A pilot study to evaluate a self-management algorithm for people with Type 1 diabetes participating in moderate intensity exercise in laboratory and real-life environments

Jacqui Charlton
Matriculation Number: 07016308

A thesis submitted in partial fulfillment of the requirements of Edinburgh Napier University, for the award of Master of Science by Research (MScRes).

March 2013

Authorship declaration

I, Jacqui Charlton confirm that this dissertation is entirely my own work.

1. Where I have consulted the published work of others this is always clearly attributed;
2. Where I have quoted the work of others the source is always given. With the exception of such quotations, this dissertation is entirely my own work.
3. I have acknowledged all main sources of help;
4. If my research follows on from previous work or is part of a larger collaborative research project, I have made clear exactly what was done by others and what I have contributed myself;
5. I have read and understand the penalties associated with plagiarism

Signed:

Matriculation number: 07016308

Date: 24.3.13

Word count: 32,350

Acknowledgements

This piece of work has been an invaluable learning experience that has increased my knowledge and research skills. It has, as expected, caused a rollercoaster of emotions and challenges, and I would like to express my gratitude to everyone who has helped me along the way.

I wish to thank my supervisors; Dr. Lynn Kilbride, Dr. Johnny McKnight, Dr. Rory MacLean and Dr. Mark Darlison, who gave me support, guidance, and a lot of patience, during my studies.

I would also like to thank Dr. Martin Maxwell for sharing his research experiences, and giving me continuous encouragement, reassurance and support.

Finally, I couldn't have performed this study without the people with diabetes who gave up their time, and put in a lot of effort to help me succeed in completing this study. I am very grateful for their participation and enthusiasm, and I hope the results in return, can help them.

Abstract

Background

Limited evidence is available to advise people with Type 1 diabetes about self-management strategies for maintaining acceptable glycaemic control when exercising. It is recognized that hypoglycaemia is a potential risk and this is a major barrier towards exercise participation for these people. Related research exploring this topic has mostly been performed in laboratory environments.

Aim

Following a specifically designed self-management algorithm, the impact of the algorithm and environment (real-life versus laboratory) was investigated regarding the attainment of acceptable glucose concentrations during and after 40 minutes exercise at 70% VO_2 max.

Methods

Nine individuals with Type 1 diabetes (five male, four female) completed the pilot study over a 2 week period. All used a basal bolus analogue insulin regimen and exercised regularly. On Days 1 and 3 of each week they undertook 40 minutes of moderate intensity exercise (day 1 and 8 in the laboratory, and day 3 and 10 in real-life environments). All were instructed to follow the self-management algorithm. Data were collected for glucose concentrations at 10 time-points during and after exercise.

Results

Statistical analysis used a 3-way repeated measures ANOVA for time-points, environment and day, which demonstrated a highly significant main effect on time-points [$F(9, 72) = 4.088$, $p = < 0.005$, partial eta squared = 0.338. During exercise the mean blood glucose difference was significantly lower from baseline to: 20 minutes during, 2.21mmol/l (SE±0.354) ($p=0.011$), and 40 minutes at end 3.41mmol/l (SE±0.511) ($p=0.007$). However, the different environments did not have a significant main effect on the mean glucose concentration of participants [$F(1, 8) = 1.489$, $p = 0.257$]. For the study period, 8 out of 9 participants experienced at least one hypoglycaemic episode. For hypoglycaemic episodes, the main differences between environments occurred: during exercise (laboratory n=5, real-life n=1), and during 8-12 hours post-exercise (laboratory n=3, real-life n=8).

Conclusion

There were differences in glycaemic patterns between environments when using a descriptive analysis. Despite post-exercise insulin reduction, nocturnal hypoglycaemia occurred in the real-life environment, and algorithm adjustments regarding carbohydrate consumption at bedtime were required for prevention. Therefore, a self-management recommendation for evening exercisers would be to perform blood glucose monitoring 8-12 hours after post-exercise insulin and consumption of carbohydrate. A larger study with the sample size to demonstrate significance, using the adjusted algorithm would clarify the reliability and efficacy of the algorithm in real-life.

Contents

Chapter One

Background

1.1 Introduction

This chapter provides information to underpin the rationale of this study and includes an overview about Type 1 diabetes and patient self-management, healthcare, and the importance of achieving optimal glycaemic control. The short and long-term problems regarding blood glucose management are described, giving an insight into the challenges individuals encounter in their daily lives. Finally, self-management when performing physical activity will be discussed, concluding with the importance of the results of this research.

"Diabetes is a condition primarily defined by the level of hyperglycaemia giving rise to risk of microvascular damage (retinopathy, nephropathy and neuropathy). It is associated with reduced life-expectancy, significant morbidity due to specific diabetes related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and diminished quality of life." (World Health Organization (WHO) 2006, p. 5).

Diabetes Mellitus can been described as a modern day health endemic. The estimated number of people with diabetes worldwide is 347 million (Danaei et al 2011cited by WHO 2013). With the prevalence of both Type 1 and Type 2 increasing globally, this has been shown to result in economic and social burdens for the person with diabetes and health systems, regarding both daily and long-term care (Dunning and Ward 2008). There are two main types of diabetes: Type 1 caused by pancreatic beta cell destruction resulting in absolute insulin deficiency, and Type 2 which accounts for around 85% of those people with diabetes and is characterised by a relative insulin deficiency and resistance to insulin (Williams and Pickup 2004). Both types have different disease pathologies and thus require different treatments and approaches to healthcare.

The current study presented in this thesis is directed to improve a common aspect of daily patient self-management regarding strategies for participation in physical

activity. From the author's clinical experience and the characteristics of Type 2 diabetes, problems with erratic blood glucose and difficulties with tablet medication, insulin and dietary management when participating in exercise, do not appear to be such arduous challenges when compared with those with Type 1 diabetes. Thus for the purpose of this study, the target population was people with Type 1 diabetes.

1.2 Type 1 diabetes management and care

The most recent figures from the annual Scottish Diabetes Survey (2011), shows that Type 1 diabetes affects 28,272 people in Scotland. This demonstrates that diabetes is a fairly common chronic condition for many of the general public. Type 1 diabetes is an autoimmune disease which causes a destruction of the insulin–producing beta cells found in the pancreas, and results in an abolition of insulin production (Watkins 2003). Insulin replacement is vital for survival otherwise death will occur, and the usual current treatment is insulin injection therapy (Dunning and Ward 2008).

Presently, the most common method of insulin therapy attempts to mimic the natural beta cell activity in relation to glucose ingestion and energy requirements. This therapy is called a basal bolus regimen and involves administering a once or twice daily injection of a 24 hour acting insulin to provide background insulin (basal), and giving calculated fast-acting analogue insulin injections before meals or snacks containing carbohydrate (CHO) food (bolus). Exercise levels and CHO quantities influence the insulin dose calculation, and to attain optimal glycaemic control, a balance between the CHO amount, subsequent exercise and fast-acting insulin dose is essential otherwise hypoglycaemia or hyperglycaemia occurs.

Treatment and care of diabetes focuses on education and patient empowerment to promote self-management, and within the Diabetes Health Care Professional (HCP) team, one of the main roles of the Diabetes Specialist Nurse (DSN) is to facilitate this to the best of the individuals' abilities. The author has practiced as a DSN for 14 years, with specialist interest in caring for patients with Type 1 diabetes. Within daily living, there are multiple factors which impinge upon an individual's glucose homeostasis. These are associated with diet, exercise, stress and lifestyle issues (Perry and Gallen 2009). Promoting self-management to achieve optimal glycaemic

control around lifestyle is one of the difficult challenges of the role of the DSN. Limited evidence-based guidelines makes offering advice and guidance difficult. The guidelines available i.e. National Institute for Clinical Excellence (NICE) (2009) and Scottish Intercollegiate Guidelines Network (SIGN) (2010), offer general recommendations in lifestyle management in an attempt to achieve standardized best practice in the UK. However, advice is vague and for individuals to live their chosen lifestyle they must strive to adjust their treatment to maintain optimal glycaemic control and prevent the following complications.

1.3 Acute and long-term complications of Type 1 diabetes

People with Type 1 diabetes have an on-going and lifelong risk of developing physical problems due to abnormal glucose metabolism. These potential problems can be divided into acute and long-term complications (Watkins 2003).

Acute complications

Acute complications of Type 1 diabetes relate to hypoglycaemia and hyperglycaemia. Both can cause a varying range of unpleasant symptoms depending on the blood glucose concentration, and may require external assistance depending on the severity of the episode. They can be life-threatening and may require immediate attention to prevent medical intervention, and also cause psychological distress and have a major impact on an individual's life when attempting to avoid occurrence by treatment and lifestyle modification.

- *Hypoglycaemia*

  Hypoglycaemia is a term used for any blood glucose concentration under 4.0mmol/l (SIGN 2010), and is a common day-to-day phenomenon when living with Type 1 diabetes. Clinical symptoms include light headedness, tremor, confusion, unsteadiness, drowsiness and sometimes unconsciousness. The onset of hypoglycaemia is rapid and the speed of deterioration is dependent on active insulin and activity levels. Its rapid onset makes hypoglycaemia one of the most feared complications of diabetes (Frier 2008), and its prevention is one of the main aims of diabetes management. Hypoglycaemia is usually caused by either the administration of a greater insulin dose than required, increased exercise or inadequate CHO consumption (Dunning and Ward 2008). The treatment will depend on the actual

blood glucose concentration and patient state, and will range between the person consuming dextrose, drinking glucose-containing fluids, massaging glucose gel into the buccal cavity and finally the administration of intramuscular Glucagon or intravenous glucose. Hypoglycaemia is an acute emergency that may have serious consequences. For example, the Driver and Vehicle Licensing Agency (DVLA) published a driving regulations update and report (DVLA 2011), which stated that the penalty for a person with insulin-treated diabetes sustaining two severe hypoglycaemic episodes within a 12 month period, would result in a loss of their license to drive.

- *Hyperglycaemia*

  Whereas hypoglycaemia is classed as a low blood glucose concentration, hyperglycaemia is generally termed as a blood glucose concentration over 9mmol/l (Montague et al 2005). Clinical symptoms include lethargy, polydipsia, polyuria, nocturia, blurred vision and weight loss. If blood glucose concentrations reach 17mmol/l or above, a person is at potential risk of developing diabetic ketoacidosis (DKA), which is a medical emergency (Riddell and Perkins 2006) and can cause death if untreated. However, people with Type 1 diabetes may lapse into hyperglycaemic ranges on a regular basis and suffer from symptoms, but not encounter an emergency clinical state. Hyperglycaemia may be caused by either the administration of a reduced insulin dose, decreased exercise or increased CHO consumption (Dunning and Ward 2008). In comparison to hypoglycaemia, hyperglycaemia has a slower rate of progression to an emergency state, although mild hyperglycaemic symptoms can be unpleasant and debilitating for the individual. For hyperglycaemia in a non-ketotic state, the treatment is the administration of insulin, the dose being dependent on a range of individual issues i.e. blood glucose, current active insulin, preceding physical activity and CHO, and the underlying cause.

<u>Long-term complications</u>

As described above, hypoglycaemia and hyperglycaemia are a day-to-day phenomenon of living with diabetes. Other potential consequences are long-term complications, which are usually caused by sustained poor glucose and hyperglycaemic concentrations over years (Diabetes Control and Complications Trial

Research Group 1993). An indicator of this situation, which is monitored ideally every 3 – 6 months, is a laboratory blood test called an HbA1c, which gives the average blood glucose concentration over the previous 14-16 weeks (SIGN 2010), and clarifies overall glycaemic control and highlights patients with poor glycaemic control.

For Type 1 diabetes the main micro and macro-vascular long-term complications include: retinopathy, nephropathy, neuropathy, cardiovascular problems and sexual dysfunction (Shaw and Cummings 2006). Depending on the stage of the complication, these symptoms can have a major impact on the quality of life and psychological well-being. The prevention or the delay of progression of long-term complications has not been incorporated into the research aim of this study. However, it is acknowledged that improvement of glycaemic control and increasing exercise behaviour for people with Type 1 diabetes, will affect many physiological factors. These factors could potentially minimise the risk of development, or progression of long-term problems, especially cardiovascular complications of diabetes. However, on the other hand, incorporating regular exercise into an individuals' daily life may precipitate daily self-management problems due to the effect on glycaemic control.

1.4 Type 1 diabetes and exercise

The impact of exercise on glycaemic control will now be discussed. The term physical activity or exercise has many interpretations, and for the purpose of this study, the defined term stated by the Scottish Intercollegiate Guidelines Network (SIGN) for diabetes (2010 p.17) was applied:

"Exercise is a subset of physical activity which is performed with the goal of enhancing or maintaining an aspect of fitness (e.g. aerobic, strength, flexibility, balance). It is often supervised (e.g. in a class), systematic and regular (e.g. jogging, swimming, attending exercise classes)".

The term VO_2 max is the maximal capacity of an individuals' body to utilize oxygen during exercise i.e. volume, oxygen, maximum (Wilmore and Costill 2004). In order to distinguish exercise intensity, a percentage value for VO_2 max is the current

measurement used (Nagi 2008). For the general population aged 18 – 64 years old, Department of Health (2009) recommended moderate intense exercise or exercise at 60 - 70% VO_2 max, taken for 30 minutes duration for 5 days per week. This alludes to 60-70% of an individuals' maximum exercise capacity. To allow for individual adaptation and flexibility, this recommendation was amended to 2.5 hours per week rather than 5 days, for people with diabetes by SIGN (2010) and the World Health Organisation (WHO) (2010). By undertaking these recommendations, for a person with Type 1 diabetes, exercise can improve their quality of life and psychological well-being (Guelfi et al 2005), and also reduce cardiovascular risk factors that impact on mortality (Brazeau et al 2008).

In view of this, exercise recommendations should be incorporated into diabetes patient education to support, encourage and empower patients to achieve the 2.5 hour weekly target. To achieve these goals, patient motivation is crucial, in order to gain knowledge and experience to effectively manipulate insulin doses and carbohydrate intake (Kilbride et al 2011a). As current advice is not evidence-based, and self-management is generally achieved through trial and error over time (Gallen 2004, Guelfi et al 2005), difficulties frequently arise during education when advising people with Type 1 diabetes on self-management when participating in exercise. Patients are often uncertain about diabetes management around exercise, and when using ad hoc self-management strategies they can experience acute complications (Kilbride et al 2011a) which cause confusion, upset, frustration and sometimes can be a reason for stopping all participation in exercise. These experiences and emotions were previously highlighted throughout a focus group analysis regarding patient perspectives relating to diabetes and exercise management (Kilbride et al 2011a).
The main implications for individuals are the potential risk of acute complications that can be a result of mismanagement.

Hypoglycaemia and exercise

Hypoglycaemia associated with exercise is the main deterrent for participation due to fear and anxiety (Brazeau et al 2008). Prior to exercise, hypoglycaemia delays the start of an exercise session as a person needs to consume CHO and wait until the blood glucose has risen to an acceptable level before exercise. During exercise they

may encounter a further hypoglycaemic episode due to depleted liver glycogen stores (Ertl and Davis 2004, Gravelling and Frier 2010). Hypoglycaemia during exercise results in diminished performance due to changed glycaemic levels, and the cessation of the exercise session. Post-exercise hypoglycaemia is also a risk especially for afternoon and evening physical activity which can result in nocturnal hypoglycaemia; a common fear for patients (Brazeau et al 2008, Lumb and Gallen 2009).

From clinical experience, the usual advice given by the author to prevent hypoglycaemia occurring from exercise was to recommend insulin dose reduction prior to the exercise. However, from experience with working with patients, and the focus group analysis describing challenges in Type 1 self-management regarding exercise (Kilbride et al 2011a), this tended to be the least preferred preventative measure for patients due to the uncertainty surrounding their physiology, insulin time actions and the required size of the dose reduction. The alternative action to prevent hypoglycaemia developing was increased CHO consumption. This intervention also presented problems as it was sometimes difficult to define the type and amount of CHO required and if, for example, weight management was one of the reasons for performing physical activity in the first place, increasing the CHO intake and also the associated calorific intake, was not desirable for some individuals.

Hyperglycaemia and exercise

For all patients, hypoglycaemia prevention is the ultimate goal during exercise, and a common strategy used by people with Type 1 diabetes is to purposely cause hyperglycaemia. When discussing exercise management with patients, many consume extra CHO and aim for a higher blood glucose before exercise. This tactic was also reported by Wallymahmed et al (2007) in a study regarding the relationship between glycaemic control, physical activity and hypoglycaemia avoidance in people with Type 1 diabetes. By achieving hyperglycaemia, when the blood glucose falls during exercise it will not decrease sufficiently to cause hypoglycaemia. Whilst this intervention is commonly used and can assist in the prevention of hypoglycaemia (Kilbride et al 2011a), some patients experienced hyperglycaemic symptoms thus affecting performance, with possible ketone formation, and over time, may run the risk of increased long-term complications.

1.5 Conclusion

Both insulin dose adjustment and dietary modification are management strategies used to overcome the acute complications whilst exercising, and must be used to ensure safety for an individual (Lumb and Gallen 2009). However, more evidence based guidance is required to ensure that this can be achieved effectively. Information about exercise self-management strategies are scarcely found in clinical practice in the form of national guidelines, local policies, and patient information leaflets or websites, which clarifies the lack of evidence. Also whilst research is rare, another important factor is that all studies have been performed only in a laboratory environment and not evaluated in real life situations (Grimm et al 2004, Peter et al 2005, West et al 2010). The real-life environment means performing habitual exercise in a participants' usual location.

This lack of evidence makes the implementation of recommendations of 2.5 hours of exercise per week (SIGN 2010) a challenge, which instigated this current study. For the above recommendations, the exercise intensity of 70% VO_2 max is required, which is equivalent to jogging, cycling, aerobics classes and brisk walking, and are all popular methods of exercise. As a DSN, when discussing exercise patterns with patients, it became apparent that physical activity after work and before consuming the evening meal was popular for many people. With this in mind, a self-management algorithm for 70% VO_2 max exercise, taken 3 hours after a fast-acting analogue injection taken at lunchtime, and before the evening meal would help many people, and from clinical experience, patients specify that approximately 30-40 minutes is their usual time duration.

Evidence generated to inform patients and HCPs of self-management strategies during and after moderate intensity exercise is much needed for a large number of people. If this specific area of research is ignored, then people with Type 1 diabetes will be challenged with physical and psychological barriers and problems when participating in exercise, and they will continue to use ad hoc strategies that have safety implications with potential complications, and may precipitate long-term debilitating health problems.

Chapter 2

Literature Review

2.1 Introduction

The previous chapter provided a general diabetes overview and introduced the complexities for people with Type 1 diabetes when performing exercise. This chapter is necessary to underpin the current study and focused on three areas:

- The challenges that people with Type 1 diabetes experience when exercising.
- Management strategies regarding insulin dose adjustment and dietary changes, and the effects on glycaemic control of people with Type 1 diabetes (not athletes) during and after exercise at moderate intensity.
- Research performed in the real-life environment, and the replication of laboratory-based self-management research strategies compared with the real-life environment.

2.2 Design

A systematic review was conducted which followed the general principles used by Kennedy (2008), which was also described in the SIGN recommendations for literature critiques (SIGN) (2001). The approach and format undertaken are detailed in table 2.1.

Table 2.1
Systematic review approach

1. Identification of aims and objectives
2. Determine key words to highlight potentially relevant studies
3. Identify appropriate literature following the search strategy
4. Implementation of inclusion and exclusion criteria to select studies
5. Assess and critique the selected literature
6. Present the analysis of relevant studies

2.3 Search Strategy

A systematic literature search was performed using CINAHL (Cumulative Index of Nursing and Allied Health Literature), MEDLINE, Cochrane Controlled Trails Register and SPORTdiscus databases. The key Medical Subject Headings (MeSH) search terms selected were: “Type 1 diabetes”, “physical activity”, “moderate intensity exercise”, “sport” and “running”, as they were the key terms used within the published literature. Other related search terms of “glycaemic control”, “insulin adjustment” and “self-management” were used initially, but due to lack of published evidence, it was decided that the term ‘Type 1 diabetes’ applied as an alternative. Using “Type 1” as the main key-term, the number of hits in searches increased and gave assurance that all related abstracts were found. The search strategy included MeSH and terms were truncated with (*) to allow for multiple spellings and endings. From the selected publications any additional related literature found in the reference lists were also assessed.

2.4 Inclusion and exclusion criteria

All abstracts retrieved through the search were reviewed using the inclusion and exclusion criterion as described below.

Inclusion

Results were limited to: a) adults or individuals over 18 years, b) use of analogue basal bolus regimens, c) moderate intensity exercise or running for a short period of time (< 2 hours), d) publications using English language e) research published in the past 10 years. This timeframe was decided because basal bolus regimens have been common practice for the past 15 years but analogue insulin has only been available on prescription for the past 10 years (Roach 2008). Prior to this period, older fast-acting insulin types were administered but it may be difficult to extrapolate data from studies using these insulins compared with modern insulin types which have different pharmacokinetics.

Exclusion

The exclusion criterion were: a) studies which included other types of diabetes rather than Type 1, because they have a different pathophysiology, treatment and glycaemic responses to exercise, b) Studies including different types of sport i.e.

endurance, intermittent, and high intensity, because the physiological response on the body was different, requiring different insulin and CHO adjustments., c) Literature relating to athletes and professional sportspersons, because the intensity and supreme fitness levels of these subjects would not be replicated by the more general population, d) Articles which only described cellular activity, because insulin replacement therapy in relation to patient experiences, were not discussed, e) Exercise programmes and their effects on long-term behaviour and glycaemic control, because the present study was concerned only with the acute response to exercise, f) Studies of older insulin types and regimens, because of the difficulty to extrapolate data and use in conjunction with current therapies.

2.5 Results

The search strategy for the four databases is shown in Appendix 1a. The search results are shown in Table 2.2. From the search, 31 publications were included in the review, and from these, 21 key studies were analysed and described individually in the literature review. The remaining 10 studies contained some relevant information and were included as narrative inclusions.

The literature review was performed in 2010 prior to performing the current study, but it has been acknowledged that since the initial review, some related recent research has been published which is described in the discussion chapter.

Table 2.2: Search results

Potentially relevant papers identified by literature search: 203
↓
Papers excluded after evaluation of abstract: 134
↓
Papers retrieved for detailed examination: 69
↓
Additional 7 papers included after review of reference list of included papers: 76
↓
Papers excluded after review of full paper: 45
↓
Papers assessed for methodological quality and included in review: 31

Search terms	**Initial hits**		
Type 1 diabetes	29,694		
Physical activity	8,085		
Moderate intensity exercise	2,027		
Sport	646,959		
Running	103,421		
Combined search terms	**Potential**	**Reviewed and included**	**Excluded**
Type 1 and physical activity	C= 46 S=0 M=0 Total=46	American Diabetes Association(2002) Brazeau et al (2008) Butler (2006) Kilbride et al (2011a) Peter et al (2005) Nagi and Gallen (2010) Wallymahmed et al (2007)	31
Type 1 and moderate intensity exercise	C=9 S=3 M=6 Total=18	Brazeau et al (2008) Nagi and Gallen (2010) Wallymahmed et al (2007) West et al (2010)	10
Type 1 and sport	C=13 S=75 M=6 Total=94	Lumb and Gallen (2009) Perry and Gallen (2009) Gallen (2005) Kavookjian et al (2007) Kilbride et al (2011b) Jimenez et al (2007)	68
Type 1 and running	C=27 S=7 M=11 Total=45	Brazeau et al (2008) Ertl and Davis (2004) Francescato et al (2004) Gallen (2005) Graveling and Frier (2010) Grimm et al(2004) Hermandez et al (1999) Lumb and Gallen(2009) Peter et al (2005) Pierce (1999) Rabasa-Lhoret et al (2001) West et al (2010)	25
Reference list searches		DAFNE (2002) Riddell and Perkins (2006) Guelfi et al (2005) Fery et al (1987) Robertson et al (2008) Biankin et al (2003) Sandoval and Davis (2006)	

Abbreviations:
1**. Initial hits**: C=CINAHL, S=SPORTDiscus, M=MEDLINE

The literature search results identified that little was written in the area of diabetes and moderate intensity exercise, especially outside the laboratory environment. The following review focused around the three areas; 1) challenges for people with Type 1 diabetes, 2) self-management strategies, 3) and the study environment, with the purpose of examining each key publication with discussions regarding the relevance in this study. A table displaying the key publications with a summary of the main points is shown in Appendix 1b.

2.6 The challenges people with Type 1 diabetes experience when exercising.

In order to undertake a study examining the impact of exercise on people with Type 1 diabetes, and the effect of specific self-management strategies, it was necessary to first determine that problems in this area existed. It was important to ensure that research undertaken and the evidence generated was worthwhile, valuable, and beneficial for both patients and HCPs. From clinical experience, the author was aware of the difficulties faced by patients when exercising. However, these difficulties were an issue for a minority of individuals encountered, and by chance may have experienced similar problems. Evidence from the literature was necessary to ensure the certain presumptions were relevant and correct.

Brazeau et al in 2008 published a quantitative study with the aim to determine barriers for people with Type 1 diabetes participating in physical activity, which addressed the opinions of the author. The examination of 103 people with Type 1 diabetes (mean age 43.5 ± sd 11.6 years) who had varying exercise behaviours, when attending routine clinic appointments, completed a diabetes-specific barriers measure (BAPAD1 scale). The results demonstrated that the highest barrier scores were associated with fear of hypoglycaemia, work schedule, loss of glycaemic control and low fitness levels respectively. Also demonstrated was that exercising with another person, resulted in significantly fewer barriers ($p<0.001$), and by

exercising with a companion familiar with hypoglycaemia, acted as a supportive measure and served also to boost confidence. Participants having an evening CHO snack after exercise as a preventative strategy, also significantly reduced fears of hypoglycaemia ($p<0.007$), thus providing glucose to replenish glycogen stores, and preventing hypoglycaemia (Ertl and Davis 2004). Another finding was that participants with knowledge of peak actions and pharmacokinetics of insulin also had reduced fears of hypoglycaemia ($p=0.021$).

The strength of this study was the large sample of Type 1 participants with different exercise behaviours, which provided a representation of real-life barriers and problems during the performance of exercise. The major limitation of the study was the lack of demographic data regarding treatment and exercise behaviour characteristics of the participants, which without these raised questions concerning the results presented. Another factor was the number of participants actively involved in regular exercise was not stated. This is important as regular exercisers and exercise-naïve patients may have different perspectives in relation to barriers and although this has not been described in other studies, it is a consideration derived from clinical experience. Another limitation was the fact the type of insulin participants used was not described. From clinical experience, if some were using a twice daily regimen compared to a basal bolus regimen this could increase hypoglycaemia and self-management problems due to the inflexibility of the insulin time-action and dose-adjusting practicalities. Another issue not clarified was that participants were questioned about their CHO snacks consumed at bedtime for nocturnal hypoglycaemia prevention, but the findings were not presented regarding types or amounts consumed and the effects experienced on individuals' glycaemic control, which would have been useful for this current study.

However, this study did provide information for practical aspects of the current study, relating to the algorithm design and participant information guidelines. The key messages taken were:

1). Knowledge of insulin pharmacokinetics improved anxiety levels in people with Type 1 diabetes.

2). Hypoglycaemia risk does cause anxiety, hence, accurate data collection for hypoglycaemic episodes were emphasised to the participants as preventative strategies are one of the main aspects of performing research in this area.
3). Incorporate CHO snack at bedtime to reduce hypoglycaemia anxiety.

Another study related to challenges faced by people with diabetes was published by Kilbride et al (2011a) who used a qualitative approach, with similar aims as Brazeau et al (2008), to explore the experiences of people with Type 1 diabetes when exercising. A focus group was used and the demographics for the four participants were: age 48.5 (± sd 2.5) years, and HbA1c 7.35 (± sd 0.5)%, and all had >2 years duration of Type 1 diabetes. This study presented detailed results regarding insulin and exercise behaviours compared with the generalisation by Brazeau et al (2008), and stated that all participants used a basal bolus insulin regimen and counted CHO, and that they participated in exercise for 30 minutes at least 3 times a week, both of which were applicable to the current study inclusion criteria.

The issues explored were self-management, hypoglycaemia and coping strategies and the results showed from the content analysis of the transcripts that there were three emerging themes: i) trial and error; all participants stated how they "juggled" and experimented with their diet and insulin doses. ii) trade-off; despite participants experiencing difficulties with self-management and hypoglycaemia, they were all motivated and considered that the benefits of exercise out-weighed the associated problems. iii) Locus of control; all participants were motivated and took control over implementing and adjusting their self-management strategies. The results demonstrated that participation in any form of exercise provoked inconsistency, unpredictability and variability in glucose control, and highlighted the substantial amount of time and effort required by patients to self-manage effectively. There was no single strategy that could be used for all types of exercise for both during and after, and different management was required for each exercise situation. Again, as highlighted by Brazeau et al (2008), participants identified a specific limitation which was their knowledge regarding physiology and insulin pharmacokinetics.

The study gave an in-depth description which demonstrated the difficulties and motivation required by patients to succeed in performing exercise whilst maintaining

acceptable glycaemic control. However the main limitation was the sample size of four participants which was small, compared to the large sample size in the Brazeau et al study (2008). Another potential disadvantage was that the participants were regular exercisers who had overcome hypoglycaemia fears by motivation and determination, and in order to understand their individual requirements for adjusting insulin and CHO, they may have forgotten about previous difficulties encountered. This study provoked uncertainty regarding whether a standardized approach for self-management was possible to achieve acceptable glycaemic control. Inconsistency and variability in glycaemic control, however, may exist because of lack of pharmacokinetic and physiology knowledge of the participants. It did confirm that people with Type 1 diabetes do have fears, concerns and difficulties relating to exercise. It also emphasised the gap between available current research and evidence, and applying findings to every-day self-management and patient education.

These studies demonstrated that anxieties and lack of information regarding self-management strategies existed, with the major focus centering around the prevention of hypoglycaemia (Brazeau et al 2008, Kilbride et al 2011a). Kilbride et al (2011a) described glucose variability, whereas Brazeau et al (2008) highlighted the loss of glycaemic control, which both suggest difficulties in achieving acceptable glycaemic control. This reinforces and clarifies the authors initial presumptions and supports the necessity for the current study to develop information regarding how to exercise safely, and from the patient perspective, how to take away the arduous task of trial and error in self-management approaches. In order to develop a self-management tool, practical strategies regarding exercise and diabetes were also examined.

2.7 Self-management strategies

The existing problems regarding exercise and Type 1 diabetes previously highlighted, lead to the next area to explore in the literature, which are self-management strategies designed to overcome these difficulties. There is general consensus amongst authors that different types of sport, intensity and duration require altered approaches to treatment adjustment because of the different effects

on glucose levels (Guelfi et al 2005, Kilbride et al 2011a, Kilbride et al 2011b, Perry and Gallen 2009, Robertson et al 2008). However, as discussed previously in section 1.2, current national guidelines for HCPs are vague, general and non-specific (NICE 2009, SIGN 2010). In order to support these national guidelines, review publications were found in the literature search which highlighted evidence of experiential opinions and recommendations from physicians with specialist knowledge in the area of diabetes and physical activity. The relevant publications are described below, however only the key relevant messages to the current study are stated as the reviews all offer a general overview of diabetes and exercise.

In order to understand the rationale behind self-management strategies, an understanding of specific physiology and metabolism factors in Type 1 diabetes was necessary. A literature review regarding self-management problems to overcome the physiological response to exercise in Type 1 diabetes was published by Riddell and Perkins (2006). The review adopted an educational stance to inform HCPs about the physiological effects of exercise on a person with Type 1 diabetes. Related research was incorporated into the article, although specific details and analysis of individual studies were not included. The relevant aspects included in the review were that large excursions in blood glucose concentrations were a challenge in self-management, with one of the reasons being that the absorption of subcutaneously injected insulin may increase with exercise. Also, self-injected circulating insulin does not decrease during exercise, whereas in a non-diabetic individual, insulin production would decrease. Another factor is that in a non-diabetic individual the release of glucagon would counter-act hypoglycaemia caused by exercise, however, in Type 1 diabetes this mechanism is impaired. Hence, all of these factors contribute to the risk of hypoglycaemia. Another challenge is that hyperglycaemia can be exaggerated in Type 1 diabetes due to increased hepatic glucose production, which happens to provide glucose for energy during exercise. This is also difficult for an individual to predict and prevent with self-management strategies.

Similar to the Riddell and Perkins (2006) review, Ertl and Davis (2004) published a review that was specifically aimed at hypoglycaemia and physiology which analysed relevant studies. The key message was moderate intensity exercise caused hypoglycaemia unless adjustments were made to exogenous insulin and glucose

intake. To counteract this, it was recommended that insulin be reduced before and after exercise (although timing issues were not stated), to account for increased insulin sensitivity with Glut 4 receptors and increased skeletal muscle glucose uptake. These two physiology reviews highlighted comparable issues regarding hypoglycaemia (Ertl and Davis 2004, Riddell and Perkins 2006) to underpin the rationale for insulin and CHO adjustment for the current algorithm design.

In 2004, Gallen published a narrative description that combined the physiological challenges described above, with management strategies to normalise blood glucose and prevent hypoglycaemia. Forty references were cited within the review which provided a wide range of narrative descriptions of key findings from original studies, although the individual studies were not critically analysed. Experiential descriptions and recommendations were given by the author which were not supported with evidence and were vague. However, a practical point for the current study was after exercise 60-120 grams (g) of CHO should be taken with insulin to replenish glycogen stores, which were emphasised by authors elsewhere describing physiology (Ertl and Davis 2004, Peirce 1999, Riddell and Perkins 2006). The drawback of the recommendation by Gallen (2004), was that it was not evidence based or related to any particular intensity or duration of exercise.

In a review by Perry and Gallen (2009), again the physiology of Type 1 diabetes and exercise with evidence based management strategies were described. A narrative description of key findings from original studies was provided but these individual studies were not critically analysed. Again, only experiential descriptions and recommendations were given by the authors. However, there were relevant messages from this review which demonstrated that multiple variables control glucose homeostasis, but advice for individuals differed as described by Riddell and Perkins (2006). In relation to self-management, the reduction of post-exercise bolus insulin dose prevented nocturnal hypoglycaemia, however, the amount of reduction was not stated. It was also suggested that a pre-exercise blood glucose target be between 7.0 -12.0 mmol/l, however, this also was not evidence based. The lack of research performed in real-life environments was highlighted and it was acknowledged that evidence is required to support the practical considerations suggested by the authors.

Once gathering these practical considerations and self-management strategies as described, the information must be disseminated amongst HCPs. The American Diabetes Association (ADA) (2002) provided an update for HCPs regarding the role of physical activity in diabetes management. Six publications from 1990-1995 were reviewed to give clinical recommendations for HCPs when advising patients on exercise management. The results gave a narrative description of physiological issues and management strategies for Type 1 and Type 2 diabetes. Information was given regarding pre-exercise physical assessment, and preparation regarding warm-up and cool-down periods. The Information was very vague but implied that any exercise can be performed by people with Type 1 diabetes and hypoglycaemia can be avoided by manipulation of CHO and insulin, but did not highlight the difficulties in which to achieve this. The key messages for the current study were to avoid exercise if blood glucose > 13.9mmol with ketosis, or blood glucose > 17mmol without ketosis. In relation to hypoglycaemia prevention, it emphasised the importance to eat CHO if blood glucose <5.5mmol before exercise. However, these strategies were again not evidence based.

Following a similar structure, Jimenez et al (2007) published similar recommendations as those by the ADA (2002), but aimed for certified athletic trainers regarding Type 1 diabetes management on behalf of the American National Athletic Trainers Association. This was a practical over-view with a narrative description of Type 1 diabetes and exercise management, aimed at trainers with no diabetes knowledge and was based on 91 cited publications. The only relevant key message from this review was that it did highlight the complex intricacies of Type 1 management that a HCP working in diabetes may assume that lay persons understand. The array of variables that HCPs were required to consider when advising a patient were also described by Perry and Gallen (2009), and Riddell and Perkins (2006).

With regard to HCPs, a narrative description by Lumb & Gallen (2009), reviewed management strategies for exercise and Type 1 diabetes, based upon patient scenarios, and cited 28 references but were not critically analysed. The results provided experiential descriptions and recommendations for different intensities and

types of exercise but they were not supported by evidence. However, this review did highlight issues which were included in the current algorithm design. Lumb and Gallen (2009) stated if severe hypoglycaemia occurred in the previous 24 hours, exercise should be performed with caution, if at all, a point also highlighted by Gravelling and Frier (2010). Lumb and Gallen (2009) also discussed the peak hypoglycaemia risk-time after moderate intensity exercise occurring 60-90 minutes post-exercise, and during the night, which was also suggested by Robetson et al (2008), but was not evidence based. An important factor stated in the review, was an insulin dose reduction of 30% was advised after exercise for hypoglycaemia prevention, although again there was no evidence basis. Lumb and Gallen (2009) stipulated that management strategies be tailored to individuals, which were highlighted by several authors and probably stemmed from glucose variability (Jimenez et al 2007, Perry and Gallen 2009, and Riddell and Perkins.

A further review by Nagi and Gallen (2010), on behalf of the British Clinical Diabetologists Committee, presented a position statement to assist diabetes HCPs to familiarise themselves with issues regarding exercise management. A narrative description of key findings from 41 publications without critical analysis, were discussed alongside experiential opinions and descriptions from this well-recognised expert group. The key messages in relation to long-term complications that came from this review revealed no evidence to suggest that moderate intensity exercise had a detrimental effect on non-proliferative retinopathy. Also physical activity (apart from high intensity, strenuous exercise) should not be restricted in people with nephropathy. Treadmill use should not be undertaken by people with significant neuropathy for safety reasons. These recommendations were of interest, although were not applicable for the current study as selected participants were complication-free. Advantages and disadvantages for specific dose-adjusting were described, but insulin-adjusting for use after exercise was not mentioned. However, it was highlighted to reduce basal insulin in order to prevent nocturnal hypoglycaemia, which was also suggested by Lumb and Gallen (2009), but stated this may also cause morning hyperglycaemia, a fact relevant in the current study.

Finally, Kavookjian et al (2007) conducted a systematic review to assess and summarise evidence and gaps in the literature regarding interventions for exercise

among people with diabetes. The aim was to establish evidence regarding exercise in all types of diabetes for learning, behavioural, clinical and humanistic outcomes. The results focused mainly on Type 2 diabetes with a limited Type 1 review. However, some relevant conclusions were found, the first being that self-management and glycaemic control intervention studies were all conducted in artificial environments i.e. laboratory, with no translation into the patients' daily life. In addition, blood glucose monitoring was described as essential to evaluate self-management strategies regarding CHO and insulin in relation to the exercise intensity and time of day. Although no analysis of diet or insulin dose-adjusting intervention studies were provided, which was acknowledged by the authors.

The above publications which reviewed current exercise and diabetes literature and provided HCPs with knowledge for use within clinical practice, also gave a general overview regarding the effects of exercise and possible self-management strategies to overcome them. The problem with these findings was they did not give specific evidence based practical guidance, but only experiential opinions for patient care and education. However, despite several claims by authors (Gallen 2004, Kavookjian et al 2007, Lumb and Gallen 2009, Perry and Gallen 2000) that there was a lack of evidence to support self-management for exercise participation, this literature search did identify some publications to underpin the design of the current self-management algorithm.

2.8 Self-management algorithm design: Before exercise

After examination of the review publications, the next section of the literature search was to identify specific evidence-based insulin dose-adjustment and dietary management strategies, and the subsequent effects on glycaemic control for both during and after moderate intensity exercise. The section has been divided into before and after exercise.

The issues applicable to self-management before performing afternoon exercise include: 1). Pre-exercise insulin reduction, 2). Target blood glucose concentration and 3). CHO consumption.

2.8.1 Pre- exercise fast-acting analogue reduction

The reduction of insulin before performing exercise is an important factor to consider as national guidelines and review publications advise on pre-exercise insulin reduction (ADA 2002, Lumb and Gallen 2009, Nagi and Gallen 2010, NICE 2009, Perry & Gallen 2009, SIGN 2010). In relation to the current study, evidence was needed to support this recommendation when performing exercise 3 hours after administering a meal-time insulin injection. This time followed the peak action of the preceding fast-acting analogue dose, and subsequent hypoglycaemia risk time (Rabasa-Lhoret et al 2001, Robertson et al 2008, West et al 2011), which confirmed that the time of the highest risk of hypoglycaemia after fast-acting analogue administration, was 40-90 minutes following injection.

The only studies found relating to pre-exercise insulin dose-adjustment associated with moderate intensity exercise, investigated the effect of adjustments of insulin and CHO before breakfast, and within 1 to 3 hours of commencing exercise (Rabasa-Lhoret et al 2001, West et al 2011). In these studies, the strategies and data collected were aimed at preventing hypoglycaemia during or immediately following exercise, without focusing specifically on post-exercise hypoglycaemia; an important issue for patient safety and anxieties (Brazeau et al 2008, Graveling and Frier 2010). No research was found for any other time of the day, or for adjusting 3 hours after fast-acting analogue insulin. Despite the different timings of exercise, the two studies by Rabasa-Lhoret et al (2001) and West et al (2011), were reviewed as the exercise intensity and duration were similar to the current study and thus may provide clarification regarding the effects of exercise on glycaemic control, especially post-exercise. Both studies also offered a rationale for possible insulin adjustment in this current study as both were designed at preventing hypoglycaemia.

West et al (2010) performed a quasi experiment to examine pre-exercise insulin reductions before running at 75% VO_2 max and the consequent 24 hour effect on glycaemic control. Seven participants attended four study visits and were randomised to conditions which administered the full breakfast fast-acting analogue dose or a reduction of 25, 50 or 75% immediately before breakfast. All participants undertook all conditions. After 2 hours, participants completed 40 minutes running at

75% VO_2 max on a treadmill. Blood glucose was tested every 15-30 minutes during and immediately after exercise, and every 2 hours until bedtime, and then on awakening. The results showed the pre-exercise blood glucose ranged between 11 - 15mmol in all four conditions. The full-dose condition experienced three hypoglycaemic episodes within 180 minutes of exercise, although each of the other conditions only had one single hypoglycaemia episode (not significant). All conditions demonstrated decreases in blood glucose ($p<0.01$). During exercise and 21 hours post-exercise, all conditions demonstrated hypoglycaemia, but the 75% reduction condition experienced fewer episodes ($p<0.05$), and achieved more acceptable 24 hour post-exercise blood glucose concentrations.

This study followed a strict protocol regarding timings of insulin administration and exercise, which followed a robust exercise protocol to achieve 75% VO_2 max. Data were collected at specific times to ensure precise and appropriate data collection. The results showed that if performing moderate intensity exercise within 2 hours of a fast-acting analogue dose, the dose should be reduced by 75%.

However, several limitations were revealed on analysis. The first discrepancy was that hypoglycaemia was stated as blood glucose <3.5mmol, but the accepted hypoglycaemia range for someone with diabetes in the UK is 4.0mmol/l or below (Diabetes UK 2012, NICE 2009, SIGN 2010). Hence, some hypoglycaemic episodes may have been missed. Also the results were presented as mean glucose values which may conceal hypoglycaemic episodes and so there was a possibility that more participants were hypoglycaemic or between 3.5-4.0mmol/l. Data were not presented to clarify this. With regard to the 75% reduction group, the mean blood glucose concentrations at the end of exercise were 11.0mmol/l, 1⁻ ¹, (s□ 0.7), and the participants were given correction doses at this time, thus possibly contributing to post-exercise hypoglycaemia. Data for up to 21 hours post-exercise regarding glucose and dose adjustments (adjustments decided by participants), including blood glucose concentrations during the night were not described. These data were taken from the real-life environment, and the authors described the difficulties concerned with analysing data when participants self-managed and used different strategies with CHO amounts, insulin dose, monitoring and injection times. These were not correlated nor described in conjunction with blood glucose concentrations or

hypoglycaemia episodes, which makes data analysis and extrapolating appropriate evidence impossible. Another limitation was that the required sample size to gain 80% power was determined with the use of 33 participants, based on data from Rabasa-Lhoret et al (2001). The West et al (2010) study recruited seven participants, which would have influenced the lack of statistical significance. Again, as described by Brazeau et al (2008) and Kilbride et al (2011b) the intra-individual variability of blood glucose across participants was highlighted by the authors as a limitation, and would affect the mean glucose figures.

Despite these limitations, there were issues to be considered for the current study:

1. The glucose-lowering effect of the fast-acting analogue insulin began approximately 10 minutes after injection, with peak-action at 60 minutes and duration up to 5 hours. The peak-action is an important factor to consider as it did not occur during this study exercise session time, however, the duration was up to 5 hours which would coincide with participants exercise times in the current study.
2. The range of the starting blood glucose concentration was 11 - 15.0mmol/l (1⁻¹), which is hyperglycaemic. Despite the high starting glucose concentrations and insulin reduction 2 hours prior to the start of exercise, participants still experienced a glucose drop during exercise. For the full dose condition, this drop was 6.1mmol/l (s 0.4).
3. A discussion point was the reported variability of blood glucose concentrations in a controlled laboratory environment. This is an important factor to consider when analysing and discussing data in the current study.

Another similar study by Rabasa-Lhoret et al (2001) performed a randomised, cross-over laboratory based study to evaluate pre-meal insulin dose reductions for exercise at different intensities and durations to minimize hypoglycaemia. Eight males with Type 1 diabetes participated, and all used a basal bolus regimen using pre-meal fast-acting analogue insulin, and Ultralente for the basal insulin. The pre-meal fast-acting analogue insulin was adjusted 90 minutes before exercise. The participants took either the full insulin dose or a reduction dose of 25 or 50%. Exercise was then performed at: 25% VO_2 max for 60 minutes, 50% VO_2 max for 30 and 60 minutes, and 75% VO_2 max for 30 minutes. The blood glucose was monitored for 18 hours post-exercise.

The results demonstrated firstly that increased physical activity for any intensity from 25, 50 and 75% VO_2 max, without reduced insulin doses or additional CHO, caused hypoglycaemia. Again, hypoglycaemia was defined as a blood glucose < 3.5mmol/l which is the same as West et al (2010). Sixty exercise sessions were performed which resulted in 24 minor hypoglycaemic episodes. Two episodes occurred in the 90 minute rest period before exercise, and four episodes during exercise. The remaining 18 episodes occurred within the 18 hour post-exercise period. From these, more than two-thirds of hypoglycaemic episodes happened in the patient group who took the full pre-meal dose. In relation to hypoglycaemia, during exercise at 75% VO_2 max the mean decrease in glucose was 2.7mmol/l (± 0.38) with the 75% reduction compared with 3.0mmol/l (± 0.71) with the full dose group. Despite this, the starting blood glucose was higher at 9.8mmol/l (±1.1) in the 75% reduction group, and the overall glucose profile during exercise was higher (p=0.05). The study demonstrated that a 75% reduction was required to maintain acceptable post-exercise glucose.

This study was of a complicated design, which succeeded in conducting 60 individual exercise sessions. It followed a robust protocol to ensure that appropriate dose-adjusting and exercise intensity were performed. The results demonstrated that pre-meal insulin reduction were required prior to exercise within 90 minutes of fast-acting analogue injections and were similar to the results of West et al (2010).

There were several limitations when extrapolating data for evidence in the current study. In comparison with West et al (2010), the sample size was small, although this was not discussed by the authors and the power calculation was not specified. Other limitations included issues that the data were not presented regarding the time that hypoglycaemia occurred within the 21 hour study period, especially the 18 episodes that occurred post-exercise which is crucial to ascertain the probable cause. Also, despite participants being examined for 18 hours post-exercise, blood glucose results were only described for the following one hour post-exercise period, which was similar to West el al (2010). After exercise, the participants used their usual insulin doses rather than reduced dosages but the authors failed to describe blood glucose concentrations and any insulin adjustments.

The relevant key messages for the current study were limited due to the lack of post-exercise data:

1. In the discussion Rabasa-Lhoret et al (2001), does recommend that exercise performed after lunch may require reductions in insulin prior to the following meal to prevent delayed hypoglycaemia at night. This recommendation was based on the post-exercise hypoglycaemia episodes despite limited published data, and this is relevant in the current study.
2. The results demonstrated that improved glucose profiles were maintained by starting with higher pre-exercise glucose concentrations, however, the actual levels were not stated.

In these two studies, exercise was performed in the early morning and the adjustment of fast-acting analogue insulin dose and CHO was made at breakfast time. This time of day ensures that participants have fasted overnight which eliminates the effects of any delayed CHO absorption or previously injected active insulin. In Type 1 diabetes, insulin resistance can occur in the early morning which sometimes requires increased insulin doses compared to the rest of the day (Pang and Narandran 2008). Thus, it is of interest, that for 30-45 minutes of exercise at 75% VO_2 max, a 75% reduction of the insulin dose was still required to prevent hypoglycaemia during and after exercise (Rabasa-Lhoret et al 2001, West et al 2010). As stated by Riddell and Perkins (2006), hypoglycaemia would occur because of an overdose of insulin before exercise, and with increased insulin absorption during exercise, its action and sensitivity can therefore last for several hours post-exercise. This has been demonstrated by West et al (2010) as the full dose group that exercised after 2 hours had a blood glucose drop of 6.1 after 45 minutes exercise, compared with the full dose group that exercised after 90 minutes, had a 3.0mmol/l decrease after 30 minutes of exercise shown by Rabasa-Lhoret et al (2001). The differences between the glucose decrease were probably due to the different exercise durations and demonstrated by the different insulin actions, which was reflected in the duration of fast-acting analogue action at 5 hours, which is applicable to the current study.

Although data were collected, Rabasa-Lhoret et al (2001) and West et al (2010) did not publish findings for the 18-21 hour post-exercise blood glucose concentrations and hypoglycaemic episodes. This may have been due to difficulties with data collection as the participants self-managed and did not follow dose-adjusting guidelines outside the laboratory environment. Because of ad hoc strategies and glucose variability (Kilbride et al 2011a, Jimenez et al 2007, and Riddell and Perkins 2006) this may have made data extrapolation difficult. However, both studies described post-exercise hypoglycaemia, although only Rabasa-Lhoret et al (2001) stated the exact figure of 18 episodes. Post-exercise hypoglycaemia was applicable to the current study and clarified the need for post-exercise insulin reduction. In both studies the variations of individual self-management were not described, thus making data analysis of strategies and blood glucose concentrations difficult to correlate and probably contributed to the reason for the lack of published data and discussion. This was an important factor to consider in the current study design from a patient perspective and also for HCPs when advising patients regarding safety and well-being.

2.8.2 Blood glucose targets.

Another area to consider when educating people with Type 1 diabetes regarding exercise management was to provide information about target blood glucose concentrations for patient guidance, which also would help to determine the success of their self-management. From clinical experience, pre-exercise blood glucose targets were an issue debated between HCPs and patients. As previously discussed, West et al (2010) and Rabasa-Lhoret et al (2001) showed that the starting mean blood glucose concentrations of participants were 11-15mmol/l and 9.8mmol/l respectively. A target blood glucose concentration was not stated and therefore assumed that participants controlled their own individual starting blood glucose concentration.

With regard to this, in general, current literature has recommended that exercise should not be performed if an individual is hyperglycaemic. The literature review published by Lumb and Gallen (2009), suggested that from clinical guidelines, exercise should be avoided with blood glucose concentrations over 14mmol/l

because of reduced circulating insulin. The rationale for this advice was determined because of a further increase in mobilisation of glucose from liver and fat stores when exercising, hence, further hyperglycaemia can occur if the individual has limited amounts of injected insulin acting to transport glucose into the cells (Riddell and Perkins 2006). A higher pre-exercise blood glucose may increase the risk of ketoacidosis in this situation (ADA 2002, Fery et al 1987, Lumb and Gallen 2009). American guidelines state that exercise should be avoided if blood glucose is over 13.9mmol/l with ketosis, or 17mmol/l without ketones (American Diabetes Association 2002). However, these publications are based on experiential opinions and clinical knowledge rather than research.

These publications also do not incorporate patient behaviour and preference, which on discussion with patients is to aim for higher concentrations, which were demonstrated in the West et al (2010) and Rabasa-Lhoret et al (2001) studies. A study regarding these issues was performed by Wallymahmed et al (2007) which confirmed that people with Type 1 diabetes (not athletes) avoided hypoglycaemia by aiming for higher blood glucose before and during exercise. This study assessed the relationship between glycaemic control, self-reported physical activity, aerobic capacity and hypoglycaemia avoidance in people with Type 1 diabetes. Fifty patients attending a routine diabetes clinic appointment participated. The mean age 36 ±9.2 years (range 18-52), duration 18 ±8.8 years, HbA1c 9.1±1.3%. Aerobic fitness was assessed by a sub-maximal step-test, and physical activity, hypoglycaemia and hypoglycaemia avoidance was measured by a non-validated questionnaire.

The results showed that 60% reported participating in regular vigorous exercise (RVE) and had significantly worse HbA1c; 9.5 ±1.35, compared with those not regularly exercising or not vigorously active (NVA); 8.5±1.2% ($p<0.002$). The implications for higher HbA1c levels, are that frequent regular exercisers who strive to achieve higher blood glucose concentrations for longer periods of time during exercise, are in danger of producing damaging effects for long-term complications due to prolonged poor glycaemic control. The RVE group reported they aimed for higher starting blood glucose (although targets were not stated), before exercise, levels compared to the NVA group (8 individuals vs 0 individuals $p<0.03$). In the RVE group 83% reported taking precautions to avoid hypoglycaemia. From these, 77%

increased the consumed amount of CHO, 7.7% reduced their insulin intake, 12.8% increased the consumed amount of CHO plus insulin reduction. The suggestions from these above data may be that patients were unable to understand how to adjust insulin effectively.

A strength of this study (Wallymahmed et al 2007), was the large sample size which provided a description of exercise and diabetes behaviour and management within a normal population with Type 1 diabetes, and confirmed that people with Type 1 diabetes aimed for higher blood glucose concentrations during exercise to prevent hypoglycaemia.

There were several limitations with regard to utilizing data for the current study. First there was no report of the level of target blood glucose, which would have been useful when deciding on the pre-exercise blood glucose target in the current algorithm. The study used a non-validated questionnaire, and the questionnaire was not published. Also it was difficult to extrapolate data and information for the current study algorithm because specific areas i.e. dose adjustments, food amounts, glucose concentrations during exercise, hypoglycaemic events related to exercise, were not described in sufficient detail. Another limitation was that hypoglycaemia was not defined. This is essential as patients often classify hypoglycaemia with different glucose concentrations as seen in the current recommendations (Diabetes UK 2012, NICE 2009, SIGN 2010), and studies; Grimm et al 2004, Rabasa-Lhoret et al 2001 and West et al 2010.

However, relevant key messages were found and used in the current study:

1. Patients consumed more CHO before and during exercise in order to achieve higher blood glucose concentrations, despite advice being given by HCPs in the clinic on insulin dose reduction. The interpretation once again suggested that patients do not understand or have not been given adequate advice by HCPs to adjust their insulin doses. This is comparable to findings from Brazeau et al (2008) and Kilbride et al (2011a).
2. The HbA1c was higher in participants who exercised regularly, which might suggest that participants purposely aimed for higher glucose concentrations.

From this section of the literature review, it was shown that although optimal blood glucose targets at exercise were not incorporated into any reviewed study aims (Grimm et al 2004, Rabasa-Lhoret et al 2001, West et al 2010), the publications suggested that blood glucose concentrations recommended prior to the commencement of exercise should be higher. Gallen (2004) recommended a glucose concentration between 7-10 mmol/l, before exercise which was slightly different from that of 7-12mmol/l which was published 4 years later (Lumb and Gallen 2009). However, a study analysing an algorithm for 50% VO_2 max exercise (Kilbride et al 2011b), aimed for the pre-exercise blood glucose target at 10mmol/l. The resulting blood glucose concentration remained high but stable during exercise, which suggested that the target of 10mmol/l could be lowered. This glucose pattern was also demonstrated by Rabasa-Lhoret et al (2001). As discussed previously, Wallymahmed et al (2007) showed that patients who exercised regularly, purposely had blood glucose concentrations higher during exercise in order to avoid hypoglycaemia. This strategy has also been highlighted during patient discussions in clinical practice and also with participants in the focus group described by Kilbride et al (2011a).

There are clearly discrepancies in the published literature with large variations of acceptable blood glucose among authors (Gallen 2005, Kilbride et al 2011b, Lumb and Gallen 2009, Wallymahmed et al 2007). However, patient preference of glucose appears to be higher than recommended in current guidelines (Diabetes UK 2012, NICE 2009, SIGN 2010). A balance should be sought to consider hypoglycemia prevention, patient comfort and long-term effects of hyperglycaemia.

2.8.3 Pre-exercise CHO consumption

The next area of the literature review to explore is CHO consumption which is a common strategy used by patients to prevent hypoglycaemia and initiate hyperglycaemia (Wallymahmed et al 2007), However, limited evidence is available regarding CHO amounts and types to be consumed prior to and during exercise, although CHO consumption in general is recommended in guidelines to prevent hypoglycaemia (Diabetes UK 2012, Francescato et al 2004, NICE 2009, SIGN 2010).

One study was found in the literature review which addressed this issue. Grimm et al (2004) compared different amounts of consumed CHO with insulin dose adjustment for people with Type 1 diabetes who exercised at different intensities and for different durations. Sixty-seven people with Type 1 diabetes participated, all had acceptable glycaemic control (HbA1c <7.5%, sd not reported) and used a basal bolus regimen with fast-acting analogues and Neutral Protamine Hagedorn (NPH) insulin which is an older intermediate-acting insulin. They were placed into 4 different treatment groups depending on their usual exercise self-management strategies. These were: 1). consuming 10-20g of CHO hourly for the duration of the exercise. 2). consuming 10-20 g of CHO hourly for the exercise duration plus reducing the daily insulin dose by >10%. 3). no extra CHO but reduced daily insulin dose by >10%. 4). no extra CHO or insulin dose reduction. Each participant performed an exercise programme of three different intensities and durations. For the purpose of this review the groups using the intensity of 60-75% VO_2 max and 20-60 minutes duration were analysed.

The results demonstrated that exercise sessions for 20-60 minutes at 60-70% VO_2 max, required 20-60g of CHO to prevent hypoglycaemia. From the results the recommendations in general for intense and moderate exercise duration require a 20-30% reduction of total daily insulin dose (not stating analogue or NPH). In the study from 265 exercise sessions, there were 6 hypoglycaemic episodes which all occurred at least four hours after exercise, and was much less than that demonstrated by Rabasa-Lhoret et al (2001) and West et al (2010).

This study had a large sample size, and was the only study found that specifically evaluated CHO amounts prior to exercise. The mean age of participants was not stated, although the inclusion criterion was 18-35 years old, which is a young age group compared to all other studies in the exercise and diabetes field. The limitations found were again related to hypoglycaemia levels, with hypoglycaemia stated as a blood glucose concentration of <2.8mmol. This is a dangerously low value, compared with UK guidelines of <4.0mmol (Diabetes UK 2012, NICE 2009, SIGN 2010). The insulin types used in the study were fast-acting analogues or NPH. NPH is an earlier type of intermediate-acting insulin which peaks between 4-8 hours after injection, which would affect post-exercise glycaemia in this study. The amount and

type of insulin dose adjustment were not specified and was reported only as a 10% reduction of the total daily dose which could be either fast-acting analogue or NPH. From the data, hypoglycaemia occurred post-exercise, but participant dose adjustment strategies after exercise were not described. Also the type of CHO that was consumed prior to exercise was not described. This is a major limitation as the glycaemic index of CHO can cause large fluctuations on absorption and the effect on the rise of blood glucose.

However, despite the limitations, the important key message taken from this study was that hypoglycaemia occurred at least four hours after the finish of exercise despite insulin reduction and CHO consumption prior to exercise. The study showed that 20-60g CHO was necessary for 75% VO_2 max to prevent hypoglycaemia. These findings were used in the current algorithm design.

Relating to Grimm et al (2004), although not an original study but an experiential report, Biankin et al (2003) suggested that physiological elements which affected glycaemic control, included CHO digestion and intestinal absorption or the glycaemic index (GI) of CHO foods. This report also stated that exercise at > 75% VO_2 max can delay absorption, but 50-70% VO_2 max should not affect the rate absorption. No other literature in this area was found, however these dietary and physiological issues were relevant to the current study due to consumed CHO prior to exercise when the blood glucose concentration was low. An applicable recommendation from the Dose Adjusting For Normal Eating (DAFNE) Group (2002), stated that 10g of CHO raised the blood glucose concentrations by 2.5 mmol/l, which is information given to patients within NHS education sessions throughout the UK and also acknowledged by Diabetes UK (2012). This recommendation was appropriate for inclusion to the current study.

The above literature therefore indicates that there are multiple factors to consider when deciding CHO consumption before exercise i.e. type of CHO, the GI index and the amount, and needs to be balanced with the amount of active fast-acting analogue insulin, and the intensity and duration of the exercise. This is a complex area, for which there are many gaps and weaknesses in the limited evidence

available for inclusion in this current study, and highlights the need that further research is required.

2.9 Self-management design: After exercise

Following on from pre-exercise self-management, post-exercise issues will now be discussed. The literature search found no studies on the effects of insulin and/or CHO adjustment after exercise, to maintain acceptable glycaemic control, and thus avoid the complication of hypoglycaemia.

Rabasa-Lhoret et al (2001) and West et al (2011) reported post-exercise hypoglycaemia, and from a patient perspective, Frier (2008) experientially described the patient's fear and concerns of hypoglycaemia, especially overnight after evening exercise. As suggested by Rabasa-Lhoret et al (2001), delayed hypoglycaemia is a potential problem, particularly for those who exercise in the afternoon, which is relevant to this current study. From this, hypoglycaemia can occur overnight and it is often more severe when people are asleep, and therefore more difficult to detect. In the review discussed by Ertl and Davis (2004), a detailed account described how hypoglycaemia can occur up to 12 hours post-exercise. This is a result of the replacement of utilized glycogen stores within the liver and muscles, which were used to provide energy during exercise. The review also highlighted the increased risk of nocturnal hypoglycaemia in some patients after evening exercise. However, evidence-based preventative strategies are limited and this gap has been acknowledged by previous authors who provide recommendations on post-exercise self-management based on clinical experience rather than research based evidence (Ertl and Davis 2004, Perry and Gallen 2009). For a HCP, it is therefore important to discuss risks with patients during education sessions and provide information regarding prevention.

The important factors to consider in post-exercise management include: 1). Post-exercise insulin reduction, 2). CHO intake, and 3). Target blood glucose at bedtime. These will now be discussed to underpin the self-management algorithm.

2.9.1 Post-exercise fast-acting analogue reduction

The risk of delayed or nocturnal hypoglycaemia is increased after exercise, and from a physiological stance, Ertl and Davis (2004) described increased insulin sensitivity post-exercise due to the increase in Glut 4 receptors. These receptors are responsible for muscle uptake of glucose in conjunction with replenishing glucose stores which supports the necessity of insulin reduction. Similarly, Sandoval and Davis (2006) described the dysfunctional autonomic regulation of metabolism after exercise and delayed hypoglycaemia, but did not recommend insulin adjusting strategies for prevention.

From the literature review, all recommendations for post-exercise insulin adjusting were based on experiential opinions. Perry and Gallen (2009), described evidence-based percentage adjustments for pre-exercise bolus doses, but only suggested post-insulin reductions with no guidance to the amount. Lumb and Gallen (2009) recommended a 30% decrease of post-exercise insulin dose which was not evidence-based. Peirce (1999) suggested a 30-50% post-exercise insulin-dose reduction, depending on exercise intensity and duration but again this was not evidence-based and vague. Rabasa-Lhoret et al (2001) also suggested a 50-75% pre-exercise insulin-dose reduction, but specific reductions for post-exercise meal doses were not recorded. The consensus of opinions from these authors all recommend dose reductions, however, amounts were variable and not evidence-based. This is a major gap in the literature as no published research was found regarding post-exercise insulin dose adjusting to assist hypoglycaemia prevention.

2.9.2 Long-acting analogue reduction

Another self-management strategy used by HCPs to prevent nocturnal hypoglycaemia was basal insulin adjusting. Insulin Glargine (Lantus) is a basal insulin replacement designed to mimic natural insulin secretion to suppress glycogenolysis and to facilitate bolus insulin action. After injection, Lantus takes one hour to start a glucose lowering effect, and remains stable for an approximate 24 hour period (Peter et al 2005). Within clinical practice, HCPs advise patients to reduce their Lantus dose after exercise to prevent delayed or nocturnal hypoglycaemia. However, because of the effect on the subsequent 24 hour blood

glucose profile, there is an increased risk of hyperglycaemia during the following day, and therefore it is not ideal.

In relation to basal insulin adjustment, the only related publication found was by Peter et al (2005), which studied the effects of the absorption of Lantus on blood glucose after exercise in Type 1 diabetes. Using a randomised cross-over design, thirteen participants with Type 1 diabetes, using a basal bolus regimen were given their usual Lantus dose administered into the thigh, on the evening before visit 1 and visit 2. On both visits, the usual fast-acting analogue insulin dose was given immediately before breakfast. They were then randomly assigned to perform a 30 minute bout of exercise one hour after one of the visits at 65% VO_2 max. For data collection, blood glucose concentrations were monitored for the following 210 minutes.

The results demonstrated that the fasting blood glucose concentrations were similar on both days; exercise day, 8.4mmol/l and non-exercise day, 8.2mmol/l. Then during the 210 minute post-exercise period there were no differences in glucose levels ($p=0.345$). However, during exercise, the glucose concentrations were significantly lower ($p=0.001$) which is likely due to the full fast-acting analogue dose being given and not reduced. Also there were no statistical differences in plasma Lantus insulin levels during ($p = 0.506$) or after ($p =0.116$) exercise on both days.

This study provided strong evidence for an important area in diabetes management. The positive outcome of the study demonstrated that plasma Lantus levels remained stable during and after the 210 minutes post-exercise period. However, again sample size was not discussed, and two further important limitations were noted that would affect clinical practice and the extrapolation of data. The first was that blood glucose concentrations were recorded at 15 minute intervals from baseline to 3 hours and 30 minutes post-exercise. But the authors failed to study blood glucose concentrations for the following 24 hours when hypoglycaemia was a potential risk because of the Lantus time-action. Secondly, there was no adjustment made to the fast-acting analogue insulin dose pre-exercise which was the likely cause of the blood glucose decrease during exercise.

Despite this, the relevant key messages taken from this study were:

1. The Lantus dose was not a contributing factor to hypoglycaemia during, or in the initial period after exercise. The plasma Lantus levels during 30 minute sessions of 65% VO_2 max exercise were not different between exercise and non-exercise visits. The Lantus absorption from injection sites after exercise was a previous concern of the author prior to performing this literature review, due to the potential increased hypoglycaemia risk which is currently discussed by HCPs with patients.
2. The suggestion from this study was that the usual Lantus dose can be safely administered, although it must be highlighted that the nocturnal glucose response after exercise was not studied.

2.9.3 Pre-bed blood glucose target and CHO amounts

To prevent nocturnal hypoglycaemia, CHO consumption before bedtime is another common self-management strategy used by patients and advised by HCPs. In view of this, Brazeau et al (2008), stated that participants who consumed a CHO snack before bedtime to prevent nocturnal hypoglycaemia were significantly less fearful of hypoglycaemia ($p=0.007$). Increased CHO consumption before bedtime was reported as a possible intervention which may reduce overnight hypoglycaemia and thus balance increased insulin sensitivity and glucose uptake during the restoration of muscle and liver glycogen after exercise (Ertl and Davis 2004, Riddell and Perkins 2006). However, despite the importance of these preventative hypoglycaemia factors for both psychological and safety reasons, no research regarding CHO snacks at bedtime after participating in exercise was found.

2.10 Algorithm design

All of the above issues regarding strategies before and after exercise are essential to incorporate into patient education. From this literature review, no publications have been found that provide a strategy that incorporates recommendations for patients to follow before and after performing moderate intensity exercise. All research has focused on one specific area i.e. before exercise insulin adjusting. An algorithm with written guidance to support verbal education which incorporates before and after exercise self-management strategies would be unique.

The author of this current study designed a similar formatted algorithm for exercise at 50% VO_2 max, which is the equivalent to fast walking and was incorporated into a recent study by Kilbride et al (2011b). The study aim was to develop and evaluate an algorithm for diabetes self-management before, during and after exercise at 50% VO_2 max in a laboratory environment for people with Type 1 diabetes exercising within 2 hours of fast-acting analogue insulin and food. Fourteen people with Type 1 diabetes participated in the study over 2 weeks, with mean demographics: age 38 yrs, BMI 25 kg/m² and HbA1c 7.5% ± 0.7%. All used a basal bolus analogue insulin regimen, CHO counted, and exercised regularly. On Days 1 and 3 of each week they undertook 40 minutes of moderate exercise at 50% VO_2 max. During week 1 participants self-managed their insulin and CHO, and in week 2 followed the self-management algorithm stipulating a 30% fast-acting analogue insulin reduction pre- and post-exercise, and recommended CHO amounts based on the current glucose concentration. Continuous blood glucose monitoring was performed. The starting blood glucose target was 10mmol/l.

These study results were discussed in relation to the usage of the algorithm as a self-management tool and not the effect on glycaemia as the exercise type was different to the current study. The relevant issues for the current study were that the measured glucose reproducibility and variability during and after exercise was poor. On a positive note, on discussion with the study participants, they found the algorithm was a useful and easy tool to understand and follow.

With regard to the current study, a potential problem was the variability of glucose concentrations within subjects despite controlling the environment, exercise intensity and insulin dose adjustment which was demonstrated, and the authors acknowledged that this type of research does generate difficulties with analysis when using standard statistical techniques (Kilbride et al 2011b), and was also highlighted by West et al (2010). However, although this study used a different type of exercise and time of the day, an advantage of this study was that this method of informing patients of self-management strategies, by use of an algorithm was effective, and would be an ideal teaching resource.

There were sections of the 50% VO_2 max algorithm that were appropriate for a 70% VO_2 max algorithm:

1. To achieve stable blood glucose concentrations, the starting blood glucose aim would be between 7-8 mmol/l. This is in contrast to previous research described in section 2.8.2, and considers patient comfort by avoiding hyperglycaemia.
2. From reviewing the data and results, for post-exercise the algorithm remained unchanged indicating a 30% reduction in the following meal analogue dose for 50% VO_2. This is evidence-based and gives the only information found from the literature search regarding post-exercise adjusting.
3. If the exercise was undertaken during the evening, 10 – 30g of extra CHO would be recommended before bedtime, which was not suggested in other research.
4. Long-acting analogue doses would not be adjusted, based on data from Peter et al (2005).
5. From experience when using the 50% VO_2 max algorithm with patients and reviewing its usage, some amendments to the design were necessary to make the algorithm easier to use with regard to insulin dose and CHO adjusting information, an example being to insert bullet points with specific guidelines.

2.11 Study environment

Following on from the algorithm development, it was important to ensure the information was safe for patients to use in their own exercise environment as all of the literature discussed so far in this review has been performed in a laboratory environment. Hence, the final section of this literature review was to identify any related research performed in a real-life environment, where the replication of laboratory-based self-management research findings were applied into the real-life environment, and then to demonstrate any differences regarding the impact on glycaemic control between environments.

After selecting the relevant publications, it became evident that all studies regarding the evaluation of self-management strategies and the maintenance of glycaemic control surrounding exercise, were based in a laboratory environment using either a treadmill or bicycle, and not applied to real-life situations. However, it has been acknowledged that this apparatus can also be used in real-life (Grimm et al 2004, Peter et al 2005, Rabasa-Lhoretet et al 2001, West et al 2010). It was apparent that

the major difficulty when conducting this type of research was blood glucose and behavioural variability with exercise, hence the need for a controlled laboratory environment as described by Jimenez et al (2007).

Depending on the individuals' real-life environment, possible factors that influence the exercise intensity i.e. seasonal weather conditions or road or grass surfaces can increase or decrease the intensity (Potteiger 2010), and have a profound effect on glycaemia data collected. Another situation would be when exercising in a gym in a real-life environment, when the duration of exercise included recovery breaks which would affect blood glucose concentrations. Similarly, when participating in team sports or playing against an opponent, the intensity and duration of exercise can be affected by others, in addition to their own performance which could vary from day-to-day. These issues make it difficult to ensure that the same intensity and duration of exercise is maintained and may influence results and data within a scientific experiment. Probably in order to minimize these variables as much as possible, previous studies were performed in a controlled laboratory environment.

A further complication in data analysis, despite the use of controlled environments, was that glycaemic variability within participants was a phenomenon which offered researchers complex and intricate dilemmas when designing studies and analysing data in exercise and Type 1 studies (Jimenez 2007, Kilbride et al 2011a, Kilbride et al 2011b, Riddell and Perkins 2006, West et al 2010). From a self-management perspective, the accuracy and compliance of participants for insulin dose adjusting and CHO counting was considered paramount, as even the slightest change to insulin or CHO amounts may influence blood glucose concentrations. Other issues such as stress levels or hormonal effects on blood glucose concentrations, were never considered during patient recruitment nor recorded on experiment days, all of which could have a profound effect on glucose levels.

As discussed previously, several studies (e.g. Peter et al 2005, Rabasa-Lhoret et al 2001, West et al 2010), collected data following exercise, but only the minimum of data was presented in these publications which could not be used in the current study. During these studies, the participants when leaving the laboratory environment managed blood glucose concentrations, insulin doses and CHO without

any guidance from the researchers and used ad hoc management strategies for the post-exercise study time-period. These data were not included in the analysis and discussions of the publications because of the possible variability and inconsistencies in individuals' self-management. Such differences between participants would make extrapolating data and findings in patient management or related studies difficult.

From the difficulties described above, the only publications found within a real-life environment were case studies, and described individuals rather than groups of patients in experiments (Butler 2006, Gravelling and Frier 2010).

Butler (2006) presented the following case study which described the training and management programme for a person with Type 1 diabetes who planned to swim the English Channel. A 38 year old male with Type 1 diabetes trained for a year prior to the Channel swim. The training sessions could be interpreted as taking place in a laboratory or controlled environment (swimming pool), and lasted between 1 – 7 hours per session. A swim of the Channel, on the other hand, would correspond to a real-life environment.

The results gave a narrative description of insulin dose-adjusting but adjustments were only described in percentage terms not in actual units. The training sessions (controlled environment) and the swim (real-life environment) resulted in differences in blood glucose concentrations, but hypoglycaemia only occurred in the real-life situation. A motivational strength of this study demonstrated that through trial and error with self-management strategies, people with type 1 diabetes can succeed in sport. However, a major limitation was the omission of glucose concentrations which were not described during training, and were only stated as satisfactory before and after the Channel swim. Narrative dose adjusting was described, which makes it is difficult to understand the precise dose-adjustment strategy despite being an important area of the management plan.

The key messages taken from this case study were:

1. It was suggested that people with Type 1 diabetes discuss their exercise and self-management plans with diabetes HCPs, and that success in self-management is

achieved by trial and error, which again indicated insufficient evidence to underpin education suggested by Gallen (2004), Kavookjian et al (2007), Lumb and Gallen (2009), and Perry and Gallen (2009)

2. The study demonstrated differences in blood glucose concentrations and hypoglycaemia episodes between environments i.e. swimming pool (laboratory) and the Channel (real-life).

Another case study was published by Graveling and Frier (2010) which focussed on the potential risk of recurring hypoglycaemia during endurance exercise. A 27 year old person with Type 1 diabetes was discussed, and the article was based on severe hypoglycaemia episodes prior to running a marathon, and resulted in one further severe hypoglycaemia episode during the following marathon. The publication presented a description of the individuals' pathophysiology and clinical markers relating to Type 1 diabetes, describing the previous 48 hours before exercise and the subsequent following risk of exercise induced hypoglycaemia.

The publication provided a good description of pathophysiology related to hypoglycaemia and endurance exercise, however, specific insulin dose-adjusting and CHO consumption adjustments were not described. An important recommendation derived from this publication was an occurrence of a severe hypoglycaemia episode in the preceding 48 hours prior to an exercise session should result in the postponement of the session. This corresponded with recommendations from Riddell and Perkins (2006), although they did not stipulate a time-frame.

In both of the above publications, the management strategies and outcomes were descriptive with limited discussion surrounding specific exercise intensity, duration or time. Moreover, the interpretation of insulin dose and CHO adjustment in relation to glycaemic control was difficult to determine. These publications were of interest because they were thought-provoking and generated ideas for patient management, however, they cannot underpin recommendations for similar patient populations and situations.

The environment in which research is performed is an interesting concept and the application of laboratory findings into real-life patient self-management has not been analysed in any research as far as the author is aware, regarding exercise and Type 1 diabetes. In regard to this, one must consider whether laboratory findings can be replicated into real-life situations and whether study interventions will have the same effect on individuals glycaemic control depending on the environment. This consideration was fundamental in the current study.

2.12 Justification of study

The literature review was structured following these three areas which identified gaps in the literature but also provided useful information in relation to moderate intensity exercise for people with Type 1 diabetes:

2.12.1 The challenges that people with Type 1 diabetes experience when exercising.

A major factor that instigated this current study was that people with diabetes were anxious about exercising, with their main concern being hypoglycaemia. The primary strategy adopted to prevent hypoglycaemia was to precipitate hyperglycaemia by consuming CHO before and after exercise, particularly at bedtime (Brazeau et al 2008, Kilbride et al 2011a, Wallymahmed et al 2007). It was apparent that the lack of understanding surrounding insulin pharmacokinetics made insulin adjusting difficult to use as a preventative measure for patients (Brazeau et al 2008, Kilbride et al 2011a). The difficulties experienced by patients suggested a lack of evidence-based education or information to encourage and achieve current exercise recommendations (Diabetes UK 2012, SIGN 2010, WHO 2010). The evidence supports the initial presumptions regarding the importance of this current study.

2.12.2 The self-management algorithm design

There were no published self-management algorithms identified for direct use in patient care. All the research was performed in the laboratory environment, studying one aspect of self-management (Grimm et al 2004, Peter et al 2005, Rabasa-Lhoret al 2001, West et al 2010). This current study will attempt to pool all related evidence regarding self-management strategies before and after exercise together, in order to

provide one resource in the form of a self-management algorithm. However, in order to do this, gaps in the evidence, and discrepancies in experiential opinions for moderate intensity exercise were identified regarding: 1) Insulin adjustment after 3 hours of insulin administration, 2) pre-exercise CHO intake, 3) target blood glucose concentrations, and 4) post-exercise insulin and CHO adjustment, for prevention of delayed hypoglycaemia risk. The algorithm design was devised after considering the appropriate key messages from individual studies, and the experiential opinions in the absence of experimental evidence, as described in section 2.8.

2.12.3 The study environment

No research was found comparing environments or research, based in a real-life environment. The impact of a self-management algorithm in the current study was analysed in both the laboratory and real-life environments, and was the first time that this approach was used.

Comparisons between glycaemic responses in the two environments would provide information about the reproducibility of laboratory research findings into everyday life scenarios. However, glycaemic variability surrounding exercise in both environments was described by authors (Kilbride et al 2011b, West et al 2010), but further clarification is needed.

2.13 Conclusion

A self-management algorithm is essential to fill the gap in current research with regard to self-management after moderate intensity exercise in real-life. This should incorporate strategies to prevent hypoglycaemia to assist people with Type 1 diabetes perform normal exercise, at a commonly preferred time of the day i.e. before an evening meal. It would also provide HCPs with evidence-based guidelines evaluated during real-life situations which is an essential part of holistic patient education (Perry and Gallen 2009, Rabasa-Lhoret et al 2001), and will support patients achieving the current recommendations for exercise (Diabetes UK 2012, SIGN 2010, WHO 2010.

Therefore, the aim and objectives of the current study are:

Aim:

To test the effectiveness of a self-management algorithm for adults with Type 1 diabetes, during moderate intensity exercise within and outside the laboratory environment.

Objectives:

1. To examine the effects of a self-management algorithm on glycaemic control during a running session of 40 minutes exercise at 70% VO_2 max and also for the following 12 hours in the real-life environment.
2. Propose self-management algorithm adjustments to prevent hypoglycaemia and improve glycaemic control in the real-life environment.
3. To investigate the impact of the environment (real-life versus laboratory) on blood glucose concentrations during and after the exercise session.

Chapter Three

Methodology

In this chapter the study design is described and justified.

3.1 Research approach.

A quantitative study design was selected for this study as objective measurements and statistical analysis were appropriate for data analysis. There were no requirements for the researcher to ascertain descriptions of personal self-management, attitudes, and perceptions from participants that were related to performing exercise.

A quasi-experimental design was selected, as this design type involved selecting groups and observing changes which occurred over time as a result of an intervention (Bryman 2008). In relation to the current study, the participants performed 40 minutes of moderate intensity exercise both in a laboratory environment and a real-life environment. The effects of the intervention, being the self-management algorithm, were analysed in both environments, and the blood glucose concentrations were analysed over time, between baseline and up to 12 hours post-exercise for changes and differences between environments.

Quasi-experiments are often used in natural settings, where the use of an artificial environment is inappropriate to use in order to answer the research question (Gerrish and Lacey 2009). This was a key issue with the current study where the laboratory exercise sessions were controlled by the researcher and possibly such sessions could be considered as an artificial environment. However, the real life environment sessions were performed outside where the participant chose to jog or run and therefore provided strong ecological validity in the study (Bryman 2008). This inferred that the findings from the real-life sessions could be applied directly into everyday lives of people with Type 1 diabetes when they perform exercise at a similar intensity.

Although it is acknowledged that a randomised controlled trial (RCT) is the gold standard for experimental studies (Bryman 2008), it was considered inappropriate to

randomise participants into comparison groups for the current study. One participant group would have to be a control group which meant they would have to self-manage their diabetes (adjust insulin and CHO amounts). However, the participants within a control group may use different methods to adjust their insulin and CHO intakes with some having more success than others. In order to overcome this problem, the control group would be given guidelines regarding self-management, though some may class this advice as an intervention (Bryman 2008). Such a procedure has the danger of making the standardisation of the control groups' self-management and subsequent analysis difficult. However, in a quasi-experiment design there is no control group, and participants act as their own control, hence individual differences would have less of an effect. For these reasons a quasi-experiment was chosen for the present study.

3.2 Population and sample

The study used a purposive sampling technique to ensure suitable participants were approached, which resulted in the recruitment of nine participants. This particular technique was appropriate because of the rigorous inclusion and exclusion criteria and the necessity not to involve non-exercising participants, as the intensity and duration of the exercise may have been too difficult to achieve for non-exercisers. A power calculation was not performed for this pilot study due to the lack of related research and evidence.

The inclusion and exclusion criteria for the participants are listed below. These criteria were selected to ensure that the study aim and objectives were achievable and that patient safety was assured.

Inclusion

- People with Type 1 diabetes for over 2 years duration: This time period was decided because within 2 years of diagnosis, pancreatic function is often fluctuating. For example, if a person was producing their own insulin on a study day, then the resulting hypoglycaemia would bias data, since the injected dose of insulin or the exercise performed, would not have contributed directly to the hypoglycaemic episode.

- Between 18 – 60 years old: People under 18 years old often have erratic glycaemic control caused by fluctuating hormone levels, which again could bias results. There were also concerns that the use of the exercise protocol at 70% VO_2 max may prove difficult for some older people, in view of the cardiovascular risk.
- HbA1c under 10.0%: An HbA1c over 10% is regarded as poor glycaemic control (SIGN 2010). These patients rarely have blood glucose levels under 12.0mmol/l and may have difficulty achieving the starting pre-exercise blood glucose level of 8.0mmol/l. There is also the risk of diabetic ketoacidosis caused by reductions of insulin doses within the algorithm.
- Using basal bolus insulin regimen with fast-acting analogue insulin: This is the most common insulin regimen for active people with Type 1 diabetes, and allows greater flexibility to manage lifestyle activities.
- Hypoglycaemic awareness: A complication of suffering Type 1 diabetes for a long-time is the potential to lose the ability to detect hypoglycaemia, which can result in moderate and severe episodes. For participant safety, it was essential that they were able to detect falling blood glucose concentrations during the exercise sessions. Patients were also at possible risk of delayed hypoglycaemia especially at night, and so study participation may put people at risk if hypoglycaemic awareness was impaired.
- Participates in exercise twice a week or more: 70% VO_2 max exercise is of moderate intensity and the study required participants to jog for 40 minutes whilst maintaining the level of intensity. A person not familiar with regular exercise may find this intensity uncomfortable.
- English speaking: It was considered unsafe to have a person included within the study if the guidelines describing insulin doses, for example, were not clearly understood. If the participant did not understand how to perform the real-life exercise sessions, or to follow the algorithm, then these problems may put them at risk and also bias results.

Exclusion

- Pre-Proliferative/Proliferative retinopathy: This condition may be exacerbated during the strenuous exercise sessions causing retinal bleeding.

- Neuropathy/Foot ulceration: Running may cause increased pressure within a training shoe, and could cause friction and potential skin abrasion that could progress to ulceration.
- Blood Pressure >150/90: Hypertension is an indicator of cardiovascular disease. This study requires exercise at 70% VO_2 max which may increase the risk of cardiovascular problems.
- Cardiovascular disease / history of angina: Increased exercise levels causing hypertension could exacerbate angina, myocardial infarction or stroke.
- Orthopaedic problems: This may inhibit the participant from running, or cause deterioration of an orthopaedic condition.

Suitable participants who attended two large NHS hospitals within one Health Board were identified via the local diabetes database. At the time of recruitment, the data base had 261 (Hospital A) and 99 (Hospital B) eligible participants who fell within the inclusion and exclusion criteria. However, it was unknown if these patients were regular exercisers as this data was not collected on the database. The invitation stipulated that to participate in the pilot study they must exercise at least twice a week. The Invitations from the Diabetes Specialist Nurse and Consultant Physician containing the relevant study information were posted to these eligible participants over a four-month period (see appendix 2). The other students named on this patient information sheet performed separate exercise studies, and the potential participants could choose which study to take part in.

3.3 Methods and data collection instruments

To answer the research questions and to examine the effects of exercise and the self-management algorithm strategies on blood glucose, the instruments used to collect data included blood glucose monitors and participant diaries (see appendix 3). The data collection was carried out over two, four-day periods on days 1 - 4 and 8 – 11 as shown below in Table 3.1.

Table 3.1

Three-week study period: This is an example of a study schedule. Days 1 and 8 could be performed on any day between Monday and Wednesday, with subsequent days 3 and 10 on any day between Wednesday and Friday.

Week 1	**Any day of the week**
Environment	**Pre-test Laboratory session**
Exercise	Sub-maximal incremental walking test performed on treadmill
Data collection and tasks performed	1. Study rationale and design explained 2. Study checklists completed 3. Consent performed 4. TrueResult blood glucose meter demonstrated 5. Study schedule and visit dates decided. 6. GP information letter sent

Week 2	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
Week 3	**Day 8**	**Day 9**	**Day 10**	**Day 11**	**Day 12**	**Day 13**	**Day 14**
Environment	**Laboratory session:**	**No exercise**	**Real-life session:**				
Exercise	Treadmill running which was programmed using their personal 70% VO_2 max Measurements.		Running using Polar wrist watch and Training Heart Rate				
Data collection	**Data collection methods start:** 1.Self Blood Glucose Monitoring 2.Continuous Blood Glucose Monitoring	**Continue: 1, 2, 3, 4.**	**Continue: 1, 2, 3, 4.**	**Data collection methods stop**			

	3.Monitoring diary 4.Hypolycaemia diary						

3.3.1 Self-management algorithm

The self-management algorithm as shown in Table 3.2 was followed by participants on days 1, 3, 8 and 10. The algorithm incorporates evidence and experiential opinions that were found in the literature review and discussed in the previous chapter. The participant copy did not contain references to support each section.

Table 3.2

Algorithm for Insulin and Carbohydrate adjusting for exercising at 70% VO_2 max

Before exercise

Lunchtime insulin

- If exercising within 2 hours of eating a meal, reduce the bolus/meal dose by 75%. *(Rabasa-Lhoret et al 2001, West et al 2010).*

Blood glucose

- Aim for blood glucose of 8mmol/l immediately before exercise.
- If blood glucose over 12mmol, check for ketones and take a correction dose.
- If blood glucose over 17mmol **do not** exercise *(American Diabetes Association 2002, Ertl and Davis 2004, Gallen 2004, Riddell and Perkins 2006).*

Food

- If blood glucose under 8 mmol/l have the following carbohydrate (*DAFNE 2002, Grimm et al 2004)*:

Blood glucose prior to exercise	Amount of CHO (g)
Under 4	30
4 - 6	20
6 - 8	10
8 or over	0

After exercise

Bolus/meal insulin

- Eat within 2 hours of exercise and reduce the bolus/meal dose by 30% *(Ertl and Davis 2004, Gallen 2004, Rabasa-Lhoret et al 2001, Riddell and Perkins 2006).*
- After 2 hours return to usual dose

Long acting insulin

- Take usual Lantus or Levemir dose *(Peter et al 2005).*

Blood glucose

- If blood glucose at 8 mmol/l or under before bedtime have 10-20 grams of CHO.

3.3.2 *Blood glucose monitoring*

For the purpose of the study, frequent blood glucose monitoring was essential to determine the effects of the algorithm described in Table 3.2, and the environment effects on glycaemic control. To ascertain the blood glucose concentration of an individual, the only current methods are invasive: Self Blood Glucose Monitoring (SBGM), Venepuncture then sending samples to a laboratory, or a Continuous Glucose Monitor System (CGMS). Venepuncture is painful, time-consuming and resource intensive, with delayed time for obtaining the result, and so SBGM and CGMS were the chosen methods.

A. Self Blood Glucose Monitoring

Participants were required to perform SBGM prior to each bolus insulin dose and meal which was equivalent to four times a day. The tests taken by participants were also used for CGMS calibration. For the exercise sessions, SBGM was performed at baseline, 20 minutes during and 40 minutes after exercise. This was to detect that the glucose concentration was safe for participants. Another SBGM test was also carried out before the following meal and insulin dose. These tests used whole blood and gave point of time results. During the data collection period, to confirm hypoglycaemic episodes, participants were also asked to test and record results whenever they suspected having a low blood glucose concentration. SBGM was used for analysis from baseline to before evening meal time-points (table 3.3), as immediate results were required during the exercise session and the CGMS would not be recording results within the first 2 hours.

There are a multitude of self-blood glucose meters on the market. The TrueResult blood glucose system was chosen because of ease of use, size (ideal for carrying in the real-life sessions), precision and the wide glycaemic test range which is beneficial for accurate measurements down to 1.1mmol/l (Home diagnostics 2009).

B. Continuous Blood Glucose Monitoring System

*C*GMS was described by Maia and Araujo (2007) as an effective management tool to identify postprandial hyperglycaemia and to detect hypoglycaemia. The Minimed iPro was the monitor used in this study which showed an accurate overall assessment of the past, present and immediate future of glycaemic status (Klonoff 2005). The

CGMS does not directly measure glycaemia, but the glucose concentration in the subcutaneous interstitial fluid which mimics the fluctuations in glycaemia (Melki et al 2006). Previous studies comparing CGMS and SBGM tests reported a time lag between results and real-time (Melki et al 2006) and this has been a cause for concern amongst HCPs regarding the accuracy of CGMS data. However, a recent comparison during sessions of 50% VO_2 max exercise showed a good correlation between the two methods of testing (Kilbride et al 2011b).

The participants were connected to the CGMS prior to the exercise sessions on days 1 and 8 and then removed 3 days later. To ensure accuracy, a minimum of one SBGM result during every 24 hour period was added into individual participants' CGMS database, to allow for correlation of results after the system was removed and downloaded. To increase precision, the four pre-meal tests were also included, with any additional hypoglycaemic test results. The SBGM results were extrapolated from the monitoring diary. In the current study, data were recorded every 10 minutes for the two, four-day data collection periods. The whole data-set is important as hypoglycaemic episodes may have been missed especially during the night and it was considered inappropriate to instruct participants to perform frequent SBGM tests (Melki et al 2006). Patients often experience undetected hypoglycaemic or hyperglycaemic experiences (Deiss et al 2006), which would go unnoticed without a CGMS method of recording, and therefore the usage was essential for the recognition of these conditions. CGMS results were used for analysis for the 2 to 12 hour time-points shown in Table 3.3.

3.3.3 Monitoring diaries

On day 1, the participants were advised how and when to record data using monitoring diaries, which were in a paper format (appendix 3). However, it was acknowledged that accuracy was dependent on the participants being conscientious and fastidious. The diaries were used to record:

1). Blood glucose concentrations.

These measurements were recorded before each meal at breakfast, lunch, evening and bedtime. Extra tests were advised if participants felt any hypoglycaemic or hyperglycaemic symptoms to enable prompt treatment.

2). Insulin dose.

The insulin dose data collection was essential to ensure participants had followed the algorithm. The usual insulin dose plus the adjusted dose were recorded to clarify that a 30% fast-acting analogue reduction had been given. This strategy within the algorithm would affect the overall data and therefore documentation to verify that this procedure was performed was considered vital.

3). CHO intake.

This part of the data collection and its accuracy could be subjective to the participant. Some participants may have been CHO counting for a long-period of time which may have instilled complacency in some, as was often seen in clinical practice. The importance of the accuracy in CHO counting was highlighted on day 1. The intake was checked when participants experienced hypoglycaemia to ensure the cause was not due to decreased CHO consumption. Participants were asked to consume the evening meal within 2 hours of finishing the exercise session.

3.3.4 Hypoglycaemia diaries

The hypoglycaemia diary is shown in Appendix 3. For the current study, hypoglycaemia was defined as: participants experiencing symptoms of hypoglycaemia confirmed with a SBGM of <4.0 mmol/l, or a SBGM <4.0 mmol/l without symptoms. These parameters followed the SIGN (2010) guidelines, although it has been acknowledged that some studies described in the literature review used lower concentrations (Grimm et al 2004, Rabasa-Lhoret et al 2001, West et al 2010). The term “severe” hypoglycaemia was used if help was required from a third party to instigate treatment. If hypoglycaemic unawareness occurred and participants experienced hypoglycaemic symptoms, but had a SBGM > 4.0 mmol/l, they were also asked to complete the diary. The CGMS also recorded hypoglycaemia and the data sheets highlighted blood glucose < 2.2mmol/l. This would ensure that if participants were unaware of the development of nocturnal hypoglycaemia or even failed to awaken, the CGMS monitor would confirm overnight glucose concentrations. In the diary, the time of hypoglycaemia in relation to exercise was reported, because it was essential to differentiate between possible causative factors within the algorithm, and to ascertain whether exercise was the cause of the episode.

3.4 Exercise intensity and study equipment

The equipment used to perform the study included heart rate monitoring and exercise equipment. The type of exercise chosen to perform at 70% VO_2 max exercise, was running. In the laboratory sessions, which were situated in the University, the treadmill was the piece of equipment that was considered best to replicate running in a real-life environment. The 70% VO_2 max and 40 minute duration of the laboratory exercise session, was precisely controlled, and measured safely and effectively by participants running on a motor-driven treadmill (Potteiger 2010). The intensity was controlled by manipulating the speed and grade to ensure that 70% VO_2 max was achieved, as pre-determined by the pre-test described in section 3.4.2.

3.4.1 Exercise Intensity

Exercise intensity can be monitored by three different methods (Wilmore and Costill 2004): 1). the training heart rate (THR), 2). metabolic equivalent (ME) or 3). ratings of perceived exertion (RPE).

1). Training Heart Rate

Measuring the heart rate is the recommended method for clarifying exercise intensity as it is closely correlated with the energy and heart expenditure (Wilmore and Costill 2004). The THR is a measurement of heart rate that is equivalent to a percentage of an individuals' VO_2 max. The THR range is an accurate method because if the exercise period utilised more energy and oxygen consumption, the individual would run to the same heart rate. This fact is important, as external variables i.e. weather conditions or ground conditions may affect the toughness of exercise and could be different on both real-life exercise session days.

2). Metabolic Equivalent

The ME relates to the oxygen requirements needed for energy expenditure required for certain activities, but is an approximation and does not account for individual variables i.e. metabolic efficiency, physical conditioning and environmental factors. The metabolic efficiency and physical conditioning can vary between participants. For real-life sessions environmental factors such as the weather, inclines and hills, and road or grass surfaces can affect performance and exercise intensity.

Consequently, the ME was not incorporated into the data collection methods of this current study.

3). Ratings of Perceived Exertion

The RPE is a method of subjectively measuring the intensity of exercise, and is a simple and convenient tool to use (Karavatas and Tavakol 2005). Individuals rate the intensity of exercise by matching their physical state and perceived exertion with a comparable numbered scale (Wilmore and Costill 2004). However, one commonly used scale called the BORG scale (1998) has been criticised for reliability and consistency (Chen et al 2002, Karavatas and Tavakol 2005). Also a meta-analysis of RPE scales showed inconsistencies regarding the ratings and physiological measures i.e. heart rate (Chen et al 2002). The ratings can also be influenced by current mood, motivation and other emotional factors at the time of the test (Pandolf 1982). An individual's RPE is subjective and for these reasons, this method was also not chosen for use in the current study.

When evaluating a specific type of physical activity and its possible effects, it was important to ensure that the equipment, techniques and protocols were designed for the item being measured (Potteiger 2010). With regard to this, the THR was used. During the laboratory exercise sessions, the intensity of 70% VO_2 max was established by following the individual treadmill speed which was determined from the sub-maximal incremental walking tests described in section 3.4.2. However, during the real-life sessions, it was more difficult to achieve this scenario. From the THR, each participant was given an individual heart rate measurement to achieve during the real-life sessions, which gave a low and high range of heart rate specific to their 70% VO_2 max. The use of a Polar wristwatch and by exercising within the THR parameters, was the easiest way for the participants to ensure they were performing exercise at 70% VO_2 max when in real-life sessions. This ensured that in both environments, the same exercise was performed.

3.4.2 Pre-test: Sub-maximal incremental walking test

A sub-maximal incremental walking test (appendix 4) was designed by a member of the research team (Kilbride et al 2011b) and was performed to determine 70% VO_2 max, which is acknowledged as moderate intensity exercise. The test consisted of 3

minute workloads with progressive increments in treadmill speed and gradient. For this test, the participants were given the opportunity to familiarise themselves with walking on the treadmill and were fitted with a heart rate (HR) monitor (Polar) and a face mask for a breath gas analysis to measure VO_2. During the test, the HR and VO_2 were recorded at the last 30 seconds of each stage. The blood glucose concentration was also recorded using SBGM at the beginning, at 10 minutes into the test and at the end. The end-point of the test was at, or just before 85% of the participant's age-predicted maximum HR. For safety reasons, however, in the event of a monitoring system failure or if a participant experienced chest discomfort, light-headiness, confusion, dyspnoea, nausea, blood glucose under 4mmol/l, or overall feelings of discomfort, the test was terminated. The pre-test was essential to standardize the exercise intensity.

3.5 Study procedure

The study ran over a three week period (Table 3.1) for each participant. The three-week time-period was necessary to accommodate laboratory room bookings, opening times and equipment use, whilst also avoiding weekends for CGMS downloading. Within the study period, participants visited the laboratory for three exercise session visits, and performed two exercise sessions in a real-life environment, which took place in an area outside and chosen by the participant. The visit checklists and procedures used throughout the study can be found in Appendix 4.

3.5.1 Week 1: Pre-test laboratory session

The study checklists and consent (Appendix 4) were performed at the pre-test laboratory session prior to performing the pre-test. The study design was described to the participant and questions were discussed. The pre-test was performed, then the study schedule described below and shown in Table 3.1 was discussed, and the following exercise session dates were decided with the participant before they completed the visit. The participants' GP was informed by letter as shown in Appendix 5.

3.5.2 *Weeks 2 and 3: Laboratory treadmill sessions*

The following weeks on Day 1 and 8, the participants attended the laboratory. Data collection methods were explained and commenced prior to the exercise session. On arrival the CGMS was connected to the participant, SBGM was demonstrated and the participant performed a test under observation to ensure they were able to use the meter correctly. Monitoring and hypoglycaemia diaries were discussed again and participant usage and accuracy was highlighted. Information sheets to explain usage were given to emphasise verbal information.

Exercise was performed 3 hours after administering the previous fast-acting analogue dose of insulin and the lunchtime meal. It was considered important to determine the time of the previous dose and meal because exercising within 3 hours may result in fast-acting analogue insulin still circulating and thus increase the risk of hypoglycaemia. Participants administered their normal lunch insulin dose and had the usual amount of CHO for that insulin amount. Participants had previously been asked not to consume afternoon snacks to ensure no food was eaten within 3 hours of the exercise session. The self-management algorithm (table 3.2) was used when the participants had tested their pre-exercise blood glucose using the SBGM.

Participants then undertook a 40 minute period of treadmill running in the laboratory environment whilst following the self-management algorithm. Blood glucose concentrations using the SBGM were taken at baseline before exercise commenced, 20 minutes into the exercise session and also 40 minutes at the end of exercise. If participants felt that their blood glucose was changing, it was checked for reassurance and safety. CGMS was not used for the exercise sessions because the system can take up to two hours to calibrate and to start recording blood glucose concentrations.

3.5.3 *Weeks 2 and 3: day 2 and 9 with no exercise*

An explanation was given to participants that no exercise should be taken on days 2 and 9 in between the laboratory and real-life exercise sessions. This was because of the risk of exercise causing hypoglycaemia, and thereby influencing the following days' glycaemic control and glycogen stores on days 3 and 10. Participants should

not have experienced any hypoglycaemia episode 24 hours prior to undertaking a study exercise session, because there is an increased risk of a further occurrence (Graveling and Frier 2010). It was important to stress during the discussions on days 1 and 8, delayed hypoglycaemia experienced after the effects of exercise could prevent participants from performing in the real-life sessions.

3.5.4 *Weeks 2 and 3: Real-life exercise sessions*

On Day 3 and 10, participants undertook their own running session at 70% VO_2 max outside the laboratory environment either outside or in a chosen sports hall, whilst following the self-management algorithm. This part of the experiment was discussed on days 1 and 8 when the data collection methods were explained. Again, exercise was performed 3 hours after administering the previous fast-acting analogue dose of insulin and meal and the importance of this was highlighted for the reason described in the laboratory session section. Only running was performed, and participants were asked not to use a different type of exercise, in order to replicate the laboratory session.

The controlled exercise session within the laboratory was replicated in real-life exercise by participants using the Polar wristwatch and the THR, thus ensuring, when possible, the maintenance of 70% VO_2 max. This was a difficult situation to replicate and was dependent on the participant following guidelines. The participant had to observe their heart rate and duration of exercise during the session. Again participants tested their blood glucose via SBGM at the start of exercise for baseline measurements, 20 minutes later and 40 minutes at the end of the session. If participants felt hypoglycaemic or thought that their blood glucose was changing, they were advised to perform extra tests. At this time, however, although the CGMS was recording blood glucose, to reduce possible variability between blood glucose testing systems, the SBGM was used only for data collection. There should have been no differences in the replication of the laboratory session into real-life, and to achieve this, the participant had to conduct it themselves without the researcher to prompt, check the timings, and observe that the THR was within the correct range.

3.6 Validity and Reliability

From the participant inclusion criterion and study design, some issues may affect the data collected. A confounding internal variable described a component that may have an effect on the findings of the effectiveness of an intervention (Bryman 2008). For the current study the confounding variables suspected were: glycaemic control, participant data collection, equipment and selection bias.

With regard to glycaemic control, one variable to consider could be the participants' different levels of glycaemic control. There are several issues involved here, the first being that participants with higher HbA1cs or erratic glycaemic control, may find it difficult to achieve the target starting blood glucose of 8.0mmol/l. This may result in participants having lower starting glucose concentrations (which would result in CHO consumption) or higher than the target level, which could cause prolonged hyperglycaemia at 20 minutes and 40 minutes at the end of the session. Also, depending on the level of hyperglycaemia, a postponement of the exercise session may be necessary.

If participants experienced different hypoglycaemic awareness they may classify hypoglycaemia as different glucose concentrations i.e. under 3.0, 3.5 or 4.0mmol/l, which could be another confounding variable. In this study the frequency of hypoglycaemia is a measure to determine the effectiveness of the algorithm, and it was crucial to collect accurate data. In an attempt to alleviate these issues, the participants were informed at all sessions that a hypoglycaemic episode is a blood glucose episode of 4.0mmol/l or less, and any episodes measured at this level should be recorded.

Another variable could be the equipment being used and the data collection methods. Measurement validity is concerned with the measurement tool reflecting the concept it was supposed to denote (Bryman 2008). As described earlier, all participants used the same equipment and were instructed on the usage, with written information to support understanding. All these factors assured the validity of the study. Education and the reinforcement of this information were given at all study visits, especially on the importance of accuracy of recording-keeping in diaries.

Selection bias may occur as this quasi-experiment used participants who were available and willing to participate (Parahoo 1997). The inclusion and exclusion criteria used in the current study was narrowly defined, however most people with Type 1 diabetes use basal bolus regimens, and by keeping the HbA1c level under 10% excluded individuals with very poor glycaemic control, who may have had difficulty achieving the target starting blood glucose. It was also deemed to be important that to test the algorithm on participants, they should be experienced exercisers who could perform the exercise intensity and duration required. Also participants performed exercise in both environments and acted as their own control which lessened variability.

External variables described by Parahoo (1997) are in relation to applying findings to similar populations in different settings. The individuals recruited in this study were motivated and had a positive approach with regard to their general and diabetes health. After the study, if the algorithm is used outwith the study environment and in patients' everyday lives, it would be envisaged that individuals wanting to use the algorithm would be motivated to want to exercise and maintain acceptable glycaemic control.

3.7 Ethical considerations.

Prior to performing this research, issues regarding patient protection were reviewed. Bryman (2008) described the following four main issues that support ethical principles: patient safety, informed consent, confidentiality, and deception. These issues are concerned with patient protection but can also be applied to the researcher to ensure safe and competent care (Nursing and Midwifery Council 2007, Royal College of Nursing 2009). The current study was approved by a local and national ethics committee who considered patient safety and the method used for patient consent, which ensured these issues were safeguarded.

3.8 Data analysis

To establish the effectiveness of the algorithm a comparison was made between the controlled laboratory exercise and the participants' real-life exercise. Participant data were analysed on all four exercise days, plus days 2 and 4 and up to the 12 hour post-exercise period of days 4 and 11.

Days 1 and 8 were compared to examine laboratory exercise and glycaemic response, and also days 3 and 10 to determine real-life exercise and the glycaemic response whilst following the algorithm. Analytical comparison was made between days 1 and 8, and 3 and 10, to establish differences in controlled exercise compared to real-life, and to answer the question whether the algorithm can be applied to the real-life situation. Data analysis from the real-life exercise sessions underpinned algorithm amendments.

Ten time-points detailed in Table 3.3 were selected for measurement and analysis, as these were specific time-points that would allow the examination of treatment adjustment strategies. For the data between base-line until before evening meal, the SBGM recordings were used, and between 2 – 12 hour time-points the CGMS recordings were used. A description is given below for the time-points that correspond to each algorithm section:

a). During exercise. The time-points of baseline, 20 minutes mid-way and 40 minutes at the end of the exercise session are incorporated into this algorithm section. These data will correspond to pre-lunch insulin dose adjusting, the starting blood glucose and CHO consumed prior to exercise.
b). Before evening meal within 2 hours of end of exercise. This time point will provide information regarding the need for CHO consumption at the finish of exercise, which was not incorporated into the algorithm.
c). 2 - 6 hours post-exercise. The time-points of 2, 4, 6 hours after the evening meal will be used in this algorithm section. These data will analyse the effect of reducing the evening meal fast-acting analogue dose by 30%.
d). 8 – 12 hours post-exercise. The time-points of 8, 10, 12 hours after evening meal will be used in this algorithm section. These data will relate to basal insulin dose adjustments or CHO consumption at bedtime.

Statistical analysis was performed using IBM Statistic Package for Social Sciences software (version 18, SPSS inc. Chicago, IL), for data storage and basic analysis. The units of analysis were based on blood glucose concentrations. All data were checked for suitability for parametric analysis then analysed using repeated measures of variance (ANOVA) on 3 factors (two environments x 10 separate time

points x two separate exercise sessions in week 1 or 2) with Bonferroni adjustments to demonstrate differences. Time-points are shown in Table 3.3.

Table 3.3
The algorithm strategies and sections with the time-points for analysis to influence algorithm adjustment. X= the time-point to be used for analysis.

Time-points	Baseline	20 minutes	40 minutes	Before evening meal	2 h	4 h	6 h	8 h	10 h	12 h
Pre-exercise fast-acting analogue dose reduction	×	×	×	×						
Pre-exercise blood glucose target	×	×	×	×						
Pre-exercise CHO amounts	×	×	×	×						
CHO consumption at finish of exercise				×	×					
Post-exercise fast-acting analogue dose reduction				×	×	×	×			
Long-acting analogue reduction								×	×	×
Pre-bed blood glucose target						×	×	×	×	×
CHO consumption at bedtime						×	×	×	×	×

To evaluate the effectiveness of the algorithm descriptive analysis was also performed to evaluate the number of participant episodes for glucose ranges of: hypoglycaemia (≤4.0mmol/l), 4-9mmol/l and hyperglycaemia (≥9.0mmol/l) at each time-point. This was performed as extreme outliers may not be highlighted on statistical analysis.

The data analysis would confirm whether the algorithm maintained acceptable glycaemic control. The findings would either instigate refinements within the algorithm, or allow the prediction of glycaemic control whilst exercising at moderate intensity when following the algorithm to prevent hypoglycaemia or hyperglycaemia. The comparison of environments would also show whether laboratory research can be applied to clinical practice and real-life scenarios.

Chapter Four

Results

4.1 Introduction

The following chapter will describe the findings of the study.

4.2 Participant demographics

Nine participants that matched the inclusion/exclusion criteria (five males, four females) were included in the study. All participants completed the study and performed all exercise sessions. No participant failed to perform an exercise session due to hypoglycaemia in the preceding 24 hours. The demographic data are presented as means ± standard deviation: age 39.3 years ± 10.5 (range 24 – 56), BMI 24.8 ± 1.7kg/m², weight 75.6 kg ± 6.2 kg, HbA1c 7.9 ± 0.7 %, duration of diabetes 16.8 years ± 14.2 (range 4 – 46 years). All performed CHO counting and insulin dose adjustments using an analogue basal bolus regimen. The insulin types were: fast-acting analogue: Humalog (n=3), Novorapid (N=6), and basal analogue: Lantus once daily (n=7), Levemir (n=1), Isophane taken three times a day (n=1). All participants engaged in exercise for more than two sessions a week. All had hypoglycaemic awareness, with no long-term complications or orthopaedic problems.

4.3 Statistical analysis

This was performed using the mean blood glucose concentrations and standard deviations, and a 3-way repeated measures test (ANOVA).

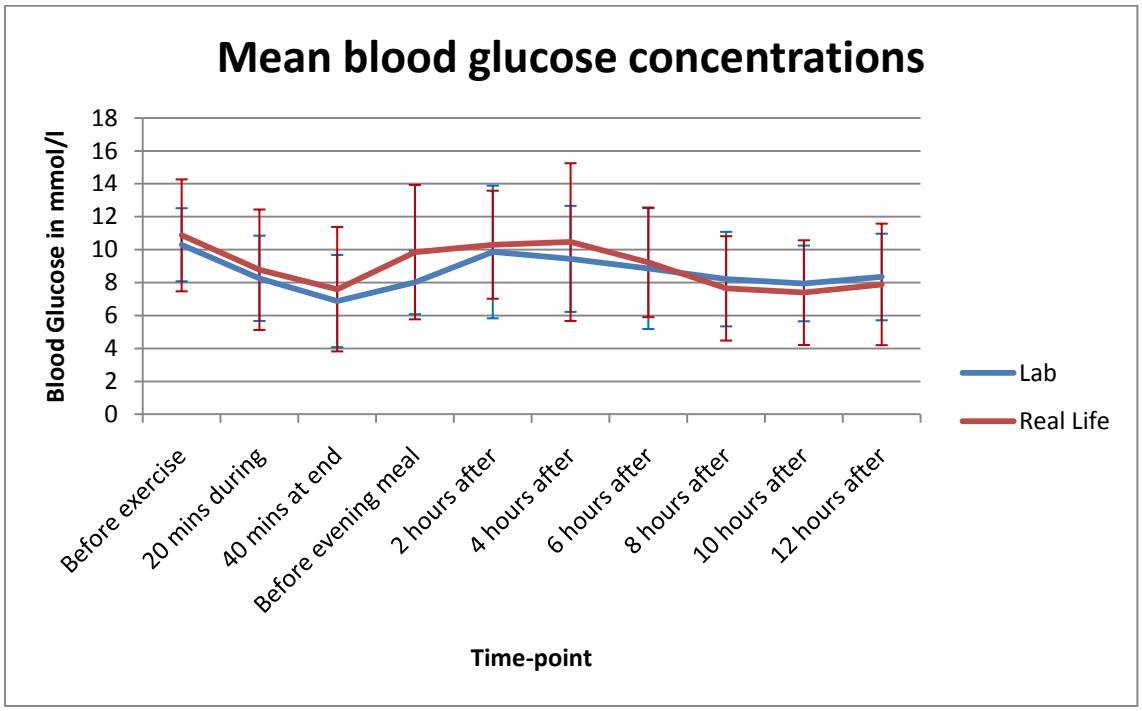
4.3.1 *Mean glucose concentrations*

The pooled data of mean glucose concentrations taken at the specific time-point with standard deviations in the laboratory and real-life sessions are shown in Table 4.1. Figure 4.1 displays the comparison between environments. The mean glucose concentrations revealed similar results in both environments. However, the glucose concentrations appeared to be more variable at the real-life time-points which were recognised by the larger standard deviations, compared with the laboratory time-points (Table 4.2).

Table 4.1
The mean glucose concentrations (and standard deviations) at each time-point in the laboratory and real-life environments.

	Baseline	20 minutes during exercise	40 minutes at end	Before evening meal	2 h	4 h	6 h	8 h	10 h	12 h
Laboratory Blood glucose (mmol/l)	10.3 (2.2)	8.3 (2.6)	6.9 (2.8)	8.0 (1.9)	9.9 (4.0)	9.4 (3.2)	8.9 (3.7)	8.2 (2.9)	8.0 (2.3)	8.3 (2.6)
Real-life blood glucose (mmol/l)	10.9 (3.4)	8.8 (3.7)	7.6 (3.4)	9.9 (4.1)	10.3 (3.3)	10.5 (4.8)	9.2 (3.3)	7.7 (3.2)	7.4 (3.2)	7.9 (3.7)

Figure 4.1
A comparison of mean glucose concentrations in laboratory and real-life sessions. The error bars represent standard deviations.



4.3.2 *Environmental differences between exercise sessions*

Data were tested for normal distribution and suitability for parametric analysis using the mean glucose concentrations at all time-points together with tests of normality using the Kolmogorov-Smirnov test. The significant levels ranged between 0.131-

0.200. A quantile-quantile (Q-Q) scatterplot revealed a straight line at all time-points, the linearity of the points suggested that the data were normally distributed. Hence, parametric statistical tests were used as a normal distribution was demonstrated.
The 3-way ANOVA was conducted to explore any differences in glycaemic control between: environment, exercise sessions and time-points. Bonferroni adjustments were used to control the probability of finding Type 1 errors. Statistical significance was set at $p<0.05$. Data are presented as means ± standard deviation.

The four exercise sessions were analysed using a 3-way ANOVA to investigate differences in blood glucose measured in mmol/l across the 10 time-points, in the two environments, and in the two sessions (i.e. week one and week two). The 3 factors were: environment (laboratory (L) or real-life (RL)), the time-point (before exercise, 20 minutes during, 40 minutes (end of session), before evening meal, 2 hours after, 4 hours after, 6 hours after, 8 hours after, 10 hours after and 12 hours after), and exercise session (first or second).

Differences between time-points

There was a highly significant main effect on time-point [$F(9, 72) = 4.088$, $p < 0.005$, partial eta-squared = 0.338, which represents a large effect size]. Post-hoc Bonferroni pairwise comparison indicated that the blood glucose at 20 minutes (mean 8.4mmol/l) was significantly lower ($p=0.011$) than before exercise at baseline (mean 10.6mmol/l), with a mean blood glucose difference of 2.20 (se±0.354). A similar significant decrease was also shown between baseline and 40 minutes at the end of exercise (mean 7.2mmol/l) ($p=0.007$) with a mean blood glucose difference of 3.41mmol/l (se±0.511). This demonstrated that a significantly lower blood glucose concentration occurred as a consequence of exercise. There were no significant differences between other time-points, all p-values >0.05.

Differences between environments

One of the principal research questions asked in this study was to establish whether any differences occurred in glycaemic control when using the algorithm in two different environments. With the overall mean glucose concentrations, the 3-way ANOVA verified that the environment did not have a significant main effect on the glycaemic control of participants [$F(1, 8) = 1.489$, $p = 0.257$]. This referred to the

comparison of all mean glucose concentrations for both environments, without examining change in blood glucose over time.

Differences between exercise sessions

The participants performed two exercise sessions in each of the two environments. As described in section 3.5.4, the exercise intensity and duration, and self-management strategies were the same for both environments. It was thought that participants may have become familiar with their exercise sessions and become lenient and diligent in their self-management following the algorithm, thus avoiding an adverse effect on glycaemic control. However, this concern transpired not to be an issue, as there was no significant main effect identified on glycaemic control between the separate exercise sessions [$F(1, 8) = 0.384$, $p = 0.553$].

Interactions between environment, time-points and exercise sessions

When investigating 2-way interactions regarding glucose control between the variables, there were no significant effects on environments and times [$F(9, 72) = 0.499$, $p = 0.871$], or environments and exercise sessions [$F(1, 8) = 0.778$, $p = 0.404$], or exercise sessions and times [$F(9, 72) = 1.616$, $p = 0.127$].

There was also no significant 3-way interaction effect on environments, times and exercise sessions [$F(9, 72) = 1.280$, $p = 0.263$].

4.4 Descriptive analysis

A descriptive analysis was also performed as the characteristics of these statistical tests along with the small participant numbers used would not reveal the extreme glucose episode outliers. It would also describe the blood and subcutaneous glucose results within ranges and the environment differences between time-points, to identify the effects of each specific self-management strategy.

Across the four exercise sessions all data were analysed for the occurrence of glycaemic episodes in different ranges. There were 18 individual participant episodes (9 participants X 2 sessions) for each time-point. The number of participant episodes for glucose ranges of hypoglycaemia (≤4.0mmol/l), 4-9mmol/l and hyperglycaemia (≥9.0mmol/l), were analysed for each algorithm section. The frequency of individual participant episodes for each of these ranges, were stated as

numbers. Table 3.2 in the methodology chapter shows the algorithm section and self-management strategy with the relevant affected time-points. The data obtained from the time-points were reviewed to establish whether algorithm adjustments were required. These adjustments were based on patterns and trends of glucose results.

Table 4.2 shows the percentage of episodes for each blood glucose range (SBGM for baseline to before teatime) and subcutaneous glucose measured by the CGMS (2 to 12 hours), in the time-points within the algorithm sections. The percentages were not based on the whole time-period but only the specific algorithm section and the number of individual measurements during the time-point range.

Table 4.2

A summary of episode percentages and numbers in the algorithm sections for each glucose range.

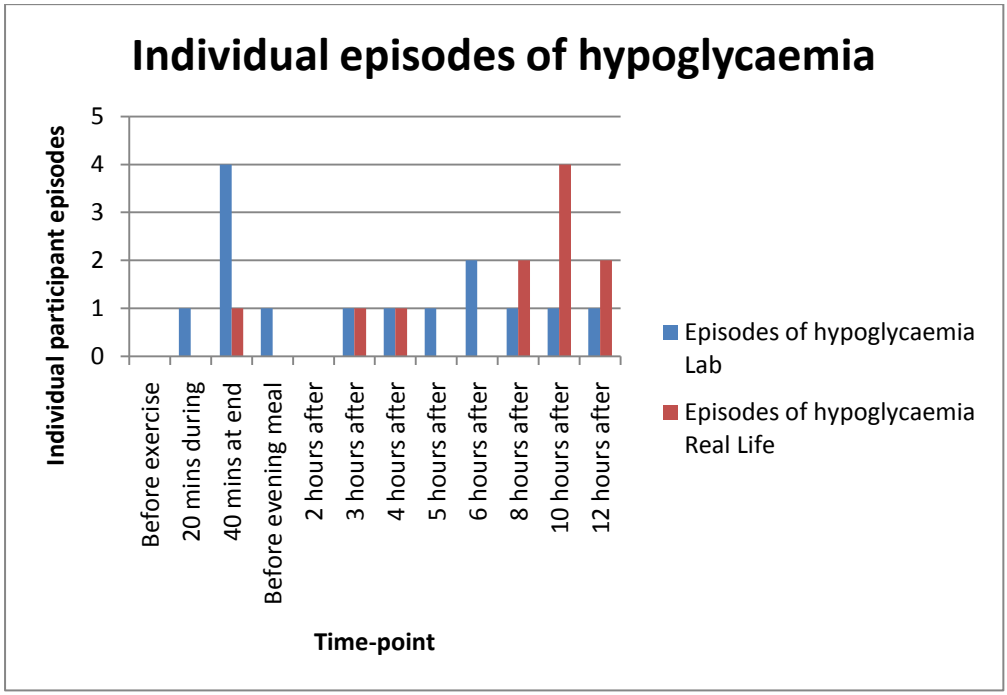
Algorithm section	**Baseline-40 minutes**		**Before evening meal**		**2 – 6 hours after**		**8 – 12 hours after**	
Environment	**Lab**	**Real-life**	**Lab**	**Real-life**	**Lab**	**Real-life**	**Lab**	**Real-life**
Blood glucose range								
Under 4mmol/l	13.9% (5)	2.8% (1)	5.6% (1)	0 (0)	5.6% (3)	1.9% (1)	5.6% (3)	14.8% (8)
4 – 9mmol/l	52.8% (24)	77.8% (34)	55.6% (10)	50% (9)	46.3% (25)	46.3% (25)	53.7% (29)	61.1% (33)
Over 9mmol/l	33.3% (25)	19.4% (19)	38.9% (7)	50% (9)	48.1% (26)	51.9% (28)	40.7% (22)	25.9% (14)

4.4.1 ≤ *4.0mmol/l or hypoglycaemia range*

With reference to a concentration < 4.0mmol/l the terminology “hypoglycaemia” was used. Because hypoglycaemia is a major problem for people with Type 1 diabetes in their ability to perform exercise, its prevention was therefore an important challenge in this study. It was essential to analyse the data and the frequency of hypoglycaemia in the participants in order to determine the effectiveness of the

algorithm, and the changes that were necessary to increase the probability of hypoglycaemia prevention. The statistical analysis used mean blood glucose concentrations which meant that hypoglycaemic concentrations would have been undetected. The chart shown in Figure 4.2 demonstrates the hypoglycaemic episodes in the laboratory and real-life environments at each of the ten time-points.

Figure 4.2
Number of individual episodes of glucose concentrations of ≤ 4.0mmol/l at each time-point at two sessions, and in both environments. Participant number = 9.



As demonstrated in Figure 4.2, prior to the start of exercise no participants in either the laboratory or real-life groups were hypoglycaemic. During exercise, 36% (5 episodes) of all hypoglycaemic episodes for the whole laboratory study time-period occurred at this time-point. However, at this time-point in the real-life environment, the frequency of hypoglycaemia was lower (1 episode). Before the evening meal, hypoglycaemia was reduced to only one episode after the laboratory session. At the 2 – 6 hour algorithm section, increased hypoglycaemia occurred after the laboratory sessions compared to the real-life sessions.

In order to identify any hypoglycaemic episodes, it was decided to view all CGMS data after exercise for low subcutaneous glucose concentrations out-with the 2 hourly time-point intervals. Additional hypoglycaemia episodes were noted at 3 hours for both laboratory and real-life sessions (1 episode each) and 5 hours, for laboratory (1 episode) and zero for real-life environments. For the following 8 – 12 hour algorithm section, there was a change in the occurrence of hypoglycaemia between environments, with increased episodes in the real-life sessions. Furthermore, during the real-life sessions and for the whole 12 hour period, the highest number of hypoglycaemic episodes were recorded at this time-point (8 episodes), which accounted for 73% of all hypoglycaemic episodes over the whole time-period.

For the whole experimental period from baseline to 12 hours post exercise, in the laboratory sessions 7.0% (14 episodes) and the real-life sessions 5.5% (11 episodes), of episodes were hypoglycaemic glucose concentrations. Of the participants in this study, 8 out of 9 experienced at least one episode of symptomatic hypoglycaemia or a glucose concentration ≤ 4.0mmol/l within the study period (minimum number = 1 , maximum number = 3).

These observations were based on episodes of glucose concentrations and not determined through statistical analysis.

Hypoglycaemic unawareness

From the data, hypoglycaemic episodes were extrapolated from the hypoglycaemia diaries and CGMS. When an episode was noted in the CGMS data sheets, but not recorded in the monitoring or hypoglycaemia diaries, and the SBGM result was not used for CGMS calibration, it was presumed that the participant was unaware of their low glucose value. Hypoglycaemic unawareness was noted in 32% (8 episodes (laboratory=5, real-life=3)) of the 22 episodes, plus 3 episodes at 3 and 5 hours. These episodes occurred in different participants at time-points between 4 – 12 hours, when participants were probably asleep.

Hypoglycaemia on non-exercising days

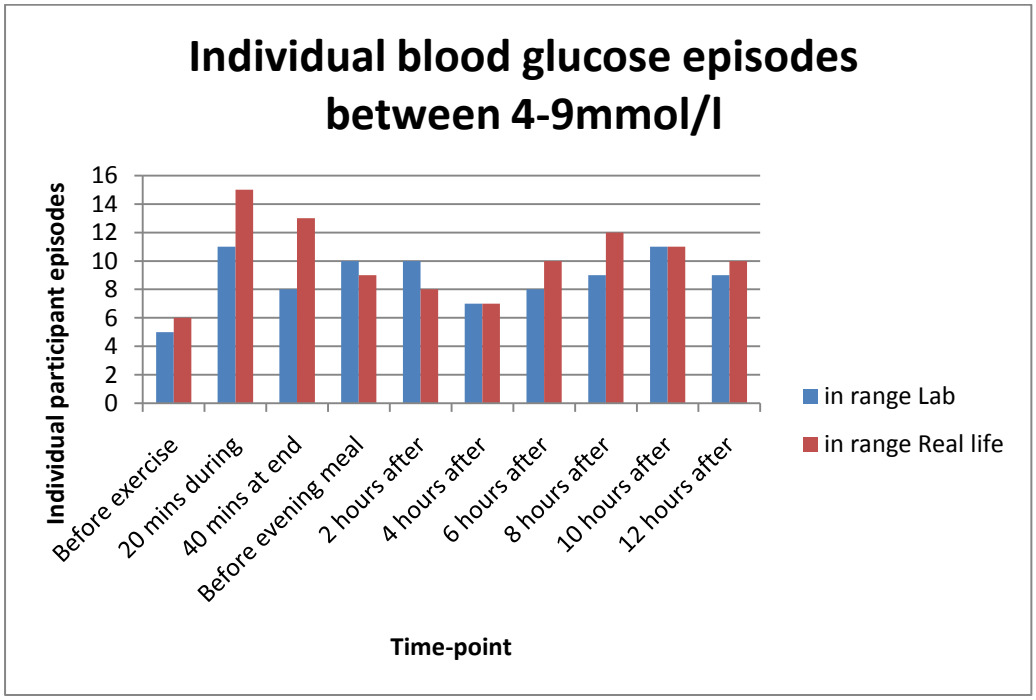
To identify whether the hypoglycaemia episodes were an effect of exercise or just a normal consequence of Type 1 diabetes, the hypoglycaemic episodes were

analysed from SBGM, CGMS and hypoglycaemia diaries on non-exercise days (day 2 and 9). Three hypoglycaemic episodes occured at 3, 6 and 12 hours after evening insulin injections and CHO intake. For two of the individuals, a hypoglycaemic episode occurred at the same time on exercise days, which suggested that this was a normal feature for the individual and not the result of increased physical activity. The frequency of hypoglycaemia was much less on non-exercising days which clarified the assumption that exercise caused hypoglycaemia. It also suggested that the algorithm needed further modification in order to achieve similar results as demonstrated on non-exercising days.

4.4.2 *4 – 9 mmol/l or acceptable glucose range*

The blood glucose range decided as an acceptable target level in this study was set between 4-9mmol/l. It was necessary to ascertain the frequency of episodes within this target range to determine the effectiveness of the algorithm, and also when comparing both environments to establish whether differences had occurred. Figure 4.3 demonstrates the episodes within the 4-9mmol/l range in both environments at each time-point. There were 18 individual participant episodes for each time-point in both environments.

Figure 4.3
Number of individual episodes of glucose concentrations in the target range of 4-9mmol/l at each time-point in two sessions, within both environments. Participant number = 9.



In the algorithm, the target starting blood glucose concentration was 8.0mmol. Because it was extremely difficult to achieve a specific blood glucose value, the range of 7.5-8.5mmol was chosen to represent an in-target value. From 18 participant episodes (9 participants X 2 sessions), this was achieved in 22% (4 episodes) of laboratory participants and 5.6% (1 episode) of real-life participants. However, the use of the 4-9mmol/l target, gave similar starting results in both environments as shown in figure 4.3.

With a higher starting blood glucose concentration of ≥9mmol/l (see Figure 4.4) the commencement of exercise caused the blood glucose concentration to drop. After the first 20 minutes of exercise, a drop in blood glucose was demonstrated in both environments (Figure 4.3). The blood glucose concentration continued to drop during the next time-point which resulted in increased hypoglycaemia (Figure 4.2), and subsequently a slight decline was recorded by 40 minutes in the 4-9mmol/l range. However, when combining the whole period of time during exercise, 52.8% (19

episodes) of episodes in the laboratory sessions and 77.8% (28 episodes) of those in the real-life sessions were within the target range (4-9mmol/l).

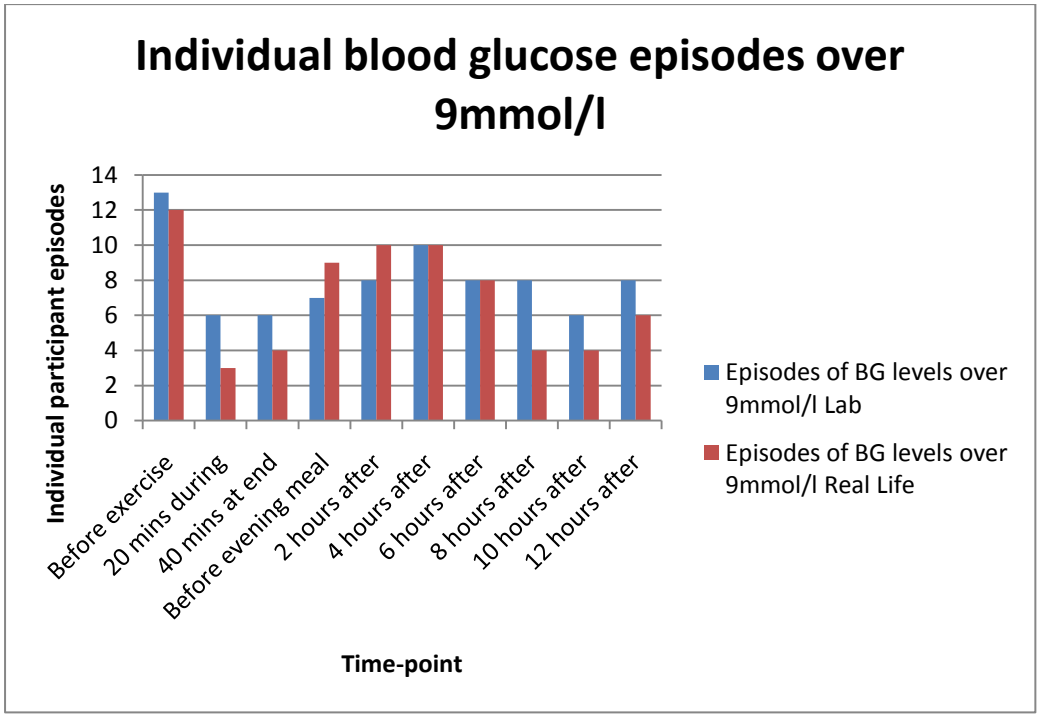
After the initial effects of exercise and the lowering of blood glucose concentrations, approximately half of the participants before the evening meal, achieved 4-9mmol/l values in both environments, which also continued during the 2 – 6 hour algorithm section, and did demonstrate a decline in hypoglycaemic episodes which coincided with CHO consumption. During the following algorithm section of 8 - 12 hours after the evening meal, the participants achieved slightly better glycaemic control (laboratory 53.7% (29 episodes), real-life 61.1% (33 episodes)), but a decline in episodes occurred at the 12 hour time-period. This corresponded with changes at the same time-period in glucose concentrations ≥9.0mmol/l (Figure 4.4).

Overall, the patterns suggested that the real-life sessions achieved greater 4-9mmol/l episodes compared with the laboratory sessions, except before the evening meal and 2 hours after the exercise time-points. For the whole of the experimental period from baseline to 12 hours post-exercise, in the laboratory sessions 51.2% (83 episodes) and the real-life sessions 57% (95 episodes), episodes were in the acceptable range. However, these observations were based on episodes of glucose concentrations and not determined through statistical analysis.

4.4.3 ≥ *9.0mmol/l or hyperglycaemic glucose range*

In this study, hyperglycaemia was classified as a glucose concentration of 9.0mmol/l or above. It is appreciated that often people with Type 1 diabetes purposely aim for higher blood glucose concentrations before, during and after exercise, in an attempt to prevent hypoglycaemia. The rationale supporting the algorithm design was an attempt to maintain acceptable glycaemic control and the prevention of hypoglycaemia and hyperglycaemia and corresponding symptoms.

Figure 4.4
Number of individual episodes of glucose concentrations ≥ 9mmol/l at each time-point for two sessions within both environments. Participant number = 9.



A high number of participants started with an elevated blood glucose concentration, which did not delay the start of exercise, and no participant administered extra fast-acting insulin at this point. In both environments during exercise, the pattern of hyperglycaemic episodes dropped from baseline to the 20 minute time-point and remained at a similar episode frequency until 40 minutes at the end of the exercise session. The number of participants who experienced blood glucose concentrations over 9.0mmol for the whole exercise time period was: laboratory sessions 33.3% (12 episodes) and real-life sessions 19.4% (7 episodes).

From the end of exercise to 4 hours after the evening meal, the pattern of hyperglycaemic episodes increased, and measurements taken before the evening meal probably coincided with a decline in physical activity and glucose-lowering effect of the lunchtime insulin dose. Four hours after the evening meal, hyperglycaemia was anticipated because of a blood glucose increase after CHO consumption. Between 4 and 12 hours after the evening meal and fast-acting

analogue injections, there was a decline in the incidence of ≥ 9.0mmol/l episodes, which corresponded with an increase in nocturnal hypoglycaemia (Figure 4.2).

For the whole experimental period from baseline to 12 hours post-exercise, in the laboratory sessions 41.3% (67 episodes) of participants and in the real-life sessions 35.8% (58 episodes) of participant episodes had glucose concentrations over 9mmol/l. From the monitoring diaries there appeared to be no difference in CHO consumption between environments and exercise sessions, which could cause hyperglycaemia.

4.5 Time point glucose trends

Although the sample size in the current study was small, there was consistency between the two environments with each time-point glucose trend or change in direction from the previous time-point, apart from 4 hours after exercise (Table 4.5). The 4 hour time-point also showed the greatest standard deviation in the real-life sessions (sd ± 4.79) (Table 4.2). The trends appeared to be consistent with the predicted changes in glycaemia relating to physiology: a blood glucose decline during exercise, a rise in glucose concentrations after exercise and CHO consumption, a decline 4 to 12 hours after the evening meal and fast-acting analogue insulin injection, when delayed hypoglycaemia was a risk. Despite these trends being detected, their statistical significance has not been demonstrated, however they will be useful for patient education.

Table 4.3

Blood glucose trend at time-points

	Laboratory glucose trend	Real-life glucose trend
20 minutes	Lower	Lower
40 minutes	Lower	Lower
Before Tea	Higher	Higher
2 hours after	Higher	Higher
4 hours after	**Lower**	**Higher**
6 hours after	Lower	Lower
8 hours after	Lower	Lower

10 hours after	Lower	Lower
12 hours after	Higher	Higher

4.6 Conclusion

The 3-way ANOVA test showed no differences in glycaemic control when following the algorithm in the laboratory and real-life environments, but significant differences were demonstrated between time-points during exercise, confirmed also by the mean blood glucose values in Figure 4.1. However, when a descriptive analysis was performed using episodes of glycaemic ranges i.e. hypoglycaemia, 4-9mmol/l and hyperglycaemia, two important differences in glucose concentrations were apparent. The first difference between environments involved the hypoglycaemia episodes during and at 40 minutes at the end of exercise with higher episode numbers in the laboratory environment. While the second difference was apparent during the 8 to 12 hour period after the evening meal and fast-acting analogue insulin injection with an increase in hypoglycaemic episodes in the real-life environment. However, it is acknowledged that these differences were observed patterns and thus were not statistically analysed. The increased hypoglycaemic episodes were acknowledged for patient safety, which highlighed the potential risk and possible deterrent for people with Type 1 diabetes involved in physical activity.

Chapter Five

Discussion

5.1 Introduction

In this chapter the results of the study will be discussed in conjunction with other related literature to emphasise the importance of this research, and its contribution to the evidence base. Each algorithm section will be discussed separately. In view of the first two study objectives, the real-life environmental data and corresponding self-management strategy will be analysed. The similarities and differences with regard to the glycaemic response in different environments will also be discussed in each section to determine if a particular environment has differences regarding patterns and frequency of episodes of glucose concentrations.

Before exercise

When evaluating the algorithm sections before performing exercise, the blood glucose response and in particular, any hypoglycaemic episodes during exercise are important factors to consider. This will determine the effect of the administered insulin dose and CHO consumption prior to exercise.

5.2 Pre-exercise algorithm section and effect on glycaemic control during a 40 minute exercise session.

The 3-way ANOVA showed a significant blood glucose decrease at time-points during the 40 minute exercise session (see table 4.2). This anticipated glucose decrease as described by several authors (Peter et al 2005, Rabasa-Lhoret al 2001, West et al 2010), resulted in five episodes of hypoglycaemia in the laboratory environment during exercise, compared to only one in real-life. One possible explanation for the difference in hypoglycaemia episodes may be related to the fact that participants during real-life exercise were not exercising as intensely. If they were performing at a lower VO_2 max, this would cause less hypoglycaemia, caused by a lower glucose value being required for energy production (Nagi 2005). When participants controlled their exercise intensity during real-life sessions without supervision by a member of the research team, compared with supervised sessions

in the laboratory they were able to decrease their intensity as they wished. However if this was the case one would not expect the finding from this study which showed a greater increase in nocturnal hypoglycaemia after the real-life sessions, as described in section 5.6.

Another possible explanation for the increased hypoglycaemic episodes observed during exercise in the laboratory environment agreed with the findings of Brazeau et al (2008). When analysing barriers to exercise, hypoglycaemia was a major deterrent, however if participants exercised with another person this significantly resulted in fewer anxiety episodes caused by the hypoglycaemia risk ($p<0.001$). This was an interesting observation, because in the laboratory environment, the researchers constantly observed the participants, and regularly checked their physical state, hence, they may have felt safe, compared with the real-life environment, when they were without a researcher which may have instigated participants to take preventative strategies. However, the participant's monitoring diaries did not show increased CHO consumption during real-life sessions, a finding one might have expected if participants had used preventative strategies.

The real-life sessions demonstrated better glycaemic control with more episodes in this target range (4-9mmol/l). In both environments, at 20 minutes into exercise, there was an increase in 4-9mmol/l episodes, which declined by 40 minutes which was a result of increased hypoglycaemia. This however, was expected due to glucose usage for energy and falling blood glucose concentrations as described by Nagi (2005).

Finally, when considering blood glucose episodes over 9.0mmol/l, in both environments the mean blood glucose value was similar although higher than the target at baseline. This observation agrees with Wallymahmed et al (2007), who noted that patients' aim for hyperglycaemia prior to commencing exercise. These reasons were not explored for study participants starting with a higher blood glucose concentration in our study, however Rabasa-Lhoret et al (2001) and West et al (2010) both described hyperglycaemic baseline concentrations. One can only speculate that participants had possibly self-managed to achieve a higher blood glucose concentration, or had difficulty in achieving such a specific glucose value of

8.0mmol/l. During the pre-assessment visit at week one, participants were not given guidance regarding insulin doses or CHO consumption at lunchtime on exercise days, although they were informed of the target blood glucose concentration of 8.0mmol/l at the start of the exercise session. However, by starting with higher blood glucose concentrations, glucose was utilised for energy and caused an increase of episodes into the acceptable range of glucose during exercise (Riddell and Perkins 2006). During the exercise sessions in both environments, the number of hyperglycaemic episodes decreased from baseline to 40 minutes and was the anticipated effect caused by glucose transfer into skeletal muscle for energy usage (Riddell and Perkins 2006). Another factor to consider was that the mean starting blood glucose values were higher in both environments. If 8.0mmol/l had been achieved, there may have been more hypoglycaemic episodes during exercise.

Due to these results, the pre-exercise self-management strategies in the algorithm worked well in the real-life environment, as only one hypoglycaemic episode out of a possible 36 episodes occurred, and 77% of glucose episodes were within the acceptable range. Unfortunately, these results cannot be compared because similar research was unavailable in the literature. The causative self-management strategies will now be discussed along with algorithm adjustments.

5.2.1 *Pre-exercise fast-acting analogue dose reduction*

When considering physiological response to exercise, insulin dose reduction is a logical self-management strategy to prevent hypoglycaemia prior to exercise (Riddell and Perkins 2006, Ertl and Davis 2004). The current study design involved the use of the full normal dose of fast-acting analogue insulin at lunchtime before the exercise, and no studies were found where exercise started 3 hours after the insulin dose. However, since performing the original literature review and this current study, Iscoe and Riddell (2011) published a similar study which investigated the effects of exercise 5 hours after insulin administration. Their aim was to compare the delayed risk of hypoglycaemia and hyperglycaemia in athletes with Type 1 diabetes while performing 45 minutes of continuous moderate intensity exercise (Group 1) and moderate intensity exercise with intermittent high intensity exercise (Group 2); both sessions were performed in the afternoon. Eleven participants were recruited: ages

35.1 ±3.5 years, duration of diabetes 15.6 ±5.6 years, HbA1c 7.8 ±0.4%, six used insulin pump therapy and five used a basal bolus regimen. Participants had interstitial glucose measured by CGMS and analysed for the following 12 hours, although the reported results were not described in time-points but just grouped into one 12 hour period. The glucose was monitored for one sedentary day and one exercise day (randomized to Groups 1 or 2), then repeated 1-4 weeks later for one sedentary day while performing the other exercise type (Groups 1 or 2). On exercise days, it was stated that the lunchtime fast-acting analogue insulin was given 5 hours prior to exercise performed at 1700 hours, designed to mimic the normal exercise time for many people (a factor used in this study design). The time-period is later than exercise performed in this current study, however, due to insulin actions both are similar as out-with the peak action, and within the duration of 6 hours. Post-exercise insulin doses were not reduced. A low GI snack was given to participants at bedtime to prevent nocturnal hypoglycaemia. For the purpose of the comparison with the current study, the data for the moderate intensity exercise group were explored.

Iscoe and Riddell (2011) did not reduce insulin doses prior to exercise, although participants were not given pre-exercise guidelines and were permitted to self-manage how they preferred. The blood glucose decrease during exercise was 5.1mmol/l (±0.7), with 64% of the participants becoming hypoglycaemic during exercise. This high incidence of hypoglycaemia was in contrast to the results observed in the current study. These results reported by Iscoe and Riddell (2011) are confusing because the hypoglycaemia risk should be minimal due to the time when circulating fast-acting insulin would be decreasing after 5 hours. It has to be assumed that this observation was caused by patient self-management prior to starting exercise, despite not being described in the publication.

All other previous studies in the literature review described a fast-acting insulin dose reduction 30 – 120 minutes before exercise (Lumb and Gallen 2009, Rabasa-Lhoret et al 2001, West et al 2010). In the current study, consideration was initially given to reduce the pre-exercise lunch dose by 10 or 20 % but the author decided against this because of the concern regarding hyperglycaemia at the start of the exercise session, since West et al (2010) demonstrated the peak action was 60 minutes after administration, which was before 3 hours used for the start of exercise in the current

study. If participants had reduced their lunch doses during the current study, it would have resulted in even higher glucose concentrations at baseline. To support this factor, pre-exercise insulin reduction resulting in hyperglycaemia at the start of exercise, was demonstrated in both the Rabasa-Lhoret et al (2001) and West et al (2010) studies.

In the current study, the administration of the full lunchtime insulin dose was effective when considering the episodes of glucose concentrations previously described. With regard to the algorithm changes, a reduction for the pre-meal insulin dose was not implemented because of the potential threat of hyperglycaemia, and cancellation of an exercise session from blood glucose concentrations over 17mmol/l as recommended by Lumb and Gallen (2009), American Diabetes Association (2002) and Fery et al (1987).

5.2.2 Pre-exercise CHO amounts

A common strategy used by patients prior to exercise, to prevent hypoglycaemia, is the consumption of extra CHO. From the algorithm, amounts of fast-absorbed glucose in the form of Lucozade and Dextrosol tablets were given to participants depending on the blood glucose concentrations, to achieve the blood glucose concentration of 8.0mmol/l. This was based on DAFNE principles (DAFNE Group 2002), which state that 10g of CHO would raise the blood glucose by 2.5mmol/l, and from the real-life results this appeared to work. For the participants with starting concentrations around 8.0mol/l (n=6), they had glucose concentrations ranging between 4.5-8.0mmol/l at 40 minutes, and the CHO amount taken before exercise appeared to prevent hypoglycaemia. However, one participant with the lowest blood glucose of 6.9mmol/l consumed the recommended amount of glucose but still developed hypoglycaemia (3.8mmol/l). Although this is based on only one participant, the avoidance of hypoglycaemia is of paramount importance and it was recommended therefore that the glucose/CHO amount be increased if the starting blood glucose value was less than 7.0mmol/l as shown in the amended algorithm (table 5.1).

Since performing the current study, an updated literature search revealed one publication by West et al (2011) examining CHO before exercise. The study

compared the consumption of two different types of CHO (Isomaltulose (ISO; low GI) and Dextrose (DEX; high GI)), taken 2 hours prior to a 45 minute running session at 80% VO_2 max, during which the glucose response was measured. Eight participants with Type 1 diabetes performed the study. The pre-exercise starting blood glucose level was 12.2 ± 0.5mmol/l with ISO compared to 15.0mmol/l (no sd presented) with DEX. During exercise there was a similar drop in blood glucose in both groups: ISO 4.4mmol/l ±0.4 vs DEX 5.8mmol/l ±0.3 (p=0.11). Immediately at the end of exercise the blood glucose in ISO group were significantly lower than DEX group (p=0.05). In the 3 hour period after exercise, the blood glucose concentrations were lower in the ISO Group compared with the DEX Group at all time-points (p=0.05). There were no hypoglycaemic episodes in the 2 hours pre-exercise or during exercise. The study concluded that the consumption of ISO prior to exercise maintained more acceptable blood glucose concentrations before, during and after exercise, compared with the consumption of DEX. One limitation of the study was that the ISO and DEX amounts were not stated. Another potential problem present from a participant point of view, were the potential hyperglycaemic symptoms which may have occurred at the start of exercise from high glucose concentrations.

Although this study by West et al (2011) was performed 2 hours prior to exercise, the results were considered sufficiently useful to incorporate them into the amended algorithm (table 5.2), which suggested a low GI lunch could prevent high starting glucose values and ensure a steady CHO absorption rate. Current practice is to consume dextrose prior to exercise, however West et al (2011) demonstrated that a low GI CHO snack or meal before exercise, may be more effective for glucose control.

5.2.3 Pre-exercise blood glucose target

The target starting blood glucose concept was not highlighted in any other similar research (Rabasa-Lhoret et al 2001, West et al 2010). For the current study, this was decided at 8.0mmol/l based on the presumption that hypoglycaemia precipitated by the exercise session was a minimal risk due to the time of the previous insulin injection (West et al 2010). Previous research suggested a starting level of 10 – 15mmol/l (Lumb and Gallen 2009, West et al 2010), which the author considered too high in an ideal scenario in view of patient comfort regarding possible

hyperglycaemic symptoms. However, when designing the algorithm, it was acknowledged that the possible need to increase the target to 10.0mmol/l if hypoglycaemia was detected during the real-life sessions, and to comply with patient preference of hyperglycaemia, to give reassurance and as a preventative approach for hypoglycaemia (Wallymahmed et al (2007).

In the current study, the mean starting blood glucose was 10.9mmol/l (sd±3.4). In the West et al (2010) study, the mean starting blood glucose for the full insulin dose Group, 2 hours prior to exercise was 9.4mmol/l (sx 0.5), and from all those seven participants there were no hypoglycaemic episodes reported. Iscoe and Riddell (2011) did not state the mean starting blood glucose although from the blood glucose graph it appeared to be around 10.5mmol/l. Both of these studies do not specify a target starting blood glucose, although the level may be decided by the participant. Brazeau et al (2008) and Wallymahmed et al (2007) reported that people with Type 1 diabetes aim for higher starting glucose concentrations and the above findings are consistent with this.

The further danger of hyperglycaemia during exercise is the risk of developing ketoacidosis. Since the initial literature review, an additional short report has been published by Bracken et al (2011), which presented analysis from the West et al (2010) study. This sub-section of the study investigated the impact of pre-exercise insulin reductions on ketogenesis after running. They found that large reductions (25, 50 or 75% insulin reduction) in the pre-exercise fast-acting analogue insulin doses did not affect beta-hydroxybutyrate (ketone) formation, to the extent that ketoacidosis occurred. Participants performed a 45 minute run at 75% VO_2 max, beta-hydroxybutyrate concentrations were then tested at the end of the run and up to 3 hours after. Ketoacidosis was defined as beta-hydroxybutyrate concentrations ≥3.0mmol/l (normal range 0.0 – 0.6mmol/l). Results showed normal beta-hydroxybutyrate concentrations during exercise. Immediate post-exercise beta-hydroxybutyrate concentrations demonstrated a significant increase which ranged between 0.03mmol/l to 0.06mmol/l ($p > 0.05$). However, all of these values are in the normal range, and are not therefore a cause for concern. Unfortunately the corresponding blood glucose concentrations were not stated. These values would have been useful in interpreting data into clinical practice.

These new data provide reassurance that hyperglycaemia caused by insulin reduction or aiming for a higher starting glucose can be safe strategies for people with Type 1 diabetes, although the findings are in contrast to recommendations and guidelines previously stated by the American Diabetes Association 2002, Fery et al 1987, and Lumb and Gallen 2009. These studies all advise avoidance of exercise if blood glucose is over 17mmol/l. However, they do not take into account the recent findings from Bracken et al (2011), which suggested that by considering the recent glycaemic pattern and if a solitary pre-exercise high concentration is caused by exercise-insulin reduction, it is safe to exercise. This knowledge will be highlighted in the amended algorithm.

It is acknowledged this current study had a small sample size, but in view of all the above, along with the low hypoglycaemia risk, the target blood glucose concentration before exercise could safely remain at 8.0mmol/l. It will be highlighted that glucose concentrations less than this may increase the risk of hypoglycaemia. However, if patient preference is a higher starting concentration, this is safe to do so but consideration must be given to the recent glycaemic pattern and to ensure fast-acting analogue insulin is in circulation (Bracken et al 2011), plus overall glycaemic control (HbA1c).

<u>After exercise</u>

Next to consider are the glucose concentrations and self-management strategies for the 12 hours following exercise which will be analysed and incorporated into the post-exercise section of the algorithm.

5.3 End of exercise prior to the evening meal

In both environments before the evening meal a similar glucose pattern was demonstrated, which showed an increase in mean blood glucose concentrations and hyperglycaemic episodes from the end of the exercise session to the evening meal. This corresponds with the physiological description by Riddell and Perkins (2006) whereby gluconeogenesis and glycogenolysis was increased in response to increased energy demands during exercise. As described by West et al (2010), the last fast-acting analogue insulin dose was administered at lunchtime in the current

study, and it would be expected to peak therefore around 60 minutes, with a duration of 5 hours, so the hypoglycaemic action would thus end by the evening meal. This would account for the increasing blood glucose concentrations in both environments at this time-point.

The blood glucose concentration taken before the evening meal provided information regarding any self-management interventions between the end of exercise and the evening meal. Carbohydrate consumption at the end of the exercise sessions were not included in the algorithm, as no evidence was found in the literature to support this, apart from an experiential opinion by Gallen (2004) who recommended consumption of CHO to prevent hypoglycaemia. This was an area of uncertainty in the algorithm design when relating the exercise sessions to physiology that there might be two outcomes. The first being hypoglycaemia as glycogen stores would be replaced at the end of exercise (Montague et al 2005), or hyperglycaemia due to glycogenolysis and the depletion of lunch insulin (Nagi 2005).

The results used to clarify this notion was the use of the 3-way ANOVA pairwise comparison between 40 minutes and before the evening meal which showed a non-significant difference in the change in blood glucose between time-points ($p=0.803$), and so hypoglycaemia was not a potential risk, and during the real-life sessions hypoglycaemic episodes did not occur. Also examining the trend of blood glucose in Table 4.4, revealed blood glucose to be on the increase, although this is not statistically proven. This would suggest that if CHO was consumed at the end of exercise, increased hyperglycaemia would result. Since the initial literature search, there have been no new publications in relation to this topic. Due to these factors, CHO at the end of exercise will not be introduced into the amended algorithm.

5.4 The effect on glycaemic control during 2-6 hours after insulin and evening meal.

The following algorithm section was 2-6 hours after the evening meal. Again there was little difference between environments for the mean glucose concentrations during this time-period, although one of the main issues in this algorithm section was glucose variability which was the highest in both environments within the full 12 hour

study-period with standard deviations at time-points ranging between; 3.2 – 4.0mmol/l in the laboratory, and 3.3 – 4.8mmol/l in real-life. Factors that could cause this increased variability is the GI of the CHO type consumed at the evening meal, and also activity levels, where many people will be inactive during this period before bed. This finding cannot be compared with Iscoe and Riddell (2012) as they did not report the time of the glucose concentrations. Glucose variability in individual participants is an important factor to consider regarding reproducibility of findings, and is discussed further in section 5.7.

Similar glucose patterns occurred in both environments, participants achieved exactly the same number of episodes within the range of 4-9mmol/l, and there were also similar frequencies of increased hyperglycaemia. This response of increased blood glucose concentrations from before evening meal were expected because of the absorption of CHO food and 30% dose reduction of pre-meal fast-acting analogue insulin and there were no changes in prevailing insulin to CHO ratios. These two self-management strategies relating to this algorithm section are discussed below.

5.4.1 *Post- exercise fast-acting analogue dose reduction.*

Post-exercise insulin reduction after exercise is not a commonly used strategy in clinical practice despite hypoglycaemia risk due to physiological actions (Riddell and Perkins 2006, Ertl and Davis 2004). In the current study, in order to evaluate the strategy of 30% fast-acting insulin reduction, the time-points at 2, 4 and 6 hours after the evening meal were examined which coincided with the insulin peak action and duration.

The frequency of hypoglycaemia and hyperglycaemia were considered important physiological factors in this study. In the real-life experiments the statistical analysis showed no differences in blood glucose between environments at the time-points, however, the variability was considerable as shown by high standard deviations. The frequency of glucose episodes in the 4-9mmol/l range (46.3%), and over 9.0mmol/l (51.9%) (shown in Table 4.4), must therefore be considered as well as in the overall mean result. This appears to suggest stable, though slightly higher glucose concentrations, albeit minimal hypoglycaemia. These data were to be expected, as

post-prandial hyperglycaemia is a common phenomenon in Type 1 diabetes and can occur because subcutaneous insulin acts more slowly than absorbed glucose from CHO food. In contrast, Rabasa-Lhoret et al (2001) recommended a post-exercise dose reduction of 50-75%. It is thought that this would cause increased hyperglycaemia as even with the 30% reduction, 52% of results were above 9 mmol/l in the current study.

Again, since the initial literature review there are no new publications on this topic. The similar study published by Iscoe and Riddell (2011) did not adjust the post-exercise dose and only used CHO at bedtime as an intervention to prevent nocturnal hypoglycaemia. From the above data, no amendments were made to the algorithm and that by reducing the dose by 30%, the hypoglycaemia risk was minimised. This approach was also recommended by Lumb and Gallen (2009).

5.5 The effect on glycaemic control during 8-12 hours after insulin and evening meal.

In the next algorithm section which covered the period 8-12 hours after the evening meal, the standard deviations were the lowest in both environments demonstrating less variability. This observation occurred because the participants were asleep, and not performing daily living activities nor consuming CHO, all of which influence blood glucose concentrations. In view of the frequency of 4-9mmmol/l glucose episodes, a slight increase was shown in the real-life environmental studies, but more importantly, differences in the hypoglycaemia and hyperglycaemia patterns were found.

Hypoglycaemia was an important area to investigate in this section, as participants will generally be asleep. The real-life sessions showed an increase in hypoglycaemia episode frequency with eight episodes occurring out of a possible fifty-four participant episodes (15%), compared with three out of fifty-four (5.5%) in the laboratory environment. These data were found in participants CGMS and hypoglycaemia diaries. This observation has not been demonstrated in any previously related research as far as this author is aware, because the reported time-periods were limited to 3 hours post-exercise (Peter et al 2005, Rabasa-Lhoret et al

2001, West et al 2010). However, several authors have commented on the risk of delayed hypoglycaemia, but no research studies appear to be available to demonstrate this (Guelfi et al 2005, Lumb and Gallen 2009, Perry and Gallen 2009, Riddell and Perkins 2006).

Since the initial literature review, described in section 5.2.1, the publication by Iscoe and Riddell (2011) included nocturnal hypoglycaemia analysis, and demonstrated that five out of eleven participants (45%) in the moderate intensity exercise group, experienced glucose concentrations ≤4.0mmol/l during 0300 to 0600 hours, in comparison with non-exercising days where only two out of eleven episodes occurred. This factor was also apparent in the current study during non-exercising days where one episode from a possible 18 occurred during the 8-12 hour time-point. These findings are very similar to the current study despite different self-management strategies being used post-exercise, and Iscoe and Riddell (2011) stated that insulin sensitivity was increased post-exercise and thus accounted for the hypoglycaemic effect. Hypoglycaemia would also be caused by the probable physiological response to exercise and the replenishment of glycogen stores in the liver and muscles (Riddell and Perkins 2006), however, this would not account for the differences between the laboratory and real-life environments.

Due to the delayed glucose lowering effect after exercise (Ertl and Davis 2004), the hyperglycaemic episode frequency decreased in both environments. However, the laboratory hyperglycaemic episodes were greater compared with those in the real-life environment, resulting in 22 episodes compared with 14 episodes respectively. The cause of the hyperglycaemia difference is difficult to interpret, as is the increased hypoglycaemia in the real-life environment. Insulin reductions cause hyperglycaemia, but exercise can also instigate hypoglycaemia. As the exercise sessions were the same in both environments, it is difficult to understand why the physiological response is different between environments, and highlights the need for further investigation.

The self-management strategies applicable to this algorithm section which contributed to these results will now be discussed.

5.5.1 Long-acting analogue dose adjustment

Long-acting insulin or basal dose reduction is a commonly used strategy to prevent hypoglycaemia in clinical practice despite the lack of evidence to support the recommendation. The time-points at 8, 10 and 12 hours after the evening meal were examined in relation to this section of the algorithm. As discussed previously, it was important to avoid hypoglycaemia at these time-points and was highlighted in the real-life environment of the current study when eight hypoglycaemic episodes out of a possible 54 episodes occurred. These data, along with the glucose patterns for the following day, related to the effects of the basal insulin dose.

The study conducted by Peter et al (2005), suggested that Lantus would not be a contributing factor to hypoglycaemia occurring during, or in the 3 hour period, following a 30 minute exercise session at 65% VO_2 max. However, the nocturnal glucose response post-exercise and specifically at the 8 – 12 hour time-period was not studied. In the current study, hypoglycaemia episodes increased during the night, however, the hypoglycaemia frequency decreased during the following day. Considering this observation, it does not appear necessary to reduce the Lantus dose which may cause possible risk of hyperglycaemia the following day. This topic has not been studied by any other researchers and so comparisons cannot be made at this stage. However, it has been recognised that previous authors have suggested the basal dose may need to be reduced (Lumb and Gallen 2009). Since the initial literature review there have been no new publications relating this topic, and in the similar study by Iscoe and Riddell (2011) they did not reduce the basal insulin dose.

5.5.2 Before bed blood glucose concentration and CHO amounts

For people with Type 1 diabetes, the consumption of CHO at bedtime is a customary strategy for the prevention of nocturnal hypoglycaemia, even when exercise has not been performed. The strategy of consuming a bedtime snack was described by Brazeau et al (2008) which showed participants who did this were less anxious about nocturnal hypoglycaemia ($p=0.007$), but unfortunately failed to state if the intervention actually prevented nocturnal hypoglycaemia. In the current study, 10-20g of CHO before bed was advised if the blood glucose was below 8mmol/l at bedtime to prevent nocturnal hypoglycaemia, however, this was not evidence based,

although the DAFNE collaborative (2010) do recommend CHO consumption if the blood glucose is below 9.0mmol/l at bedtime. When reviewing the participants CGMS data, the period between 8 – 12 hours post-exercise corresponded with the early hours of the morning. If increased CHO in the region of 20-40g were given at bedtime this may cause hyperglycaemia within the post-exercise 4 – 6 hour time-period which would be around midnight. Although used at a different time-period, West et al (2011) showed the delay in absorption of low GI CHO, and the subsequent stable effect on glycamic control. Hence, if low GI foods i.e. certain fruits, porridge and cereals containing bran (as stated by Diabetes UK 2012), were consumed at bedtime this would be absorbed slowly and cause a delayed rise in blood glucose. A potential advantage of this over adjusting basal insulin is that it would not have a knock on effect on the full 24 hour time-period as would be the case if the basal insulin dose was reduced.

The recent publication by Iscoe and Riddell (2011) used a bedtime snack strategy. The participants who performed moderate-intensity exercise before the evening meal did not reduce the post-exercise evening meal insulin dose, but consumed a 30g low GI CHO snack at bedtime, without taking fast-acting analogue insulin. The idea behind this snack was to prevent nocturnal hypoglycaemia. However, 45% of participants still experienced nocturnal hypoglycaemia. Unfortunately the individual blood glucose concentrations before bedtime were not stated, although a graph appeared to demonstrate a value of approximately 9.5mmol/l. It was therefore difficult to decipher the change in blood glucose levels during the night. However, the authors stated that the CHO snack at bedtime was insufficient, and reducing the basal insulin dose might be more beneficial.

This CHO strategy may not be accepted by some people with Type 1 diabetes if the main reason for performing exercise is for weight loss or weight maintenance, as extra CHO will contain an increased calorific content. In this instance, the basal insulin dose may need to be reduced. Both basal insulin reduction and the consumption of extra low GI CHO snack are options to prevent hypoglycaemia and should be dependent on patient choice. These options were included in the amended algorithm and patients are permitted to choose their preferred approach.

The consumption of CHO at bedtime may also help alleviate patient anxieties regarding nocturnal hypoglycaemia (Brazeau et al (2008).

In relation to bedtime, a target blood glucose concentration was not stipulated in the self-management algorithm, however, after reviewing the findings, a blood glucose of 10.0mmol/l at bedtime was advised with regard to prevent hypoglycaemia. This will also help patients determine the amount of CHO they consume to achieve this target at bedtime using the DAFNE recommendations (DAFNE collaborative 2010).

5.6 Nocturnal hypoglycaemia risk

When considering hypoglycaemia, issues arose after data analysis, which were not contemplated during the study design. Firstly it was important to ascertain whether exercise caused the overnight hypoglycaemia episodes in participants or whether this was a normal feature of participants diabetes control. Analysis of the overnight glucose results on non-exercising days was therefore performed. This showed that on non-exercising days, one participant had a glucose concentration under 4.0mmol/l at 12 hours compared with eight hypoglycaemic episodes in the real-life exercise session days. This confirms that exercise is likely to be a significant factor in causing overnight hypoglycaemia.

A new and important finding in this study was revealed from the descriptive analysis. This showed that it was apparent from the monitoring and hypoglycaemia diaries and CGMS calibration, that a number of participants were not aware of low glucose episodes during the night whilst asleep. This was a big concern for patient well-being and safety. During the 3 – 12 hour time-points, 18 hypoglycaemic episodes occurred within both environments. From these episodes two participants had an episode that lasted for two consecutive time-points (both after real-life sessions at 8-10 and 10-12 hour time-points) which indicated one extended hypoglycaemia episode. From the 18 episodes, eight were not documented in the participant diaries or CGMS calibrations, and thus it was assumed that the participants had hypoglycaemia unawareness at that time. Iscoe and Riddell (2011) used CGMS in their study, although they failed to stipulate if any nocturnal hypoglycaemic episodes occurred and unawareness was never discussed in previous publications.

The CGMS was an essential data collection tool in this worrying finding, although it had been acknowledged that discrepancies may occur with the time-lag difference (Melki et al 2006) compared with plasma glucose, and that results may be debated with regard to being an accurate low glucose episode, as the results were based on interstitial fluid. These concerns were recognised but considering no other method was available to monitor glucose overnight, other than invasive blood extracting methods, these data were used for the algorithm evaluation.

As delayed hypoglycaemia was shown in this study to be a genuine problem, it is vital to educate patients about the risk, and how it might be prevented. This will be incorporated into the algorithm by recommending occasional SBGM monitoring in the time-period of 8-12 hours post-exercise. This clinical finding needs to be highlighted to HCPs involved in diabetes care, and incorporated into patient education for those who wish to exercise.

5.7 Glucose variability

Another issue not considered in the initial objectives of the current study was the concept of individual variability. Patient individuality is occasionally discussed by expert authors in review articles when recommending exercise management strategies, and they advocate that insulin and CHO adjustments must be tailored to the individual (ADA 2002, Kavookjian et al 2007, Lumb and Gallen 2009, Perry and Gallen 2009). This variability of glucose was also found and described by previous researchers. In the West et al (2010) study which investigated a similar intensity of 75% VO_2 max, authors discussed the problem with the intra-individual variability. They acknowledged that this could contribute to the lack of statistical significance. Also, in the qualitative study described by Kilbride et al (2011a), participants highlighted that any form of exercise provoked inconsistency, unpredictability and variability in glycaemic control. This may be caused by a multitude of external and internal factors i.e. diet, physical activity, stress, lifestyle as discussed by Perry and Gallen (2009) and Riddell and Perkins (2006). In the current study, participants were not asked at exercise sessions if they were experiencing factors such as stress, which may have contributed to any irregularities in glycaemic control. When considering stress, performing in the laboratory environment could be considered as a stressful situation by some participants.

The mean glucose concentrations at each time-point in both environments were similar with a 0.3-0.7mmol/l difference. The exception occurred, however, before the evening meal (1.9mmol/l difference) and 4 hours after (1.1mmol/l difference) with higher levels identified in the real-life sessions (see Table 4.1 and Figure 4.1). The standard deviations of the individual mean glucose results were an important factor to consider. The highest figure was seen at the 4 hour time-point in the real-life sessions, with a blood glucose level of 10.5mmol/l (sd ± 4.8mmol/l). The mean values or the ANOVA used in this current study did not highlight the extreme levels of individual participants episodes of hypoglycaemia nor even those of hyperglycaemia. For this reason a descriptive analysis was also undertaken.

Iscoe and Riddell (2011) presented far lower standard deviations of glucose concentrations after performing 45 minutes of moderate intensity exercise during the evening. Standard deviations were highest in Groups 1 (2.6 ±0.51mmol/l) and group 2 (2.8 ±0.44mmol/l) compared with those from the sedentary days (2.0 ±0.31mmol/l) ($p=<0.05$). Unfortunately there was no information differentiating between types of insulin therapy and demonstrated the erratic effect that exercise can have on glycaemia. When considering glucose variability after exercise, the nighttime minimum and maximum glucose concentrations were between 5.0mmol/l (±0.7) to 12.4mmol/l (±1.3). The night glucose range for the laboratory sessions in the current study were 8.0mmol/l (±2.3) to 9.4mmol/l (±3.2), and in the real-life sessions 7.4 mmol/l (±3.2) to 10.5mmol/l (±4.8). This demonstrated that the actual mean glucose range was wide with small standard deviations (Iscoe and Riddell 2011), compared with the current study which revealed a smaller mean glucose range but large standard deviations. The two study designs were similar, but the main differences in the two studies which may account for the variations observed, were Iscoe and Riddell (2011) controlled the meal-times and CHO amounts consumed throughout the whole study period, whereas the participants in this study consumed their normal amounts at their own decided times. The aim was to try and mimic normal life behaviour and not to dictate times that may indispose participants. Furthermore, in the current study, the post-exercise insulin dose was reduced and participants only consumed CHO at bedtime if their blood glucose levels were under 9.0mmol/l. In the Iscoe and Riddell (2011) study, participants did not reduce post-exercise insulin and consumed a fixed amount of CHO at bedtime. The variability in meal and insulin

injection times may have caused the wider glucose variability in the current study, however, Iscoe and Riddell (2011) demonstrated an increased variability on exercising days compared with sedentary days, which was a similar finding in the current study.

The above issues do question whether a larger study using statistical analysis would show any significant differences in glucose variability as shown by the large standard deviations, and therefore may be beyond the control of the participant or researcher in a real-life study design. Small participant numbers have not helped the situation both in the current study and those of Iscoe and Riddell (2011) and West et al (2010). For a further study, specific timings for meal-times and insulin dosing may be required as a way of reducing glucose variability. However, some variability would be expected because of multiple factors than can affect glycaemic control.

5.8 Effectiveness of the self-management algorithm

Despite variability, when comparing the impact of environments on the glucose response for individual participants, for the whole period from baseline to 12 hours post-exercise, a similar frequency for hypoglycaemic episodes occurred where the laboratory environment had 14 hypoglycaemic episodes, and the real-life environment had 11. However, some differences did occur in the times of the hypoglycaemic episodes as was previously described. Hypoglycaemia prevention was a primary aim of the study, but another was also to achieve glucose values less than 9mmol/l. The results showed that over one-third of episodes, during the whole time-period, were above 9mmol/l, (laboratory environment 40.5% and real-life environment 33.9%). This may be viewed negatively by HCPs, with the implication that the algorithm was ineffective. However, one might consider that 9mmol/l was too tight a target, and some HCPs may aim for a target <11.0mmol/l especially with regard to post-prandial hyperglycaemia in the 2-4 hour time-point range. In both environments, around half of all episodes were in the acceptable 4-9mmol/l range, 48.3% in the laboratory and 53.3% in real-life. This figure could depict that the algorithm was unsuccessful, however, the chosen range of 4–9 mmol/l may be considered by HCPs as too stringent considering the difficulties encountered around exercise. Across the whole time-period of 13 – 15 hours, when considering patient

preference of running blood glucose concentrations higher with exercise (Wallymahmed et al 2007), this figure may be acceptable. Difficulties do arise, however, when making such statements on small sample sizes, together with the challenges of analysing data using descriptive methods rather than statistical tests.

5.9 Summary of self-management strategies and amendments after data analysis

The analysis of each algorithm section with regard to self-management strategies and the effect on glycaemic control have been described. From these factors, a summary of key changes can be seen in Table 5.1, which states the current self-management strategies with new amendments after analysing the data and considering the new evidence since the initial literature review.

Table 5.1
Summary of amendments

Current algorithm	New algorithm
Pre-exercise fast-acting analogue dose reduction: no change to meal bolus insulin dose if taken at least 3 hours prior to exercise	No change
Pre-exercise blood glucose target: To aim for a blood glucose of 8.0mmol/l.	No change
Pre-exercise CHO amounts: CHO amounts as per algorithm (see table 3.2)	For the meal prior to exercise, consume low GI CHO. Immediately prior to exercise if the blood glucose is <7.0mmol/l, increase the recommended amount by 10g extra CHO.
Post-exercise fast-acting analogue dose reduction: Reduce dose by 30%	No change to the 30% reduction
Long-acting analogue: Take usual dose.	Basal insulin to be reduced if patient exercise goal was to lose weight
Pre-bedtime blood glucose concentration and CHO amounts: If blood glucose below 8.0mmol/l take 10-20 g of CHO. No specific target level stipulated.	Consume 20-40g of low glycaemic index food. At bedtime, aim for a blood glucose concentration of 10mmol/l.
	Nocturnal hypoglycaemia risk: It is essential that patients when exercising in the evening occasionally perform a blood glucose test 8-12 hours after administering the evening meal fast-acting analogue insulin dose.

These amendments for the self-management strategies will be incorporated into the self-management algorithm as shown below in table 5.2.

Table 5.2: Amended self-management algorithm

Amended algorithm for Insulin and Carbohydrate adjusting for exercising at 70% VO_2 max

Before exercise
Lunchtime insulin

- Have slowly absorbed carbohydrate and if you are exercising within 2 hours of eating a meal, reduce the bolus/meal dose by 75%.

Blood glucose

- Aim for blood glucose of 8mmol/l immediately before exercise.
- If blood glucose over 15mmol, check for blood ketones and consider taking a correction dose.
- If blood glucose over 17mmol **do not** exercise unless this is: 1). A "one-off" high blood glucose level and previous blood glucose levels have been acceptable, 2). You have given a bolus/meal insulin dose within 5 hours.
- If you have blood ketones over 0.6 **do not** exercise.

Food

- If blood glucose under 8 mmol/l have the following quickly absorbed carbohydrate i.e. sugary drink or dextrosol.

Blood glucose prior to exercise	Amount of CHO (gm)
Under 4	40
4 - 6	30
6 - 8	20
8 or over	0

After exercise
Bolus/meal insulin

- Eat within 2 hours of exercise and reduce the bolus/meal dose by 30%.

Long-acting insulin

- Take usual Lantus or Levemir dose.

Blood glucose

- Before bedtime have 30-40 grammes of slowly absorbed CHO i.e. cereal, banana.
- Aim for a blood glucose of 10mmol/l.
- It is important to test blood glucose occasionally 8-12 hours after evening meal to check for night-time hypoglycaemia.

If you would prefer not to eat CHO at bedtime you can reduce your long-acting insulin, however this can affect your blood glucose for the following 24 hours. You should discuss this with your diabetes team.

5.10 Summary of the impact of the environment

Objective three was to evaluate differences in glucose concentrations between environments. The exercise session environments were designed to mimic each another, and the self-management algorithm used was exactly the same for both environments. Participants were questioned how they would perform the real-life sessions to ensure consistency. One might predict therefore, that there would be no difference between the glucose response in each environment. As described, statistically, no difference was found, but these pilot study findings were based on only 9 participants. The findings cannot be compared with other results in the literature since no studies, as far as this author is aware, have been published comparing environments in this manner. This remains an important issue for patients, because differences regarding hypoglycaemia were shown in the descriptive analysis, but will require further investigation using a larger study, with a full power analysis. From this analysis the following key messages were obtained:

1. Using statistical analysis, the two environments did not have a different effect on the glycaemic control when following the self-management algorithm. This observation must provide reassurance that previous laboratory based research and subsequent findings can be used in patient education to advise on self-management strategies during exercising and subsequently clarify the reproducibility of clinical research in everyday life. However, it must be taken into consideration that the sample size was a limitation of this study. The sample size appears to be a common problem with this type of research and was highlighted by several authors (Iscoe and Riddell 2011, Kilbride et al 2011b, Rabasa-Lhoret et al 2001, West et al 2010).
2. Glucose variability was apparent from the large standard deviations that were demonstrated in both environments, thus supporting previous findings (Jimenez et al 2004, Kilbride et al 2011b, Riddell and Perkins 2006, and West et al 2010). This variability provoked difficulty in extrapolating data, particularly from the statistical analysis with extreme outliers between environments e.g. hypoglycaemia and hyperglycaemia were not highlighted.
3. The descriptive analysis emphasized these outliers, and differences in time-points were found when analysing the mean and individual participant hypoglycaemic episodes. This factor suggested that in the laboratory environment, there was an

increased risk of hypoglycaemia during exercise, and in the real-life environment an increased risk during the night between 8 – 12 hours after insulin doses and the evening meals (also demonstrated by Iscoe and Riddell 2011). In contrast, during the night the laboratory environment demonstrated increased hyperglycaemic episodes. A comparison between other studies with regard to overnight glycaemia cannot be made as data was not presented (Rabasa-Lhoret et al 2001, West et al 2010). With regard to this, it would appear that there was a difference between environments.

The statistical analysis does suggest that laboratory based findings can be applied into a patient's everyday lifestyle when performing a comparable exercise, however, they should be aware of the glucose-lowering effect during exercise and the delayed risk of hypoglycaemia especially 8-12 hours after the post-exercise insulin dose. This is an important finding for patient safety and education regarding prevention of hypoglycaemia, although it has been acknowledged this was not demonstrated statistically.

5.11 Strengths and limitations

It is important that the strengths and limitations of the study are considered. These will be combined with potential amendments and adaptations for a follow-on study which will be discussed in the recommendations chapter.

This study has certain characteristics that make it different to previously-related studies regarding moderate intensity exercise in Type 1 diabetes. No other research was performed where the principal focus was to examine post-exercise self-management strategies, rather than pre-exercise strategies. A key difference supporting a post-exercise focus, was the recording and analysis of the glucose response for 12 hours post-exercise. This included the data collection of the glucose response overnight; a very important time for patients who greatly fear overnight hypoglycaemia. Previous research has only concentrated on the glucose response in the immediate post-exercise time-period. Other research has been performed after breakfast (Peter et al 2005, Rabasa-Lhoret et al 2001, West et al 2010), despite many people exercising or wishing to exercise in the early evening following work.

The timing of the exercise in this study was influenced by patients who described their normal exercise routines, which often was before the evening meal.

As discussed by Bryman (2008), in order to have ecological validity, the study design must incorporate or mimic the real-life situation that is under investigation. This was an important concept in the planning stages of this study and one of the objectives and strengths of the study. This is the only study to incorporate a real-life environment into the study design as all other research, other than case studies by Butler (2006) and Gravelling and Frier (2010) have been performed in a controlled laboratory environment. But despite this, laboratory findings regarding self-management strategies were used by HCPs to advise patients on exercise management in daily life, but they were not evaluated in that environment (Grimm et al 2004, Peter et al 2005, Rabasa-Lhoret et al 2001, West et al 2010). In the current study, the participants managed to perform the required exercise sessions in the real-life environment on day 3 and 10, and this allowed the comparison of controlled laboratory exercise and every-day exercise. This has demonstrated that participants were able to effectively follow instructions which included an ecological component in the exercise study. The combination of these attributes made this study unique, while addressing an important gap in the evidence base.

Another strength of the study is the everyday practicality for ordinary people with Type 1 diabetes to use a commonly-used insulin regimen and exercise. This is important as some of the previous research including expert opinions, has focused on elite athletes and it is therefore not applicable to the more general population. One of the major concerns prior to commencing the study was that of patient compliance with self-management and adherence to the study protocol, and also performing data collection. However, the participants were compliant and adhered to guidelines regarding SBGM, insulin dose, monitoring diaries and also not exercising on days 2 and 9. This was confirmed by a review of the participants' diaries and questioning them during exercise sessions.

Another strength related to the participants' role, was that despite potential difficulties, the participants performed the study without experiencing any significant problems. The patient involvement and interaction were intensive, as were the researcher expectations, and also demands on patient compliance were

considerable when performing such research in a laboratory environment, and even more so when including a real-life component. When conducting a research programme which involves humans, it is important to consider their feelings, both physical and mental, during participation. Despite the intensive demands on the participants, their overall comment of enjoyment was apparent and they felt they developed a greater understanding of the effects of exercise on their body, especially when provided with their CGMS data after the study. Several participants also mentioned the appreciation of support received in the laboratory, and the time and communication with an exercise expert and diabetes nurse. This feedback was reassuring for the research team.

Another strength was the use of CGMS, which was invaluable for overnight glucose monitoring. This method of data collection for glycaemic control had not been used in other similar research (West et al 2010, Peter et al 2005, Rabasa-Lhoret et al 2001). The CGMS enabled frequent glucose monitoring without disturbing the participant whilst sleeping. It also provided data regarding hypo-unawareness. Calibration was not a problem with participants in this study, although occasional blood glucose concentrations were not recorded on the CGMS data sheet. However, this was for short and limited times, and as results were provided every 10 minutes it was not an issue. Concerns regarding measurement validity as described in section 3.6 were not encountered, although the accuracy of these data may be questioned by some HCPs. In the authors opinion the data was valid and applicable for use in clinical care.

There were, nevertheless, several limitations to this study, the main one being the sample size, although in spite of this one significant result was found. Recruitment to the study was more difficult than initially thought, although similar difficulties were noted by other research teams (West et al 2010, Kavookjian et al 2007, Peter et al 2005, Rabasa-Lhoret et al 2001) regarding recruitment for the correct sample size, in order to achieve the statistical power.

One deterrent could have been the commitment in time and effort that was required by the participants to adhere to the demanding study protocol. They performed five exercise sessions over a 3 week period, at a particular time of day, three of which would involve travel to the laboratory. The target population was of working age, had

busy lives and work schedules which may have influenced their decision not to participate in the study. In order to increase participant numbers, further recruitment from other diabetic clinics was an option, however, there was insufficient time to do this.

Another deterrent may have been the strict inclusion criteria which was required for the purpose of patient safety. Participants were required to have acceptable glycaemic control and use a basal bolus regimen, and participate in regular exercise which did reduce the number of eligible participants.

Apart from the sample size, there were also limitations with the data collection methods. During the real-life environment sessions, the participants were relied upon to accurately collect data for this study and some may criticise the impact this method of data collection had on the reliability of the data. Similar studies have used research staff to collect all study data (West et al 2010, Peter et al 2005, Rabasa-Lhoret et al 2001). This was not possible during the real-life sessions of this study and so the benefits of making the study clinically relevant to people lives had to be weighed up against potential issues. Despite the onus of data collection being placed on the participant, outside the laboratory the participant monitoring and hypoglycaemia diaries provided essential data regarding hypoglycaemia and hypoglycaemic unawareness, the confirmation of reducing evening meal dose by 30% and the CHO consumption at bedtime. These parameters were all verified from the diaries and they provided valuable information, despite possible concerns stated in section 3.6 regarding the accuracy of record-keeping.

Occasionally there was missing data, such as blood glucose times which were not recorded in the participants' diaries, and had to be determined by the CGMS data sheets, and time of basal insulin administration in the evening after exercise was not recorded. However, this did not impact on the overall results but it was time-consuming for data analysis. In a further study, the recommendation would be for more stringent guidelines, stressing the importance of participant record-keeping when explaining the monitoring diaries.

The Polar wristwatch was worn by participants during the real-life sessions and they were instructed with usage and given a minimum and maximum heart-rate to achieve during the 40 minute exercise sessions. These watches cannot be downloaded to verify whether the participant exercised at the expected intensity, and the researcher had to trust that the participant did this. In a further study, the author would include in the diaries to record the heart-rate at ten minute intervals in an attempt to encourage the correct exercise intensity.

With regard to the environment, an order effect could be a possible limitation as all participants performed in the laboratory environment first, followed by the real-life environment. However this order was decided to ensure participants had experience of running at 70% VO_2 max prior to undertaking the real-life session. In a further study, randomised exercise sessions should be considered.

Despite having limitations especially regarding the sample size, this study has generated useful information and data in which to perform a power calculation to perform a subsequent study with full power analysis.

5.12 Summary

In this chapter, the results of the study have been discussed whilst linking with related research and current guidelines. Important issues have been discovered that could be applied into clinical practice and patient education which will be described in the following recommendations chapter.

Chapter Six

Recommendations

6.1 Introduction

This study has several implications for clinical practice regarding evidence-based guidelines and patient education which will be discussed in this chapter. The reliability and efficacy of the algorithm and the feasibility of a further study will also be determined.

6.2 Implications for clinical practice

Healthcare research generates information for clinical practice which are; firstly to provide evidence-based recommendations for national guidelines and policies, and secondly to provide HCPs with evidence to underpin information for patients.

6.2.1 Implementation of findings into clinical care

The descriptive results may not be considered robust or sufficiently influential to incorporate into evidence-based guidelines in diabetes management such as SIGN or NICE documents. This is disappointing as several authors have commented on the gap in the current research with regard to moderate intensity exercise and post-exercise insulin adjustment in real-life situations (Brazeau et al 2008, Gallen 2005, Guelfi et al 2005, SIGN 2009, Walleymahmed et al 2007).

Despite this, the findings will be conveyed to diabetes HCPs in the local NHS for their own use. The issues stated below in section 6.2.2, could be discussed with patients with Type 1 diabetes who perform or are considering exercise. These issues could be incorporated into individual patient management plans, with the advice that they are based on findings from a small study but may help to improve glycaemic control and prevent hypoglycaemia, when performing moderate exercise. The major factor for HCPs to be aware of, and to consider and include in education sessions with patients, is the risk of delayed hypoglycaemia and the possibility of hypoglycaemic unawareness during the night after evening exercise. The findings from this study do suggest that previous laboratory-based findings regarding self-

management strategies may be applied into the real-life environment but one must be careful not to over-interpret the results; this algorithm had the same effect in the laboratory and real-life environments. This may be due to the small sample size and differences with hypoglycaemic episodes.

6.2.2 Self-management issues to implement into patient education

From clinical experience, it is unusual for patients to reduce insulin after exercise, which may increase the risk of post-exercise hypoglycaemia in some patients. Post-exercise hypoglycaemia was a crucial finding, but to implement this finding it may be difficult to encourage patients to include SBGM into their usual nighttime monitoring after exercise, although many who are motivated to exercise will be keen to be informed of this finding. However, the focus group analysis described by Kilbride et al (2011a), did highlight that motivated patients use different strategies in an attempt to improve their glycaemic control and their knowledge related to exercise. Communicating the hypoglycaemia risk to the diabetes HCP community and patient population is essential for patient safety, and prevention of developing hypoglycaemic unawareness or exacerbating the severity of hypoglycaemia unawareness. If HCPs have access to CGMS, this would be a useful tool to use with people with Type 1 diabetes who are evening exercisers. From the current study, the participants were given their own CGMS recordings and were very interested in examining data, and subsequently making changes to their own exercise management strategies.

After analysing the data and applying the findings into the real life situation and patient self-management, the following issues could be discussed with patients to consider and evaluate in their own personal self-management plans. It would have to be stressed to patients, however, that these strategies would have to be monitored and maybe modified depending on the effects on the individual:

- There is a risk of delayed nocturnal hypoglycaemia after performing moderate intensity exercise in the evening.
- After this type and time of exercise, reduce the evening meal fast-acting analogue insulin dose by 30%.

- At bedtime, have a banana or low GI snack to eat.
- Monitor blood glucose before and after exercise, then before evening meal and bedtime, then again the following morning to evaluate the insulin dose reduction and bed snack.
- Occasionally set an alarm and check blood glucose between 8-12 hours after the evening meal and fast-acting analogue insulin dose.

6.3 Future research

Determining the reliability of the glucose response of patients repeatedly using the algorithm is essential if it is to be used as evidence to support patient education in clinical practice. Unfortunately, it is difficult to determine the reliability of the algorithm within this pilot study, on a small sample size. This limited the interpretation of the current results. An additional problem was the high standard deviations when using the mean glucose concentrations, which meant a high variability in individual participants' glucose values. A further study, using results from this study to perform a full power analysis with a larger sample size, would be required to achieve statistical power to evaluate the amended algorithm and ensure findings were the result of the effects of the algorithm and not by chance. However, a descriptive analysis would still need to be performed to ensure any extreme outliers are detected as these are important clinically.

As this is the first time a complete self-management algorithm has been investigated, it would not be deemed as unusual that the algorithm requires amendments. Also, findings from recent publications by Iscoe and Riddell (2011) and West et al (2011) recommended similar adjustments which could be incorporated into the algorithm. The study highlighted areas in the algorithm sections where adjustments may increase the effectiveness and improve glycaemic control (Table 5.1 and 5.2). Although based on a small sample size, there was consistency in the data regarding glucose concentrations and patterns that emphasised specific glycaemic problems at certain time-points. In each algorithm section, the participant episodes within the acceptable range varied between 50-77.8%, and by making the suggested

amendments to the algorithm, and re-evaluating the effectiveness, the author would hope to improve this outcome, whilst reducing hypoglycaemic episodes.

The major challenges in designing and performing a larger study would be regarding recruitment and cost. A multi-centre study would have to be considered. This is not without its challenges e.g. finding suitable research sites with appropriate personnel, the organisational issues, and cost implications. If these obstacles were overcome, the benefits of running a larger multi-centre study with the outcomes for evidence-based guidelines to inform HCPs and patients would be immense, and add to the evidence-base.

Chapter Seven
Conclusion

7.1 Introduction

The initial idea and motivation behind the pilot study aims and objectives were to develop guidelines to help people with Type 1 diabetes perform exercise without the risk of hypoglycaemia. This was instigated after patients had discussed their anxieties and problems encountered with exercise in their usual daily routines. These quotes from the Kilbride et al (2011a) focus group study support this:

"You can't just take anything for granted…you've always got to be ten steps ahead of it and trying to work out what's going to happen", and

"Once you understand your own body a bit then you're not as frightened. I used to be really frightened about having hypos when I was exercising", and finally,

"I think diabetes is really quite hard work" (Kilbride et al 2011a, pp.75-75).

When deciding specific details about the current study design, there was the desire to generate convincing evidence that would be applicable to the normal population when dealing with these challenges, hence the reason for the type of exercise, intensity and time used in this study.

7.2 Related evidence

The literature review highlighted a major gap in evidence regarding self-management strategies for people exercising before the evening meal. It also clarified the vast amount of variables (type of exercise, intensity, glycaemic control, time in relation to insulin), issues, problems and questions within the exercise and diabetes realm. All the previous research had been performed in the laboratory environment and not applied into similar real-life situations. It was unclear if laboratory-based research would be relevant outside the laboratory. None of the research analysed a complete self-management tool for patients before, during and after exercise, and all had only evaluated one management strategy. Evidence regarding delayed hypoglycaemia was also poor, with only experiential opinions available to acknowledge the problem.

7.3 Self-management algorithm

This pilot study has been useful and informative as a starting point to evaluate a new idea for a self-management algorithm to be used by HCPs and patients to decrease the problems exposed to patients. The management strategies incorporated into the algorithm were based on the author's clinical experience plus expert opinions, though not always evidence-based because of lack of appropriate research. This study has been crucial to ascertain the success of combining these strategies into one self-management tool, and the current data analysis together with the recent findings from Iscoe and Riddell (2011) will underpin changes required for certain sections of the algorithm (Table 5.2).

7.4 Hypoglycaemia

This is the first pilot study to provide data demonstrating the risk of delayed and nocturnal hypoglycaemia after evening exercise. The data also highlight the worrying finding of nocturnal hypoglycaemic unawareness. Although not significantly proven, suggestions derived from this study can be disseminated to diabetes HCPs and patients regarding the importance of performing SBGM between 8-12 hours following an evening meal insulin dose with evening exercise to prevent hypoglycaemia. The data also confirm the advantages for HCPs to use CGMS in appropriate patients in order to investigate their individual hypoglycaemic risk, and to support education and identify accurate self-management adjustments.

7.5 Differences between environments

It appears that the two exercise environments in the laboratory and real-life have a similar effect on glycaemic control, and therefore previous research findings can be utilized in patient education. However in the current study, statistical analysis was performed with a small sample size, and results may have been different if performed with larger numbers. Extreme outliers were not highlighted, but the descriptive analysis demonstrated a difference with the patterns of hypoglycaemia in each environment.

7.6 Future research

A further study using a full power analysis, to evaluate the amended algorithm is necessary, and to also investigate differences between environments, as the

aetiology of the difference in hypoglycaemia episodes and nocturnal hyperglycaemia is not clear. It is inspiring that since the initial literature review, another research team had aims similar to those of the current study (Iscoe and Riddell 2011), and contact with them to discuss future research would be beneficial for the possibility of a collaborative study combining both post-exercise interventions.

Since performing the literature review and having increased awareness of related research, the author has been in contact with the West et al (2010) team to discuss research results, and consequently, a UK interest group in physical activity and Type 1 diabetes has been established. This offers a greater opportunity to increase research awareness, and to develop potential collaborations in exercise/diabetes research in the UK, with the aim to help people with Type 1 diabetes perform a normal activity safely.

7.7 Summary

This pilot study has added to the small evidence-base in self-management strategies for people with Type 1 diabetes when performing moderate intensity exercise, to achieve recommendations for health (American College of Sports Medicine 2007, Department of Health 2009, SIGN 2010, WHO 2010). The key findings regarding hypoglycaemia are essential for patient well-being, and should be incorporated into patient education to support patients to perform exercise safely.

References

American Diabetes Association (2002). Diabetes Mellitus and Exercise, *Diabetes Care.* **25** (1), pp 64-68

Biankin, S. A., Jenkins, A.B., Campell, L.V., Choi, K.L., Forrest, Q.G., Chisholm, D.J. (2003). Target-Seeking Behaviour of Plasma Glucose with Exercise in Type 1 diabetes, *Diabetes Care.* **26** (2), pp.297-301

Borg, G. (1998) *Borg's perceived exertion and pain scales*. Stockholm: Human Kinetics

Bracken, R. M., West, D.J., Stephens, J.W., Kilduff, L.P., Luzio, S., Bain, S.C. (2011) Impact of pre-exercise rapid acting insulin reductions on ketogenesis following running in Type 1 diabetes, *Diabetic Medicine* **28** (2) 218-222

Brazeau, A.S., Rabasa-Lhoret, R., Strychar, I., Mircescu, H. (2008). Barriers to Physical Activity among Patients with Type 1 Diabetes, *Diabetes Care* **31** (11), pp. 2108-2109.

Bryman, A., (2008). *Social Research Methods.* Third edition. Oxford: Oxford University Press.

Butler, J., (2006). The effect of intensive exercise on type 1 diabetes control: A case study, *Journal of Diabetes Nursing* **10** (3), pp 95-98

Chen, M.J., Fan, X., Moe, S.T. (2002). Criterion-related validity of the Borg ratings of perceived exertion scale in healthy adults: a meta-analysis, *Journal of Sports Science.* **20** pp. 873-899

Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet*, 2011, 378(9785):31–40.

Deiss, D., Bolinder, J., Riveline, J-P., Battelini, T., Bosi, E., Tubiana-Rufi, N., Kerr, D., Philip, M. (2006). Improved glycaemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring, *Diabetes care.* **29** (12), pp2730-2732

Department of Health, in partnership with other Government Departments (2009) *Be active, be healthy: a plan for getting the nation moving*. London: DOH

Diabetes in Scotland (2009). *Scottish Diabetes Survey* Available from: www.diabetesinscotland.org.uk/Publications/Scottish%20Diabetes%20Survey%202009.pdf [accessed 23.7.10].

Dose Adjusting For Normal Eating (DAFNE) Study Group (2002) Training in flexible, intensive insulin management to enable dietary freedom in people with type 1

diabetes: dose adjustment for normal eating, *British Medical Journal* **325** pp. 325-331

Diabetes Control and Complications Trial Research Group. (1993). The effect of intensive treatment of diabetes on the development and progression of long term complications in insulin dependent diabetes mellitus, *New England Journal of Medicine* **329** pp.683-9

Diabetes UK. (2012). Care. Connect. Campaign. Available at: http://www.diabetes.org.uk [accessed 5.12.12]

Driver and Vehicle Licensing Agency (DVLA). (2011). *Changes to the standards for drivers with diabetes mellitus - important update 20th September 2011* Swansea: DVLA

Dunning, T., and Ward, G., (2008). *Managing Clinical Problems in Diabetes.* Oxford: Blackwell

Ertl, A.C., Davis, S.N. (2004). Evidence for a vicious cycle of exercise and hypoglycaemia in type 1 diabetes mellitus, *Diabetes/Metabolism Research and Reviews.* **20** pp. 124-130

Fery, F., de Maertelaer, V., Balasse, EO. (1987). Mechanism of the hyperketonaemic effect of prolonged exercise in insulin deprived type 1 (insulin–dependent) diabetic patients. *Diabetologia.* **30** (5). pp. 298-304

Francescato, MP., Geat, M., Fusi, S., Stupar, G., Noacco, C., Cattin, L., (2004). Carbohydrate Requirement and Insulin Concentration During Moderate Exercise in Type 1 Diabetic Patients. *Metabolism.* **53** (9) pp. 1126-1130

Frier, B. (2008). How hypoglycaemia can affect the life of a person with diabetes. *Diabetes Metabolism Research and Reviews* **24** 87-92

Gallen, I. (2004). Helping the athlete with type 1 diabetes, *The British Journal of Diabetes and Vascular Disease* **4** pp. 87-92.

Gallen, I. (2005). The management of insulin treated diabetes and sport, *Practical Diabetes International.* **22** (8), pp. 307-312.

Gerish, K., Lacey, A., (2009). *The Research Process in Nursing.* Fifth edition. Oxford: Blackwell Publishing Limited.

Graveling, A.J., Frier, B.M. (2010). Risks of marathon running and hypoglycaemia in Type 1 diabetes, *Diabetic Medicine.* **27** pp. 585-588

Grimm, J., Ybarra, J., Berne, C., Muchnick, S., Golay, A. (2004). A new table for prevention of hypoglycaemia during physical activity in type 1 diabetic patients, *Diabetes Metabolism.* **30** 465-470.

Guelfi, K.J., Jones, T.W., Fournier, P.A. (2005). The Decline in Blood Glucose Levels is less with Intermittant High-Intensity Compared with Moderate Exercise in Individuals with Type 1 Diabetes, *Diabetes Care.* **28** (6), pp. 1289-1294

Hernandez, J.M., Moccia, T., Fluckley, J.D., Ulbrecht, J.S. (1999). Fluid snacks to help persons with type 1 diabetes avoid late onset postexercise hypoglycaemia, *Medicine & Exercise in Sports & Exercise. p*p 904-910

Home diagnostics. (2009). *Our products.* Available from: http://www.homediagnostics.com/our_products/bgm_sidekick.aspx {accessed 23rd November 2009).

Hones, J., Muller, P., Surridge, N. (2008). The Technology Behind Glucose Meters: Test Strips, *Diabetes Technology and Therapeutics.* **10** (1). pp. 10-26

Hopkins, WG., Marshall, S., Ballenham, A., Hanin, J. (2009). Progressive Statistics for Studies in Sports Medicine and Exercise Science. *Medical Sciences for Sports and Exercise* **41** pp 3-12.

Iscoe, K.E, Riddell, M.C. (2011). Continuous moderate-intensity exercise with or without intermittant high-intensity work: effects on acute and late glycaemia in atletes with Type 1 diabetes mellitus *Diabetic Medicine* **28** (7) pp. 824-832

Jimenez, C., Corcoran, MH., Crawley, JT., Hornsby, WG., Peer, KS., Philbin, RD., Riddell, MC. (2007). National Athletic Trainers Association Position Statement: Management of the athlete with type 1 diabetes mellitus. *Journal of Athletic Training* **42** (4) pp 536-545

Karavatas, S., Tavakol, K. (2005). Concurrent Validity of Borgs Rating of Percieved Exertion in African-American Young Adults, Employing Heart Rate as the Standard. *The Internet Journal of Allied Health Sciences and Practice* **3** (1) pp. 2-5.

Kennedy, C., Christie, J., Harbison, J., Maxton. F., Rutherford, I., Moss, D. (2008). Establishing the contribution of nursing in the community to the health of the people of Scotland: integrative literature review. *Journal of Advanced Nursing* **64** (5) pp. 416-439.

Kilbride L., Aitken G., Charlton J., Hill G., Davison R., McKnight J. (2011a). An exploration of issues faced by physically active people with type 1 diabetes *Journal of Diabetes Nursing*, **15** (2) 73-77

Kilbride, L., Charlton, J., Aitken, G., Hill, G., Davison, R., McKnight, J., (2011b). Managing Blood Glucose During and After Exercise in Type 1 Diabetes: Reproducibility of glucose response and a trial of a structured algorithm adjusting insulin and carbohydrate intake *Journal of Clinical Nursing* **20** (23) pp. 3423 – 3429.

Klonoff, D.C. (2005) A review of continuous glucose monitoring technology, *Diabetes Technology and Therapeutics,* **7** (8), pp.770-775

Kavookjian, J., Elswick, BM., Whetsel, T. (2007). Interventions for being active amongst individuals with diabetes. *The Diabetes Educator,* **33** (6) pp 962-988.

Lumb, A.N., Gallen, I.W. (2009). Insulin dose adjustment and exercise in type 1 diabetes: what do we tell the patient? *The British Journal of Diabetes and Vascular Disease.* **9** (6), pp. 273-277

Maia, F., Araújo, L., (2007) Efficacy of continuous glucose monitoring system (CGMS) to detect postprandial hyperglycemia and unrecognized hypoglycemia in type 1 diabetic patients *Diabetes Research and Clinical Practice,* **75 (**1), pp. 30-34

Mastrototaro, J., Shin, J., Marcus, A., Sulur, G. (2008). The Accuracy and Efficacy of real-time Continuous Glucose Monitoring Sensor in Patients with Type 1 diabetes, *Diabetes Technology and Therapeutics.* **10** (5), pp. 385-390

Melki, V., Fernandez, M., Hanaire-Broutin, H. (2006). Value and limitations of the continuous glucose monitoring system in the management of type 1 diabetes, *Diabetes Metabolism*. **32** pp. 123-129

Montague, S.E, Watson, R., Herbert, R.E. (eds) (2005) *Physiology and Nursing Practice* Elsevier: London

Nagi, D. (2008) *Exercise and Sport in Diabetes* 2nd edition Chichester: Wiley & sons.

Nagi, D., Gallen, I. (2010). ABCD position statement on physical activity and exercise in diabetes. *Practical Diabetes International* **27** (4) pp 158-163.

National Institute for Clinical Excellence (NICE) (2009). *Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults in primary and secondary care*. London: NICE

Nursing and Midwifery Council, (2007). *The Code. Standards of conduct, performance and ethics for nurses and midwives.* London: Nursing and Midwifery Council

Pandolf, K.B. (1982). Differentiated ratings of perceived exertion during physical exercise, *Medicine and Science in Sports and Exercise.* **14** (5), pp.397-405

Pang, T., Narendran, P. (2008). Addressing insulin resistance in Type 1 diabetes. *Diabetic Medicine* **25** (9) pp 1015-1024

Parahoo, K., (1997). *Nursing Research: Principles, Process and Issues.* Hamphire: Palgrave Macmillan

Peirce, N.S. (1999). Diabetes and exercise, *British Journal of Sports Medicine*. **33** pp. 161-173

Perry, E., Gallen, I.W., (2009). Guidelines on the current best practice for the management of type 1 diabetes, sport and exercise, *Practical Diabetes International.* **26** (3), pp.116-123.

Peter, R., Luzio, S.D., Dunsheath, G., Miles, A., Hare, B., Backx, K., Pauvaday, V., Owens, D.R. (2005). Effects of Exercise on the Absorption of Insulin Glargine in Patients with Type 1 Diabetes, *Diabetes Care.* **28** (3), pp. 560-565

Potteiger, J.A. (2010). *ACSMs Introduction to exercise science.* Philadelphia: Lippincorr, Williams & Watkins

Rabasa-Lhoret, R., Bourque, J., Ducros, F., Chasson, J.L. (2001). 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* **24** pp. 625-630.

Riddell, M., Perkins, B., (2006). Type 1 Diabetes and Vigorous Exercise: Applications of Exercise Physiology to Patient Management, *Canadian Journal of Diabetes* **30** (1), pp. 63-71.

Roach, P.,(2008). New insulin analogues and routes of delivery: pharmacodynamic and clinical considerations, *Clinical Pharmacokinetics* **47** (9). pp. 595-610

Robertson, K., Adofsson, P., Riddell, M.C., Scheiner, G., Hanas, R. (2008). Exercise in children and adolescence with diabetes, *Pediatric Diabetes.* **9** pp. 65-77

Royal College of Nursing, (2009). *Research Ethics. RCN guidance for nurses.* London: Royal College of Nursing

Sandoval, D.A., Davis, S.N. (2006). Metabolic Consequences of Exercise-Associated Autonomic Failure, *Exercise and Sports Sciences Reviews.* **34** (2), pp72-76

Scottish Diabetes Survey Monitoring Group. (2011). *Scottish Diabetes Survey 2011* Edinburgh: Diabetes in Scotland

Scottish Intercollegiate Guidelines Network. (2011). *SIGN 50: A Guideline Developer's Handbook.* Edinburgh: SIGN

Scottish Intercollegiate Guidelines Network, (2010). *SIGN 116: Management of Diabetes.* Edinburgh: SIGN

Shaw, K.M., and Cummings, M.H., (2006) *Diabetes: Chronic Complications* 2nd edition West Sussex: Wiley

Wallymahmed, M.E., Morgan, C., MacFarlane, I.A. (2007). Does hypoglycaemia avoidance behaviour contribute to increased HbA1c levels in physically active people with type 1 diabetes? *Practical Diabetes International.* **24** (8), pp. 418-421

Watkins, P.J. (2003) *ABC of Diabetes* 5th edition London: BMJ publishing

West, D.J., Morton, R.D., Bain, S.C., Stephens. J.W., Brachan. R.M. (2010) Blood glucose responses to reductions in pre-exercise rapid acting insulin 24 h after running in individuals with type 1 diabetes, *Journal of Sports Science.* **28** (7), pp 781-788

West, D.J., Stephens, J.W., Bain, S.C., Kilduff, L.P., Luzio, S., Still, R., Bracken, R.M. (2011) A combined insulin reduction and carbohydrate eeding strategy 30 min before running best preserves blood glucose concentration after exercise through improved fuel oxidation in type 1 diabetes mellitus *Journal of Sports Sciences* **29** (3) pp 279-289

Williams, G., Pickup, J. C., (2004) *Textbook of Diabetes* 3rd edition Oxford: Blackwell Science

Wilmore. J. H., Costill. D., (2004) *Physiology of Sport and Exercise* 3rd edition Champaign: Human Kinetics

World Health Organisation (2006). *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycaemia.* Geneva: Switzerland

World Health Organisation (2010). *Global recommendations on physical activity for health.* Geneva: WHO

World Health Organisation (2013). *Statistics and Prevalence*. Geneva: WHO

Appendix 1a
Search strategy

Wednesday, August 04, 2010 8:50:54 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S22	S10 and insulin management	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	6
S21	S10 and S11	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	25
S20	type 1 diabetes* and exercise*	**Limiters** - English Language; English Language **Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	542
S19	(("sport") and (S5 or S6 or S7)) and (S4 and S8)	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	13
S18	(("sport") and (S5 or S6 or S7)) and (S4 and S8)	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	13
S17	S14 and insulin management	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - British Nursing Index;CINAHL with Full Text;MEDLINE;SPORTDiscus	Display
S16	S14 and S15	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - British Nursing Index;CINAHL with Full Text;MEDLINE;SPORTDiscus	Display
S15	type 1 diabetes* and glycaemic control*	**Limiters** - English Language; ; English Language; Human; ; Language: English **Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - British Nursing Index;CINAHL with Full Text;MEDLINE;SPORTDiscus	Display
S14	type 1 diabetes* and exercise*	**Limiters** - English Language; ; English Language; Human; ; Language: English **Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - British Nursing Index;CINAHL with Full Text;MEDLINE;SPORTDiscus	Display
S13	S10 and insulin management	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	1
S12	S10 and S11	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	4
S11	type 1 diabetes* and	**Limiters** - English	**Interface** - EBSCOhost	Display

	glycaemic control*	Language; ; English Language; Human; ; Language: English **Search modes** - Boolean/Phrase	**Search Screen** - Advanced Search **Database** - British Nursing Index;CINAHL with Full Text;MEDLINE;SPORTDiscus	
S10	type 1 diabetes* and exercise*	**Limiters** - English Language **Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	143
S9	(("sport") and (S5 or S6 or S7)) and (S4 and S8)	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text;British Nursing Index;MEDLINE;SPORTDiscus	13
S8	("sport") and (S5 or S6 or S7)	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	4320
S7	"sport"	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display
S6	(MM "Physical Activity") or (MM "Physical Activity (Omaha)")	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display
S5	(MM "Exercise+") or (MM "Aerobic Exercises+") or (MH "Anaerobic Exercises")	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display
S4	(("insulin dependant diabetes") or (MM "Diabetes Mellitus, Insulin-Dependent")) and (S1 or S2 or S3)	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	5215
S3	("insulin dependant diabetes") or (MM "Diabetes Mellitus, Insulin-Dependent")	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display
S2	("type 1") or (MM "Diabetes Mellitus, Insulin-Dependent")	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display
S1	type 1	**Search modes** - Boolean/Phrase	**Interface** - EBSCOhost **Search Screen** - Advanced Search **Database** - CINAHL with Full Text	Display

Appendix 1b	**Key publications**
Original studies	
Brazeau et al (2008)	**Type:** A qualitative research design **Aims:** To determine barriers for people with Type 1 diabetes against participating in physical activity **Method:** 103 people with Type 1 diabetes (mean age 43.5 ± 11.6 years) attending routine clinic appointments completed a diabetes-specific barriers measure (BAPAD1 scale). **Results:** The highest barrier scores were fear of hypoglycaemia, work schedule, loss of glycaemic control and low fitness levels respectively, however P values not stated. Exercising with another person significantly resulted in fewer barriers (P<0.001). Participants having an evening CHO snack after exercise significantly reduced hypoglycaemia fear (P<0.007). Although not significant, participants with time actions and pharmacokinetics of insulin reduced the fear (P=0.021). **Strengths:** A random sample of participants with Type 1 diabetes to extrapolate data to inform the current study of participant and real life barriers to performing physical activity. **Limitations:** Numbers of people actively performing physical activity were not stated thus possibly skewing the data, depending on the number of non-exercisers. **Key message:** Hypoglycaemia risk is a feared and major barrier. Thus supporting the need for this particular study in delayed hypoglycaemia prevention. The need for patients to understand insulin actions will be demonstrated in the self-management algorithm, giving people with diabetes education regarding insulin and dietary strategies. Highlighting bed snacks depending on the bg level in the algorithm will attempt to allay nocturnal hypoglycaemia.
Grimm et al (2004)	**Type:** Comparison study **Aims:** To compare different therapeutic options related to dose adjusting and CHO ingestion on people with Type 1 diabetes exercising at different intensities and durations. **Method:** 67 participants with well controlled diabetes (HbA1c <7.5%) and placed into 4 different treatment groups. Each participant was then placed into different intensity and duration groups. It was not stated how these decisions were made. **Results:** Data very poorly presented and vague despite the complex study design. In relation to this study for 20-60 minutes exercise at 60-70 VO2 max, 20-60 grammes of CHO would need to be ingested to prevent hypoglycaemia. Recommendations in general for intense and moderate duration require 20-30% reduction of total daily dose (not stating analogue or NPH). **Strengths:** Considering a multiple array of exercise and treatment options. **Limitations:** Very difficult to decipher data. Hypoglycaemia was stated as BG levels <2.8mmol which is very low. Insulin used were fast acting analogues or NPH which is an old intermediate acting insulin with peak between 4-8 hours after injection which could bias data. Unable to extrapolate any information or evidence to incorporate into this study. **Key message:** None with regard to research questions. But when writing up data be specific and don't have too many treatment groups/variables within the study as interpretation is impossible.
Peter et al (2005)	**Type:** Randomised cross-over design **Aims:** to study the effects in Type 1 diabetes on the absorption of Lantus after exercise. **Method:** 13 participants with Type 1 diabetes using basal bolus regimen given usual Lantus dose on the evening before visit 1 and the same on visit 2. Then randomly assigned to perform 30 minute bout of exercise at 65% VO2 max on one visit. Blood samples collected to assess bg and insulin levels. **Results:** fasting bg levels similar on both days (8.4 and 8.2 respectivly). During 210 min post exercise period showed no difference in glucose (P=0.345), however during exercise glucose levels were significantly lower (P=0.001). No statistical differences in insulin levels during (0.506) or after (P=0.116) exercise on both days. **Strengths:** Insulin levels remained stable during and 210 minutes post exercise. **Limitations:** Unusual time of data collection (3 hours and 30 minutes post exercise). No description of adjustments to fast acting analogue pre-exercise which could have resulted in the glucose drop during exercise. No data collection for bg levels for following 24 hours when hypoglycaemia is a potential risk. This study is disappointing as post exercise data up to 24 hours would have been interesting for the algorithm design to support Lantus adjustment. **Key message:** Lantus would not be a contributing factor to hypoglycaemia during or in the initial period after exercise.

West et al (2010)	**Type:** Randomised quasi – experiment into 3 groups with no control **Aims:** to examine pre-exercise insulin reductions before running and the consequent 24 hour effect on glycaemic control. **Method:** 7 participants were given a reduction of 25, 50 or 75% of their usual fast acting analogue dose 2 hours prior to exercise. **Results:** Pre-exercise bg levels ranged 11-15mmol in all groups, however the intra-individual variability across participants could have contributed to a lack of statistical significance. Each group experienced 1 hypoglycaemia episode at 180 mins (not significant). All groups experienced decreases in bg levels (P<0.01). During and 21 hours post exercise all groups experienced hypoglycaemia, although the 75% experienced less (P<0.05). The 75 % reduction experienced more acceptable 24 hour post bg levels. **Strengths:** Similar participant characteristics performing moderate intensity 70% V02 max running for 45 minutes. **Limitations:** Hypoglycaemia stated as bg <3.5mmol. For the 75% reduction bg levels at finish were 11.0mmol and participants took correction doses which would have contributed to post exercise hypoglycaemia. No data regarding post exercise dose adjusting or data collection of bg levels via CGMS. Post exercise participants performed their own individualised self-management strategies which were not correlated or described with bg levels. Lack of statistical power – required sample size of 33 but recruited 7. BG levels before, during and after not described in detail. Only performed in laboratory environment not real life. **Key message:** Peak insulin concentrations occurred 60 minutes after injection. Higher starting bg levels maybe required as this study aims for 8.0mmol. Reported variability of bg levels in controlled environments and a factor to consider in future research. For the algorithm, if exercising within 2 hours reduce pre-exercise dose by 75%. A discussion with the researcher would be beneficial to get detailed results. This could be combined with this study as this looks at pre dose adjusting.

Review articles	
American Diabetes Association (2002)	**Aim:** Recommendations given for diabetes and exercise **Method:** Only 6 publications reviewed to give clinical recommendations for health care professionals when advising patients on exercise management. **Results:** A narrative description of physiological issues and management strategies for Type 1 and Type 2 diabetes. **Key messages:** Avoid exercise if BG > 13.9mmol with ketosis, or BG > 17mmol without ketosis. This information is included in the algorithm. Eat CHO if BG <5.5mmol before exercise. This information was not included as hypoglycaemia risk would be increased.
Gallen (2004)	**Aim:** A narrative description of the physiological challenges in exercise and Type 1 diabetes, and management strategies to normalise BG and prevent hypoglycaemia. **Method:** No description of search strategy. 40 references cited. **Results:** A narrative description of key findings from original studies, although individual studies not critically analysed. Experiential descriptions and recommendations given by the author which are not supported with evidence. **Key messages:** After exercise 60-120 grammes of CHO should be taken with insulin to replenish glycogen stores. However not evidence based or relating to any particular intensity or duration of exercise. Very vague information.
Jimenez et al on behalf of the National Athletic Trainers Association (2007)	**Aim:** To give recommendations to certified trainers regarding Type 1 diabetes management **Method:** No search strategy shown. 91 references cited. **Results:** A practical narrative description of type 1 diabetes and exercise management, aimed at trainers with no diabetes knowledge. **Key messages:** None. However it did highlight the complex intricacies of management that being a HCP working in diabetes can assume people understand.
Kavookjian et al (2007)	**Aims:** A systematic review to assess and summarise evidence and gaps in the literature regarding interventions for exercise among people with diabetes. **Method:** 12 databases were searched for exercise in all types of diabetes for learning, behavioural, clinical and humanistic outcomes.

	Results: The results focused mainly on Type 2 diabetes with limited Type review. **Key messages:** Self-management and glycaemic control intervention studies are conducted in artificial environments i.e. laboratory, with no translation into the patients daily life. No analysis of diet/dose adjusting intervention studies due to the nature of the review, which was acknowledged by the author.
Lumb & Gallen (2009)	**Aim:** A narrative description of management strategies for exercise and Type 1 diabetes, based around patient scenarios. **Method:** No description of search strategy. 28 references cited. **Results:** Experiential descriptions and recommendations for different intensities and types of exercise are given by the authors, which are not supported with evidence. Studies acknowledged were not critically analysed. **Key messages:** If severe hypoglycaemia occurs in the previous 24 hours, exercise should be performed with caution if at all. Peak hypoglycaemia risk time after moderate intensity exercise is 60-90 minutes post and during the night. A post exercise dose reduction of 30% advised although not evidence based. Management strategies should be tailored to individuals.
Nagi & Gallen; on behalf of the British Clinical Diabetologists Committee (2010)	**Aim:** A position statement to assist diabetes HCPs to familiarise themselves with issues regarding exercise management. **Method:** No description of search strategy. 41 references cited. **Results:** A narrative description of key findings from original studies, although individual studies not critically analysed. Experiential descriptions and recommendations given by the authors which are not supported with evidence. The information recommended was disappointing from this well-recognised expert group as the information was not analysed or limitations from studies discussed. **Key messages:** No evidence that moderate intensity exercise has a detrimental effect on non-proliferative retinopathy. Physical activity (apart from high intensity, strenuous exercise) should not be restricted in people with nephropathy. Jogging or treadmill use should be undertaken by people with significant neuropathy. Advantages and disadvantages for specific dose adjusting was described, however post bolus reduction was not mentioned, although post basal reduction was which highlighted a reduction in nocturnal hypoglycaemia but may cause morning hyperglycaemia – for this reason in the algorithm bolus was reduced to alleviate nocturnal hypos but maintain morning usual BG levels.
Perry & Gallen (2008	**Aim:** Physiology description of Type 1 and exercise and literature review regarding evidence based management strategies. **Method:** No description of search strategy. 42 references cited. **Results**: A narrative description of key findings from original studies, although individual studies not critically analysed. Experiential descriptions and recommendations given by the authors which are not supported with evidence. **Key messages:** Multiple variables control glucose homeostasis. Advice for individuals will differ. Reducing post exercise meal dose will prevent nocturnal hypoglycaemia (amount not given). Starting BG between 7-12mmol. Lack of research performed in real life environments.

Real life studies	
Butler (2006)	**Type:** Case study **Aims:** To describe the training and management plan for a person with Type 1 diabetes swimming the channel. **Method:** A review of the literature regarding pathophysiology, diet and insulin modification, hypo and hyperglycaemia risks for relating to Type 1 and exercise. A description of the individualised training and insulin/diet adjustment strategies. During the swim fast acting analogue doses were stopped and long acting analogue reduced by 30% for 2 days prior and after the swim. **Results:** The person finished the swim but experienced a hypoglycaemic episode during, and vomited on several occasions. May be due to the high energy supplements differing during the swim compared to training sessions. Training sessions of 7 hours duration maintained acceptable bg levels. **Strengths:** One of the few articles found that is undertaken in real life. Highlights the importance of regular SBGM and individualised dose adjusting. Training sessions could be classified as laboratory or controlled environments, and the swim being real life. **Limitations:** Only had 1 participant. Bg levels not described during training, although satisfactory before and after the channel swim, which could have been correlated to laboratory and real life. The

	swim took 14 hours, this study looks at moderate intensity exercise for 40 minutes. **Key message:** Insulin and dietary modification is essential. Training sessions (controlled environment) and the swim (real life) resulted in differences in bg levels and hypoglycaemia occurred in real life.
Graveling & Frier (2010)	**Type:** Case study **Aims:** A description of metabolic events in Type 1 diabetes, in the preceding 48 hours before exercise and the risk of exercise induced hypoglycaemia. **Method:** A case history describing a 27 year old person with Type 1 diabetes suffering severe hypoglycaemia then running a marathon resulting in further severe hypoglycaemia. **Results:** Description of the individuals pathophysiology and clinical markers. **Strengths:** Highlights the risk of rebound and delayed hypoglycaemia and the necessity for dietary and insulin dose adjustment. **Limitations:** Only 1 person performing a marathon not 40 minutes moderate intensity exercise. No description of post exercise dose adjustment to prevent hypoglycaemia. **Key message:** People with insulin-treated diabetes should not attempt prolonged strenuous exercise within 48 hours of experiencing a severe hypoglycaemic episode.
Wallymahmed (2007)	**Type:** Comparison study **Aims:** To assess the relationship between glycaemic control, self-reported vigorous activity, aerobic capacity and hypoglycaemia avoidance in people with Type 1 diabetes. **Method:** 50 patients attending a routine diabetes clinic appointment participated. Aerobic fitness assessed by a sub-maximal step test, physical activity, hypoglycaemia and hypo avoidance measured by a non-validated questionnaire. **Results:** 60% reported participating in regular vigorous exercise (RVE) with significantly worse HbA1c compared to those not regularly participating (NVA) (9.5% vs 8.5% $p<0.02$). The RVA group reported aiming for higher starting blood glucose before exercise levels compared to the NVA group (8 vs 0 $p<0.03$). In the RVA group 83% reported taking precautions to avoid hypoglycaemia. From these 77% ate more, 7.7% reduced insulin, 12.8% ate and reduced insulin. **Strengths:** A good description of exercise/diabetes behaviour in a normal population of people with Type 1 diabetes. **Limitations:** No description of insulin type and dose adjusting in the 83% who did. Used a non-validated questionnaire that was not shown in the paper. Difficult to extrapolate data to use in other studies as specific areas i.e. dose adjusting, food amounts, BG levels around exercise, hypos related to exercise, all not described in detail. **Key message:** Patients tend to eat more CHO around exercise to aim for higher BG levels, despite advice being given previously on insulin dose reduction.

Appendix 2
Patient study information

EDINBURGH NAPIER UNIVERSITY
Faculty of Health, Life and Social Sciences Research Ethics and Governance Committee

Information Sheet/Letter for Potential Participants

Our names are Jacqui Charlton, John Chisholm and Lorraine Steel and we are currently research students from the Faculty of Health, Life and Social Sciences at Edinburgh Napier University. As part of our degree courses we are involved with NHS Lothian in a programme of research looking at the effects of Type 1 diabetes and exercise, and ways to manage blood glucose levels. Dr. X has given us names of patients who attend the X diabetic clinic, and you have been identified as a possible participant for this research because you have type 1 diabetes.

We have 3 separate studies starting in the next few months. The information about each study is enclosed. The studies will investigate the effects on blood glucose levels for people with type 1 diabetes when performing different types of exercise. All studies are suitable for adults over the age of 18 years old.

The findings from the projects will be valuable because many people with type 1 diabetes are anxious about exercising due to the fear of hypoglycaemia and the possibility of having erratic blood glucose levels. There is limited information available regarding the effects and so gathering this information could help many people with type 1 diabetes to enjoy participating in sport and exercise.

We are looking for volunteers to participate in the projects. As have type 1 diabetes and use a basal bolus insulin regimen we would like to invite you to take part in a study. However it is important that you already participate in regular exercise.

If you decide to take part in a study you will be asked to attend the exercise laboratory at Merchiston Campus of Edinburgh Napier University in Colinton Road. Each study runs for a 2-3 week period, and the following information sheets tell you what the each study entails. As all of the study sessions involve exercise, please attend wearing flat shoes (preferably trainers) and comfortable clothing.

You will be free to withdraw from the study at any stage, you would not have to give a reason, and it will not affect your treatment. This project will also mean that we will have to look at your diabetic hospital records.

Since your participation will involve you travelling to Edinburgh Napier University you will be reimbursed for out-of-pocket expenses.

All data will be anonymised as much as possible. Your name will be replaced with a participant number and it will not be possible for you to be identified in any reporting of the data gathered. Any data collected will be kept in a secure place to which only the study team has access. These will be kept till the end of the examination process.

The results may be published in a diabetes or sport journal, or presented at a diabetes or sport conference. It will also be possible for you to obtain written or verbal feedback on your results of the study in order to help you better understand your diabetes management relating to the specific form of exercise. We will also send you information regarding the results of the study when it has finished.

If you would like to contact an independent person, who knows about this project but is not involved in it, you are welcome to contact Barbara Neades, who is a lecturer and chairperson of the research committee at Edinburgh Napier University. Her contact details are given below.

Before you decide if you would like to participate in a study it is important for you to understand why we are undertaking this research and what it will involve. Please take time to read the information sheets carefully and discuss it with others if you wish. If there is anything that you do not understand, or if you would like more information, please contact us.

If you decide to take part, please let us know which study you would like to take part in and send the completed form back to us.

Thank you very much for your time.

Kind regards,

Dr. X, Consultant Physician
Jacqui Charlton, Diabetes Specialist Nurse
Lorraine Steel & John Chisholm, Research students

Contact details of the independent adviser:

Name of adviser: Barbara Neades
Address: Edinburgh Napier University
Canaan Lane Campus
Edinburgh
EH9 2TB

Email / Telephone: b.neades@napier.ac.uk / 0131 455 5659

Please return in the pre-paid envelope.

Name:

Address:

Email:

Phone number:

I am interested in taking part in the following study/s (please tick):

1. Self management algorithm for moderate intensity
2. The effect of intermittent exercise on blood glucose levels
3. The effects of weight training on blood glucose levels

Thanks very much.

Information sheet - s*elf management algorithm for adults exercising with type 1 diabetes*

Assessment visit	In the exercise laboratory at Edinburgh Napier University. Informed consent will be obtained. Questionnaire to establish general fitness to undertake study will be completed. Blood pressure and blood glucose will be measured to make sure these are at safe levels for the exercise to take place. Heart rate monitor and face mask to measure exhaled air will be fitted. Participants will be asked to follow an exercise plan, lasting approximately 40 minutes, this will be a brisk walk/slow jogging pace on a treadmill.
Day 1 Monday	You will be connected to a watch to monitor your heart rate. You will be connected to the 24 hour blood glucose monitor and connect you up to it by means of a sensor placed under your skin. We will explain how it works. You will be asked about your usual management of insulin doses and food intakes when you exercise. We will discuss guidelines for the management of insulin doses and food intake while exercising. You will then be asked to follow these guidelines for the exercise session undertaken at this and your next 3 exercise sessions. You will be given diaries to record blood glucose levels, food intake, insulin doses and any incidences of low blood glucose to be filled in for the <u>next two 4 day periods.</u> You will then be asked to start the exercise session, which will be jogging lasting 40 minutes on the treadmill. At the end of the session you will be asked to continue wearing the heart rate and blood glucose monitors and carry out your normal routine the following day.
Day 3 Wednesday	You will be asked to undertake your own usual exercise.
Day 4 Thursday	You will be asked to return to have the monitors removed.
Day 8 Monday	In the exercise laboratory at Edinburgh Napier University. Same as day 1
Day 10 Wednesday	Same as day 3.
Day 11 Thursday	You will be asked to return for removal of the monitors. End of study.

Appendix 3
Participant folder

To compare the effectiveness of a self management algorithm during and after controlled laboratory and real life moderate intensity exercise in Type 1 diabetes

Name:

Subject ID:

Contact numbers

Jacqui Charlton 0131 455 5676 (Mon,Tue,Wed) 0131 5371747 (Thu, Fri)

Exercise lab at Merchiston campus 0131 455 2599

Diabetes Doctor on call: 0131 537 1000 and ask to bleep diabetes doctor on call

Medtronic (Minimed) helpline 01923 205142 (office hours)
01223 577379 (24 hour helpline, USA number charged at local rate)

This folder has been designed to allow you to record the information that we require for this study. On the page before each form there is information relating to the way we would like you to complete the forms.

As part of this study we would like you to complete a diary recording your food and insulin intake, exercise and hypos for each day of the study. This is each day of the two weeks that you are attached to the monitors.

Arrangements will be made with you for the collection of completed forms.

The information you record will be used to produce guidelines for future treatment of people with diabetes, so please take time to be as accurate as you can when filling out the forms.

There are also examples of completed sheets at the end of each section for your information.

Please bring this folder with you to all appointments

Guidance notes for completing hypoglycaemic (low blood glucose) episodes

Please indicate on the following sheet every episode of low blood glucose (hypoglycaemia) during this study. This is the day before and when you are attached to the monitors.

We would like you to note:

- the date and time of these
- the severity (mild or severe) with mild being that you can treat it yourself and severe being if you need help from someone else
- the symptoms you had
- any treatment you needed

Hypoglycaemic Episodes

Please record all hypo's related to exercise.
Please rate as mild or severe i.e. mild = you can treat it yourself and severe = you need help from someone else.

Date/ *Time*	Mild or severe	During exercise?	Within 2 hours of exercise?	Over 2 hours after exercise?	During the night?	Blood glucose (using meter)	Symptoms you had
	Mild / Severe	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No mmol/l	
	Mild / Severe	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	
	Mild / Severe	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	
	Mild / Severe	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	

Guidance notes for completing the daily monitoring diary

Carbohydrate (CHO) intake

This section helps us to find out how much carbohydrate you consume before, during and after exercise. When recording food intake if you know how to calculate carbohydrate portions please use these. If not give as much information about your food intake as you can. For example ***ham sandwich*** does not give enough information whereas ***2 slices of wholemeal bread spread thinly with butter with ham, tomato and lettuce*** is much more useful.

Remember to also record what you have had to drink, including any alcohol.

It is important to record all snacks and food taken between meals.

Please be accurate about the amount of food you eat. We are not making judgements on what you eat but about **how what you eat affects** your blood glucose level, especially when you are exercising.

You may use sugary food or drink when exercising or at other times please try and give accurate quantities, we are interested in what works for you. We are not looking at the healthiness of your diet. There is an example of a completed form at the end of this section.

Blood glucose monitoring

Please record your blood glucose levels before, during and after exercise.

You will be given a TrueOne meter to use for the duration of the study. Please be sure to bring this meter to all sessions so all blood glucose measures are made from the same meter.

Take the before reading approximately 10 minutes before exercising.

If you normally test your blood glucose during exercise take a reading at a convenient time to yourself but record this on the sheet.

Take the after reading within 10 minutes after completing the exercise.

Insulin dose

Please record any additional insulin dose taken as well as your usual dose.

Exercise

Describe the session of exercise you have taken, including how long you were active for, and what you did.

For example
Gentle walk for 30 mins or
20 minutes of brisk walking or
One hour of heavy gardening.

Remember not to take any structured exercise on the in-between days that you are connected to the monitors.

If you have any questions about this please contact one of the study team. The contact details are on the front of this pack.

DAILY MONITORING DIARY **Name:** **Day number after visit (1-4 or 8- 11)**

Date:

Please fill in the time	**Breakfast**	**Morning**	**Lunch**	**Afternoon**	**Evening Meal**	**E**	**Bed**
Total CHO eaten (g)							
Extra CHO before Exercise **Extra CHO during Exercise** **Extra CHO after exercise**							
Blood glucose **B=before** **D=during** **A=after** ***if not exercising record reading in before (B) section**	**B** **D** **A**	**B** **D** **A**	**B** **D** **A**	**B** **D** **A**	**B** **D** **A**	**B** **D** **A**	**B** **D** **A**
Insulin taken							
Usual insulin dose							
Exercise: **How long for?** **What did you do?**							
Hypo's Tick appropriate box if experience and fill details in hypo diary							

Guidance notes for following the moderate intensity exercise guideline

This guideline has been developed to help you to exercise safely and attempt to prevent large fluctuations in your blood glucose levels when exercising.
For the purpose of the study we would prefer you to exercise after 2 hours of injecting insulin and eating food.

Before exercise

If the exercise is more than 2 hours after your last meal then you just need to take your usual amount of carbohydrate and insulin at that time.

For example if you are having lunch at 1 o'clock and know you are going for a run straight from work at 4 o'clock then do not alter your insulin or carbohydrate at lunch time.

Aim to have your blood glucose around **8 before you start your exercise**.

If your blood glucose is less than 8 you need to take the amount of fast acting carbohydrate suggested in the guideline.

For example if your blood glucose is 6 mmol/l before you start exercising you will need to take an additional 10g CHO e.g. 3 dextrosol or 60 mls. Lucozade before exercising.

After exercise

Test your blood glucose as soon after exercise as you can.

If you normally eat straight after exercise then take your normal amount of carbohydrate and reduce your normal dose of humalog/ novorapid by one third.

For example if you normally take 9 units reduce this to 6 units.

If you exercised in the early morning, before breakfast, you need to reduce you breakfast insulin by one third.
If you exercised in the morning, after breakfast, then you need to reduce your lunch time insulin by one third.
If you exercised in the afternoon then you need to reduce the insulin taken at your evening meal by one third.
If you exercised in the evening then your supper time dose of humalog/ novorapid will need to be reduced by one third, if you usually inject and eat food at this time.

It is very important to remember to test your blood glucose before bedtime and take your normal dose of Lantus/ Levemir.

If you have exercised any time after lunch time you will need an extra 10-30g CHO at supper time to prevent night time hypos.

Appendix 4
Pre-assessment test and study visit checklist

To compare the effectiveness of a self management algorithm during and after controlled laboratory and real life moderate intensity exercise in Type 1 diabetes

Participant folder and checklist

DO NOT REMOVE THIS SHEET FROM FOLDER
TICK AND INITIAL IF CARRY OUT INTERVENTION

Name:	
Subject ID:	
Minimed Serial number:	
Date of Birth: (age 18-60)	
Consent obtained:	**Yes / No**
Copy of consent to patient:	**Yes / No**
Consent obtained by:	

Exclusion criteria	**Initials**
Diagnosed peripheral vascular disease	
Orthopaedic problems to prevent brisk walking	
Diagnosed heart disease	
Proliferative retinopathy	
Peripheral neuropathy	
Hypoglycaemic unawareness	

Measure	**Result**	**Initials**
HbA1c plus date obtained	_____ % Date:	
Exercises 3x30 mins per week	Yes / No	
Basal bolus regimen	Yes / No	
Analogue insulin (name and dose)		
Basal insulin (name and dose)		
Insulin:CHO ratio		
CHO counting	Yes / No	
Able to adjust insulin/ CHO	Yes / No	
Correction dose		
Weight kg	kg	
Height (M)	m	

BMI		
Average BP		

	Initials
TrueOne meter education - 100 strips given - 1 box lancets given	
Diary education (insulin, food, exercise, hypo and BG monitoring)	
Exercise questionnaire	
GP information letter sent	

Moderate intensity exercise in Type 1 diabetes
Visit checklists

Pre-assessment test
Participant will be asked to attend wearing trainers and comfortable clothes or may require changing facilities.

Task	**Initial**
Obtain informed consent	
Administer questionnaire to establish general fitness (attached)	
All participants will be provided with TrueOne meters to test blood glucose levels. Training will be provided at this session.	
Ask participant to measure blood glucose. If less than 4mmol-1 or more than 17 mmol-1 test will not go ahead. Reading……..mmol^{-1}	
After at least 5 minute rest take 2 measures of resting BP if average is over 165/90 can not take part in study refer to Dr McKnight at WGH (letter attached)	
a. Measurement 1: / mmHg	
b. Measurement 2: / mmHg	
c. Average: / mmHg	
Allow participants to familiarise themselves with walking on treadmill	
Fit Polar heart rate monitor	
Fit face mask for Breath x Breath analyser	
Follow test protocol as below	
Participant should have access to blood glucose meter as will be asked to test blood glucose levels half way through the test (i.e. at 20 minutes)	
Measurement at 20 mins: mmol^{-1}	

WORKLOAD	TIME(mins)	SPEED(km/h)	GRADIENT (%)	PREDICTED VO_2 (ml kg^{-1} min^{-1})
1	0 - 3	4	0	10.17

2	3 - 6	4.8	2.5	15.9
3	6 - 9	5.3	5	20.25
4	9 - 12	6	6.5	25.2
5	12 - 15	6	9.5	30.6
6	15 - 18	6	12	35.1
7	18 - 21	6	15	40.5

During the test HR and VO_2 will be monitored continuously with Rate of Perceived Exertion (RPE) being assessed at the end of each stage.

The end point for all tests is at or just before 85% of the participant's age predicted maximum heart rate or for safety reasons when;

1. The monitoring system failed.
2. A participant experienced progressive angina.
3. A participant experienced light headedness, confusion, ataxia, pallor, cyanosis or nausea.
4. A participant experienced discomfort and asked to stop.
5. A participants blood glucose falls beneath 4 mmol l^{-1}. or they experience symptoms of hypoglycaemia.

If any of the above occur please complete an adverse event form

After exercise session is completed:

Blood glucose level: mmol/l

Initials:

Carbohydrate will be available if required.
Ensure participant leaves with monitoring diaries and clear instructions to complete this on the evening before, and morning of, the next visit i.e. day 8.
Monitoring diaries will be completed from days 8 to 18 inclusive.

Visit 1 (Day 1)

1. On arrival at the laboratory the participant will be connected to their minimed monitor, and given instruction on its use.
2. They will then be taken through the procedures for recording food intake, insulin dosage, hypoglycaemia and physical activity that they will be required to complete for the duration of the study.
3. Finally the participants will be attached to the Actiheart physical activity monitor.

Ask participants about usual management of food and insulin when exercising with the attached questionnaire. If anomalies are apparent offer education.

After a period of at least 1 hour has elapsed and stable readings are obtained from the minimed meter the participant should be asked to measure their blood glucose levels using their TrueOne meter; if blood glucose levels are not above 17 mmol l^{-1} or below 4 $mmol^{-1}$, the participant will be put on a Polar heart rate monitor in preparation for their treadmill walking exercise.

Current blood glucose level: mmol/l

Initials:

Previous blood glucose time: Level:
Previous dose of insulin taken: mmol/l
Usual Insulin dose mmol/l
Time of meal:
CHO taken: g.

The participant will commence their 40 minute walk at 3$km.h^{-1}$ for 2 minutes then the intensity will be increased to elicit 60% VO_{2max} determined from the Incremental Walking Test.
During the 40 min exercise participants will have their HR and blood glucose levels continuously monitored and RPE will be assessed every 10 minutes.
Participants should be asked to measure their blood glucose levels 20 minutes through the exercise period.
This test will be terminated if:
1. The monitoring system failed.
2. A participant experienced progressive angina.
3. A participant experienced light headedness, confusion, ataxia, pallor, cyanosis or nausea.
4. A participant experienced discomfort and asked to stop.
5. Blood glucose levels dropped below 4mmol l^{-1} or the participant experiences symptoms of hypoglycaemia.
If any of the above occurs please complete an adverse event form.

Results of blood glucose taken during exercise: mmol/l

Initials:

Ensure that participants test blood glucose levels on completing the period of exercise.

Blood glucose level: mmol/l

Initials:

On completion of the test the subject would adopt their normal life style.

Participants would be asked not to perform any structured exercise on day 2.

On day 3 they will be instructed to perform their own exercise at 60% VO2 max for 40 minutes and check blood glucose levels before, during and after.

Actiheart and minimed meters to be worn continually, and arrangements will be made to collect on day 4.

Remind participants to keep monitoring diaries up to date until handing in equipment.

Day 3 – own exercise

Type:
Time of day:

Record blood glucose
Before:
During:
After:

Reduce following meal dose:

Day 4

Arrangements for collection of equipment and diaries:

Visit 2 (day 8)

1. On arrival at the laboratory the participant will be connected to their minimed monitor, and given instruction on its use.
2. Any problems from the previous week will be discussed regarding: diaries, equipment and own exercise.
3. Finally the participants will be attached to the Actiheart physical activity monitor.

After a period of at least 1 hour has elapsed and stable readings are obtained from the minimed meter the participant should be asked to measure their blood glucose levels using their TrueOne meter; if blood glucose levels are not above 17 mmol l^{-1} or below 4 $mmol^{-1}$, the participant will be put on a Polar heart rate monitor in preparation for their treadmill walking exercise.

The participant should be asked to measure their blood glucose levels using their TrueOne meter; if blood glucose levels are not above 17 mmol l^{-1} or below 4 $mmol^{-1}$, the participant will be put on a Polar heart rate monitor in preparation for their treadmill exercise.

Current blood glucose level: mmol/l

Initials:

Previous blood glucose time: Level:
Previous dose of insulin taken: mmol/l
Usual Insulin dose mmol/l
Time of meal:
CHO taken: g.

The participant will commence their 40 minute walk at 3km.h^{-1} for 2 minutes then the intensity will be increased to elicit 60% VO_{2max} determined from the Incremental Walking Test.
During the 40 min exercise participants will have their HR and blood glucose levels continuously monitored and RPE will be assessed every 10 minutes.
Participants should be asked to measure their blood glucose levels 20 minutes through the exercise period.
This test will be terminated if:
1. The monitoring system failed.
2. A participant experienced progressive angina.
3. A participant experienced light headedness, confusion, ataxia, pallor, cyanosis or nausea.
4. A participant experienced discomfort and asked to stop.
5. Blood glucose levels dropped below 4mmol l^{-1} or the participant experiences symptoms of hypoglycaemia.

If any of the above occur please complete an adverse event form.

Blood glucose level during test: mmol/l

Initials:

Ensure that participants test blood glucose levels on completing the period of exercise.

Blood glucose level: mmol/l

Initials:

On completion of the test the subject would adopt their normal life style.

Participants would be asked not to perform any structured exercise on day 9.

On day 10 they will be instructed to perform their own exercise at 60% VO2 max for 40 minutes and check blood glucose levels before, during and after.

Actiheart and minimed meters to be worn continually, and arrangements will be made to collect on day 11.

Remind participants to keep monitoring diaries up to date until handing in equipment.

Day 10 – own exercise

Type:
Time of day:

Record blood glucose
Before:
During:
After:

Reduce following meal dose:

Day 11

Arrangements for collection of equipment and diaries:

Appendix 5
GP information letter

Edinburgh Napier University

Faculty of Health, Life and Social Sciences Research Ethics and Governance Committee

Date:

Dear Dr.

Testing a self–management algorithm for people with Type 1 diabetes undertaking moderate intensity exercise.

Name of participant: _____

Date of Birth: _____

Your patient has agreed to participate in this research project (see attached patient information sheet). The research has been given approval by the NHS and X Ethics Committee. If you have any questions please contact me by email or phone.

Kind regards

Jacqui Charlton
Lecturer/Practitioner in Diabetes
Edinburgh Napier University

Contact details:

Name: Jacqui Charlton
Edinburgh Napier University, 74 Canaan Lane, Edinburgh EH9 2TB
Email / Telephone: j.charlton@napier.ac.uk / 0131 455 5676