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Post-exercise recovery for the endurance athlete with type 1 diabetes: A review and consensus statement

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Word count: 6478

Number of Figures: 4

Number of Tables: 0

Abstract

In recent years, there has been substantial progress in our knowledge of exercise and type 1 diabetes (T1D), with the development of guidelines for optimal glucose management. In addition, an increasing number of people living with T1D are pushing their physical limits in order to compete at the highest level of sport. However, the post-exercise recovery routine, particularly with a focus on sporting performance, has received little attention within the scientific literature, with most of the focus being placed on insulin or nutritional adaptations to manage glycaemia before and during the exercise bout. The post-exercise recovery period presents an opportunity for maximising training adaption and recovery, and the clinical management of glycaemia through the remainder of the day and overnight. The lack of clear guidance for the post-exercise period means that people with T1D must either develop their own recovery strategies based on individual trial and error or follow guidelines that have been developed for people without diabetes. This review provides an up-to-date consensus on post-exercise recovery and glucose management for individuals living with T1D. We aim to: 1) outline the principles and time course of post-exercise recovery, highlighting the implications and challenges for the endurance athlete living with T1D; 2) provide an overview of potential post-exercise recovery strategies that could be used by athletes with T1D to optimise recovery and adaptation, alongside improved glycaemic monitoring and management; 3) highlight the potential for technology to ease the burden of managing glycaemia in the post-exercise recovery period.

Search Strategy and Selection Criteria

References for this review were identified through searches of PubMed and other relevant biomedical databases for articles containing the terms “type 1 diabetes” or “insulin-dependent diabetes” and “exercise”, “post-exercise”, or “physical activity”, published up until 23rd December 2020 and restricted to English language publications. Additional searches were done with the following terms for various subtopics within this review: “nutrition”, “carbohydrate”, “protein”, “fructose”, “caffeine”, “glycogen”, “active cool down”, “alcohol”, “cold water immersion”, “ice baths”, “dietary protein”, “glycaemic index”, “energy expenditure”, “glycaemic control”, “management”, “hypoglycaemia”, “hyperglycaemia”, “hydration” “sleep”, “technology”, “decision”, “decision-making”, or “prevention and control”.

1. Introduction

In recent years, there has been substantial progress in our knowledge of managing blood glucose concentrations in the context of exercise and type 1 diabetes (T1D), with the development of exercise-specific guidelines ¹. Many people living with T1D now live an active lifestyle and there are numerous examples of people achieving incredible feats of physical endurance while living with the condition ^{2,3}, even reaching the highest level in their sport. However, in contrast to their counterparts without diabetes, research specifically examining the post-exercise recovery routine is scarce, with most of the focus being placed on insulin or nutritional strategies to manage glycaemia before and/or during the exercise bout. Although the guidelines by Riddell et al. ¹ do contain advice regarding the post-exercise period, this section is rather brief, and places its focus on glycaemia rather than optimising recovery. This is unfortunate, because irrespective of an individual's training or competition goals, the post-exercise recovery period provides an opportunity for maximising training adaption and recovery ⁴.

The aim of this review is to provide an up-to-date consensus on post-exercise recovery and glucose management for the endurance athlete living with T1D. First, we will outline the principles and time course of post-exercise recovery, highlighting the additional implications and challenges for the athlete living with T1D. Second, we will provide an overview of potential post-exercise recovery strategies that could be used by endurance athletes with T1D to optimise recovery and adaptation, alongside improved glycaemic monitoring and management. Third, we outline the ways in which rapid developments in technology can be used to ease the burden of managing glycaemia in the post-exercise period. The manuscript is aimed at anyone living with T1D that regularly undertakes endurance exercise for competition and/or health reasons.

1.1. Principles and Time Course of Exercise Recovery

An increasing number of individuals living with T1D are now aiming to compete at the top level of their chosen sport ⁵. This requires developing behaviours to optimise nutrition and insulin dosing during the periods before, during, and after exercise. The importance of post-exercise recovery practices have been well described for athletes without diabetes, with literally hundreds of studies investigating various ways to optimise training adaptations, rates of glycogen resynthesis and athlete safety, leading to multiple guideline papers and the incorporation of these strategies as an integral part of evidence-based training regimes ^{6,7}. For the athlete with T1D, the challenge of managing glycaemia makes this more difficult as they must also consider the effects of altered insulin sensitivity, post-exercise hyperglycaemia, depleted glycogen stores, dehydration, impaired glucose counterregulatory responses, insulin dosing, abrupt changes in the rate of muscle glucose uptake due to halt in muscle contraction, and nutritional selection (for energy/macronutrient intake) on blood glucose concentration. The lack of clear guidance for athletes living with T1D means that they often either develop their own recovery strategies, based on individual trial and error, or follow guidelines that have been developed for athletes without diabetes.

1.2. Defining the Post-Exercise Period

The post-exercise period can be simply defined as the period of time after exercise until a new bout is initiated. A bout of exercise influences glycaemia both during and after, and this can

persist for up to at least 48 hours due to changes in insulin sensitivity and muscle glucose uptake ⁸. Therefore, technically speaking, the post-exercise period includes everything from immediately post exercise and the subsequent 48 hours (and potentially longer after exhaustive endurance exercise or if there is severe muscle damage). In reality, athletes compete or train much more regularly than every 48 hours, sometimes multiple times per day (Figure 1). Rest and recovery are important aspects of an athlete's training regime for optimal performance and training adaptation ⁹. During situations of suboptimal recovery time, the athlete and/or sports coach must have a good understanding of which aspects of recovery they prioritise. The aim will be to ensure that glycaemia is stable within optimal ranges and energy substrates have recovered to as great a degree as possible to facilitate performance, while avoiding potentially dangerous glucose excursions and risk of complications.

For the athlete with T1D, it would seem that managing post-exercise glycaemia and achieving adequate recovery (e.g. replenishing glycogen stores, ensuring adequate sleep, etc.) should go hand in hand. Post-exercise late-onset hypoglycaemia is a common occurrence for people living with T1D ¹⁰, suggesting that improving the post-exercise recovery routine could reduce this risk. On the other hand, high-intensity efforts (above lactate threshold) may be related to immediate post-exercise hyperglycaemia, which appears to be more common with fasted morning exercise as compared to exercise at other times of the day ¹¹. Post-exercise hyperglycaemia may also result after moderate-intensity aerobic exercise ¹² due to a number of factors such as prolonged insulin pump suspension/removal ¹³, loss of insulin delivery (pump site failure), reduced basal insulin delivery prior to or during exercise, and poorly matched insulin administration to high rates of carbohydrate feeding. Prolonged post-exercise hyperglycaemia with or without hypoinsulinaemia may impact optimal glycogen recovery and should be managed with insulin dosing adjustments in the immediate post-exercise period to promote the complete restoration of liver and muscle glycogen stores. Excessive insulin administration in early recovery may however, increase the risk for late-onset hypoglycaemia ¹⁴. An understanding of the metabolic changes that occur during and after exercise, as well as the individual glycaemic responses with different types or intensities of exercise, may facilitate the development of nutrition and insulin dosing regimens to optimise rate of recovery.

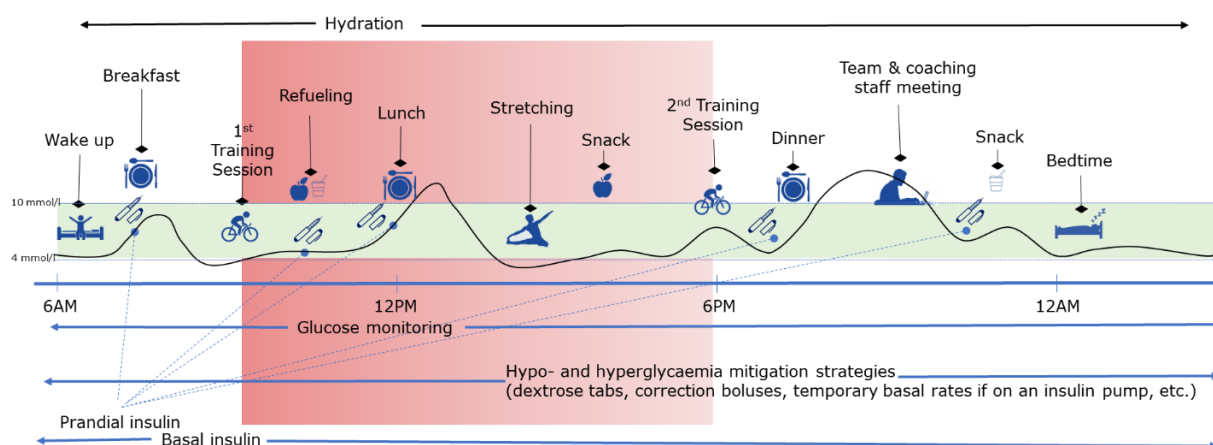


Figure 1. Challenges experienced by the athlete living with type 1 diabetes during the post-exercise recovery period

Unlike athletes without diabetes, for the athlete with T1D, the tasks of monitoring glucose, insulin dosing and carbohydrate intake for optimal glycaemia must always take priority. The athlete with T1D needs to individually balance the normal recovery requirements (replenishment of energy substrates, promotion of muscle remodelling and recovery of skeletal muscle damage), while preventing potentially life-threatening severe hypoglycaemia or ketoacidosis¹⁵ that may also prolong recovery. This figure shows an example of the tasks and challenges that an athlete with T1D must manage when training more than once per day. Note, that the tasks of managing glycaemia are in addition to the other logistical and personal challenges such as travel, media demands, work, and family commitments. In the image, the red box represents the recovery period between the 1st and 2nd training sessions, during which the athlete must make sure they are prepared for the next exercise session. In this example, recovery time will be limited to just a couple of hours between sessions meaning the athlete with T1D must have a sound strategy in place to ensure recovery, fuel for the next training session, while simultaneously managing glycaemia.

1.3. Changes in Post-Exercise Metabolism

At rest, energy consumption is low, with a carbohydrate oxidation rate of $\sim 0.1 \text{ g} \cdot \text{min}^{-1}$ depending on the diet and exercise prior to the measurements¹⁶. During exercise there are considerable changes in fuel utilisation that are determined primarily by the intensity and duration of exercise¹⁶. When exercising at intensities $>70\%$ of $\dot{V}\text{O}_{2\text{max}}$, carbohydrate will be the main fuel source¹⁶. These changes in metabolism also occur in people living with T1D whereby there is greater carbohydrate oxidation with higher exercise intensities¹⁷.

A handful of studies have investigated exercise-associated fuel metabolism in people with T1D and the impact of differing plasma glucose and insulin concentrations¹⁹⁻²³. Chokkalingham et al.²¹ compared the effects of differing insulin levels on whole-body and muscle metabolism in people with T1D during moderate-intensity exercise. Hyperinsulinemia caused an increase in blood glucose utilisation during exercise but with no sparing of intramyocellular glycogen. Subsequently, Chokkalingham and colleagues²² compared hepatic glycogen utilisation during exercise in people with T1D and people without T1D. Despite the significantly higher systemic insulin and glucose levels in those with T1D, there were no major differences in substrate oxidation nor hepatic glycogen breakdown between the two groups. Jenni et al.¹⁹ investigated the impact of different glucose levels at identical levels of low

insulinaemia on fuel metabolism during moderate-intensity exercise in people with T1D. They found that there was a higher rate of carbohydrate oxidation during exercise in hyperglycaemia than during euglycaemia with inverse findings for lipid oxidation. While these studies provide important insights into the potential effects of pharmacological insulin levels and varying glucose levels on fuel metabolism, the effects post exercise remain to be determined. Therefore, the following is drawn primarily from research conducted in individuals without diabetes.

Carbohydrate oxidation is predominant during a bout of moderate- to high-intensity exercise ¹⁶, but lipid oxidation becomes the main fuel source post exercise ²⁴, resulting in a decrease in respiratory exchange ratio (RER), even under conditions of high carbohydrate feeding ²⁴. The decrease in RER following prolonged aerobic exercise has been shown to persist to the following morning in adults without diabetes ²⁵. This shift in substrate metabolism demonstrates high metabolic priority for muscle glycogen resynthesis, whereby lipid oxidation from intra- and extra-muscular sources is elevated to meet fuel requirements ²⁶. The importance of this is evidenced by the fact that there is a strong relationship between the replenishment of liver and skeletal muscle glycogen stores post-exercise and an individual's subsequent exercise performance ^{27,28}. Commencing a bout of exercise with reduced muscle glycogen content impairs exercise capabilities ²⁹, meaning that restoration of muscle glycogen is vital if optimal performance is desired.

1.4. Muscle Glycogen Resynthesis: Insulin Independent and Dependent Phases

The process of muscle glycogen resynthesis begins immediately following exercise and is the most rapid during the first 5-6 hours of recovery ³⁰. Glycogen resynthesis post exercise occurs in a biphasic pattern, whereby there is an initial rapid phase, lasting minutes to hours, that does not require the presence of insulin, followed by a more prolonged insulin-dependent phase lasting up to 72 hours ^{31,32}. Following an exercise bout, muscle glycogen is typically restored to pre-exercise concentrations within 24-36 hours, provided sufficient carbohydrate is ingested ^{33,34}. For athletes involved in multiple training sessions or competitions on the same day or successive days, muscle glycogen stores need to be replenished more rapidly and this can be facilitated with certain carbohydrate feeding strategies, (for reviews detailing studies on people without T1D see ^{4,35,36}). When rapid recovery from prolonged exercise is the key objective, and peak performance is required within 24 hours, people without diabetes are advised to consume 1-1.3 g CHO·kg⁻¹·h⁻¹ for the first 4 hours of recovery, starting as soon as possible after exercise with frequent feeding intervals thereafter (i.e. every 30 minutes) ^{6,37,38}. These carbohydrate requirements are likely to be similar for an endurance athlete living with T1D. For athletes with T1D, who manage their insulin via exogenous administration, greater understanding of the physiology of glycogen resynthesis, may help to reduce the risk of hypo/hyperglycaemia, with the appropriate adjustments in insulin delivery to facilitate a safe and effective recovery.

1.4.1. Insulin-Independent Phase of Muscle Glycogen Resynthesis

After exercise of sufficient intensity and duration to largely deplete muscle glycogen stores, glycogen synthase activity ^{31,39} and the permeability of the muscle cell membrane to glucose increases ^{40,41}. This results in an initial rapid phase of glycogen resynthesis, which is independent of insulin signalling that typically lasts ~30-60 minutes according to studies conducted in humans without diabetes ^{32,39,42}. Glucose is the primary substrate for muscle glycogen resynthesis; however, after predominantly anaerobic exercise, lactate also becomes

a significant contributor, accounting for ~20% of total muscle glycogen resynthesis ⁴³. The initial rapid phase of glycogen resynthesis in the muscle appears to be due to contraction-induced GLUT4 translocation to the cell membrane and augmented glycogen synthase activity ^{39,44}. The rate of resynthesis during this initial phase can rapidly decline in the absence of exogenous carbohydrate ^{31,42}. Research conducted in people with T1D is very limited in this area, with the exception of a few studies conducted in the 1970s ^{31,45,46}. However, it can be assumed that provided adequate carbohydrates are consumed, this initial phase of glycogen resynthesis would be normal in the athlete with T1D (Figure 2).

1.4.2. Insulin-Dependent Phase of Muscle Glycogen Resynthesis

The second phase of glycogen resynthesis has been defined as the insulin-dependent phase ^{31,32,47}, which potentially requires additional considerations in the athlete with T1D as insulin is administered exogenously. In individuals without diabetes, insulin release due to carbohydrate intake increases blood flow to the muscle, GLUT4 translocation to plasma membrane, hexokinase II and glycogen synthase activity ⁴⁸⁻⁵⁰, all of which contribute to increased glucose uptake by the muscle and glycogen synthesis. In the absence of carbohydrate intake, this second phase occurs at a rate approximately 7-10 fold slower than the initial rapid phase ⁴⁷. Carbohydrate feeding immediately after exercise, along with the natural rise in insulin levels, has an important effect on the rate of glycogen synthesis during the slow phase. The effectiveness of the carbohydrate intake to speed muscle glycogen recovery during the second phase is directly related to the plasma insulin response ⁵¹.

During the mid to late post-exercise period (3-12 hours after exercise), the magnitude of increased insulin sensitivity can be extremely high, significantly increasing the risk of post-exercise hypoglycaemia. Therefore, individuals with T1D must take this into account and typically reduce their bolus and/or basal insulin dose accordingly post exercise ⁵², based on frequent glucose monitoring and some trial and error, to help prevent hypoglycaemia. Due to the absence of studies quantifying insulin adaptations in the post-exercise period, we usually recommend that the bolus insulin dose can be reduced by ~20-50% at the first recovery meal, along with a similar reduction in the insulin basal delivery rate (for those on pump) for ~6-12 hours or a reduction in the first basal insulin dose (multiple daily insulin injections) in the recovery period, although the precise amount will depend on the type, intensity and timing of the exercise performed. Other athletes with T1D may choose not to adjust their insulin delivery but simply consume carbohydrates at an elevated rate that preserves blood glucose concentrations.

A handful of pioneering studies conducted in the 1970s used muscle biopsies to investigate post-exercise muscle glycogen synthesis in people with T1D ^{45,46,53,54}. Maehlum et al. ⁵³ compared glycogen resynthesis rates in 6 participants with and without T1D ingesting a carbohydrate rich diet during 12 hours of recovery after exhaustive cycling exercise. The group with T1D took a fixed insulin dose after the exercise, although not enough to maintain blood glucose concentration within the target range due to the additional carbohydrates consumed. During exercise, muscle glycogen utilisation was similar in the two groups. Following exercise, glycogen synthesis rate was most rapid in the first 4 hours of recovery in both the group with and without T1D (6.4 ± 0.6 mmol glucosyl units/kg ww/h vs. 7.2 ± 0.7 mmol glucosyl units/kg ww/h in the group with and without T1D, respectively). In a subsequent experiment, the same group ⁴⁶ investigated the effect of insulin deprivation on muscle glycogen resynthesis during 12 hours of recovery after exhaustive exercise. Using a similar protocol to the previous study,

5 participants with T1D were given a carbohydrate rich diet, but this time insulin was withheld during recovery. In the first 4 hours, they reported high rates of glycogen synthesis, similar to the previous study in which they gave insulin³¹. In the subsequent 8 hours, there was no further increase in glycogen synthesis in the insulin deprivation condition despite the fact that plasma glucose concentration was 20-30 mmol/l and that glycogen synthase was activated⁴⁶. These observations provide clear support for the importance of insulin signalling in the second phase of glycogen resynthesis. However, it is important to note that these studies were not performed under physiological conditions given the likelihood of ketoacidosis with insulin deprivation and clearly lack control in terms of the exhaustive exercise bout, food consumption and blood glucose concentration. Since the completion of these studies^{31,45,46} over 40 years ago, there have been substantial improvements in insulin formulations and delivery methods and our knowledge of the effects of exercise on glucose concentrations in T1D. Therefore, the post-exercise period in the athlete with T1D should be the focus of renewed interest using rapid-acting insulin analogues with much shorter half-lives.

These studies illustrate the importance of post-exercise insulin adjustments for optimal glycogen resynthesis as well as individual basal insulin adjustments due to increased insulin sensitivity. For the athlete with T1D, the best strategies for insulin administration post exercise are likely to be highly individual and depend on particular circumstances. The priority after finishing a bout of exercise should be to first get his or her blood glucose concentration stable and within target range (4-10 mmol/l). This may be achieved by taking an insulin correction if required¹⁴ and then adding additional bolus insulin to cover the carbohydrate and protein intake consumed in early recovery to stimulate glycogen resynthesis, and muscle protein synthesis. As always, it is important to re-emphasise, that while the rate of glycogen resynthesis is important, the athlete with T1D needs to balance this with the risk of hyperglycaemia and hypoglycaemia. Athletes with T1D must also be made aware that the greater muscle insulin sensitivity after exercise can persist for up to 48 hours (or even longer following extreme exercise bouts) and this means they must be aware of delayed onset of hypoglycaemia. In addition, they should adapt their insulin doses based on individual increases in insulin sensitivity experienced during periods of increased training or competition². Athletes and their coach/trainer/nutritionist should work on developing a regular routine of post-exercise nutrition and insulin administration based on individually defined parameters and requirements. Section 2 of this statement will outline potential strategies to help facilitate this.

1.5. Liver Glycogen Metabolism During and After Exercise

Skeletal muscle glycogen metabolism has received much attention over the last 6 decades since the development of the muscle biopsy technique^{36,55}. However, the role of hepatic glycogen during and after exercise has been less well studied, primarily due to the difficulty of accessing tissues samples compared to muscle biopsy samples. Development of ¹³C-magnetic resonance spectroscopy (MRS) as a non-invasive measurement of human liver glycogen⁵⁶ has enabled repeated measurements of liver glycogen content to be made without inducing the catecholamine response that sometimes is induced by biopsy procedures. A handful of studies have used ¹³C-MRS to measure the effect of carbohydrate ingestion on the rate of post-exercise hepatic glycogen resynthesis in athletes without diabetes^{27,57,58} (see Section 2.2). Although there are no data on hepatic glycogen metabolism during the post-exercise period in athletes with T1D, Bally et al.⁵⁹ found comparable hepatic and intramyocellular glycogen stores between well-controlled adults living with T1D and a group of

matched individuals without T1D under standardised resting conditions. Future research should aim to use these techniques to investigate optimal strategies to maximise hepatic glycogen resynthesis after prolonged endurance exercise in athletes living with T1D.

1.6. Influence of Sex Hormones and Menstrual Cycle Phase on Fuel Metabolism and Glycogen Resynthesis

Within the T1D and exercise literature, the majority of published work has only included young healthy males, and those that have included females tend not to recognise the potential sex-related impact on their outcomes. As was highlighted previously,^{5,60,61} this is an important issue, as there are likely to be important sex-related differences in metabolic and neuroendocrine responses during and after exercise that will influence glycaemia, carbohydrate requirements, and glycogen resynthesis. Female athletes with T1D may experience important changes in glycaemia that are linked to the menstrual cycle phase. These changes are likely to influence insulin and carbohydrate needs before, during and after an exercise bout.

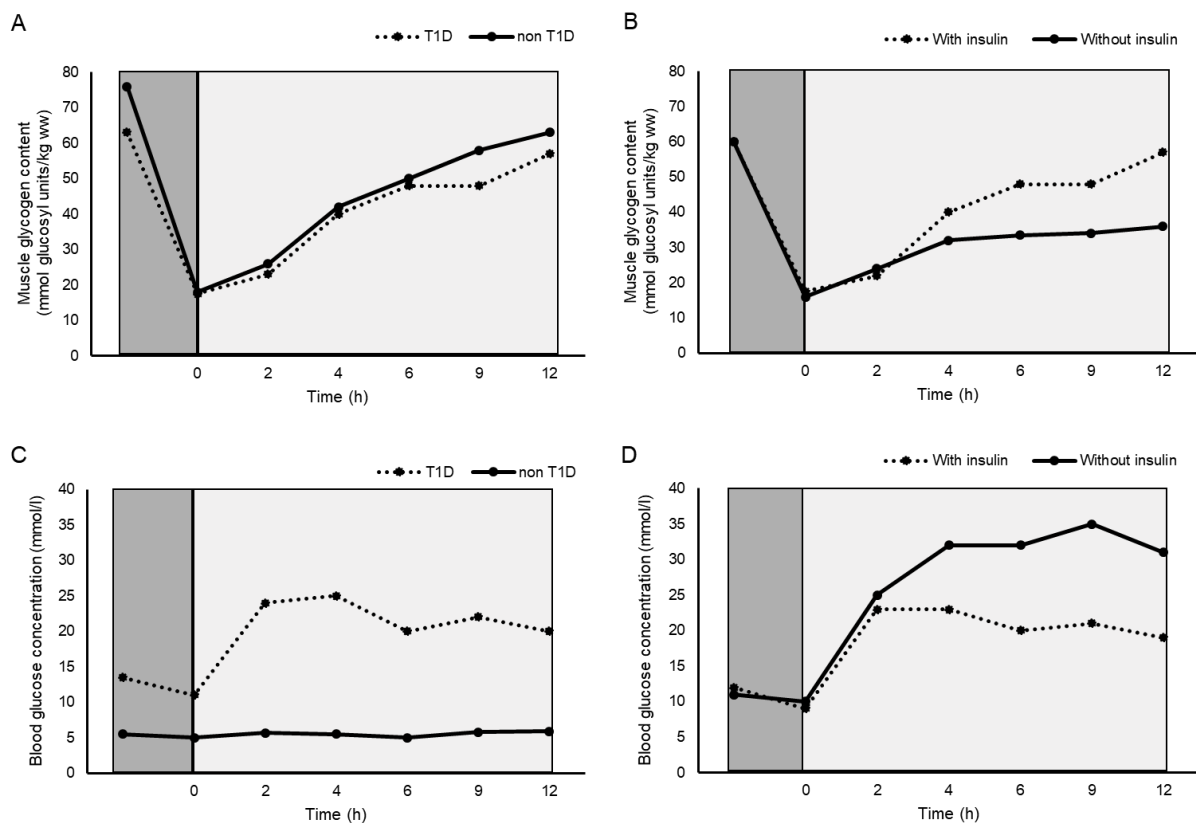


Figure 2. Muscle glycogen recovery and blood glucose concentrations after prolonged exercise. Adapted from ^{31,46}

Panel A shows the glycogen content in individuals with T1D with insulin administration and individuals without T1D. Panel B shows the effects of insulin deprivation in individuals with T1D, where the changes are apparent in the second (insulin-dependent phase). The dark grey shading illustrates the exercise period and light grey is the recovery period up to 12 hours post exercise. Panels C and D, are the corresponding blood glucose profiles to graphs A and B

above, demonstrating the importance of prioritising blood glucose concentration during recovery.

2. Strategies to Maximise/Facilitate Post-Exercise Glycogen Synthesis in Athletes Living with Type 1 Diabetes

Athletes without diabetes do not need to consider their blood glucose concentration in the same way as those living with T1D since their β -cell response is intact and insulin is produced endogenously. For those without T1D, following a bout of exhaustive exercise, replenishment of glycogen stores is the primary aim, with rate of carbohydrate absorption in the gut and glucose uptake in the muscle being the main limitation, with little concern of hyper- or hypoglycaemia ³⁹. For the athlete with T1D, maintaining blood glucose concentration within target range (4-10 mmol/l) adds an additional level of complexity that requires vigilance, frequent glucose monitoring, preferably by CGM, and often insulin dose titration. Nutritional strategies to maximise rate of glycogen resynthesis and muscle protein synthesis after exercise have been well studied in athletic populations without diabetes. Muscle damage repair and skeletal muscle reconditioning are also important determinants of recovery ⁷. A positive muscle protein balance is needed to facilitate repair of exercise induced muscle damage ⁶² and in the long-term for muscle hypertrophy for improved athletic performance, depending on the event. In this section, we outline the potential impact of timing, quantity, and type of nutrition as well as post-exercise recovery practices (cool down, ice baths, sleep) and how they could be used to simultaneously manage glycaemia and rate of recovery (see Figure 3 for a summary).

2.1. Post-Exercise Carbohydrate Intake

The quantity of post-exercise carbohydrate intake will depend on the type, duration and intensity of the exercise performed as well as blood glucose concentration and the circulating level of insulin. If maximising the rate of muscle glycogen resynthesis is the primary aim (which is common for endurance/ultra-endurance athletes that compete multiple times within a short timespan), post-exercise carbohydrate ingestion represents the most important factor determining the rate of muscle glycogen synthesis ^{34,39}. During situations in which speedy recovery of glycogen is required (<8 hours recovery between two fuel demanding sessions) athletes without T1D are recommended to consume 1-1.3 g CHO·kg⁻¹·h⁻¹ for the first 4 hours and then resume regular meal patterns to meet daily fuel needs ⁶. During such situations, athletes may choose carbohydrate-rich foods that are low in fibre and easily consumed (e.g. white rice or pasta). For the athlete with T1D, there is limited research in this area. However, it is likely that requirements are similar, provided insulin is taken in the correct amount to manage glycaemia. In recent years, low-carbohydrate or carbohydrate-restricted diets have received much attention due to suggested benefits for health, glycaemic management and sports performance. As this is a topic of debate beyond the scope of this review, interested readers are referred to a recent review by Scott et al. (2019) ⁶³.

The athlete with T1D should also be aware that addition of fat, protein and/or fibre will alter glycaemic profile of a meal ^{64,65}. The use of a hybrid closed-loop insulin delivery system that automatically changes basal insulin delivery based on unique settings customised to the individual's insulin sensitivity, real-time glucose measurements and other variables may facilitate glycaemic management during the recovery period, particularly when sleeping ⁶⁶.

2.2. Effects of the Type and Form of Carbohydrates on Post-Exercise Recovery and Glycaemia

The form in which carbohydrates are ingested (i.e. solid vs. liquid) does not appear to make a difference to the rate of glycogen resynthesis ⁶⁷. However, the type of carbohydrate is important, due to differing rates of digestion, intestinal absorption and hepatic metabolism, which are key determinants of their glycaemic impact and rate of delivery to skeletal muscle ^{39,58,68}. A handful of studies have directly compared ingestion of glucose-fructose mixtures vs. glucose alone on the post-exercise muscle glycogen repletion in individuals without diabetes ^{27,57,69,70}. Based on the evidence from these studies, post-exercise ingestion of glucose-fructose mixtures does not appear to accelerate muscle glycogen repletion compared to glucose alone. A few studies have used ¹³C-MRS to non-invasively compare the effects of glucose and fructose co-ingestion with glucose alone on post-exercise liver glycogen resynthesis in people without diabetes ^{27,57,58}. When fructose is co-ingested with glucose (either as free glucose and free fructose or sucrose) the rate of liver glycogen repletion is approximately double the rate seen when ingesting glucose alone and this effect is clearest when carbohydrate ingestion rate exceeds 0.9 g CHO·kg⁻¹·h⁻¹. The greater liver glycogen repletion seen with glucose and fructose is likely due to preferential hepatic metabolism of fructose and/or faster digestion and independent absorption kinetics. For a general overview in this area, interested readers are referred to other detailed reviews ^{71,72}.

Focusing on the athlete with T1D, these alternative, multiple transportable carbohydrates such as fructose, isomaltulose and galactose (although there is currently only data on the former) may also be beneficial for reducing the risk of exercise-associated hypoglycaemia due to the lower amount of insulin required to cover their intake ^{73,74}. Unfortunately, no studies have yet investigated glycaemic effects of fructose ingestion post exercise in people with T1D or the possible impact on glycogen resynthesis (liver or muscle).

2.3. Fluid Management

To preserve homeostasis, optimal body function and well-being, athletes should aim to have fluid management strategies for before, during and after exercise to maintain euhydration, depending on the type and duration of exercise, as well as the environment. The athlete with T1D will have to consider what they drink (i.e. if it contains carbohydrates) in addition to how much they consume to manage glycaemia and hydration. Most athletes finish a bout of exercise with a fluid deficit so will need to restore euhydration during recovery ⁷⁵. In addition to water, sweat contains substantial but variable amounts of sodium, potassium, calcium and magnesium. Therefore, athletes should not be advised to restrict sodium post exercise, particularly when large sodium losses have occurred ⁶.

Concerns that thermoregulation may be impaired in people living with T1D during exercise, particularly under hot and humid conditions, have previously been raised ⁷⁶. Data is quite limited in this area, but studies have shown that young individuals with T1D without diabetes-related complications have no differences in sweat rates during low- to moderate-intensity exercise compared to individuals without diabetes matched for age, sex, body surface area, body composition, and physical fitness ^{77,78}. However, Carter et al. ⁷⁷ found that when exercising at higher workloads (≥ 250 W·m⁻²) in the heat (35°C at 20% humidity), local sweating response in individuals with T1D was lower and core body temperature was higher compared

to participants without T1D. These findings suggest that the reduced sweat rate may lead to reduced ability to dissipate heat at higher workloads.

Whether those living with T1D experience differences in thirst perception vs. those without diabetes (i.e. thirst depending on changes in blood osmolality) has not been fully defined, although high blood glucose concentrations increasing blood osmolality are likely to signal for increased thirst sensation ⁷⁹. This is supported by Buoi et al. ⁸⁰, who found using a questionnaire that self-reported fluid intake during exercise was higher in a group of individuals with T1D compared with a group of age and sport-matched individuals without T1D. Hyperglycaemia influences the hydration status in individuals with diabetes because it alters the fluid resorption in the kidneys and causes a shift in free water from cells into the circulation. When blood glucose concentration is <9-10 mmol/l, almost all glucose in filtrate is reabsorbed in the proximal tubule and the amount of glucose in the urine is negligible. When blood glucose concentration goes >9-10 mmol/l, glucose in the filtrate can escape and glucose can be found in the urine (glucosuria) ⁸¹. The amount of glucose reabsorbed increases linearly with rising plasma glucose concentration until a maximum value is reached. Any further increase in filtered glucose load is excreted in urine ⁸¹. Because glucose needs to be dissolved in water, whenever glucose is lost in urine, water must follow. This osmotic drive increases the risk of dehydration if fluid losses are not compensated.

2.4. Co-ingestion of Additional Nutrients: Protein, Caffeine, Alcohol

Rates of glycogen resynthesis and blood glucose concentration can be affected (both positively and negatively) by the co-ingestion of other nutrients with carbohydrate ^{4,82}. Such information is useful when glycogen resynthesis is required in a short time frame.

2.4.1. Protein

In addition to carbohydrates, insulin secretion is induced through intravenous infusion or oral ingestion of certain amino acids in individuals without diabetes ^{83,84}. Studies have also shown that there is a synergistic effect of combined amino acids and/or protein and carbohydrate ingestion on insulin secretion ^{84,85}. This evidence led to the commonly used strategy in athletes without diabetes of co-ingesting carbohydrate and protein with the aim of accelerating post-exercise muscle glycogen resynthesis and taking advantage of the anabolic effects of insulin ^{4,6,7}. Indeed, there is evidence that when amino acids and/or protein are co-ingested with carbohydrate, postprandial insulin levels are augmented, leading to an increase in glycogen synthase activity, when carbohydrate intake is below the threshold for glycogen storage (e.g. 0.5-0.8 g CHO·kg⁻¹·h⁻¹) ^{82,86-88}. However, when carbohydrate intake is adequate (e.g. >1 g CHO·kg⁻¹·h⁻¹), the co-ingestion of protein has no additional effect on glycogen synthesis ^{37,89}, although there will still be effects of protein on anabolism.

The beneficial effects of protein intake in the recovery period is well described for athletes who do not have T1D. Studies have shown that performance was better in a second exercise bout 18 hours after exhaustive exercise with intake of 0.8 g CHO·kg⁻¹·h⁻¹ + 0.4 g protein·kg⁻¹·h⁻¹ compared to 1.2 g CHO·kg⁻¹·h⁻¹ during the first two hours of recovery ^{90,91}. Although muscle glycogen was not measured in these studies, metabolic data suggested the glycogen stores did not limit performance after carbohydrate only intake during the first two hours of recovery ^{90,91}. Importantly, muscle glycogen synthesis was similar during the 5-hour recovery period with intake of 0.8 g CHO·kg⁻¹·h⁻¹ + 0.4 g protein·kg⁻¹·h⁻¹ compared to 1.2 g CHO·kg⁻¹·h⁻¹ during the first two hours after exhaustive exercise ³⁷ but performance was better

when protein was added to the recovery drink. Clearly protein intake will not influence endogenous insulin production in the athlete with T1D, but it may increase insulin dose requirements. The addition of protein post exercise is recommended, provided insulin is taken, as the protein is likely to contribute to glycogen resynthesis and increase muscle protein synthesis.

2.4.2. Caffeine

Caffeine is naturally found in many foods and is frequently added to sports supplements due to its ergogenic effects in a range of sporting events. Caffeine has numerous physiological effects including increased lipolysis in adipose tissues and hepatic glucose production alongside a decrease in glucose uptake in skeletal muscle ^{92,93}. In people without diabetes, caffeine intake prior to exercise increases plasma glucose concentration (0.5 mmol/l) during moderate-intensity endurance exercise ^{94,95}, and slightly more (1.0-1.5 mmol/l) after maximal effort time-trials ^{95,96}. These responses have led to the suggestion that acute caffeine intake may attenuate exercise-associated hypoglycaemia in people with T1D ⁹⁷. Ingestion of modest amounts of caffeine (200-250 mg, equivalent to 3-4 cups of coffee) has been shown to augment the symptomatic (i.e. increased hypoglycaemia awareness) and hormonal responses (e.g. greater catecholamine release) to hypoglycaemia in participants with ^{98,99} and without ¹⁰⁰ T1D. Regular caffeine ingestion has also been shown to reduce the frequency of moderate episodes of hypoglycaemia occurring overnight in individuals with long-standing T1D ¹⁰¹.

Just one study has investigated the effects of caffeine on exercise-associated hypoglycaemia in individuals with T1D ¹⁰². However, there are currently no data to support the use of caffeine during the recovery period in athletes living with T1D. If caffeine is found to be useful for post-exercise recovery, future research should aim to define the lowest caffeine intake required to reduce the risk for hypoglycaemia because of the need to consider the possible disadvantages e.g. impaired sleep quality. The paucity of data on caffeine and exercise in individuals with T1D in conjunction with caffeine's popularity both socially and as a sports supplement, suggests that this deserves further attention.

2.4.3. Alcohol

Alcohol is an important factor to consider, as anecdotal evidence suggests that some athletes regularly consume large amounts in the post-exercise period, particularly in team sports following competition. Alcohol intake has significant effects on carbohydrate metabolism in the liver and muscle as well as negative effects on fluid balance ¹⁰³ with important implications for post-exercise recovery ¹⁰⁴. Alcohol has been shown to inhibit glucose uptake into skeletal muscle ¹⁰⁵, decrease the stimulating effect of exercise on muscle glucose uptake ¹⁰⁶ and impair glucose utilisation ¹⁰⁷. There is increased risk of hypoglycaemia when consuming alcohol ^{108,109} due to inhibition of hepatic gluconeogenesis ¹¹⁰ and this is aggravated by blunted symptoms of hypoglycaemia ¹¹¹ and impairment of cognitive function ¹¹². Therefore, athletes with T1D need to be particularly careful when consuming alcohol in the context of an exercise bout, due to the potentially additive risk of severe hypoglycaemia ¹¹³.

2.5. Non-Nutritional Recovery Modalities

Aside from the nutritional and insulin adjustment strategies, the most commonly performed recovery strategies are an active cool down (usually consisting of light aerobic activity) ¹¹⁴, cold water immersion ¹¹⁵ and massage. Here we provide a brief overview of their potential role (excluding massage) in the post-exercise routine of an athlete living with T1D.

2.5.1. Active Cool Down

Many people regularly perform an active cool down, consisting of 5-15 minutes of low- to moderate-intensity exercise, after training or competition with the aim of facilitating recovery ¹¹⁴. Although there are a number of proposed benefits, such as faster recovery of heart rate, reduced muscle soreness and more rapid reduction of metabolic by-products ^{116,117}, only a few benefits are actually supported by research (reviewed by Van Hooren and Peake ¹¹⁴). Despite uncertainty surrounding the potential benefits in terms of recovery for those without diabetes, for those living with T1D, an active cool down should be considered, as this short active phase has the potential to influence blood glucose concentration and therefore may be used to help manage post-exercise glycaemia. For example, if blood glucose is only slightly elevated (i.e. 8-12 mmol/l) at the end of an exercise bout (e.g. after high-intensity exercise, or following ingestion of carbohydrates during exercise), it may be appropriate to perform a low-intensity aerobic cool down with the aim of gradually reducing glucose concentration without the need to apply insulin (which may otherwise result in hypoglycaemia). On the other hand, if blood glucose is on the low side and/or trending down, the cool down can be reduced or eliminated and additional carbohydrates need to be consumed.

2.5.2. Ice Baths

Cold water immersion (CWI) in an ice water bath (also known as cryotherapy) is a common recovery practice ¹¹⁸. It is used by athletes involved in a variety of sports, with the aim of reducing muscle fatigue and potentially accelerating recovery between exercise sessions. However, there is still much debate about the potential beneficial effects of CWI, with contradictory evidence regarding the effects, with some studies showing even potential deleterious ones ^{119,120}. Although research has shown that CWI does not impair glycogen resynthesis rates after exercise ¹²¹, the potential impact on glycaemia during post-exercise recovery in athletes with T1D has not been investigated. Therefore, there is no evidence to support routine recommendation of CWI in the endurance athlete with T1D.

2.6. Optimising Sleep and Avoiding Nocturnal Hypoglycaemia

People with T1D tend to experience higher rates of sleep disturbances than those without diabetes ¹²². Poor sleep has particular negative implications for those with T1D as it has been linked with reduced insulin sensitivity ¹²³ and is associated with poorer glycaemic management ^{124,125}. Sleep is also critical for optimal athletic performance and for the regenerative processes and adaptations that take place during training and competition ¹²⁶.

In people living with T1D, physical activity, especially aerobic exercise, has been shown to increase the risk of nocturnal hypoglycaemia due to an increase in insulin sensitivity ¹²⁷⁻¹²⁹. Nocturnal hypoglycaemia is often particularly challenging for people with T1D, and is associated with significant risk, with over 50% of severe hypoglycaemia episodes occurring overnight ^{109,130}. In a 3-week crossover trial by Reddy et al. ¹³¹, actigraphy was used to assess sleep in individuals with T1D during periods in which they undertook no exercise, resistance training or aerobic exercise. The authors found that participants slept less on nights following aerobic exercise and there was a trend towards decreased sleep in the resistance training condition compared to a control week with no exercise.

For general information relating to napping, sleep extension and sleep hygiene practices, interested readers are referred to a review by Fullagar et al. (2015) ¹³². Specifically for the athlete living with T1D, it seems that improving time in target glycaemic range is a key component of getting a good night's sleep. A number of studies have investigated the effects of a pre-bedtime snack on reducing the risk of nocturnal hypoglycaemia ¹³³⁻¹³⁵, but with mixed

results as to the effectiveness. More recently, technology for diabetes management, including advances in closed loop systems, have demonstrated improvements in glycaemic variability and time in range overnight ^{66,136,137}.



GLUCOSE CHECK ^{AO, 1, 143}

- Check immediately post exercise due to increased risk of hypo- or hyperglycaemia ^{1, 14, 18}
- Continue to check at regular intervals (15 min) or use CGM/flash glucose monitoring due to increased risk of dysglycaemia following exercise ^{AO, 5, 143}
- Consider setting alarms to guide the timings of your checking routine ^{AO}
- Due to potentially elevated risk of hypoglycaemia overnight, CGM alarm should be set at 4.4 mmol/l (80 mg/dl) and those using a flash glucose monitoring should perform at least one scan during the night-time period ¹⁴³



INSULIN ADJUSTMENTS (including pre and post exercise)

- These are likely to be highly individual and depend on the circumstances, including but not limited to, the type, intensity, and timing of the exercise performed ^{1, 5, 11, 12, 13, 14, 18, 52}
- After exercise, the magnitude of increased insulin sensitivity can be high, significantly increasing the risk of post-exercise hypoglycaemia

If using multiple daily injections

- Consider reducing insulin dose pre-exercise ^{AO, 52}
- Reduce the first basal insulin dose in the recovery period, particularly if exercise session was >30-60 min ^{AO, 1}
- Reduce bolus insulin dose with recovery meal ^{14, 134}

If using subcutaneous insulin infusion

- Basal rate reduction 60-90 min before the start of exercise ^{AO, 5}
- When suspending the pump at the start of exercise, limit suspension to max 45-60 min. Consider a hybrid regimen ¹³
- The bolus insulin dose can be reduced by ~20-50% at the first recovery meal, along with a similar reduction in the insulin basal delivery rate for ~6-12 hours ^{AO, 5}



CARBOHYDRATE INTAKE

- Initiate carbohydrate feeding when glucose concentration is below 8.0 mmol/l (144 mg/dl), particularly if glucose is decreasing ^{AO, 5}
- When rapid recovery from prolonged exercise is the key objective, and peak performance is required within 24 h, aim to consume 1-1.3 g CHO·kg⁻¹·h⁻¹ for the first 4 h of recovery, starting as soon as possible after exercise with frequent feeding intervals thereafter (i.e. every 30 minutes) ^{6, 37, 38, 70}
- In some scenarios (e.g. focus is on enhancing the training stimulus or adaptive response), low carbohydrate availability may be deliberately achieved by reducing total carbohydrate intake, or by manipulating carbohydrate intake related to training sessions (e.g. training in a fasted state or undertaking a second exercise session with a low carbohydrate intake) ⁶³. However, there is limited information in athletes living with T1D and we do not generally recommend a low carbohydrate diet for exercise performance ^{AO, 63}
- The use of multiple-transportable carbohydrates (e.g. fructose) in combination with glucose post-exercise will promote a faster liver glycogen repletion rate than glucose alone ^{27, 57, 58}
- Fructose alone cannot be used to immediately treat low blood glucose ⁶⁸
- Fructose/glucose co-ingestion will require a lower insulin dose compared with glucose alone ^{73, 74}
- For further, detailed information on fuel and recovery, readers are referred to Table 1 in reference ⁶



PROTEIN INTAKE

- Daily protein recommendations for endurance athletes is 1.6 – 1.8 g·kg⁻¹·d⁻¹ ^{6, 7}
- Protein added to carbohydrate immediately after exercise may speed up recovery ^{4, 6, 7, 33, 37, 82, 86, 87, 90, 91}



HYDRATION

- Be aware of the effects of drinks containing high levels of carbohydrate on blood glucose concentration ^{AO}
- Hydrate with carbohydrate free drinks if glucose >10.0 mmol/l ^{AO}
- Effective rehydration requires the intake of a greater volume of fluid (e.g. 125%–150%) than the final fluid deficit (e.g. 1.25–1.5 l fluid for every 1 kg BW lost) ⁶
- Dietary sodium/sodium chloride (from foods or fluids) helps to retain ingested fluids
- Be aware of environmental conditions (hot/humid conditions) ^{76, 77}
- Excessive alcohol intake in the recovery period is discouraged due to diuretic effect and increased risk of hypoglycaemia ^{103, 108, 109}



CAFFEINE

- Caffeine in a dose of 3 mg·kg⁻¹ (200-300 mg) may reduce the risk for hypoglycaemia during and after exercise ^{AO, 93, 102}. This can be consumed alongside glucose ^{AO}.
- Avoid high levels of caffeine consumption late in the day, as this can negatively affect sleep ¹³²



COOL DOWN

- If during the last 10 min of exercise, blood glucose >10.0 mmol/l consider a more prolonged low-intensity cool down ^{AO}
- If during the last 10 min of exercise, blood glucose is 5-10 mmol/l and decreasing reduce the length of the cool down ^{AO}

Figure 3. Summary of Considerations to Maximise/Facilitate Post-Exercise Glycogen Synthesis in Endurance Athletes Living with Type 1 Diabetes

References to support each of the statements are provided within the figure where data are available. The rates of carbohydrate, protein and fluid intake suggested here are based on research conducted on individuals without type 1 diabetes (T1D). Where published evidence is lacking due to a limited number of studies in the post-exercise period in individuals living with T1D statements are based on the authors' opinion and experience. In such cases, this is denoted within the figure using AO (Author Opinion). For each of these considerations, glycaemia, insulin dose (type and whether on multiple daily injections or pump) will have to be taken into account and monitored. More detailed information relating to each topic are provided in the text. CGM = continuous glucose monitoring.

3. Potential for Technology to Aid Post-Exercise Recovery

Wide variation in training and nutrition plans, insulin requirements and diabetes experience, strongly suggest that there will never be a "one size fits all" set of guidelines that can be applied to every athlete living with T1D. What is consistent between individuals, however, is the large number of decisions that can influence glucose management and general health. Following diagnosis of T1D, the individual is launched into a process of decision-making that becomes part of his or her daily life. Indeed, it has been estimated that people with T1D must make as many as 600 decisions per day to manage their diabetes ¹³⁸. Self-adjusted insulin dosing is complex as it involves recalling the time and amount of a dose while the insulin is still active, as per the pharmacokinetics of insulin and the temporal relationship of these doses to any recently ingested food. Physical activity presents additional challenges, with the majority of decision-making based on personal trial and error rather than input from medical professionals ¹³⁹. Therefore, developing adaptable, easy to follow decision support tools that can be adjusted according to each individual's needs are likely to be extremely useful for improving not only performance but also blood glucose management and exercise participation.

Rapid developments in technologies such as continuous glucose monitoring (CGM) sensors, smart devices/wearables, and closed-loop systems all contribute to the possibility of increased time in range around exercise with less input by the user (Figure 4). The use of increasingly accurate and reliable CGM technology in particular has greatly improved our knowledge of the glycaemic responses to exercise, even during the nocturnal period ¹⁴⁰⁻¹⁴³, thereby positively affecting post-exercise recovery. CGM technology has also been essential in the ongoing development of artificial pancreas systems using closed-loop automated insulin delivery ¹⁴². These systems combine sensor glucose measurement with insulin pumps using an algorithm to direct insulin delivery ^{66,144-146}. Next generation closed-loop systems currently under investigation integrate other signals such as heart rate, skin conductance, ventilation rate and near body temperature, and add other hormones such as glucagon to help improve glucose and time in target range during and after exercise ¹⁴⁴⁻¹⁴⁷. Hybrid closed-loop systems are offering benefits for improved time in range and benefits in maintaining glycaemia within target range over night and under demanding environmental and even unplanned conditions ^{66,145,146,148}. In the future, innovative algorithmic and machine learning (artificial intelligence) approaches are likely to further facilitate decision support ¹⁴⁴. Such technology may also help to reduce some of the psychological toll and cognitive burden that T1D can have on the individual due to constantly having to calculate meal or correction boluses and account for differences in insulin sensitivity during or after exercise ¹⁴⁹. Therefore, appropriate guidance

and support should be given to individuals interested in using these technologies so that they are used to their maximum potential.

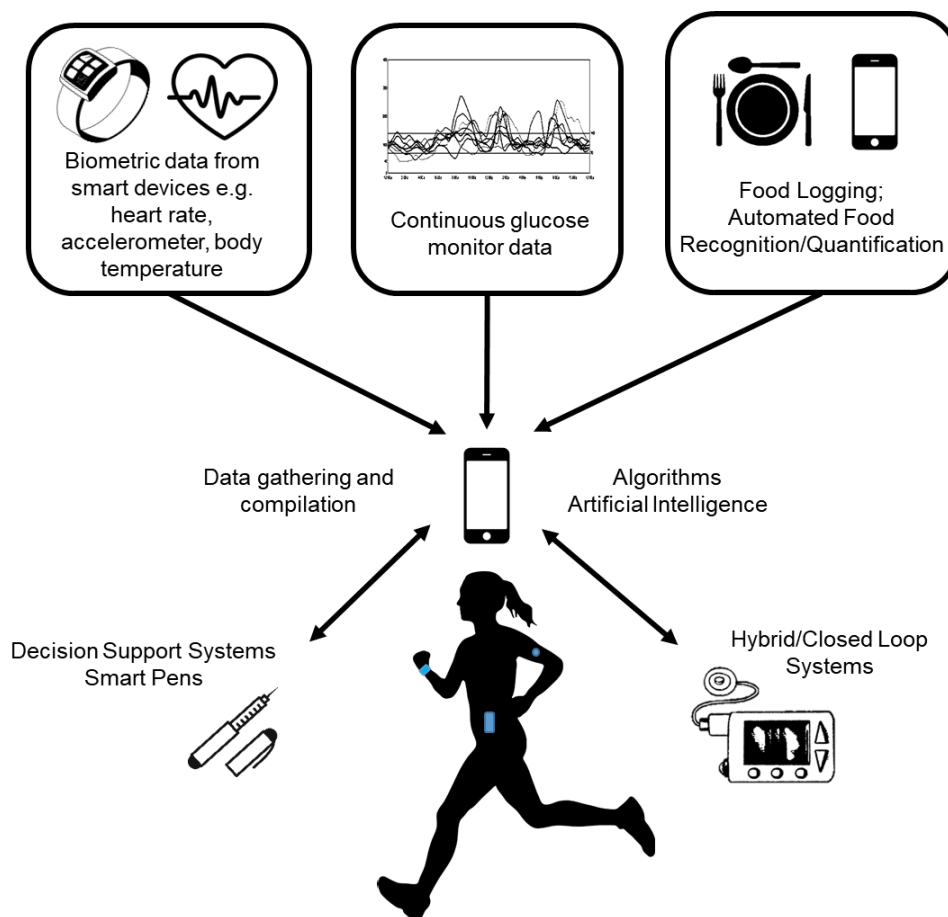


Figure 4. Proposed example of a connected virtual ecosystem to aid the decision-making processes for optimised post-exercise glycaemia and recovery in people living with type 1 diabetes. Researchers, clinicians, sports coaches, and athletes living with T1D are increasingly integrating different data sources to facilitate decision-making behaviours related to glycaemia, training, and nutrition to meet energy requirements. Rapid development of hybrid-closed loop systems are also helping to make this much more automated ^{141,142,150}. It is important to note that athletes without diabetes are also using similar data tools (e.g. glucose monitoring, food logging apps, wearables) to make decisions about their training and nutrition practices.

4. Conclusions

The post-exercise recovery phase is an extremely important, yet somewhat unexplored topic, for the athlete with T1D. Regardless of the athlete's sport or competition level, it is clear that numerous behaviours will have an impact on short- and long-term recovery, and therefore subsequent performance, training adaptation, and time in target glycaemic range. The athlete with T1D must always prioritise blood glucose management, which is essential for overall health and to optimise aspects of recovery. On the other hand, the unique ability of people

living with T1D to influence their insulin concentration through exogenous administration, suggests that greater planning and attention is needed to optimise nutrition and insulin strategy for glycogen resynthesis.

Contributors

The literature search was done by SNS. All authors (SNS, FYF, MC, JM, RD, JFPW, JJ, RC, MCR, AJ, and CS) contributed to the original draft of the manuscript. SNS, FYF, MC, MRC, and CS edited the revised manuscript. All authors approved the final submission.

Declaration of Interests

Dr. Scott has nothing to disclose. Dr. Fontana has nothing to disclose. Dr. Cocks has nothing to disclose. Dr. Morton has nothing to disclose. AJ is involved and receives a consulting fee from a startup company (Neverseond that makes sports nutrition products for athletes. Dr. Dragulin has nothing to disclose. JFPW has research collaborations with the Pfizer a/s and Novo Nordisk a/s unrelated to this work. Dr. Jensen has nothing to disclose. Dr. Castol has nothing to disclose. Dr. Riddell reports personal fees from Zucara Therapeutics, grants from Insulet, personal fees from Zealand, personal fees from Lilly Diabetes, personal fees from Novo Nordisk, personal fees from Sanofi, outside the submitted work. Dr. Stettler has nothing to disclose.

Funding Information

None

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