Diabetes Technology and Exercise

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KEYWORDS

• Type 1 diabetes • Exercise • Technology • Physical activity • Closed loop
• Automated insulin delivery • Glucose monitor • Diabetes

KEY POINTS

- Regular physical activity and planned exercise sessions are important for people living with diabetes for a variety of health and fitness reasons.
- However, the challenges around managing blood glucose concentrations mean that many people with diabetes lead a sedentary lifestyle.
- Rapid advances in technologies are already helping many individuals with diabetes reach their physical activity goals more safely and more easily.
- However, although these technological advances are exciting, there are limitations that need to be addressed with further research.
- This article provides an overview of recently developed technologies designed to help patients with diabetes to be more physically active, while also trying to improve glucose control around exercise.

INTRODUCTION

Regular physical activity (PA) is important for people living with type 1 diabetes for a variety of health and fitness reasons.[1] However, because of the challenges around managing blood glucose concentrations, many people with type 1 diabetes lead a sedentary life.[2] Advances in technologies, including continuous glucose monitoring

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(CGM), intermittent flash glucose monitoring (fGM), and automated insulin delivery (AID) systems, are helping many individuals with type 1 diabetes reach their PA goals more safely and more easily. The development of strategies that integrate the use of smartphone technologies and PA monitors provides users with important data metrics, such as activity levels, carbohydrate counting, and glucose monitoring, to help users make better-informed decisions. This article provides an overview of recent technologies that help engage patients with diabetes to be more physically active, while also trying to improve glucose control around exercise.

TYPES OF EXERCISE AND TERMINOLOGY

PA is defined as any body movement caused by the contraction of skeletal muscle that substantially increases energy expenditure compared with rest, whereas exercise is defined as a structured form of PA that is performed with the intent to maintain or improve health and fitness.[3] These terms are used interchangeably for this review. Numerous categories of PA exist that can tax various components of physical endurance, strength, balance, and/or flexibility. For those living with diabetes, and in particular type 1 diabetes, the exercise type, intensity, and duration all have major impacts on glucose homeostasis.[4] Aerobic exercise (eg, walking, bicycling, swimming, or jogging) involves continuous, rhythmic movements of large muscle groups, normally lasting at least 10 minutes at a time. Resistance exercise involves brief, repetitive muscle contractions with weights, weight machines, resistance bands, or the person’s own body weight (eg, push-ups, pull-ups, leg press). Flexibility exercises (eg, lower back or hamstring stretching) are intended to enhance the ability to move through fuller ranges of motion with little resistance. Many types of activities, such as yoga and Pilates, incorporate elements of both resistance and flexibility exercise and use components of both aerobic and anaerobic metabolism. High-intensity interval training (HIIT) is defined as brief, intermittent periods of vigorous aerobic/anaerobic exercise, interspersed with periods of rest or recovery, and is frequently used to improve fitness. Under the umbrella term HIIT, there are several protocols that have been investigated in the literature, including aerobic interval training,[5] sprint interval training,[6] and constant-load low-volume HIIT,[7] all of which are likely to have differing effects on glycemia in people with diabetes.

BENEFITS OF REGULAR PHYSICAL ACTIVITY

Regular PA can help people with type 1 diabetes achieve a variety of goals, including increased cardiorespiratory fitness, better sleep, enhanced energy levels, improved glycemic control, decreased insulin resistance, improved blood lipid profile, enhanced blood pressure control, and the maintenance of a healthy body weight.[1] In general, both regular PA[8–10] and/or a high level of cardiorespiratory fitness[11] are associated with reductions in the incidence of cardiovascular disease and overall mortality. In addition to aerobic fitness, anaerobic fitness and/or muscular strength also have independent and additive benefits for people living with diabetes,[12] including those with type 1 diabetes.[13] The American Diabetes Association (ADA)[1] and others[4,14] recommend that adults with diabetes should engage in 150 minutes or more per week of moderate to vigorous aerobic exercise, spread over at least 3 d/wk, with no more than 2 consecutive days without activity. Moreover, the ADA points out that less PA may be sufficient (ie, minimum 75 min/wk) if the activities are more vigorous. They also recommend that strength training be done 2 to 3 times per week to help maximize the health and fitness benefits of regular PA.[1] Flexibility training and balance training are also recommended 2 to 3 times/wk.[1]

TOOLS AND TECHNIQUES FOR MEASURING PHYSICAL ACTIVITY

To assist with the challenge of achieving the PA recommendations, patients may benefit from the ability to objectively measure and record their bouts of PA. However, many health care providers do not ask about patient PA patterns, and activity monitors are seldom prescribed.[15] PA levels are often suboptimal in people living with diabetes, according to self-report[16] and accelerometry[2,17] data. Monitoring PA levels objectively using accelerometry, along with behavior change interventions, increases activity levels in inactive youth with type 1 diabetes.[18]

PA and exercise events can be measured in a variety of ways, from surveys requiring user input (eg, International Physical Activity Questionnaire, Minnesota Leisure Time Physical Activity Questionnaire)[19] to automated wearable sensors that can automatically track the movements of the user and even quantify the intensity of effort by measuring heart rate.[20] The widely used International Physical Activity Questionnaire has been used in various research settings to gauge the PA levels of individuals living with diabetes.[21,22] In smaller studies, wearable sensors, such as wrist-worn smart watches, that combine accelerometry with photoplethysmography and other sensors to measure heart rate, step count, energy expenditure, and other descriptors of movement and sleep (quality and quantity) have also been used.[23,24] Although fitness trackers and smartphone apps offer some solutions for documenting PA levels in individuals, issues of reliability and accuracy remain.[23] To date, the authors know of only 2 studies that have assessed the accuracy of these devices in individuals with diabetes during exercise, with both displaying varying results in heart rate and energy expenditure measurement accuracy.[25,26] Although many wearable sensors using photoplethysmography measure heart rate levels reasonably accurately during exercise, these devices typically show poor accuracy in measuring energy expenditure during activities of low to high intensity[23,27,28] (**Fig. 1**). In general, the accuracy of measuring heart rate and energy expenditure in many sensors decreases as exercise intensity increases.[23,27,29] Some newer wearables, such as the Garmin activity monitor with Garmin Move IQ, can automatically quantify the number of active minutes per week.

ACTIVITY MONITORS IN DIABETES SELF-MANAGEMENT

Overall, consumer-based wrist monitors, from manufacturers including Fitbit, Apple Watch, and Garmin, are reasonable at estimating heart rate, daily step count, and energy expenditure for activities of light to moderate intensity. In general, these consumer products are affordable, easy to use, and accessible for the general population and could be useful for patients with diabetes to self-monitor their PA habits. It is therefore tempting, from a technology perspective, to strive to incorporate ways of detecting, characterizing, and integrating signals from various forms of exercise so that AID systems can be adapted appropriately to limit any exercise-associated dysglycemia. However, several challenges exist when trying to accurately characterize a PA event for an AID system.[24,30] These challenges include determining the physiologic thresholds for movement/exercise based on heart rate and/or accelerometry (or some other physiologic measurement) that would trigger a change in insulin delivery rate and the complicated relationship between relative exercise intensity and the body's insulin needs (**Fig. 2**). At the least, wearable sensors and smartphone applications that document activity levels are useful for determining whether patients

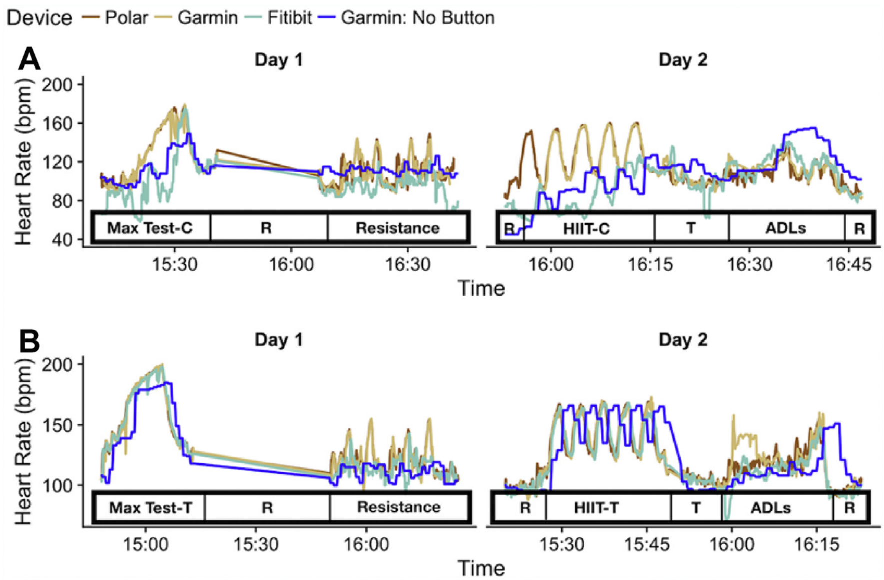

Fig. 1. Accuracy of wearable technologies during exercise and rest. (*A*) Two-day wear study protocol with R indicating rest periods and T indicating a transition period between 2 different types of activities. Data are shown from 2 different participants (*A* and *B*) wearing a Polar H10 (Polar, Kempele, Finland) heart rate chest strap (reference standard) and a Garmin vivosmart 3 (Garmin, Olathe, KS) watch and a Fitbit Charge 2 (San Francisco, CA) watch. Note, the Garmin device was worn by the participants in 2 different modes: 1 with the activity mode indicated (Garmin) and the other without (Garmin: no button). (*A*) Heart rate data during a progressive cycling test to exhaustion; (*B*) The data during a progressive treadmill running test to exhaustion. Data in (*A*) highlight the error observed during higher intensity cycling exercises in which wrist movement was less pronounced during cycle ergometer testing. (*B*) Treadmill results when the Garmin, Fitbit, and Polar data are closely matched across the exercise types. ADLs, activities of daily living; HIIT-C, high-intensity interval training–cycle ergometer; HIIT-T, high-intensity interval training–treadmill; Max Test-C, maximum test–cycle ergometer; Max Test-T, maximum test–treadmill.

are achieving their activity goals.[24] Emerging evidence suggests that wearable fitness trackers merged with smartphone technologies/apps and electronic health record systems may facilitate behavioral goal setting and improve PA monitoring in patients living with diabetes.[31]

ASSESSING PHYSICAL ACTIVITY IN PATIENTS WITH DIABETES

There is little consensus on how activity data should be described or expressed for the purposes of prescribing, tracking, or decision support around glucose management in diabetes. For example, some clinicians or researchers may simply prescribe or document the number of minutes of PA performed over a week (eg, 150 min/wk of moderate-intensity activity; 75 min/wk of vigorous-intensity activity), whereas others may express PA metrics more objectively, such as the time spent at a given metabolic equivalent (MET) for a given task (eg, 40 minutes jogging or cycling at 5 METS = 200 MET-minutes).[32] The latter approach may be preferred in certain situations of exercise prescription, because it considers the relative intensity (ie, a unit of energy expenditure relative to the individual’s energy expenditure at rest) and the

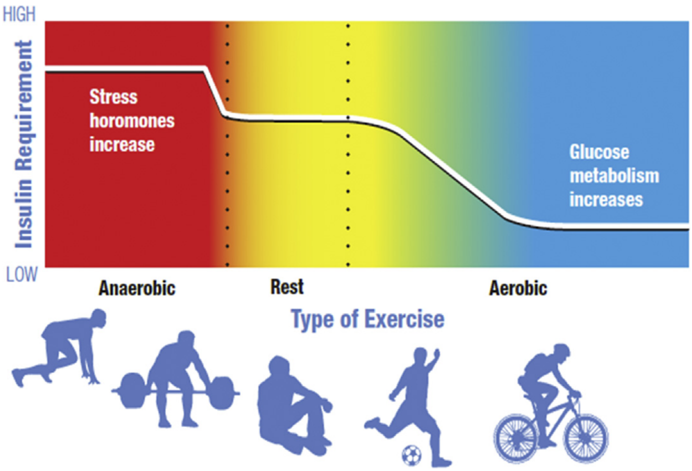

Fig. 2. Insulin needs depend on the type and intensity of physical activity performed. In general, insulin needs increase during or after intensive aerobic and anaerobic activity when stress hormone (ie, adrenaline, noradrenaline), growth hormone, and lactate levels increase. In contrast, insulin needs diminish with more prolonged mild to moderate-intensity aerobic activities when stress hormone levels are less pronounced. (*Courtesy of* Michael C. Riddell, PhD, North York, ON, Canada.)

duration of the task, although this approach may be more difficult to explain to most patients. Energy expenditure during exercise can also be expressed as kilocalories, joules, or watts, depending on the activity sensor used, whereas relative energy expenditure is often expressed relative to the individual's maximal percentage of oxygen consumption (ie, $\%\dot{V}O_{2max}$) or maximal heart rate (HR_{max}). These various technical terms used to describe PA make it cumbersome for patients, clinicians, and researchers to effectively communicate how much exercise is required, or being performed, and at what level of intensity. However, it is likely that the consideration of these terms may be necessary, because both the relative[33] and absolute[34] PA intensity influence glucose homeostasis in people living with diabetes.

For decision support with exercise, it is important to detect when spontaneous activity occurs, perhaps with accelerometry and/or heart rate. Another approach is to schedule a planned exercise event into a controller, perhaps using a smartphone application that is somehow tied to a calendar app. In any case, the relative exercise intensity and the activity duration should be considered when it comes to basal and/or bolus insulin adjustments. The relative intensity of aerobic exercise is typically gauged by estimating the $\%\dot{V}O_{2max}$ or percentage HR_{max}. Typically, as the relative exercise intensity increases, the risk for hyperglycemia increases in a J shape, whereas the risk for hypoglycemic increases in an inverted U shape, although the risk for dysglycemia depends, at least in part, on circulating insulin levels (**Fig. 3**). With very intensive aerobic/anaerobic exercise, insulin needs typically increase compared with basal conditions, whereas, with less intense exercise, insulin needs decrease markedly. Resistance-based activities can have variable effects on glycemia in type 1 diabetes.[35]

Individuals with type 1 diabetes who are in competitive events likely benefit from being able to visualize their performance and glycemia data together to better understand the relationships between glucose levels and performance. Some patients living with type 1 diabetes are very physically active and many reach the competitive

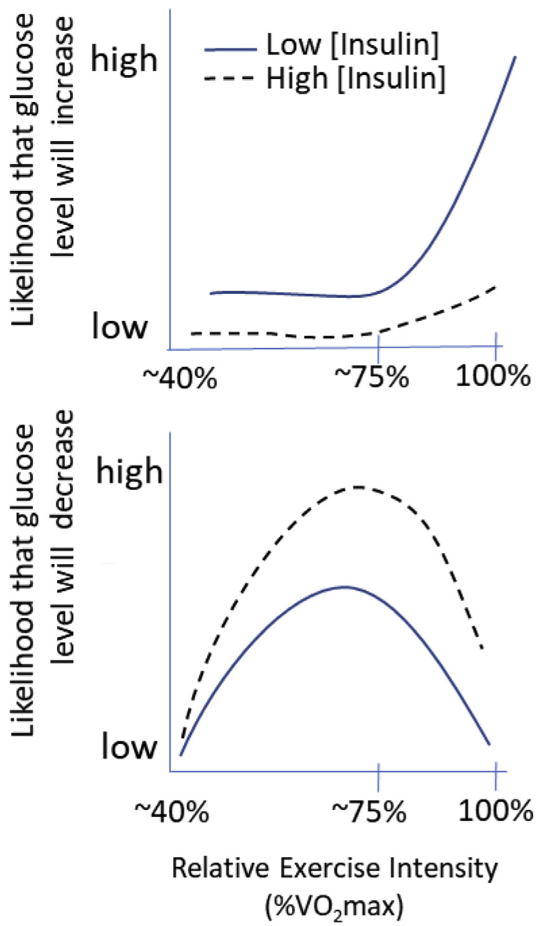

Fig. 3. Theoretic risks for exercise-related dysglycemia in type 1 diabetes. As the relative exercise intensity increases, the risk of hyperglycemia increases in a J shape, whereas the risk for hypoglycemia increases in an inverted U shape, depending on the circulating insulin levels.

or even elite level (see https://en.wikipedia.org/wiki/List_of_sportspeople_with_diabetes). Rapidly improving technologies are now enabling athletes to measure and visualize data (eg, insulin, glucose, heart rate, power output) during training or competition (**Fig. 4**) with minimal burden to the athlete. This ability facilitates communication between the athletes, their coaches, and health care providers, potentially resulting in improved time in target and performance.

EXERCISE AND GLYCEMIC TRENDS

PA comes in several forms for individuals with diabetes, all of which may affect glucose homeostasis. For example, leisure time PA (eg, walking, hiking, gardening, sport, dance) and physically demanding occupations (eg. letter carrier, general laborer, food service industry) may make glucose levels decrease and insulin dosing needs may need to be decreased and carbohydrate snacking initiated to prevent

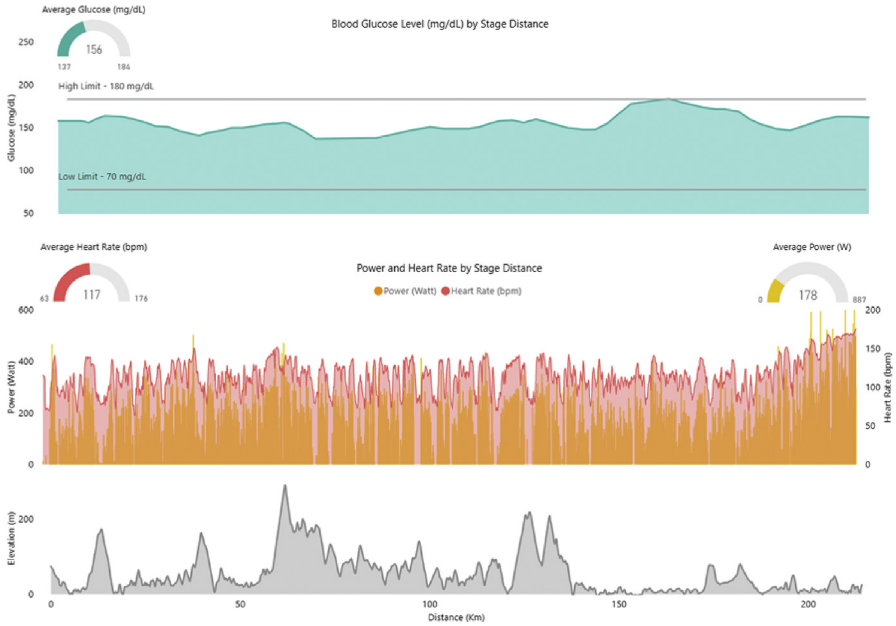

Fig. 4. Example of diabetes and physiologic performance data collection and visualization during professional cycling races. Data visualization of interstitial glucose level (Dexcom G6, Dexcom, San Diego, CA), cycling power output (Watts; Pioneer HD power meter, Long Beach, CA), heart rate in beats per minute (bpm; Wahoo TICKER chest strap), and elevation in meters (Wahoo Element cycling computer) in a 214 km professional cycling stage race. (Data courtesy of Team Novo Nordisk.)

hypoglycemia.[36] In contrast, a stressful competitive event, such as a short cross-country ski race, a swimming event, or a HIIT session, may cause glucose levels to increase rapidly,[37,38] sometimes requiring bolus insulin correction for hyperglycemia.[39] Paradoxically, symptoms of hypoglycemia, rather than hyperglycemia, ensue with intensive exercise even as glucose levels increase.[40]

Exercise duration,[41] mode,[42] relative intensity,[33] absolute intensity,[34] and fitness[34] all affect glucose homeostasis in people living with type 1 diabetes. For example, a more prolonged exercise session in an aerobically fit individual with type 1 diabetes typically increases the reliance on plasma glucose as fuel, compared with a shorter session of exercise at the same relative intensity.[41] In contrast, a brief session of very intense exercise lasting seconds to minutes tends to promote an increase in glycemia in aerobically fit individuals with type 1 diabetes,[43,44] even though a high rate of plasma glucose uptake into working muscle exists.[37] High-intensity interval-based or circuit-based exercise activities tend to have variable effects in diabetes, with some studies showing a decrease in glycemia,[45] whereas others show glucose stability[46] or an increase in glycemia.[44,47] To date, only a few investigators have attempted to use technologies that can distinguish between aerobic, anaerobic, and mixed forms of exercise for the purpose of developing more sophisticated multivariable adaptive artificial pancreas systems for PA and type 1 diabetes.[30] The inability to correctly assess the relative exercise intensity of persons with type 1 diabetes on an AID system may limit the ability of the system to make appropriate changes to insulin delivery for a range of exercise modalities.

STRATEGIES FOR IMPROVED TIME IN TARGET DURING AND AFTER EXERCISE FOR THOSE ON MULTIPLE DAILY INSULIN INJECTIONS OR OPEN-LOOP CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

Various guidelines and strategies exist to help establish and maintain glucose control during and after exercise for individuals living with diabetes.[1,4] Although individuals with type 2 diabetes can have some glucose control issues with different types of exercise, including mild to moderate hypoglycemia with predominantly aerobic exercise[48] or a small increase in glycemia with intensive interval training,[49] they have less exercise dysglycemia overall compared with individuals living with type 1 diabetes. For patients with type 1 diabetes on multiple daily insulin injections (MDI)[50] or continuous subcutaneous insulin infusion (CSII),[51] reduction in prandial (bolus) insulin at the meal before prolonged aerobic exercise, by 25% to 75% depending on the intensity and duration of the exercise, helps reduce hypoglycemia risk when the activity occurs 1 to 3 hours after a meal. This strategy of reduced bolus insulin at the meal before aerobic exercise could be incorporated into AID systems for exercise if the controller, and perhaps user, takes into account a planned exercise session later in the day.

For prolonged aerobic exercise before meals (or $\geq$3 hours after a meal), basal insulin reductions are helpful in preventing hypoglycemia. For patients on MDI, a 20% reduction in basal insulin before an active day (ie, the night before or morning of, depending on when the basal insulin is administered) is an effective strategy to reduce hypoglycemia risk.[52] Even ultralong-acting insulin degludec can be reduced by $\sim$20% to 25% the day before activity to help decrease hypoglycemia risk, although some additional carbohydrate intake may still be required and there may be a small increase in glucose levels at other times of the day.[53] Overall, based on limited observations, CSII may offer some improvements compared with MDI in managing postexercise hyperglycemia,[54] although postexercise hyperglycemia can be sufficiently managed in individuals on MDI via postexercise insulin bolus administration.[39,55] For those on CSII, reductions in basal insulin infusion rate by 50% to 80% set 90 minutes before exercise, carried throughout the exercise session, effectively attenuate the decrease in glucose level associated with prolonged aerobic exercise.[56] Note that not all physically active patients with type 1 diabetes want to wear insulin pumps and CGM devices. Pump and CGM discontinuation often occurs because the individual (often a child or adolescent) finds that the devices are burdensome during periods of increased PA.[57] It is possible that adding additional sensors (eg, heart rate monitors or other exercise wearables) during exercise may increase the burden for patients rather than reduce it.

Overall, the use of wearable technologies, such as step counters, accelerometers, and heart rate monitors, should help identify periods of increased activity and thus the requirement for insulin dose changes and/or carbohydrate feeding. In 1 study, automated weekly review of accelerometer, CGM, and insulin pump data was used to identify children with type 1 diabetes who had increased risk of nighttime hypoglycemia and preemptively adjust the nighttime basal insulin profile according to daytime activity.[58] Hypoglycemia during a PA session lasting 30 to 60 minutes can be predicted, to some degree, if the pre-exercise blood glucose level is less than 180 mg/dL (10 mmol/L) and heart rate level during exercise is greater than 120 beats per minute (ie, the 180/120 rule).[59] More complex random forest models may be incorporated into future AID systems or decision-support systems for type 1 diabetes.[59]

ROLE AND ACCURACY OF REAL-TIME CONTINUOUS GLUCOSE MONITORING AND FLASH GLUCOSE MONITORING FOR EXERCISE

For physically active people with diabetes, CGMs have advantages compared with self-monitoring of blood glucose level with a hand-held glucose meter and capillary sample. For example, the ability to track glucose levels in real time near continuously during prolonged aerobic exercise can be used to initiate carbohydrate feeding before hypoglycemia occurs.[60] However, exercise, in most forms, seems to significantly deteriorate the apparent accuracy of both real-time CGM (rtCGM)[61–64] and intermittent flash glucose monitoring (fGM)[65,66] devices, at least in part because of a significant lag effect. The significant rtCGM lag effect with exercise (15–30 minutes) may mean AID systems have a reduced ability to respond quickly to rapidly occurring changes in glucose concentration associated with aerobic or anaerobic activities. Emerging real-time intradermal CGM technologies using microneedles may help to reduce the time delay associated with exercise and other common physiologic stimuli.[67]

CLOSED-LOOP AND EXERCISE

Advances in CGM technologies, rapid-acting insulin analogues, programmable smart pumps, and smart decision-making algorithms all contribute to the possibility that glucose control can be enhanced with exercise in people living with type 1 diabetes. The recent emergence of hybrid AID systems is showing that glycemic control can be improved overall while reducing the burden on patients around self-management.[68] Current AID systems automate basal insulin delivery rate using intelligent algorithms that receive information from an interstitial glucose sensor. These systems that suspend insulin delivery before hypoglycemia ensues, based on a predicted hypoglycemic event (either during or after), show efficacy compared with standard sensor-augmented pumps (SAPs) in some exercise settings.[69] However, hypoglycemia can still occur with these approaches, particularly if prandial insulin is in circulation. Prototypes and future closed-loop systems may use other signals, such as exercise sensors, and possibly infuse other hormones, such as glucagon, to help improve glucose time in target during times of increased PA or during and after an acute exercise session. The need to reduce basal insulin delivery well in advance of prolonged aerobic exercise to get levels down in circulation by the start of exercise is a major hurdle for the use of AID systems. This hurdle could be overcome by patient preplanning either manually or with the use of a smartphone-based controller that could be set up well in advance of the activity using a calendar tool (eg, Loop-JOJO application on iOS).

Basal insulin suspension at the onset of aerobic exercise offers limited protection against the decrease in glucose concentration.[56,70,71] It is currently unclear whether insulin-only closed-loop AID systems will be sufficient for moderate to vigorous aerobic exercise, because it is difficult to decrease insulin levels in circulation rapidly if the insulin is infused subcutaneously.[72] In one insulin-only AID study by Elleri and colleagues,[73] adolescents with type 1 diabetes still developed significant hypoglycemia with unannounced exercise. However, compared with SAPs, single-hormone closed-loop systems have shown improved time in target and less hypoglycemia in a variety of exercise and post-exercise settings in which hypoglycemia is particularly common.[74–79] It is worth noting that many of these studies examined AID efficacy in exercise settings of predominantly aerobic-based activity, in which insulin needs typically decrease. As mentioned earlier, most AID systems simply increase the glucose target in their exercise modes to reduce insulin infusion rates. As expected, based on recent open-loop exercise research,[56,80] setting the AID system in exercise mode or to temp target mode well before the start of exercise seems to be more effective than setting the system at exercise start time.

In general, closed-loop systems are reasonably safe and effective for improving time in range and reducing hypoglycemia during unannounced exercise sessions in young, active people with type 1 diabetes.[74,81] These technologies generally rely on setting a temporarily higher glycemic target during exercise to pull back on basal insulin delivery, although this is an oversimplification because even if a higher glycemic target is set, glucose levels during the exercise session may still decrease to less than the set target.[82] Perhaps the most challenging exercise-related task will be creating a closed-loop system capable of adapting to all types and durations of PA for a wide range of individuals, although considerable progress is being made.

One strategy that should improve the capacity of AID systems to cope with exercise is to simultaneously measure additional physiologic variables, such as heart rate or other signals, that could be used to gauge the relative intensity of exercise and then use this information in a multivariable adaptive AID system.[83,84] The use of various exercise signals (accelerometer and heart rate) to gauge the onset of increased activity and its intensity does improve estimation (prediction) of a change in glucose in silico.[85] The addition of heart rate signals alone to a glucose dynamic model improves glucose prediction accuracy.[84] Using heart rate as an input signal should help AID systems automatically switch to an algorithm that is more conservative in insulin delivery for aerobic exercise as insulin sensitivity increases.[84] Heart rate is a reasonably accurate way to track the body's response to activity, providing objective personalized data that account for age and fitness level and reflect exercise intensity regardless of the type of exercise performed.[86] Of all the exercise signals, heart rate may be the best gauge of aerobic exercise, although these data may be better expressed as a percentage of heart rate reserve for a given individual to help account for age-related and fitness-related differences in the heart rate to work rate (ie, relative intensity) relationships.

The integration of other signals in addition to heart rate, such as ventilation rate, accelerometry, near body temperature, galvanic skin response, interstitial lactate, or interstitial ketone sensing, may help to discriminate between exercise artifacts (eg, heart rate increases caused by stress or caffeine) and various modes and intensities of exercise. However, with the current mode of insulin delivery (subcutaneous) and pharmacokinetic profile, an exercise sensor, such as a detection of an increase in heart rate, may not trigger a change in set point for the glycemic target or reduce basal insulin delivery soon enough to prevent a decrease in glycemia during predominantly aerobic exercise.[87] In the future, implantable AID systems with rapid insulin delivery (or rapidly reduced insulin delivery) directly into the intraperitoneal space may improve glucose control around exercise.

Several research groups are currently pursuing dual-hormone approaches for prolonged aerobic exercise. In general, dual-hormone approaches outperform SAP during continuous aerobic and interval-type exercise in adults with type 1 diabetes.[88] The addition of glucagon delivery to a closed-loop system with automated exercise detection reduces, but does not eliminate, hypoglycemia in physically active adults with type 1 diabetes.[89] Adjusting insulin and glucagon delivery at exercise onset within a dual-hormone closed-loop system significantly reduces hypoglycemia compared with no adjustment during prolonged aerobic exercise and performs similarly to SAP therapy when insulin is adjusted before exercise.[90] The failure to eliminate hypoglycemia during aerobic exercise in dual-hormone systems may be because the insulin levels in circulation do not decrease fast enough when the insulin delivery on the

AID decreases and perhaps because the glucagon delivery is not triggered soon enough with the current algorithms. Another approach may be to administer a small dose of glucagon (150–200 μg) just before prolonged aerobic exercise to help eliminate hypoglycemia risk.[91,92] However, future studies are needed to determine whether administration of glucagon before very intensive exercise may exaggerate hyperglycemia and possibly increase ketone production.

SUMMARY AND FUTURE DIRECTIONS

The rapid developments in wearable sensors, glucose sensors, insulins, AID systems, and other technologies are helping many people with diabetes to be more physically active, with some patients even competing at the Olympic and/or professional level. Activity wearables and mobile apps help to keep track of activity levels and provide feedback on whether the individuals are achieving their activity goals. Increasingly accurate and reliable rtCGM and fGM devices provide convenient and near-instantaneous information on glycemia during exercise and in the recovery period to facilitate decision making to reduce the risk of hypoglycemia or hyperglycemia. Advances in artificial pancreas systems that link CGM to the user's insulin pump, potentially with the addition of solubilized glucagon, through intelligent hormone dosing algorithms have the potential to ease the burden of exercise management in type 1 diabetes. The integration with automated exercise detection tools in these closed-loop systems may help to discriminate between exercise artifacts (eg, heart rate increases caused by stress or caffeine) and various modes and intensities of exercise to further reduce user input. Within elite-level sport and type 1 diabetes, data from multiple technologies, including CGM, smart insulin pens, and power meters, are now being combined to facilitate communication between the athletes, their coaches, and health care professionals. These technologies are intended to improve time in glycemic target range, and, ultimately, improve the health and performance of the athletes. Although these technologies are exciting, there are limitations that need to be addressed with further research. At present, optimal use of these technologies depends largely on patient and family motivation, competence, and adherence to daily diabetes care requirements.

DISCLOSURE

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REFERENCES

1. Colberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016; 39(11):2065–79.
2. Matson RIB, Leary SD, Cooper AR, et al. Objective measurement of physical activity in adults with newly diagnosed type 1 diabetes and healthy individuals. Front Public Health 2018;6:360.
3. Howley ET. Type of activity: resistance, aerobic and leisure versus occupational physical activity. Med Sci Sports Exerc 2001;33(6 Suppl):S364–9 [discussion: S419–20].

4. Riddell MC, Gallen IW, Smart CE, et al. Exercise management in type 1 diabetes: a consensus statement. Lancet Diabetes Endocrinol 2017;5(5):377–90.
5. Wisløff U, Støylen A, Loennechen JP, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. Circulation 2007;115(24):3086–94.
6. Burgomaster KA, Hughes SC, Heigenhauser GJF, et al. Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity in humans. J Appl Physiol (1985) 2005;98(6):1985–90.
7. Little JP, Gillen JB, Percival ME, et al. Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. J Appl Physiol (1985) 2011;111(6):1554–60.
8. Hu G, Jousilahti P, Barengo NC, et al. Physical activity, cardiovascular risk factors, and mortality among Finnish adults with diabetes. Diabetes Care 2005;28(4):799–805.
9. Moy CS, Songer TJ, LaPorte RE, et al. Insulin-dependent diabetes mellitus, physical activity, and death. Am J Epidemiol 1993;137(1):74–81.
10. Tikkanen-Dolenc H, Wadén J, Forsblom C, et al. Physical activity reduces risk of premature mortality in patients with type 1 diabetes with and without kidney disease. Diabetes Care 2017;40(12):1727–32.
11. Nielsen PJ, Hafdahl AR, Conn VS, et al. Meta-analysis of the effect of exercise interventions on fitness outcomes among adults with type 1 and type 2 diabetes. Diabetes Res Clin Pract 2006;74(2):111–20.
12. Sampath Kumar A, Maiya AG, Shastry BA, et al. Exercise and insulin resistance in type 2 diabetes mellitus: a systematic review and meta-analysis. Ann Phys Rehabil Med 2019;62(2):98–103.
13. Yardley JE, Hay J, Abou-Setta AM, et al. A systematic review and meta-analysis of exercise interventions in adults with type 1 diabetes. Diabetes Res Clin Pract 2014;106(3):393–400.
14. Diabetes Canada Clinical Practice Guidelines Expert Committee, Sigal RJ, Armstrong MJ, Bacon SL, et al. Physical activity and diabetes. Can J Diabetes 2018;42(Suppl 1):S54–63.
15. Bellicha A, Macé S, Oppert J-M. Prescribing of electronic activity monitors in cardiometabolic diseases: qualitative interview-based study. J Med Internet Res 2017;19(9):e328.
16. McCarthy MM, Whittemore R, Grey M. Physical activity in adults with type 1 diabetes. Diabetes Educ 2016;42(1):108–15.
17. Hult A, Johansson J, Nordström P, et al. Objectively measured physical activity in older adults with and without diabetes. Clin Diabetes 2019;37(2):142–9.
18. Mitchell F, Wilkie L, Robertson K, et al. Feasibility and pilot study of an intervention to support active lifestyles in youth with type 1 diabetes: the ActivPals study. Pediatr Diabetes 2018;19(3):443–9.
19. van Poppel MNM, Chinapaw MJM, Mokkink LB, et al. Physical activity questionnaires for adults: a systematic review of measurement properties. Sports Med 2010;40(7):565–600.
20. Ludwig M, Hoffmann K, Endler S, et al. Measurement, prediction, and control of individual heart rate responses to exercise-basics and options for wearable devices. Front Physiol 2018;9:778.
21. Nolan RC, Raynor AJ, Berry NM, et al. Self-reported physical activity using the International Physical Activity Questionnaire (IPAQ) in Australian adults with type 2 diabetes, with and without peripheral neuropathy. Can J Diabetes 2016;40(6):576–9.

22. Hui SS-C, Hui GP-S, Xie YJ. Association between physical activity knowledge and levels of physical activity in chinese adults with type 2 diabetes. PLoS One 2014; 9(12):e115098.
23. Reddy RK, Pooni R, Zaharieva DP, et al. Accuracy of wrist-worn activity monitors during common daily physical activities and types of structured exercise: evaluation study. JMIR Mhealth Uhealth 2018;6(12):e10338.
24. Schwartz FL, Marling CR, Bunescu RC. The promise and perils of wearable physiological sensors for diabetes management. J Diabetes Sci Technol 2018;12(3): 587–91.
25. Machač S, Procházka M, Radvanský J, et al. Validation of physical activity monitors in individuals with diabetes: energy expenditure estimation by the multisensor SenseWear Armband Pro3 and the step counter omron HJ-720 against indirect calorimetry during walking. Diabetes Technol Ther 2013;15(5):413–8.
26. Yavelberg L, Zaharieva D, Cinar A, et al. A pilot study validating select research-grade and consumer-based wearables throughout a range of dynamic exercise intensities in persons with and without type 1 diabetes: a novel approach. J Diabetes Sci Technol 2018;12(3):569–76.
27. Wallen MP, Gomersall SR, Keating SE, et al. Accuracy of heart rate watches: implications for weight management. Calbet JAL. PLoS One 2016;11(5):e0154420.
28. Shcherbina A, Mattsson C, Waggott D, et al. Accuracy in wrist-worn, sensor-based measurements of heart rate and energy expenditure in a diverse cohort. J Pers Med 2017;7(2):3.
29. Kendall B, Bellovary B, Gothe NP. Validity of wearable activity monitors for tracking steps and estimating energy expenditure during a graded maximal treadmill test. J Sports Sci 2019;37(1):42–9.
30. Turksoy K, Paulino TML, Zaharieva DP, et al. Classification of physical activity: information to artificial pancreas control systems in real time. J Diabetes Sci Technol 2015;9(6):1200–7.
31. Wang J, Coleman DC, Kanter J, et al. Connecting smartphone and wearable fitness tracker data with a nationally used electronic health record system for diabetes education to facilitate behavioral goal monitoring in diabetes care: protocol for a pragmatic multi-site randomized trial. JMIR Res Protoc 2018;7(4):e10009.
32. Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. Clin Cardiol 1990;13(8):555–65.
33. Shetty VB, Fournier PA, Davey RJ, et al. Effect of exercise intensity on glucose requirements to maintain euglycemia during exercise in type 1 diabetes. J Clin Endocrinol Metab 2016;101(3):972–80.
34. Al Khalifah RA, Suppère C, Haidar A, et al. Association of aerobic fitness level with exercise-induced hypoglycaemia in Type 1 diabetes. Diabet Med 2016; 33(12):1686–90.
35. Yardley JE, Sigal RJ, Perkins BA, et al. Resistance exercise in type 1 diabetes. Can J Diabetes 2013;37(6):420–6.
36. Buoite Stella A, Assaloni R, Tonutti L, et al. Strategies used by patients with type 1 diabetes to avoid hypoglycemia in a 24×1-hour marathon: comparison with the amounts of carbohydrates estimated by a customizable algorithm. Can J Diabetes 2017;41(2):184–9.
37. Marliss EB, Vranic M. Intense exercise has unique effects on both insulin release and its roles in glucoregulation: implications for diabetes. Diabetes 2002; 51(Suppl 1):S271–83.

38. Harmer AR, Chisholm DJ, McKenna MJ, et al. High-intensity training improves plasma glucose and acid-base regulation during intermittent maximal exercise in type 1 diabetes. Diabetes Care 2007;30(5):1269–71.
39. Aronson R, Brown RE, Li A, et al. Optimal insulin correction factor in post-high-intensity exercise hyperglycemia in adults with type 1 diabetes: the FIT study. Diabetes Care 2019;42(1):10–6.
40. Potashner D, Brown RE, Li A, et al. Paradoxical rise in hypoglycemia symptoms with development of hyperglycemia during high-intensity interval training in type 1 diabetes. Diabetes Care 2019;42(10):2011–4.
41. Shetty VB, Fournier PA, Davey RJ, et al. The time lag prior to the rise in glucose requirements to maintain stable glycaemia during moderate exercise in a fasted insulinaemic state is of short duration and unaffected by the level at which glycaemia is maintained in Type 1 diabetes. Diabet Med 2018;35(10):1404–11.
42. Guelfi KJ, Ratnam N, Smythe GA, et al. Effect of intermittent high-intensity compared with continuous moderate exercise on glucose production and utilization in individuals with type 1 diabetes. Am J Physiol Endocrinol Metab 2007;292(3):E865–70.
43. Fahey AJ, Paramalingam N, Davey RJ, et al. The effect of a short sprint on post-exercise whole-body glucose production and utilization rates in individuals with type 1 diabetes mellitus. J Clin Endocrinol Metab 2012;97(11):4193–200.
44. Riddell MC, Pooni R, Yavelberg L, et al. Reproducibility in the cardiometabolic responses to high-intensity interval exercise in adults with type 1 diabetes. Diabetes Res Clin Pract 2019;148:137–43.
45. Iscoe KE, Riddell MC. Continuous moderate-intensity exercise with or without intermittent high-intensity work: effects on acute and late glycaemia in athletes with Type 1 diabetes mellitus. Diabet Med 2011;28(7):824–32.
46. Scott SN, Cocks M, Andrews RC, et al. Hit improves aerobic capacity without a detrimental decline in blood glucose in people with type 1 diabetes. J Clin Endocrinol Metab 2019;104(2):604–12.
47. Harmer AR, Ruell PA, Hunter SK, et al. Effects of type 1 diabetes, sprint training and sex on skeletal muscle sarcoplasmic reticulum Ca2+ uptake and Ca2+-ATPase activity. J Physiol 2014;592(3):523–35.
48. Ferland A, Brassard P, Lemieux S, et al. Impact of high-fat/low-carbohydrate, high-, low-glycaemic index or low-caloric meals on glucose regulation during aerobic exercise in Type 2 diabetes. Diabet Med 2009;26(6):589–95.
49. Savikj M, Gabriel BM, Alm PS, et al. Afternoon exercise is more efficacious than morning exercise at improving blood glucose levels in individuals with type 2 diabetes: a randomised crossover trial. Diabetologia 2019;62(2):233–7.
50. Campbell MD, Walker M, Trenell MI, et al. Metabolic implications when employing heavy pre- and post-exercise rapid-acting insulin reductions to prevent hypoglycaemia in type 1 diabetes patients: a randomised clinical trial. PLoS One 2014;9(5):e97143.
51. Rabasa-Lhoret R, Bourque J, Ducros F, et al. Guidelines for premeal insulin dose reduction for postprandial exercise of different intensities and durations in type 1 diabetic subjects treated intensively with a basal-bolus insulin regimen (ultralente-lispro). Diabetes Care 2001;24(4):625–30.
52. Campbell MD, Walker M, Bracken RM, et al. Insulin therapy and dietary adjustments to normalize glycemia and prevent nocturnal hypoglycemia after evening exercise in type 1 diabetes: a randomized controlled trial. BMJ Open Diabetes Res Care 2015;3(1):e000085.

53. Moser O, Eckstein ML, Mueller A, et al. Pre-exercise blood glucose levels determine the amount of orally administered carbohydrates during physical exercise in individuals with type 1 diabetes-a randomized cross-over trial. Nutrients 2019; 11(6) [pii:E1287].
54. Yardley JE, Iscoe KE, Sigal RJ, et al. Insulin pump therapy is associated with less post-exercise hyperglycemia than multiple daily injections: an observational study of physically active type 1 diabetes patients. Diabetes Technol Ther 2013;15(1):84–8.
55. Turner D, Luzio S, Gray BJ, et al. Algorithm that delivers an individualized rapid-acting insulin dose after morning resistance exercise counters post-exercise hyperglycaemia in people with Type 1 diabetes. Diabet Med 2016;33(4):506–10.
56. Zaharieva DP, McGaugh S, Pooni R, et al. Improved open-loop glucose control with basal insulin reduction 90 minutes before aerobic exercise in patients with type 1 diabetes on continuous subcutaneous insulin infusion. Diabetes Care 2019;42(5):824–31.
57. Binek A, Rembierz-Knoll A, Polańska J, et al. Reasons for the discontinuation of therapy of personal insulin pump in children with type 1 diabetes. Pediatr Endocrinol Diabetes Metab 2016;21(2):65–9.
58. Ortiz-Rubio P, Oladunjoye A, Agus MSD, et al. Adjusting Insulin Delivery to Activity (AIDA) clinical trial: effects of activity-based insulin profiles on glucose control in children with type 1 diabetes. Pediatr Diabetes 2018;19(8):1451–8.
59. Reddy R, Resalat N, Wilson LM, et al. Prediction of hypoglycemia during aerobic exercise in adults with type 1 diabetes. J Diabetes Sci Technol 2019;13(5): 919–27.
60. Riddell MC, Milliken J. Preventing exercise-induced hypoglycemia in type 1 diabetes using real-time continuous glucose monitoring and a new carbohydrate intake algorithm: an observational field study. Diabetes Technol Ther 2011; 13(8):819–25.
61. Zaharieva DP, Turksoy K, McGaugh SM, et al. Lag time remains with newer real-time continuous glucose monitoring technology during aerobic exercise in adults living with type 1 diabetes. Diabetes Technol Ther 2019;21(6):313–21.
62. Biagi L, Bertachi A, Quirós C, et al. Accuracy of continuous glucose monitoring before, during, and after aerobic and anaerobic exercise in patients with type 1 diabetes mellitus. Biosensors (Basel) 2018;8(1) [pii:E22].
63. Moser O, Mader JK, Tschakert G, et al. Accuracy of Continuous Glucose Monitoring (CGM) during continuous and high-intensity interval exercise in patients with type 1 diabetes mellitus. Nutrients 2016;8(8) [pii:E489].
64. Li A, Riddell MC, Potashner D, et al. Time lag and accuracy of continuous glucose monitoring during high intensity interval training in adults with type 1 diabetes. Diabetes Technol Ther 2019;21(5):286–94.
65. Zaharieva DP, Riddell MC, Henske J. The accuracy of continuous glucose monitoring and flash glucose monitoring during aerobic exercise in type 1 diabetes. J Diabetes Sci Technol 2019;13(1):140–1.
66. Moser O, Eckstein ML, Mueller A, et al. Impact of physical exercise on sensor performance of the FreeStyle Libre intermittently viewed continuous glucose monitoring system in people with Type 1 diabetes: a randomized crossover trial. Diabet Med 2019;36(5):606–11.
67. Ribet F, Stemme G, Roxhed N. Real-time intradermal continuous glucose monitoring using a minimally invasive microneedle-based system. Biomed Microdevices 2018;20(4):101.

68. Boughton CK, Hovorka R. Is an artificial pancreas (closed-loop system) for Type 1 diabetes effective? Diabet Med 2019;36(3):279–86.
69. Bally L, Thabit H. Closing the loop on exercise in type 1 diabetes | Bentham Science. Current Diabetes Reviews 2018;14(3):257–65.
70. Diabetes Research in Children Network (DirecNet) Study Group, Tsalikian E, Kollman C, Tamborlane WB, et al. Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. Diabetes Care 2006;29(10):2200–4.
71. Franc S, Daoudi A, Pochat A, et al. Insulin-based strategies to prevent hypoglycaemia during and after exercise in adult patients with type 1 diabetes on pump therapy: the DIABRASPORT randomized study. Diabetes Obes Metab 2015; 17(12):1150–7.
72. Tagougui S, Taleb N, Rabasa-Lhoret R. The benefits and limits of technological advances in glucose management around physical activity in patients type 1 diabetes. Front Endocrinol (Lausanne) 2018;9:818.
73. Elleri D, Allen JM, Kumareswaran K, et al. Closed-loop basal insulin delivery over 36 hours in adolescents with type 1 diabetes: randomized clinical trial. Diabetes Care 2013;36(4):838–44.
74. Ekhlaspour L, Forlenza GP, Chernavvsky D, et al. Closed loop control in adolescents and children during winter sports: Use of the Tandem Control-IQ AP system. Pediatr Diabetes 2019;20(6):759–68.
75. Forlenza GP, Buckingham BA, Christiansen MP, et al. Performance of omnipod personalized model predictive control algorithm with moderate intensity exercise in adults with type 1 diabetes. Diabetes Technol Ther 2019;21(5):265–72.
76. Pinsker JE, Laguna Sanz AJ, Lee JB, et al. Evaluation of an artificial pancreas with enhanced model predictive control and a glucose prediction trust index with unannounced exercise. Diabetes Technol Ther 2018;20(7):455–64.
77. Breton MD, Cherñavvsky DR, Forlenza GP, et al. Closed-loop control during intense prolonged outdoor exercise in adolescents with type 1 diabetes: the artificial pancreas Ski study. Diabetes Care 2017;40(12):1644–50.
78. Petruzelkova L, Pickova K, Sumnik Z, et al. Effectiveness of SmartGuard technology in the prevention of nocturnal hypoglycemia after prolonged physical activity. Diabetes Technol Ther 2017;19(5):299–304.
79. Huyett LM, Ly TT, Forlenza GP, et al. Outpatient closed-loop control with unannounced moderate exercise in adolescents using zone model predictive control. Diabetes Technol Ther 2017;19(6):331–9.
80. McAuley SA, Horsburgh JC, Ward GM, et al. Insulin pump basal adjustment for exercise in type 1 diabetes: a randomised crossover study. Diabetologia 2016; 59(8):1636–44.
81. Dovc K, Macedoni M, Bratina N, et al. Closed-loop glucose control in young people with type 1 diabetes during and after unannounced physical activity: a randomised controlled crossover trial. Diabetologia 2017;60(11):2157–67.
82. Petruzelkova L, Soupal J, Plasova V, et al. Excellent glycemic control maintained by open-source hybrid closed-loop AndroidAPS during and after sustained physical activity. Diabetes Technol Ther 2018;20(11):744–50.
83. Turksoy K, Hajizadeh I, Hobbs N, et al. Multivariable artificial pancreas for various exercise types and intensities. Diabetes Technol Ther 2018;20(10):662–71.
84. Hobbs N, Hajizadeh I, Rashid M, et al. Improving glucose prediction accuracy in physically active adolescents with type 1 diabetes. J Diabetes Sci Technol 2019; 13(4):718–27.

85. Jacobs PG, Resalat N, El Youssef J, et al. Incorporating an exercise detection, grading, and hormone dosing algorithm into the artificial pancreas using accelerometry and heart rate. J Diabetes Sci Technol 2015;9(6):1175–84.
86. Zisko N, Skjerve KN, Tari AR, et al. Personal Activity Intelligence (PAI), sedentary behavior and cardiovascular risk factor clustering – the HUNT study. Prog Cardiovasc Dis 2017;60(1):89–95.
87. Stenerson M, Cameron F, Payne SR, et al. The impact of accelerometer use in exercise-associated hypoglycemia prevention in type 1 diabetes. J Diabetes Sci Technol 2015;9(1):80–5.
88. Taleb N, Emami A, Suppere C, et al. Efficacy of single-hormone and dual-hormone artificial pancreas during continuous and interval exercise in adult patients with type 1 diabetes: randomised controlled crossover trial. Diabetologia 2016;59(12):2561–71.
89. Castle JR, El Youssef J, Wilson LM, et al. Randomized outpatient trial of single- and dual-hormone closed-loop systems that adapt to exercise using wearable sensors. Diabetes Care 2018;41(7):1471–7.
90. Jacobs PG, El Youssef J, Reddy R, et al. Randomized trial of a dual-hormone artificial pancreas with dosing adjustment during exercise compared with no adjustment and sensor-augmented pump therapy. Diabetes Obes Metab 2016;18(11): 1110–9.
91. Rickels MR, DuBose SN, Toschi E, et al. Mini-Dose glucagon as a novel approach to prevent exercise-induced hypoglycemia in type 1 diabetes. Diabetes Care 2018;41(9):1909–16.
92. Steineck IIK, Ranjan A, Schmidt S, et al. Preserved glucose response to low-dose glucagon after exercise in insulin-pump-treated individuals with type 1 diabetes: a randomised crossover study. Diabetologia 2019;62(4):582–92.