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Exercise management in type 1 diabetes: a consensus statement

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Running title: Exercise management in T1D

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Abstract

Type 1 diabetes (T1D) is challenging condition to manage for a variety of physiological and behavioural reasons. Regular exercise is important, however management of the different forms of activity is a particular struggle for both the individual with T1D and the health care provider. People with T1D tend to be at least as inactive as the general population, with a large percentage of individuals not maintaining a healthy body mass nor achieving the minimum number of minutes per week of moderate-to-vigorous aerobic activity. Regular exercise can improve health and well-being and can help individuals to achieve their lipid, body composition, fitness and glycaemic goals. However, several additional barriers to exercise may exist for the person with diabetes including fear of hypoglycaemia, loss of glycaemic control, and inadequate knowledge around exercise management. This review provides an up to date consensus on exercise management for individuals with T1D who exercise regularly, including glucose targets for safe and effective exercise, and nutritional and insulin dose adjustments to protect against exercise-related glucose excursions.

Introduction

Despite tremendous advances since the discovery of insulin almost 100 years ago, type 1 diabetes (T1D) remains a challenging disease to manage (1,2). A majority of patients living with T1D are not at a healthy body weight (~60% are overweight or obese), suffer from hypertension (~40%) and/or dyslipidaemia (~60%) (3) and are not engaging enough regular physical activity (4). Regular exercise helps patient achieve a number of goals. It improves the cardiovascular disease risk profile in paediatric patients (5) and reduces HbA1c (-0.3%) in that particular segment of the patient population (6). Body composition, cardiorespiratory fitness, endothelial function and blood lipid profile (i.e. triglycerides, total cholesterol) all improve with regular physical activity in children and young people with T1D (7). These cardiometabolic improvements are all important, given that cardiovascular disease is the leading cause of morbidity and mortality in persons with T1D (8). In adults, both retinopathy and microalbuminuria are less common in those who are more physically active (9). Active adults with T1D tend to have better chance of achieving target HbA1c levels, blood pressure levels and a healthier body mass index when compared to inactive patients (3). Regular exercise also lowers total daily insulin needs (10). Having a high exercise capacity in adulthood with T1D is associated with less risk for coronary artery disease, myocardial ischaemia and stroke if you have diabetes or not (11). In a large cross sectional study of 18,028 adults with T1D, patients who fall in the most active category of physical activity levels (exercising two or more times per week) had better HbA1c levels, a more favourable body mass index, less dyslipidaemia, hypertension and fewer diabetes-related complications (retinopathy, microalbuminuria), compared to those who were less habitually active (3). In general, patients with T1D who are more active tend to have less diabetic ketoacidosis and less risk for developing severe hypoglycaemia with coma (3), except for with older women where this latter relationship is reversed; those most active have higher rates of severe hypoglycaemia (with coma) when compared with those who are inactive (3). However, several barriers may exist for exercise including: a fear of hypoglycaemia; a loss of glycaemic control, lack of time; access to facilities; lack of motivation; issues around body image and a general lack of knowledge around exercise management (12–14).

The physical activity prescription for all adults living with diabetes, including those living with T1D, is 150 minutes of accumulated physical activity each week, with no more than 2 days in a row with no activity. Resistance exercise is also recommended two to three times a week. Getting this much exercise is difficult for a large majority of patients; with less than 20% of patients performing aerobic exercise more than two times per week and 60% of the patient population performing no structured exercise at all (3). For children and adolescent, at least 60 minutes of physical activity should be performed per day (15). Physical inactivity and prolonged sitting times increase gradually with age and are linked to high HbA1c levels in youth with T1D (16) and inactivity appears to be more common in females than in males (3).

Regular exercise should be encouraged and supported by health care professionals (HCPs), for a number of reasons, but primarily because the overall cardiometabolic benefits outweigh the immediate risks if certain precautions are made. In this review, the basic categories of exercise are described from a physiological perspective as are the starting points for nutritional and insulin dose adjustments to keep patients in a targeted glycaemic range. This review summarizes our consensus on the available strategies that help incorporate exercise safely into the daily T1D management plan for those adults who are regularly engaging in exercise, sport and/or competitive events. It is hoped that these new guidelines for exercise management will improve patient control and engage more individuals with T1D to be more physically active.

Search strategy and selection criteria

We searched PubMed.gov and other relevant biomedical databases for articles pertaining to ‘type 1 diabetes’ OR ‘insulin-dependent diabetes AND ‘exercise’ OR ‘physical activity’; published between 01/1990 to 07/2016 and filtered for human and restricted to English publications. Additional searches using the search terms ‘nutrition’ OR ‘dietary carbohydrate’ OR ‘dietary protein’ OR ‘glycemic index’ OR ‘hypoglycaemia’ OR ‘energy expenditure OR ‘glycemic control’ OR ‘management’ OR ‘hypoglycemia’ OR ‘hyperglycemia’ OR ‘prevention & control’ were conducted for various subtopics within this review.

Physiology of Physical Activity and Exercise

Modalities of exercise

Understanding the metabolic and neuroendocrine responses to the various types of exercise undertaken by people with T1D is critical for determining appropriate nutritional and insulin management strategies. Exercise is generally classified as *aerobic* or *anaerobic*, depending on the predominant energy systems used to support the activity, although a majority of exercise activities include a mix of energy systems. Aerobic exercise involves repeated and continuous movement of large muscle groups (e.g. walking, cycling, jogging, and swimming) that rely primarily on aerobic energy-producing systems. Resistance (strength) training is a type of exercise using free weights, weight machines, body weight, or elastic resistance bands that rely primarily on anaerobic energy-producing systems. High intensity interval training (HIIT), involves alternating between brief periods of vigorous exercise and recovery periods at low-to-moderate intensity (e.g., from 20 seconds to 4 minute intervals of exercise and rest, for up to ~10 cycles) (17). Both aerobic and resistance type activities are recommended for a majority of people living with diabetes (15,18) and recent guidelines also now incorporate HIIT as a training modality with established benefits for individuals with prediabetes or type 2 diabetes (18). In some studies, HIIT has been shown to be more effective than continuous aerobic training in improving cardiovascular fitness and various parameters related to glucose metabolism including insulin sensitivity and glycaemic control in type 2 diabetes (19). At present, it is unclear what form(s) of exercise are best for improving cardiometabolic control in type 1 diabetes (20).

Neuroendocrine and metabolic responses to exercise

Individuals without diabetes

The metabolic responses to different forms of exercise are distinct. However, in almost all forms of exercise, no matter the intensity or duration, blood glucose concentrations are normally held within a tight range (4-6 mmol/l). During aerobic exercise, insulin secretion drops and glucagon secretion rises in the portal vein to facilitate glucose release from the liver to match the rate of glucose uptake into the working muscles (21). Exercise can increase glucose uptake into muscle by up to 50-fold; a phenomenon independent of insulin signalling (22), so the drop in insulin in the circulation does not limit glucose provision to the working body. Although the main determinant of glucose production for aerobic exercise is a rise in glucagon levels, there is also neural control of glucose release and other counterregulatory hormones play a supportive role (23). With increased exercise duration, there is reduced reliance on muscle glycogen as fuel and a greater reliance on lipid oxidation and plasma-derived glucose (24). If insulin levels do not fall during aerobic exercise, the rise in counterregulatory hormones is less effective in promoting hepatic glucose production (21).

As the intensity of exercise increases above ~50-60% of maximal oxygen consumption (VO_2max), fat oxidation decreases, particularly in those who are untrained, and CHO are the preferred fuel (25). Prolonged high-intensity exercise is supported by both muscle glycogen and blood glucose utilization with minimal contributions from lipid and protein (26). During predominantly anaerobic activities (27) and during a HIIT session (28), circulating insulin concentrations do not drop as markedly as compared to purely aerobic activities, in part because the duration of activity is typically shorter. High rates of external power output during HIIT increase reliance on muscle phosphagens and glycogen, with lactate levels rising markedly in the circulation (28). Insulin levels increase above baseline levels in early recovery from a HIIT session to offset the rise in glucose caused by the elevations in counterregulatory hormones and other metabolites (27).

Dysglycaemia during exercise in individuals with T1D

In T1D, the glycaemic responses to exercise are influenced by the location of insulin delivery, the amount of insulin in the circulation, the pre exercise blood glucose concentration, the composition of the last meal or snack, as well as the intensity and duration of the activity (29) (Figure 1).

During aerobic exercise, most individuals with T1D have a drop in glycaemia, unless carbohydrates (CHO) are ingested, because insulin levels cannot be lowered rapidly enough at the start of the activity, and levels may rise in the systemic circulation (30), perhaps because of increased subcutaneous adipose tissue blood flow during exercise (31). Even if basal insulin infusion rates are halved 60-min before the start of exercise in patients on continuous subcutaneous insulin infusion (CSII), circulating free insulin levels do not drop at exercise commencement and levels tend to rise transiently during the activity (32). Higher insulin levels in circulation during exercise promotes increased glucose disposal relative to hepatic glucose production, and may delay lipolysis, another feature that increases the muscles reliance on glucose as a fuel. Hypoglycaemia develops in a majority of patients within ~45 minutes of activity (33,34). Trained individuals with T1D have greater reductions in blood glucose concentrations during aerobic exercise when compared to less fit patients (35), possibly because the overall work rate is higher in those more aerobically conditioned. As such, both trained and untrained individuals with T1D typically require increased CHO intake, and/or insulin dose reduction, for prolonged aerobic exercise (see below). High intensity interval sprint training promotes increased oxidative capacity of skeletal muscle in T1D and attenuates the rates of glycogen breakdown (36), which may protect against post-exercise hypoglycaemia, at least in theory. Perhaps in line with this, individuals who are aerobically conditioned have reduced glucose variability compared to those unconditioned (37). Low insulin levels due to aggressive reductions in administration or a skipped insulin dose can cause hyperglycaemia prior to and during aerobic exercise (38) and ketosis may develop, even with mild activity (39).

Compared to continuous moderate-intensity aerobic exercise, resistance exercise is associated with better glucose stability (40), although it may cause a modest rise in some individuals (41). Compared to aerobic exercise, performing a HIIT session attenuates the drop in glycaemia (42), as does performing resistance exercise before aerobic exercise (43), possibly because of increases in counterregulatory hormones and various metabolites that limit glucose disposal (44). In situations of brief and intense anaerobic exercise (e.g. sprinting, weight lifting, some competitive sports) (41,45), or during HIIT (28), glucose levels typically rise.

Dysglycaemia post-exercise in individuals with T1D

Immediately after aerobic exercise, glucose uptake into muscle drops but overall glucose disposal is still elevated for hours in recovery to help replenish glycogen stores (46). Hypoglycaemia risk is elevated for at least 24 hours in recovery from exercise with the greatest risk for nocturnal hypoglycaemia occurring after afternoon activity (47). As mentioned above, weight lifting, sprinting and intense aerobic exercise can promote elevations in glycaemia that may last for hours in recovery. Although a conservative insulin “correction” post-exercise may be prudent in some situations (48), over-correction with insulin can promote severe nocturnal hypoglycaemia and death (49). HIIT appears to increase risk for nocturnal hypoglycaemia compared to continuous aerobic exercise in some (50), but not all (51,52) studies.

Exercise Goals and Glycaemic Targets

Individuals with T1D should perform exercise for a variety of health reasons. The evidence that regular exercise training improves metabolic control in adults with T1D is somewhat limited (20,53), although in youth it appears to be helpful (7). Exercise readiness questionnaires for adults with diabetes who may be at increased risk for adverse events can be found at eparmedx.com. Patient goals for exercise should be considered before making management decisions (e.g. metabolic control and prevention of complications, fitness, weight loss, competition/performance). This is a critical element of the diabetes management plan. For example, exercise for weight loss requires strategies that focus on reducing insulin levels during and after exercise, as opposed to consuming additional CHOs. By contrast, if maximising sports and exercise performance is the primary goal, then sport-specific nutritional guidance is needed and a modified insulin plan to match increased nutritional requirements should be considered (54). For all patients, blood glucose monitoring before, during and after exercise is critical for informing strategies and maintaining stable and safe glycaemia.

The appropriate blood glucose concentration for the start of exercise should be individually tailored. Based on consensus, a reasonable starting range for most patients doing aerobic exercise lasting up to an hour is between 7-10 mmol/l. This range balances performance considerations against hypoglycaemia risk. Higher levels may be acceptable in some situations where added protection against hypoglycaemia is needed. Achieving and maintaining circulating glucose in this range is challenging. The glycaemic response to exercise is variable and based on several factors including the duration and intensity of exercise (44,55), the starting level of glycaemia (34), the individual's aerobic fitness (35) and the amount of insulin in circulation (56,57) (Figure 1). Anaerobic and a HIIT session can be initiated with a lower starting glucose level (5-7 mmol/l) since glucose concentrations tend to remain relatively stable, fall to a lesser extent compared to continuous aerobic exercise, or rise slightly (Figure 1). Strategies to cope with a range of glucose concentrations near the start of exercise are provided in Table 1. If glucose level is too high because of insulin omission, risk of ketosis and further hyperglycaemia can occur (39) and work effort probably rises. Although it is unclear if there is an optimal glycaemic range for exercise performance, clinical experience and limited field study investigation (58) suggest that maintaining a concentration between ~6.0-8.0 mmol/l may be ideal.

Contraindications and cautions for exercise

While few exercise limitations should be placed on patients, some considerations are important:

A. Ketones

- Elevated blood ketones (≥1.5 mmol/l) before a bout of exercise should be addressed prior to the start of the session via insulin administration and/or CHO feeding (Table 1). The cause of elevated ketone levels should be identified (illness, diet manipulation, a recent bout of prolonged exercise, insulin omission, etc.). Both prolonged endurance type activities (marathons, trekking, etc.) and very low CHO diets can elevate blood ketone levels in patients and the HCP should define appropriate levels and provide tailored guidance for each individual. Blood ketone levels of ≥ 3.0 mmol/l should be managed immediately by a qualified HCP (e.g. emergency department, physician, etc.).

B. Recent hypoglycaemia

- Severe hypoglycaemia (defined here as a blood glucose ≤2.8 mmol/l or a hypoglycaemic event requiring assistance from another individual) within the previous 24 hours is a contraindication to exercise, due to the significant increased risk of a more serious episode during the exercise (59). Where minor hypoglycaemia (blood glucose 2.9-3.9 mmol/l, with the ability to self-treat) has occurred, the increased risk of a recurrence must be taken into account (60). Vigilance around monitoring should be stressed and exercise should be avoided if the setting is deemed particularly unsafe (e.g. swimming/trekking alone).

C. Diabetes-related complications

- Overall the health benefits of being physically active outweigh the risks of being sedentary for people with diabetes. Those with complications can derive numerous health benefits from lower intensity physical activities, with little risk for any adverse events (61). In those with long-standing disease, or with HbA1c levels well above target, vigorous exercise, heavy weight-bearing activities and competitive endurance events are contraindicated, particularly if the patient has unstable proliferative retinopathy, severe autonomic dysfunction or renal failure (61).

D. Failure to be prepared for exercise-associated hypoglycaemia

- In preparation for exercise, individuals with T1D should be aware of their starting glucose concentrations, have blood glucose monitoring equipment and snacks to treat hypoglycaemia. They should also be advised to wear/carry diabetes identification.

Nutritional Management

<u>Goals for nutritional management</u>

Nutritional management for people with T1D should incorporate strategies that optimise glycaemic control, while promoting long-term health (62). The main strategies around nutrition for exercise and sport discussed in this section are primarily to maximise athletic performance and are based largely on studies conducted in highly trained healthy individuals without diabetes (63), with limited studies in people with T1D. The application of these strategies must consider the individual's insulin management plan and specific advice targeting nutrition for both athletic performance and glycaemic management (see Glycaemic Management section below). A registered dietitian with specialist diabetes and sports knowledge is the most qualified to help active people with T1D.

An individualised meal planning approach is central to improving performance and glycaemic outcomes. Daily CHO intake should relate to the fuel cost of training in the athletic subpopulation and hypoglycaemia prevention for all active people. Balancing insulin dose to CHO intake during exercise is essential. A variety of CHO and insulin adjustment strategies can be used, such as reducing the pre-exercise bolus insulin dose by 30-50% up to 90 minutes before aerobic exercise (64), consuming high glycaemic index (GI) CHO (30-60g /hour) during sport or replacing CHO post-exercise for anaerobic exercise. Personal tolerance of ingested CHO particularly during exercise is a key factor in individualising recommendations. The distribution of macronutrient intake over the day should take into account the timing of exercise so that liver and muscle glycogen stores are maximised before the activity and replenished in early recovery (63). This strategy should include CHO feeding well before exercise (~4 hours) and early in recovery (63,65).

Daily energy and macronutrient balance

Athletes with T1D need sufficient energy to meet the demands of their daily activity. These will vary with age, sex, body composition and activity type (66). Total energy requirements differ with individual aims. Predictive equations can be used to estimate resting energy expenditure (67); however they should serve only as a guide as they may over or underestimate actual requirements. An appropriate macronutrient balance and micronutrient intake (63), coupled with a glycaemic control strategy, is required to maximise performance. The optimal macronutrient distribution will vary depending on an individualised assessment and exercise goals. A guide to the distribution of the total daily energy intake is 45-65% CHO, 20-35% fat and 10-35% protein, with higher protein intakes indicated for individuals wanting to lose weight (68).

The major nutrients required to fuel performance are CHOs and lipids, while the addition of protein is needed to help foster recovery and maintain nitrogen balance (63,69). Protein requirements range from 1.2- 1.6 g/kg body weight (BW) /day and will vary with training type and intensity and CHO availability (63,70). Higher intakes may be needed for recovery from injury or for individuals on energy restricted diets (71) to maintain lean body mass.

CHO needs before, during and after exercise

Distinction should be made between CHO needs for performance and CHO required for hypoglycaemia prevention (Table 2). CHO requirements will alter insulin management strategies and vice versa. The majority of studies in T1D investigate the amount and distribution of CHO to prevent hypoglycaemia rather than to optimise performance, although the two may be at least partially related (34,64,72,73). As an example, although only 15-20 grams/hr of CHO may be required to prevent hypoglycaemia in people who reduce their insulin levels in anticipation of exercise; this amount of CHO may be insufficient for performance. It has been shown that it is possible to implement larger CHO supplementation (up to 75g/hr) for prolonged competition greater than 2.5 hours (marathons and other endurance type races) without adversely impacting glycaemia as long as insulin dose is titrated appropriately (54). In general, CHO requirements during shorter, intermittent high intensity and anaerobic activities can be much less (Table 2).

Nutritional needs for recovery

Post-exercise nutrition requirements to maximise muscle recovery and muscle protein synthesis have been well studied in the athletic population without diabetes (74). For replenishment of glycogen content after exercise, CHO intake is essential (63). For athletes with T1D, it is important to ensure rapid and adequate replenishment of muscle and liver glycogen stores to help prevent late-onset hypoglycaemia. Glycogen replacement strategies may also be important to help prevent euglycaemic ketosis in exercise recovery (75). Ingesting protein (~20-30 grams) in addition to CHO in the post-exercise period is beneficial for muscle protein synthesis, but it does not appear to facilitate glycogen replenishment, at least in non-diabetic athletes (63).

Role of high and low GI foods for maintenance of euglycaemia

The GI of a CHO-rich food can be used to assist with the selection of CHO type for exercise; with high GI sports drinks and gels providing rapidly released CHO to increase blood glucose levels during endurance events and for the treatment of hypoglycaemia. Low GI foods have been suggested pre-exercise to sustain CHO availability and maintain euglycaemia, while higher GI meals/snacks consumed post-exercise may enhance recovery. Low and moderate GI snacks may also be preferred for long distance activities (like trekking and long distance cycling) at low to moderate workloads. Low GI CHO (isomaltose) consumed 2 hours before a high intensity run showed improved blood glucose responses during exercise compared to a high GI CHO (dextrose) (76). A low GI meal and bedtime snack consumed after evening exercise prevented postprandial hyperglycaemia compared to a high GI meal and snack, with both meal types protective against hypoglycaemia for ~8 hours (77). Protection beyond 8 hours with a snack is lost and hypoglycaemia risk remains significant (77).

Fluid Replacement

Adequate fluid intake before, during and after exercise is necessary to avoid dehydration and for optimal performance (65). Water is the most effective drink for low intensity and short duration sports (i.e. ≤ ~45 min), as long a glucose levels are at or above target (≥7 mmol/l). Sports beverages containing CHO (6-8%) and electrolytes are useful for athletes with T1D in longer duration, higher intensity exercise as a hydration and fuel source and to prevent hypoglycaemia (34,78). However, it is important to ensure these are not over consumed as this can result in hyperglycaemia. Milk-based drinks containing CHO and protein can assist recovery and prevent delayed hypoglycaemia (73).

Low-CHO high-fat diets and exercise

People with T1D may choose a low-CHO high-fat (LCHF) diet for a variety of reasons. A recent review on LCHF diets and sports performance in subjects without T1D concluded that despite increasing the muscles' ability to utilise fat over time, there was no evidence of performance benefits (79). Long-term studies have yet to be conducted on the health, glycaemia, or performance effects of LCHF diets in T1D. A concern with these diets is that they may impair the capacity for high intensity exercise (80).

Variation in CHO intake (i.e. periodisation throughout the training cycle according to fuel needs and performance) has been suggested by some researchers as a way to help promote skeletal muscle adaptation to training (81). Additionally, various exercise-nutrient protocols (i.e. training in a fasted state or withholding CHO intake at meal before or after exercise) are used to manipulate CHO availability. These approaches have not been studied in individuals with T1D where manipulation of dietary CHO as part of training presents unique challenges for insulin therapy and requires careful glucose monitoring.

Sports nutritional aids and T1D

The use of ergogenic aids is a widespread performance enhancement strategy used by athletes. The evidence for ergogenic aids on performance is limited in athletes with T1D.

Caffeine intake in athletes without diabetes has shown improvements in endurance capacity and power output (82). Caffeine intake (5-6 mg/kg body mass) before exercise attenuates the drop in glycaemia during exercise in individuals with T1D but may increase late-onset hypoglycaemia risk (83).

Glycaemic Management Recommendations

There is high between- and within-patient variability in glucose responses to the various forms and intensities of exercise (Figure 1); therefore glycaemic management is based on frequent glucose monitoring, adjustments to both basal and/or bolus insulin dosing and the consumption of CHOs during and after exercise. These recommendations are intended to serve as a starting point for insulin adjustments and CHO intake that can then be individualised (Figure 2).

Clinical management strategies should be built around exercise types and individual aims and implemented, taking into account the factors summarised in Table 3. Generally, sustained aerobic exercise requires more substantial reductions in insulin dose and/or higher CHOs than a shorter-term HIIT session. In stark contrast, brief anaerobic exercise (sprinting, weight lifting) may require increased insulin delivery, which is typically given in early recovery rather than before exercise for obvious safety reasons (48). Strategies for insulin dose adjustments and/or CHO intake during and after planned exercise are presented in Table 4.

Insulin adjustment for prolonged activities: bolus insulin approaches

Pre-exercise meal insulin bolus dose reductions and/or additional CHO consumed during exercise are typically needed to avoid hypoglycaemia during prolonged exercise (>30 minutes) (34,55,64,84–86). Bolus dose reductions require pre-planning and are probably only appropriate for exercise with a predictable intensity performed within 2-3 hours after a meal. As shown in Table 5, the extent of mealtime dose reduction is proportional to both the intensity and duration of the activity. This approach is safe and effective; even reducing the bolus insulin dose by as much as 75% does not appear to increase ketone production during exercise (86).

Another strategy is to combine the reduction of the pre-exercise insulin bolus dose (by 75%) with the ingestion of a low GI snack/meal (87). Importantly, this method also reduces the risk of pre-exercise hyperglycaemia. However, protection against hypoglycaemia with this approach is lost if the exercise is performed an hour or more after the snack (87). As such, this combined approach may be preferable only for early postprandial exercise.

<u>Basal insulin approaches</u>

Late postprandial hypoglycaemia (4+ hours after a meal) following aerobic exercise is driven partly by circulating basal insulin concentrations. Elevated insulin sensitivity post-exercise, and perhaps a blunting of glucose counterregulation appear to place individuals at risk for at least 12 hours. Reducing circulating basal insulin levels can ameliorate this risk. For patients on multiple daily insulin injections (MDI), clinical observations and limited experimental data (88) demonstrate that reducing long acting basal (as well as prandial) insulin before exercise reduces hypoglycaemia risk during and after the activity, but may promote hyperglycaemia at other points during the day. Therefore reduction in basal insulin dose for MDI patients should not be routinely recommended but may be a therapeutic option for those having unusual days with considerably more planned activity (e.g. camps, tournaments). In general, basal insulins with a relatively short half-life such as NPH-insulin or insulin detemir seem to lead to less hypoglycaemia in conjunction with exercise when compared to longer basal insulins such as glargine (89), although the mechanism for this is unclear. While ultra-long acting insulins (e.g. insulin degludec with a 25hr half-life) pose similar risks for hypoglycaemia with endurance exercise to that of insulin glargine (90), dose reductions for exercise would have to be implemented at least 48 hours before planned exercise. This is not recommended, as it would compromise overall control.

CSII offers flexibility to modify basal infusion delivery and to obtain a relatively quick effect (within ~1-2hrs) (91). Suspension of basal insulin infusion at the onset of 60-min exercise reduces hypoglycaemia risk during the activity, but it may increase post-exercise hyperglycaemia risk (92). Moreover, glucose levels may still drop 2-3 mmol/l over 30-60 minutes even when basal insulin is dramatically reduced (or completely suspended) (64,92,93), due to the lag time in the change in circulating insulin levels. Where practical, a basal rate reduction, rather than suspension, should be attempted well before the start of exercise (60-90 minutes). An 80% basal reduction at the onset of exercise helps mitigate post-exercise hyperglycaemia, compared to basal suspension, and appears to be associated with reduced hypoglycaemic risk both during and after the activity (64). However, the optimal timing of basal rate insulin reductions for aerobic and HIE activities and the maximal safe duration for insulin pump suspension is unclear and remains open to debate. To limit the risk of compromised glycaemic control and ketosis a time limit of <2hours is proposed based on rapid acting insulin pharmacokinetics (91).

Post-exercise hyperglycaemia is a common complaint for patients doing intense exercise, particularly if insulin levels are reduced. CSII seems to offer advantages over MDI in managing early post-exercise hyperglycaemia (94) and late-onset post-exercise hypoglycaemia (95), due to the increased flexibility around basal insulin adjustments. Overcorrection of post-exercise hyperglycaemia via repeated insulin dose administration results in increased risk for severe late-onset hypoglycaemia, which may even be fatal (49).

<u>Strategies to reduce the risk of post-exercise late-onset hypoglycaemia</u>

Increased insulin sensitivity lasts up to 24-48 hours following exercise (46). Very few studies have tested various nutrient or insulin dose adjustments to prevent hypoglycaemia after exercise. Nocturnal hypoglycaemia after exercise is a major occurrence for individuals with T1D (96), with increased risk for afternoon exercise (47,97). Immediate increases in post-exercise insulin sensitivity can be accommodated for by reductions in the bolus insulin at the meal after exercise by ~50%, along with a low GI snack at bedtime (77). In one study of 16 youth, a ~20% temporary pump basal rate reduction from bedtime for 6 hours reduced nocturnal hypoglycaemia risk (95). Similarly, in another study of ten males on MDI, a 20% basal rate reduction on the exercise day along with a “free” CHO snack at bedtime (0.4 g CHO/kg body mass) reduced hypoglycaemia risk overnight (88). Individuals at high risk of severe nocturnal hypoglycaemia (e.g., recurrent hypoglycaemia, and those sleeping alone), should take additional preventive measures including blood glucose checks at 2-3AM and/or use a real time CGM system with alarms and automatic pump suspension (98). A snack alone, without changes to basal insulin therapy, does not appear to entirely eliminate nocturnal hypoglycaemia risk (77) and alcohol intake may increase risk (99).

Glucose monitoring, CGM and other emerging tools for exercise management

A range of treatment regimens exists for people with T1D. CSII offers better flexibility in basal insulin adjustments and the management of exercise-associated hyperglycaemia (100). CSII is associated with reduced post-exercise hyperglycaemia compared to MDI (94), but can create frustrating challenges for sports requiring pump disconnection (101). CSII can also contribute to a greater sense of being “diseased” for some individuals and may promote stigma (101). Prolonged pump disconnect (> 60 minutes) should be managed with reconnecting, testing and re-infusion if necessary, or a change to basal insulin provision by needle. CGM provides comprehensive information on blood glucose levels, real-time trends in glucose levels and rates of glucose change in glucose, which can be used to prevent lows during exercise (102), even in unique settings when self-monitoring of blood glucose (SMBG) is difficult to perform (103). Current sensors are reasonably accurate for exercise (104,105); however, the lag time in glucose equilibrium with the interstitial space and the rapid turnover in glucose during exercise may impact accuracy (i.e. overestimate glucose value when levels are dropping and underestimate it when levels are rising) (106,107).

Structured educational sessions can be implemented using downloads of SMBG, CGM and CSII (108). CGM now offers the option to add “followers” who can view glucose levels in real time and potentially alert the patient while he/she is playing sports. Threshold suspension of insulin delivery in CSII may offer additional protection against exercise-associated hypoglycaemia according to some limited data (109). The development of a fully artificial pancreas for exercise remains an elusive goal (110).

Summary

Regular physical activity should be a routine objective for patients with type 1 diabetes for a variety of health and fitness reasons. Considerable challenges remain for the person with T1D, and their HCP team, in exercise/sports management. A number of small observational studies and a limited number of clinical trials have been published to date that help to inform the consensus recommendations here. More studies are needed to determine how to best prevent exercise-associated hypoglycaemia with basal rate insulin dose adjustments and how to manage in the post-exercise recovery period. In general, aerobic exercise is associated with reductions in glycaemia while anaerobic exercise may be associated with a transient rise in glucose levels. Both forms of exercise can cause delayed-onset hypoglycaemia in recovery. A sound understanding of the physiology of different forms of exercise and the variables that can influence glycaemia during exercise and sport should underpin the implementation of safe and effective glycaemic management strategies. For aerobic exercise, reductions in insulin administration before the activity (basal and/or bolus) can help ameliorate hypoglycaemia risk, as can increasing CHO intake to 60 grams per hour or more. For anaerobic exercise, conservative insulin dose corrections may be required, although this too may increase the risk for nocturnal hypoglycaemia, particularly if the exercise is performed late in the day. In all instances, more vigilance around glucose monitoring is needed before, during and after the activity.

Contributors

The literature search was conducted by MCR, IWG and CES. All authors (MCR, IWG, CES, CET, PA, ANL, AK, RR-L, RM, CH, FA, PF, CG, BB, PG, TWJ, ISM, TH, AP, AP, and LML) contributed to the original draft of the manuscript. MCR, FA and CES edited the revised manuscript. All authors approved the final submission.

Declaration of interest

The authors declare no relevant conflicts of interests that influence the content of this consensus review.

Table 1. Pre-exercise blood glucose concentrations and initial glucose management strategies.

Starting blood glucose concentrations	**General Recommendations***
Below Target (<5 mmol/l)	▪ Ingest 10–20 g of glucose before starting exercise ▪ Delay exercise until blood glucose > 5mmol/l (90 mg/dL) and monitor closely for hypoglycaemia
Near target (5-6.9mmol/l)	▪ Ingest 10 g of glucose before starting aerobic exercise ▪ Anaerobic exercise and HIIT sessions can be started
Target (7-10mmol/l)	▪ Aerobic exercise can be started ▪ Anaerobic exercise and HIIT sessions can be started but glucose levels may rise
Slightly above target 10.1-15.0 mmol/l)	▪ Aerobic exercise can be started ▪ Anaerobic exercise can be started but glucose levels may rise
Above target (>15 mmol/l)	▪ If the hyperglycaemia is unexplained (not associated with a recent meal), check blood ketones. If ketones are modestly elevated (up to 1.4 mmol/l), exercise should be limited to a light intensity for only a brief duration (<30 minutes) and a small corrective insulin dose may be needed before the exercise begins. If blood ketones are elevated (≥1.5mmol/l), exercise is contraindicated and management should be initiated rapidly as per the advice of the HCP/team. ▪ Mild to moderate aerobic exercise may be started if blood ketones are low (<0.6 mmol/l) or if urine ketones are less than 2+. Blood glucose levels should be monitored during exercise to help notify if glucose is rising further. ▪ Intense exercise should be initiated only with caution as it may promote a further rise in glycaemia.

*Note: The CHO intake amounts shown here are to help with glucose stability at the start of exercise. For aerobic activities lasting greater than 30 minutes, additional CHOs will likely be needed (see Table 2). Blood glucose levels at the start of exercise must also be viewed within a wider context. Factors to consider include directional trends in glucose concentrations, insulin levels, patient safety and individual patient preferences based on experience. CHO intake will need to be higher if circulating insulin levels are high at the onset of exercise. See Nutritional Management section. HIIT= high intensity interval training.

Table 2 CHO requirements for endurance (aerobic) exercise performance and hypoglycaemia prevention

Situation	**Endurance exercise performance (Athletes with and without diabetes)**	**Hypoglycaemia prevention under low insulin conditions**	**Hypoglycaemia prevention under high insulin conditions**
Pre-exercise meal (low fat, low GI)	A minimum of 1g CHO/kg BW according to exercise intensity and type	A minimum of 1g CHO/kg BW according to exercise intensity and type	A minimum of 1g CHO/kg BW according to exercise intensity and type
Immediately pre-exercise (high GI)	No CHO required for performance	If BG < 5mmol/l ingest 10-20g CHO	If BG < 5mmol/l ingest 20-30g CHO
Up to 30 min duration	No CHO required for performance	If BG < 5mmol/l ingest 10-20g CHO	May require 15-30g CHO to prevent or treat hypoglycaemia
30- 60 min duration	Small amounts of CHO (10-15 g/hr) may enhance performance	Low- moderate intensity (aerobic): Small amounts of CHO (10-15 g/hr) depending on the exercise intensity and BG High intensity (anaerobic): No CHO required during exercise unless BG is < 5 mmol/l then ingest 10-20g CHO. Replace CHO needs post-exercise.	May require up to 15-30g CHO/30 min to prevent hypoglycaemia
60- 150 min duration	30-60g CHO/hr	30-60g CHO/hr to prevent hypoglycaemia and enhance performance	Up to 75 g CHO/hr to prevent hypoglycaemia and enhance performance*
> 150 min duration (Mixture of CHO sources)	60-90g CHO/hr spread across the activity (e.g. 20-30g CHO/20 min) Use CHO sources that utilize different gut transporters (e.g. glucose and fructose)	Follow sports nutrition guidelines (60-90g/hr) with appropriate insulin adjustment for glycaemic management	
Post- exercise meal	1-1.2g CHO/kg body BW	Follow sports nutrition guidelines to maximise recovery with appropriate insulin adjustment for glycaemic management	

Note: These guidelines are based on the following references (63,111,112) and on the expert opinion of the authors. BW= body weight, BG= blood glucose concentration. * Note: CHO consumption at a high rate may cause gastric upset in some individuals and may contribute to hyperglycaemia during and after the activity. To increase CHO absorption rate during exercise, and maintain hydration status, sport beverages containing glucose and fructose may be preferable.

Table 3 Examples of factors that need to be considered before making adjustments for exercise.

Factor	Effect
Subcutaneous insulin injection and its adjustments	• Difference in injection site and depth affect insulin absorption characteristics (113,114). • Lipodystrophy. • Misunderstanding of insulin pharmacokinetic often leads to inappropriate insulin adjustments, including excessive insulin corrections (stacking), which may be particularly dangerous after exercise. • Rapid acting (30), regular and intermediate acting (115,116), but likely not long acting (117) insulin absorption rates are increased with exercise.
CHO intake	• Variation in CHO quantity (including inaccuracy to evaluate intake) and type will impact glycaemic excursions (118).
Self-monitored capillary glucose measurements and CGM	• Errors in SMBG sampling or measurement errors (SMBG, CGM) may result in inappropriate insulin dose estimations (119,120). • CGM accuracy, while improving, can be compromised by poor SMBG accuracy and calibrations methods (121). • Lag time in CGM may impact accuracy during exercise (104,106).
Medications/ alcohol	• Insulin sensitivity may be impacted (99) as might glucose monitoring tools (120).
Physiological cycles	• Diurnal endocrine variation, menstrual cycle and pregnancy impact insulin sensitivity and impact glycaemic patterns (122).
Changes in work and sleep patterns	• Require changes in timing of insulin basal dose administration. • Timing of exercise should be considered relative to insulin sensitivity and nocturnal hypoglycaemia risk (47).
Intercurrence illness and stress	• May require changes in both basal and bolus insulin dose (123). • Vigorous exercise contraindicated.

Table 4. Therapeutic adjustment options (insulin and/or food intake) to minimize glycaemic excursions for prolonged aerobic and brief high intensity aerobic/anaerobic exercise.

Adjustment	Prolonged endurance exercise (predominantly aerobic)	Brief intense exercise (aerobic and anaerobic)
Pre- exercise meal bolus dose insulin reduction	Advised when exercise occurs within ~120min of bolus dose The magnitude of reduction vary according to timing, type, duration and intensity of exercise (see Table 5)	Bolus reduction not advised May require additional conservative bolus dose correction if hyperglycaemia develops
Pre-exercise basal insulin dose reduction in (MDI patients) by ~20%	Useful especially if exercise occurs less than every 3 days or if exercise levels are elevated throughout the day May also be useful if on twice daily intermediate insulin	Basal reduction not advised
Basal nocturnal insulin dose reduction (MDI & CSII) following exercise by ~20% to reduce nocturnal hypoglycaemia	Particularly important if the exercise occurred in the afternoon or early evening	Useful for helping limiting post-exercise hypoglycaemia after a HIIT session
Temporary basal rate change (CSII)	Reduce basal rate to as low as total suspension of normal basal during exercise To take into account rapid acting insulin pharmacokinetics, this basal rate reduction should ideally occur well before exercise start (up to 90 minutes before) Normal basal rates can be resumed either at the end of exercise, or later in recovery depending on glucose trends	Increased basal rate may be needed to help prevent/treat hyperglycaemia either during or immediately after exercise
Pre-exercise CHO intake	See Table 2	Not usually needed
Intra-exercise CHO intake	Typically up to 60g/h if no insulin dose adjustments have been made See Table 2 for additional information	Not usually needed
Pre-exercise or post-exercise sprint	May help reduce hypoglycaemia risk	May increase hyperglycaemia risk Consider a prolonged aerobic cool down
Post-exercise CHO intake	Useful to reduce risk of hypoglycaemia and enhance recovery (see Nutritional Management section) May need a specified insulin bolus depending on length and intensity of exercise (may need a reduced insulin to CHO ratio)	Useful to reduce risk of hypoglycaemia and enhance recovery but should be delayed if hyperglycaemia is initially observed (see Nutritional management section) May need a specified insulin bolus strategy (e.g. may need a reduced insulin to CHO ratio)

Table 5: Suggested pre-exercise meal bolus percent reduction for exercise started within 90min of a meal.

	Exercise duration	
Exercise intensity	30 minutes	60 minutes
Mild aerobic (~25%VO_2max)	- 25%*	- 50%
Moderate aerobic (~50% VO_2max)	- 50%	- 75%
Heavy aerobic (70-75% VO_2max)	- 75%	N-A
Intense aerobic/anaerobic (>80% VO_2max)	No reduction recommended	N-A

Notes: Recommendations based on the following references (51,55,72,124); N-A: Not assessed, since the exercise intensity is typically too high to sustain for 60min for most individuals; * Estimated from the 60min study.

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Figure 1: **Blood glucose trends and different forms of exercise.** High patient variability exists in the blood glucose responses to different form of exercise, as denoted by the arrows and grey shading. In general, aerobic exercise lowers glycaemia, anaerobic exercise raises glycaemia and mixed activities is associated with relative glucose stability. The individual responses depend on a number of additional factors including the duration/intensity of the activity; initial blood glucose level; individual fitness; levels of insulin, glucagon, other counterregulatory hormones in circulation; and the nutritional status of the individual.

Figure 2: Decision tree for aerobic exercise and mixed aerobic and anaerobic activities lasting 30 min or longer. This decision tree can serve as a starting point for decision-making for aerobic exercise. Notes: [1] Mixed activities that include anaerobic bursts of exercise may require less carbohydrate intake and/or less insulin dose reductions compared continuous moderate aerobic activities. If both resistance and aerobic exercise are to be performed, suggest performing resistance first to help attenuate the drop in glycaemia. [2] In some situations, increased carbohydrate feeding rather than insulin dose reduction may help improve endurance performance in prolonged activities. [3] In other situations, both bolus and basal insulin dose reductions may be preferred to help limit CHO needs. Consider CGM where patient or parent preference dictates, or with history of nocturnal or severe hypoglycaemia.