Title: HOME-BASED HIGH-INTENSITY INTERVAL TRAINING REDUCES BARRIERS TO EXERCISE IN PEOPLE WITH TYPE 1 DIABETES

Running title: Home-HIT and type 1 diabetes

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NEW FINDINGS

- This symposium review provides an overview of the recent work investigating whether a virtually monitored home-based HIT (Home-HIT) intervention reduces the fear of hypoglycaemia and other common exercise barriers in people with type 1 diabetes.

- Home-HIT seems to offer a strategy to reduce fear of hypoglycaemia, while simultaneously removing other known barriers preventing people with T1D from taking up exercise because it is time-efficient, requires no travel time or costs associated with gym memberships, and allows people to exercise in their chosen environment.

ABSTRACT

People with type 1 diabetes (T1D) are recommended to engage in regular exercise for a variety of health and fitness reasons. However, many lead a sedentary lifestyle and fail to meet the physical activity guidelines, in part because of the challenge of managing blood glucose concentration and fear of hypoglycaemia. A number of strategies designed to help people with T1D to manage their blood glucose during and after exercise have been investigated. Although many of these strategies show promise in facilitating blood glucose management during and after exercise, they do not target the many other common exercise barriers that people with T1D face, such as difficulty with cost and travel time to gyms, limited access to exercise bikes and treadmills and a possible dislike for exercising in front of others in public places. In this symposium review we provide an overview of ongoing research into a virtually monitored home-based high-intensity interval training (Home-HIT) programme that is designed to reduce these other common barriers to exercise. The conclusion of this review is that Home-HIT seems to offer a strategy to reduce fear of hypoglycaemia, while simultaneously removing other known barriers preventing people with T1D from taking up exercise such as being time-efficient, requiring no travel time or costs associated with gym memberships, and giving them the opportunity to exercise in their chosen environment, reducing embarrassment experienced by some when exercising in public.

INTRODUCTION

People with type 1 diabetes (T1D) are recommended to engage in regular exercise due to its recognised physiological and psychological benefits (Chimen et al., 2012). However, many people with T1D lead a sedentary lifestyle and fail to meet the physical activity guidelines (Makura, Nirantharakumar, Girling, Saravanan, & Narendran, 2013; Tielemans et al., 2013; Wadén et al., 2008), in part because of the challenge of managing blood glucose concentration around exercise and fear of hypoglycaemia (Brazeau, Rabasa-Lhoret, Strychar, & Mircescu, 2008; Lascar et al., 2014; Scott, Shepherd, Andrews, et al., 2019). Examples of strategies designed to help people with T1D to manage their blood glucose during and after exercise include adding short periods of high-intensity exercise to traditional moderate-intensity exercise (Vanessa A. Bussau, Ferreira, Jones, & Fournier, 2006; V. A. Bussau, Ferreira, Jones, & Fournier, 2007; Fahey et al., 2012; Guelfi, Ratnam, Smythe, Jones, & Fournier, 2007); combining resistance training and endurance training (Yardley et al., 2012); the use of closed-loop pump technology (Bally & Thabit, 2018); mini-dose glucagon injections (Rickels et al., 2018); insulin adjustments and modifications to carbohydrate intake before and during exercise (Sybil A. McAuley et al., 2016; Moser et al., 2019; Zaharieva et al., 2019); and high-intensity interval training (HIT) (Scott et al., 2019a, 2019b). Although many of these strategies show promise in facilitating blood glucose management during and after exercise, they do not target the many other common exercise barriers that people with T1D face, such as difficulty with cost and travel time to gyms, limited access to exercise bikes and treadmills and a possible dislike for exercising in front of others in public gyms. This symposium review gives an overview of the recent work conducted by our research group investigating whether a novel virtually monitored home-based HIT (Home-HIT) intervention not only reduces the fear of hypoglycaemia, but also reduces other common exercise barriers previously reported in the literature.

COMMON BARRIERS TO EXERCISE IN PEOPLE WITH TYPE 1 DIABETES

In addition to commonly cited barriers to exercise faced by the general population such as lack of time, work commitments, bad weather and cost (Korkiakangas, Alahuhta, & Laitinen, 2009; Trost, Owen, Bauman, Sallis, & Brown, 2002), further barriers exist for many people with T1D including fear of hypoglycaemia and inadequate knowledge around exercise management among patients and their healthcare professionals (Brazeau et al., 2008; A. Kennedy, Narendran, Andrews, Daley, & Greenfield, 2018; Kime, Pringle, Rivett, & Robinson, 2018; Lascar et al., 2014; Scott, Shepherd, Andrews, et al., 2019). Many people with T1D report that they find it difficult to manage their blood glucose and physical activity levels, and the majority of their decision making on optimal strategies was reported to be based on personal trial and error rather than on input from medical professionals (Kime et al., 2018).

In healthy individuals without T1D, tight control mechanisms exist so that glucose uptake into peripheral tissues is precisely matched by the rate of hepatic glucose production to thus maintain euglycaemia (Gagliardino, 2005). At the onset of moderate-intensity aerobic exercise in individuals without T1D, insulin secretion by the β-cells of the pancreas is suppressed to below fasting levels. Alongside this there is an increase in glucagon secretion from the α-islets of the pancreas into the portal vein which stimulates release of glucose from the liver to match the rate of glucose uptake into the working muscles (Bally et al., 2016; Koyama et al., 2001). Other counterregulatory hormones including adrenaline, growth hormone, aldosterone and adrenocorticotropic hormones are also released which stimulate hepatic glucose production and adipose tissue lipolysis, as well as inhibiting skeletal muscle glucose uptake in order to protect against hypoglycaemia (Chan & Sherwin, 2013; Donovan & Watts, 2014).

However, in people with T1D, the glucoregulatory responses to moderate-intensity exercise are impaired. Because insulin is supplied exogenously, circulating systemic insulin levels decrease only slowly, and may in fact rise, during prolonged aerobic exercise because of increased blood perfusion and absorption rates from the subcutaneous adipose tissue injection sites (Mallad et al., 2015; S. A. McAuley et al., 2016; Ronnemaa & Koivisto, 1988). The high circulating insulin concentration limits the release of glucagon and, therefore reduces hepatic glucose production. The combination of high circulating insulin concentrations with contraction-induced skeletal muscle GLUT-4 translocation also has been proposed to increase skeletal muscle glucose uptake in people with T1D and may thus lead to decreases in blood glucose during exercise (Camacho, Galassetti, Davis, & Wasserman, 2005). Higher insulin concentrations will also suppress adipose tissue lipolysis and free fatty acid mobilisation and therefore fat oxidation in the skeletal muscle (Saltiel, 2016). This combination of changes in fuel selection and oxidation in T1D results in an imbalance between peripheral glucose disposal and hepatic glucose production and eventually results in hypoglycaemia. Consequently, a bout of moderate-intensity exercise is associated with a rapid decline in blood glucose concentration in T1D. A decrease of 4.43 $mmol/L.h^{-1}$ on average was reported by García-García, Kumareswaran, Hovorka, and Hernando (2015). This is important, as the current American Diabetes Association (ADA) guidelines for people with T1D are to accumulate 150 minutes of moderate to vigorous aerobic exercise per week (Colberg et al., 2016). Therefore, it is not surprising that many people with T1D avoid aerobic exercise, especially if they have had a previous bad experience of exercise-related hypoglycaemia (Brazeau et al., 2008). Because of the increased risk of complications in people with T1D, regular exercise should be encouraged as the overall cardio-metabolic benefits outweigh the immediate risks, provided certain precautions are taken to avoid hypoglycaemia during and following an exercise bout. These precautions are best described in the exercise recommendations of the ADA (Colberg et al 2016), and in the most recent consensus statement (Riddell et al., 2017). Higher habitual physical activity levels are also associated with lower incidence (Balducci *et al.*, 2006; Tielemans *et al.*, 2013) and severity (Balducci *et al.*, 2006) of complications in people with T1D.

HOME-HIT MAY HELP SOME INDIVIDUALS WITH TYPE 1 DIABETES TO OVERCOME COMMON BARRIERS TO EXERCISE

Recent work from our laboratory demonstrated that unlike traditional moderate-intensity continuous training (MICT), HIT does not cause acute reductions in blood glucose concentrations in people with T1D (Scott et al., 2019a, 2019b). Furthermore, 6 weeks of HIT in people with T1D led to similar increases in $\dot{V}O_{2peak}$ compared to MICT (Scott et al., 2019b), despite the weekly training volume being 54-90 minutes less during HIT than MICT. However, during these studies (Scott et al., 2019a, 2019b), HIT was performed under optimal conditions with high levels of researcher supervision, meaning the "real world" potential of HIT for people with T1D was still unclear. Furthermore, the HIT protocol used a cycle ergometer, introducing additional barriers to exercise such as difficulties with access to equipment or facilities (including distance and cost) and potential embarrassment due to negative body image if performed within a gym setting (Brazeau et al., 2008; Lascar et al., 2014). One suggestion is the use of home-based exercise programmes to help reduce some of these common exercise barriers.

Although home-based interventions remove many of the traditional barriers to exercise, such as travel time and cost of gym memberships, research has shown that additional barriers are created (Bachmann & Bachmann, 2018). Many of these barriers centre around feelings of competency, and lack of support and feedback from exercise specialists (Bachmann & Bachmann, 2018). These barriers may be particularly important for people with T1D as advice and encouragement around managing diabetes for exercise has been identified as a major facilitator to exercise participation (Brazeau et al., 2008). Advances in wearable technology provide the opportunity to facilitate feedback between the exerciser and healthcare provider, potentially increasing feelings of competency (Hawkins et al., 2017). For people with T1D, a time-efficient Home-HIT intervention that does not result in a drop in blood glucose concentration may offer an exercise strategy that reduces the two major barriers to exercise: lack of time and fear of hypoglycaemia. In addition, virtual-monitoring during Home-HIT allows feedback, and does not require special facilities or equipment, or involve travel time to gyms (Figure 1).

A recent feasibility study conducted by our group (Scott, Shepherd, Andrews, et al., 2019), demonstrated that a virtually-monitored (Figure 2 and 3) Home-HIT intervention is effective for people with T1D, resulting in high adherence to training that leads to increased $\dot{V}O_{2peak}$ and reduced insulin dosage. Importantly, Home-HIT did not reduce blood glucose concentrations for up to 1h post exercise and carbohydrate was not needed to correct blood glucose during the majority of training sessions (94%). These data, in combination with qualitative feedback from an online survey, suggest that virtually-monitored Home-HIT is a safe strategy that reduces the major barriers to exercise including fear of hypoglycaemia and perceived lack of time. These findings are supported by another study that investigated this virtually-monitored Home-HIT in obese individuals with elevated cardiovascular disease (CVD) risk (Scott, Shepherd, Hopkins, et al., 2019). This study tested a wide range of factors associated with health, including aerobic capacity, fasting blood lipid profile, insulin sensitivity, body composition, aortic pulse wave velocity, brachial artery function (flow-mediated dilation), and a range of skeletal muscle adaptions measured using immunofluorescence microscopy in muscle biopsy samples. This comprehensive approach (Scott, Shepherd, Hopkins, et al., 2019) allowed a full assessment of Home-HIT in comparison to fully supervised laboratory-based HIT and home-based MICT programmes and provided robust evidence that Home-HIT is physiologically effective in obese individuals at elevated CVD risk. The study also showed that adherence and compliance over 12 weeks without researcher supervision was high, providing further support for the use of this exercise mode in people with T1D.

BENEFITS OF HOME-HIT IN PEOPLE WITH TYPE 1 DIABETES

A strength of the Home-HIT study (Scott, Shepherd, Andrews, et al., 2019) was the multi-disciplinary approach of combining physiological data with a qualitative evaluation of this training intervention by the participants. This is the first study to qualitatively assess the acceptability of an exercise-training programme in people with T1D designed to overcome the major barriers to exercise. The blood glucose data were supported by the survey responses as the participants reported that they were comfortable doing Home-HIT at any time of day because they felt that their blood glucose concentrations were more stable. This supports the conclusion that HIT reduces the fear of hypoglycaemia, which is the major barrier to take up exercise for people with T1D. The survey results also confirm the time-efficiency of Home-HIT as a major advantage. The training sessions during the Home-HIT intervention lasted between 12 and 20 minutes, meaning the weekly time commitment of Home-HIT was at least 90 minutes less than the recommended 150 minutes of endurance exercise (Colberg et al., 2016). The convenience of not having to travel added to the time-efficiency of Home-HIT. Many participants also liked exercising at home because there was more privacy, the programme was free and required no equipment. Importantly, the current study and previous research has shown that embarrassment during exercise due to poor body image and the cost of exercise due to gym memberships are barriers to exercise, which suggests that Home-HIT removes many traditional exercise barriers (Brazeau et al., 2008; Lascar et al., 2014; Scott, Shepherd, Andrews, et al., 2019).

Fear of hypoglycaemia means that people with T1D regularly stop to check their blood glucose concentration when performing traditional MICT recommended by the American Diabetes Association (Colberg et al., 2016). The survey responses in the study by Scott, Shepherd, Andrews, et al. (2019) provide evidence that stopping to check blood glucose and correct accordingly with carbohydrate during exercise can be frustrating as it means that an already time consuming MICT session is even longer as the individual has to wait for their blood glucose to stabilise before they can recommence the exercise. The participants in the Home-HIT study (Scott, Shepherd, Andrews, et al., 2019) were able to complete every session in the study without stopping to check their blood glucose concentration. In addition, out of the 188 completed Home-HIT sessions in this study there were only 10 occasions in which participants had to ingest carbohydrates following exercise because of falling blood glucose concentrations. This further highlights the acceptability, time efficiency and ability to fit Home-HIT into their daily routine. The data on carbohydrate consumption and blood glucose concentration during and after the exercise would suggest that HIT may provide a more stable blood glucose concentration during and following exercise sessions, which may lead to better glycaemic control in the long term. Amy Kennedy et al. (2013) suggested that previous research may have failed to show improved glycaemic control with exercise training because calorie intake and insulin dose around the time of exercise has not been controlled. Therefore, the long-term effects of Home-HIT on 24h glycaemic control should be tested further.

The survey responses (Scott, Shepherd, Andrews, et al., 2019) also highlighted that lack of motivation was often a key barrier to achieving physical activity guidelines prior to the study, in line with the findings of Lascar et al. (2014). Importantly, data from the survey suggests that the design of the HIT intervention contributed to improving participant motivation to exercise. These motivating factors included the range of exercises available and the progression in number of intervals. Home-HIT exercises were chosen by the research team to provide a range of difficulties, from simple low-impact exercises to complex movements with higher impact. This allowed participants to modify exercise sessions, choosing exercises that elicited the desired HR response, but were suitable for their gradually improving level of mobility and fitness. This may have contributed to the improved motivation through increasing enjoyment and by enhancing participants' sense of mastery and competency, which are recommended as core components of successful behaviour change interventions (Nice, 2014). Unlike previous low-volume HIT studies (Gillen et al., 2012; Hood, Little, Tarnopolsky, Myslik, & Gibala, 2011), the number of intervals increased from 6 to 10 in our study as participants progressed. Participants also said they liked the sense of achievement of completing more intervals as they progressed, suggesting future studies should use progression to help personalise training to individual fitness levels.

Participants also indicated in the qualitative survey (Scott, Shepherd, Andrews, et al., 2019) that the virtual-monitoring system contributed to their motivation, as it provided instant feedback on exercise intensity and allowed progression to be tracked by the researchers and feedback could be given if needed. This supports previous work, where receiving HR information during exercise enhanced engagement through feelings of competence in sedentary adults (Hawkins et al., 2017). In addition, a study in which 1,150 sedentary individuals were given a HR monitor came to the conclusion that the technology could teach individuals how to exercise at an intensity most likely to elicit health changes (Miller et al., 2014). Support and supervision from exercise professionals is known to be a key factor needed to build motivation (Morgan et al., 2016) and likely to increase confidence to exercise at higher intensities. Therefore, the improved feedback through remote monitoring likely contributed to the high adherence observed. The feeling of being "watched" by the research team may also have extended the period of external motivation traditionally felt after specialist exercise advice (Markland & Tobin, 2010; Rouse, Ntoumanis, Duda, Jolly, & Williams, 2011). Such extrinsic motivation can facilitate adoption to exercise and result in adaptive outcomes when accompanied by more autonomous motivation (e.g., facilitated through self-monitoring) (Thøgersen-Ntoumani & Ntoumanis, 2006). Finally, the use of HR monitoring to provide feedback to participants and exercise specialists has a number of advantages over other technologies such as pedometers and accelerometers. Firstly, HR is the most accurate way to track the body's adaptive response to exercise training, providing objective personalised data that accounts for age and fitness level (Zisko et al., 2017). HR also reflects exercise intensity regardless of the type of exercise performed (Zisko et al., 2017). Such monitoring systems provide a relatively inexpensive (~£40 per HR monitor and mobile application) strategy to engage with participants and improve uptake, adherence, compliance and ultimately health outcomes.

FUTURE DIRECTIONS

The virtually-monitored Home-HIT investigations completed so far (Scott, Shepherd, Andrews, et al., 2019; Scott, Shepherd, Hopkins, et al., 2019) were designed as proof of concept studies, and as such the sample sizes were small. Nonetheless, these promising data provide strong evidence that virtually-monitored Home-HIT offers an effective strategy to improve physical activity participation in at-risk populations (i.e. those with type 1 diabetes and obese individuals with elevated cardiovascular disease risk), and therefore should be explored further using larger cohorts and longer follow up times. The use of a HR monitor and mobile phone app system was an important addition that allowed objective measurement of whether participants completed the exercises at the correct intensity.

CONCLUSIONS

The research described in this review suggests that virtually monitored Home-HIT already is, and can be further developed into a safe, acceptable and effective strategy to reduce common barriers to exercise for patients with T1D. The authors, therefore, expect that in the future Home-HIT will increase exercise participation and health in people living with T1D. Further research should be conducted in larger cohorts, using longer follow up times to assess the true potential of Home-HIT.

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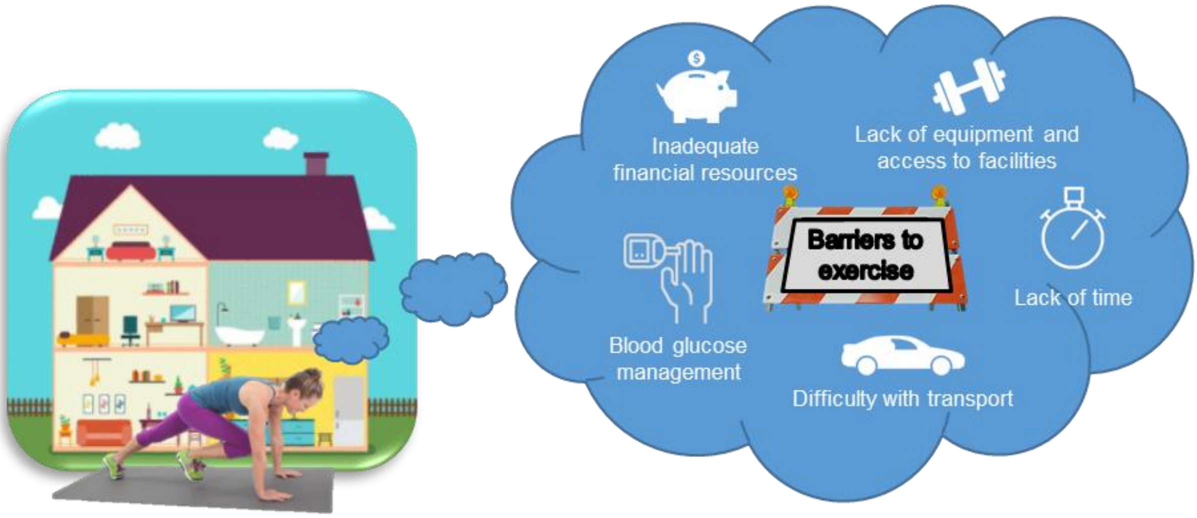

Figure 1. Home-based high-intensity interval training (Home-HIT) may help to reduce common exercise barriers in people with type 1 diabetes

Home-HIT uses the principles of laboratory-based HIT, whereby there are short high-intensity intervals interspersed with recovery periods. Home-HIT is time efficient and may help reduce the risk of hypoglycaemia. Home-HIT does not require transport and costs associated with transport and gym memberships and does not require expensive specialist exercise equipment. The Home-HIT protocol uses simple on-the-spot bodyweight exercises which allows HIT to be performed without equipment in one's own home. As such, Home-HIT may offer an exercise strategy that reduces the two major barriers to exercise: lack of time and fear of hypoglycaemia, but is also, inexpensive and requires no facilities, equipment or travel time to gyms.

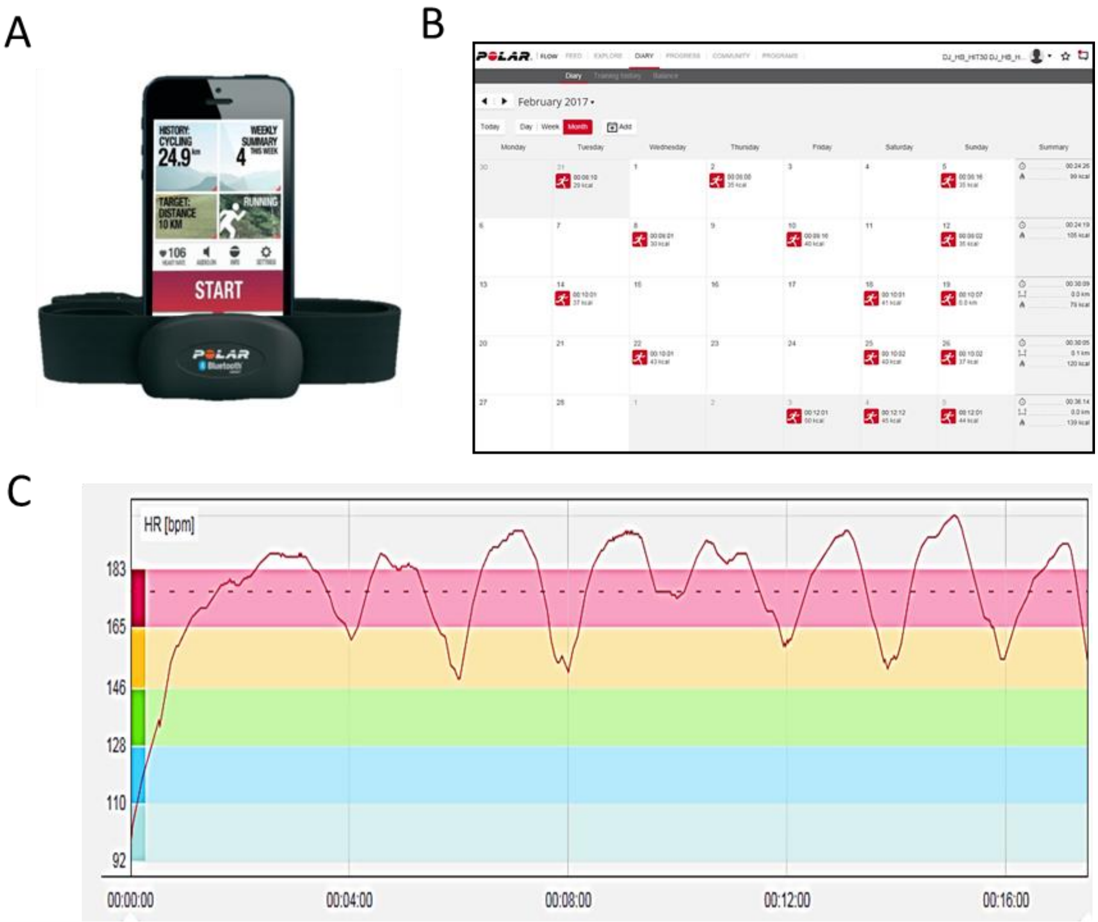

Figure 2. Methods used to monitor adherence and training intensity during home-based exercise

In the studies conducted by our Research Group (Scott, Shepherd, Andrews, et al., 2019; Scott, Shepherd, Hopkins, et al., 2019), A) participants were provided with a Polar H7 heart rate (HR) monitor and mobile phone application Polar Beat®. B) HR data from each session was downloaded to Polar Flow, a cloud-based storage application so that adherence and compliance could be remotely recorded by the researchers. C) Shows an example of a HR trace from a participant during a Home-HIT session. The HR traces can then be analysed to provide information on compliance to the prescribed workload. The research team were able to determine the number of intervals by looking at the peaks and troughs in the HR traces.

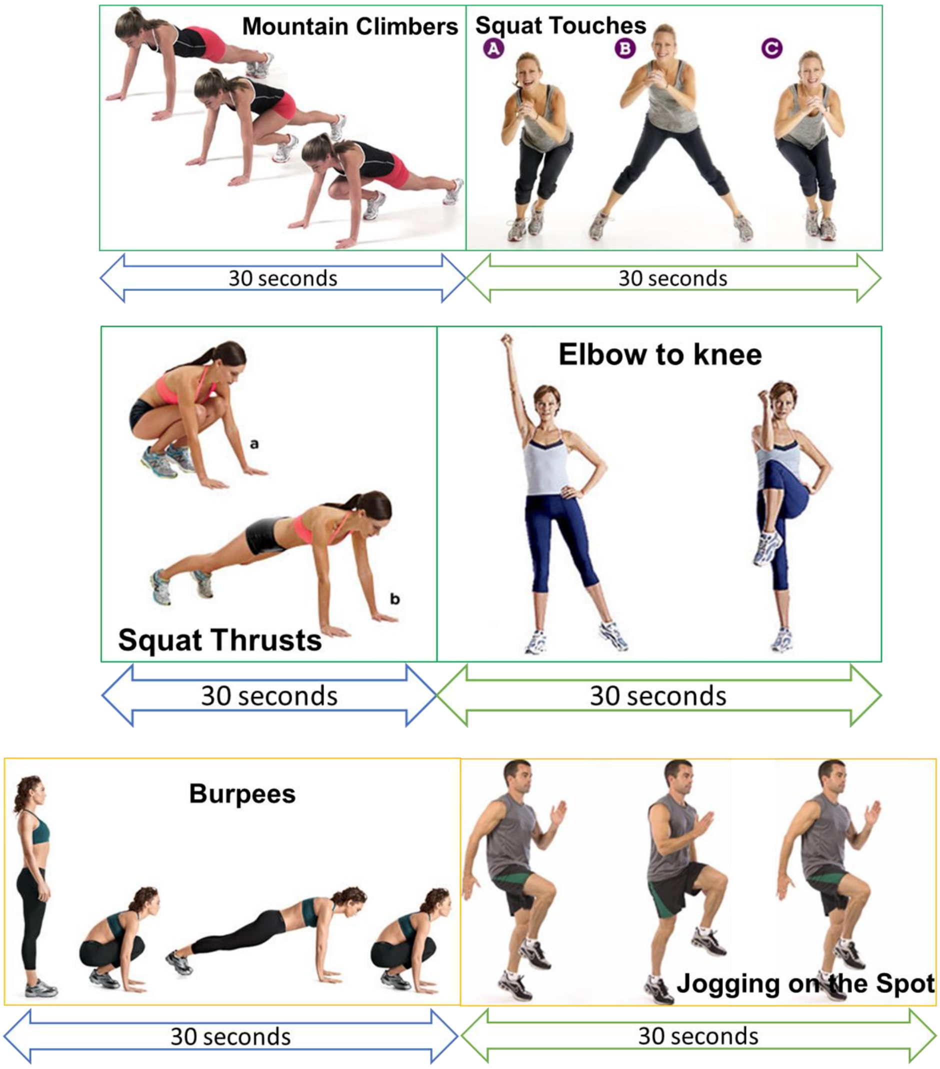

Figure 3. Example of exercises performed during home-based high-intensity interval training (Home-HIT) programme

In the Home-HIT studies (Scott, Shepherd, Andrews, et al., 2019; Scott, Shepherd, Hopkins, et al., 2019) participants were asked to perform repeated 1-minute bouts of exercise interspersed with 1 minute of rest in a place of their own choosing. Participants were advised to achieve ≥80% of their predicted heart rate maximum (HRmax; 220–age) during the intervals. The 1-minute intervals were composed of two different sequential 30-second body weight exercises with no rest in between (examples shown above). Participants were provided with 9 exercise pairs, detailed in an exercise pack, and were free to choose which pairs of exercises they completed during each session. During studies the number of intervals that participants were advised to complete increased as participants progressed through the programme.