



UNIVERSITY OF OXFORD

**The Development of a Complex Dietary and Physical Activity
Intervention to Improve Glycaemic Control and Prevent Undesirable
Weight Gain Using Novel Technology, in Young Adults with Type 1
Diabetes Mellitus**

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Wolfson College, Oxford

A Thesis Submitted for the Degree of Master of Science by Research in the
University of Oxford

Michaelmas Term, 2011

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ABSTRACT

Intensive insulin treatment for type 1 diabetes has been shown to prevent or delay the progression of microvascular and macrovascular complications. Improvements in glycaemic control however, may be associated with undesirable weight gain, which could interfere with treatment compliance. Physical activity may potentially improve insulin sensitivity, reduce insulin requirements and prevent undesirable weight gain. Current diabetes education programs provide little or no information on weight gain prevention, are resource intensive and have shown unsustainable improvements in glycaemic control. The use of e-health platforms in diabetes is a promising approach for sustainable education and support provision from a distance. The objective of this thesis was to provide a rationale and describe the processes required for the development of an intervention to improve glycaemic control without weight gain, using a mobile phone-based e-health platform in young adults with type 1 diabetes.

To further investigate the extent to which treatment intensification may lead to weight gain and physical activity reduces insulin requirements, two systematic reviews were conducted. The results of the reviews contributed to the development of the components and processes of the proposed intervention and helped in defining the specifications of the e-health platform through which the intervention would be delivered. A complete diabetes package would include sustained dietary education, portion control, carbohydrate counting and physical activity monitoring. Some of the components of the intervention were evaluated, including the validation of a novel carbohydrate and calorie counting smartphone application against standard food composition tables. A dietary audit provided information on patients' ability to estimate the carbohydrate and calorie content of food from photographs, further highlighting the need for the proposed intervention.

This thesis provides a basis on which a formal evaluation of the different intervention components could be based, to determine their impact on the provision of diabetes care in clinical practice.

300 words

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ABBREVIATIONS

Abbreviations	Explanation
ADA	American Diabetes Association
BDA	British Diabetic Association
BMI	Body Mass Index
BMR	Basal Metabolic Rate
CAD	Coronary Artery Disease
COMA	Committee of Medical Aspects of Food and Nutrition Policy
CP	Carbohydrate Portion
CVD	Cardiovascular Disease
DAFNE	Dose Adjustment for Normal Eating
DCCT	Diabetes Controlled and Complications Trial
DIT	Diet-Induced Thermogenesis
DKA	Diabetic Ketoacidosis
DRV	Dietary Reference Values
DSN	Diabetes Specialist Nurse
FAO	Food and Agriculture Organisation
GPS	Geographical Positioning Systems
HbA1c	Glycated Haemoglobin
HOMA	Homeostatic Model Assessment of Insulin Sensitivity
IAA	Insulin Autoantibodies
ICA	Islet Cell Autoantibodies
METS	Metabolic Equivalent
MeSH	Medical Subject Headings
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NLEA	Nutritional Labeling and Education Act
NRUCTs	Non-Randomised and Uncontrolled Clinical Trials
PAL	Physical Activity Levels
PAR	Physical Activity Ratio
QUALY'S	Quality Adjusted Life Years
RCT	Randomised Controlled Trials
SMBG	Self Monitoring of Blood Glucose
TEE	Total Energy Expenditure
UCT	Uncontrolled Clinical Trial
UKPDS	United Kingdom Prospective Study

1. Introduction

1.1 Background

Type 1 diabetes is a leading cause of morbidity and mortality in young people and although its incidence is highest in childhood, later onset in adulthood also occurs (1). It is common in people with a strong family history, with approximately 6% of children of an affected father developing type 1 diabetes, compared to approximately 3% of children of an affected mother. With population prevalence between 0.4 and 0.6%, the risk of siblings developing diabetes is 12 to 15 times greater than the general population (2,3).

Type 1 diabetes results from the autoimmune destruction of the insulin-producing β -cells of the pancreas, with consequent insulin deficiency, leading to complete insulin dependency (4,5). The aetiology of the disease is poorly understood and the risk factors are still being investigated. Several genetic influences have been involved in the pathogenesis of type 1 diabetes such as genetic defects of the β -cells of the pancreas, and immune defects, such as the presence of insulin (IAAs) or islet cell (ICAs) autoantibodies (4). Exposure to several environmental factors has also been linked to increased risk of developing type 1 diabetes, such as viral infections, i.e. rubella (6) and mumps (7), and exposure to toxins (N-nitroso derivatives), together with several pre-natal and early post-natal factors such as high birth weight and increased maternal age at the time of delivery (8).

1.2 Prevalence of Type 1 Diabetes

Type 1 diabetes accounts for around 5-10% of all cases of diabetes (9). Its incidence is characterised by wide differences between populations, ranging from very low in South America, to very high in Europe and especially Northern Europe (1). More specifically, in Western Southern America approximately 0.7 cases are diagnosed with type 1 diabetes per

100,000 per year (10), while in Finland, which has the highest incidence in the world, approximately 41 cases are diagnosed per 100,000 per year (11,12). The incidence in the UK has been increasing by 3% per year over the last three decades (13) and in the Oxford region the overall incidence in children aged 0-15 in the period 1986 to 1996 was 18.6 cases/100,000/year, with the increase largely confined to those aged less than five years (14).

Worldwide, around 3.2 million deaths are attributable to diabetes each year (15). The cost of diabetes (both type 1 and type 2) to the UK National Health Service (NHS) is estimated to be around 5% of the budget and the cost to patients' quality of life and life expectancy is equally burdensome (16). Among children diagnosed with type 1 diabetes aged 10, boys will lose 16.6 years of life and 29.3 Quality Adjusted Life Years (QALY's), and girls will lose 17.9 years of life and 31.8 QALYs (17).

1.3 Burden of Disease

Although the prognosis of diabetes is poor, its complications are potentially preventable. The most severe acute complications of type 1 diabetes are hypoglycaemia and diabetic ketoacidosis. Hypoglycaemia is the most common side effect of treatment and severe hypoglycaemia affects around 10% of patients each year. Diabetic ketoacidosis (DKA) is more common in younger patients. It results from absolute (total insulin omission) or relative (illness or inappropriate reduction in insulin dose) insulin deficiency and is associated with 3-5% mortality (5).

Long-term complications of type 1 diabetes include retinopathy, nephropathy and neuropathy as well as increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease. The increased mortality associated with type 1 diabetes is mainly attributable to cardiovascular disease (18).

1.4 Treatment

The primary aim of type 1 diabetes treatment is to achieve insulin profiles that mimic non-diabetic pancreatic insulin secretion patterns. Over the years, technological advances and innovations in medical and nutritional research, such as the development of human insulin analogues and the introduction of simpler, smarter and faster blood glucose meters, have made this possible. This area is discussed in greater detail in Chapter 6. Non-diabetic insulin secretion patterns can be achieved through treatment intensification, which involves frequent blood glucose monitoring and matching insulin doses to carbohydrate intake, which is the primary nutrient that affects the postprandial rise in blood glucose levels (19).

There is conclusive evidence that treatment intensification reduces the burden of diabetes-related microvascular and macrovascular complications. In the Diabetes Control and Complications Trial (DCCT) intensification of glycaemic control reduced the risk of microvascular complications by about 2/3 when compared to conventional treatment (less than 3 insulin injections per day), and showed that the target glycated haemoglobin (HbA1c) level should be about 7% (20). An 11-year follow-up of the primary cohort showed that patients previously randomised to the intensive group had a 42% reduction in macrovascular disease compared to patients previously randomised to conventional treatment (21).

1.4.1 Limitations of Current Treatment

One of the main components of the DCCT that contributed to a reduction in diabetes-related morbidity was treatment intensification, supported by rigorous supervision through regular contact between patients and the diabetes team. However, implementing the DCCT strategy in routine clinical practice can be prohibitively resource intensive. Patients in the intervention group were heavily dependent on the diabetes team, requiring on average 32, 20-minute

telephone conversations with the diabetes specialist nurse each year, who were offering advice on insulin dose adjustment (22). This raises questions regarding treatment sustainability, patient autonomy and the extent to which patients acquire the skills to effectively self-manage their condition.

Following the DCCT's evidence that intensification of glycaemic control reduces the microvascular and macrovascular complications of type 1 diabetes, a number of structured education programs have been implemented to support the development of diabetes self-management skills and to enhance patient autonomy. The Dose Adjustment for Normal Eating (DAFNE) program is currently the leading approach for type 1 diabetes education in the UK (23). This intensive 5-day outpatient course uses adult education principles to teach patients to match their insulin dose to carbohydrate intake on a meal-by-meal basis, and unlike the DCCT there is no intensive healthcare input after the initial training period. Tested in a randomised controlled trial (RCT), DAFNE significantly improved patient quality of life, treatment satisfaction and glycaemic control and showed an absolute reduction in HbA1c of 1%, over a six-month period. However, the mean HbA1c remained unacceptably high at 8.4%, and had deteriorated to 8.9% within a year (23), raising questions about its wider effectiveness and sustainability. Despite the limited evidence of the effectiveness of DAFNE, the National Institute for Health and Clinical Excellence (NICE) published guidance, recommending that structured education courses such as DAFNE should be made available to all people with diabetes from the time of diagnosis, onwards (24).

1.5 Intensification of Glycaemic Control and Weight Gain

In clinical practice, apart from the limited evidence of the effectiveness of structured diabetes education programs, intensification of glycaemic control has been associated with undesirable

weight gain, which may act as a barrier to treatment compliance. For example some patients, especially adolescent girls and women (25-27), develop disordered eating habits and intentionally omit insulin injections in an attempt to induce weight loss (25,28-30). Indeed, up to 1/3 of people with type 1 diabetes, and more commonly females, report regular omission of prescribed insulin doses, in an attempt to control their weight (31). This behaviour is dangerous since it not only leads to poor glycaemic control but also to higher rates of diabetes-related complications, including the potentially fatal diabetic ketoacidosis.

In the general population, being overweight or obese has been associated with increased risk of cardiovascular disease (CVD), gallstones, certain types of cancer and type 2 diabetes (32,33). In type 1 diabetes, coronary artery disease (CAD) is the principal cause of long-term morbidity and mortality. Prospective studies suggest that visceral adiposity, which is a characteristic of metabolic syndrome, is associated with increased cardiovascular risk (34,35). In type 1 diabetes, however, it has yet to be demonstrated whether cardiovascular risk is increased by weight gain resulting from intensification of glycaemic control.

1.6 Need for a Program of Research

There is overwhelming evidence that intensification of glycaemic control improves the poor prognosis of type 1 diabetes. The DCCT approach however, can be resource intensive and structured education programs such as DAFNE have only shown short-term, modest improvements in glycaemic control (20,23). In addition, weight gain can be a barrier to treatment compliance (36).

Current interventions mainly focus on optimising glycaemic control by teaching patients to match their insulin doses to carbohydrate intake and give little or no attention to preventing weight gain (23). The challenge is to develop an intervention that is more effective and less

resource intensive, aiming to optimise glycaemic control, improve self-management skills and to promote patient autonomy, while focussing on preventing undesirable weight gain, and providing sustainable treatment effects.

1.7 Improving Intervention Delivery Methods

During the twentieth century and into the twenty-first, new healthcare technologies have improved the quality of diabetes care. In the 1980s, and after urine testing was proven unsatisfactory and inadequate in accurately reflecting blood glucose levels (37), self-monitoring of blood glucose (SMBG) was described as one of the most important developments in diabetes management (38,39). Nowadays, SMBG is a fundamental part of treatment, with the emerging technologies providing reliable and easy to use blood glucose monitoring systems. Additionally, insulin delivery methods have evolved, with needles and syringes being superseded by insulin pens and continuous subcutaneous insulin infusion pumps (“pumps”), which are convenient, easy to use and carry around, and are more accurate. Most importantly, insulin pens and pumps enable patients to intensify their insulin treatment using “basal bolus” regimens that mimic the physiologic insulin secretion by providing sustained background plasma insulin levels with pre-prandial insulin boluses, offering greater flexibility and control (40).

Despite these advances, diabetes management is still a complex process, the treatment of which entails a degree of interaction between patients and healthcare professionals. Patient motivation is important for behavioural change and improved treatment adherence. To achieve sustainable treatment effects, frequent patient contact is required and even nowadays patient treatment, education and monitoring mainly operates on a face-to-face

basis, which can be resource intensive and impractical for both patients and healthcare professionals.

Over the last decade, several studies have addressed the feasibility, safety and efficacy of telecommunication devices in the management of long-term conditions, by providing the potential for more accessible and efficient healthcare (41,42). E-health interventions have been shown to be useful in the efficient and effective collection of patient health information, reaching patients unable to attend clinic appointments and enabling remote monitoring, consultations and patient education (43,44).

Studies have demonstrated the feasibility and acceptability of e-health platforms in type 1 diabetes for downloading patient data and for monitoring patients from distance, but failed to show significant improvements in HbA1c (41). RCT evidence however, revealed improved treatment adherence, with 40% more patients transmitting SMBG readings in the group using a mobile phone-based e-health system compared to the control group, after a 9-month follow-up. Some evidence of improved glycaemic control was also shown, with a significantly higher proportion of patients in the intervention group achieving HbA1c levels $\leq 8\%$ compared to the control group (45). These findings indicate that e-health is valued by users and suggest that such platforms could be used to deliver more complex, intensive interventions. The use of e-health platforms in healthcare will be discussed in greater detail in Chapter 5.

1.8 Intervention Components

1.8.1 Intensification of Glycaemic Control

The existing evidence-base suggests that a remotely delivered, dietary, educational intervention could offer sustained treatment, monitoring and support through a mobile

phone-based e-health platform. The proposed intervention would aim to optimise glycaemic control through frequent SMBG (at least 4 times/day), a basal bolus insulin regimen and through understanding the effect of carbohydrate on blood glucose levels and insulin requirements (20). The program would incorporate additional educational components to enable patients with the insulin dose adjustment process.

1.8.2 Prevention of Undesirable Weight Gain

Intensification of diabetes treatment through insulin injections results in less glycosuria and to the reversal of the metabolic rate from catabolism to anabolism, leading to positive energy balance and to weight gain (46). Insulin also contributes to weight gain as it is a lipogenic hormone that inhibits lipolysis and promotes lipogenesis (47). Furthermore, sub-optimal physical activity could result in positive energy balance and consequently to weight gain (33). It is therefore important for the proposed intervention to address the concept of energy balance, by giving equal attention to both energy intake and energy expenditure.

Energy balance or weight stability depends on energy intake matching energy expenditure. For weight loss, energy expenditure should exceed energy intake and for weight gain energy intake should exceed energy expenditure. Increased physical activity is an important component of diabetes management as it has been shown to reduce the risk of heart disease, stroke and depression (48-50). It has also been suggested that it improves insulin sensitivity and reduces insulin requirements, which could potentially prevent undesirable weight gain. Together with intensive insulin treatment and carbohydrate counting, encouragement of physical activity and a basic knowledge of the calorific content of foods are needed, to achieve energy balance and avoid the undesirable effects of weight gain on diabetes treatment.

1.9 Overall Objective

The overall objective of this thesis is to provide a rationale and describe the processes required for the development and evaluation of a complex dietary and physical activity intervention intended to improve glycaemic control without undesirable weight gain, using a mobile phone-based e-health platform, in young adults with type 1 diabetes.

To assess whether there is sufficient evidence to justify the development of the proposed intervention, the relationships between (i) interventions designed to intensify glycaemic control and body weight and (ii) physical activity, insulin sensitivity and insulin requirements were examined by systematically reviewing the literature and, where possible, conducting meta-analysis to quantify the effect sizes.

2. The Effect on Body Weight of Interventions Designed to Intensify Glycaemic Control in Adults with Type 1 Diabetes: A Systematic Review and Meta-analysis

2.1 Introduction

In patients with type 1 diabetes, insulin deficiency and hyperglycaemia result in glycosuria, osmotic diuresis, catabolism and consequent weight loss (46). With insulin initiation these processes are reversed, weight is rapidly regained and, with intensified treatment, weight gain may be even more apparent (47,51).

Intensification of glycaemic control has been demonstrated conclusively to reduce the risk of microvascular and macrovascular complications in patients with type 1 diabetes (20,21,52). Undesirable weight gain resulting from intensification of glycaemic control, however, has been associated with an increase in blood pressure and lipid levels (36) and could also operate as a barrier to compliance with diabetes treatment (47). The emotional consequences of weight gain may enhance patients concerns about weight and body image, leading to poor self-esteem and self-management neglect. Furthermore, there is evidence that overweight adolescents are more likely to become overweight adults (26).

Intensification of glycaemic control can improve the poor prognosis of type 1 diabetes, but weight gain may be an inevitable consequence. The objective of this systematic review was to assess whether weight gain is observed in RCTs of interventions aiming to intensify glycaemic control compared to conventional treatment, in adult patients with type 1 diabetes.

2.2 Methods

2.2.1 Inclusion and Exclusion Criteria

The trials eligible for inclusion in this systematic review specified that the intervention should include and administer at least three insulin injections daily but allowed for a variety of other components targeted at intensifying glycaemic control. Interventions in primary care, outpatient and community settings were included with a minimum sample size of five in each treatment arm (54) and a minimum follow-up period of at least three months so that any changes in weight and HbA1c would be apparent. Participants had to be ≥ 18 years of age with type 1 diabetes based on the diagnostic criteria specified by the authors.

The criteria used to exclude trials were: failure to specify the type of diabetes; <three insulin injections per day in the intervention group; inclusion of pregnant women; use of combination therapy with oral hypoglycaemic agents and insulin. Studies that compared different types of insulin were excluded, as they were not comparing intensified vs. conventional insulin treatment. Studies that compared different insulin delivery methods (such as pumps vs. multiple daily injections) were also excluded, as it has been reported that treatment with insulin pumps improves glycaemic control, reduces insulin requirements and may result in weight loss (291). This could dilute the effect size of treatment intensification on body weight. Furthermore, in the NHS, insulin pumps are not suitable for everyone. This type of treatment is expensive, requires a lot of healthcare professional training and expertise, time and effort by patients who also have to meet the National Institute for Health and Clinical Excellence (NICE) guidelines on insulin pump therapy (292). Although it is hoped that in the future all diabetes specialist centres will be able to provide this treatment option to their patients, for now, wide adoption of insulin pump therapy is unlikely (293). Therefore, there still remains a need to address the effect of multiple daily injection therapy on weight gain.

2.2.2 Search Strategy and Study Selection

The Cochrane Register of Controlled Trials from 1986, MEDLINE (1950), EMBASE (1980), CINAHL (1982) and PsychINFO (1967) databases were searched for RCTs evaluating interventions intended to intensify glycaemic control in adult patients with type 1 diabetes, without restriction on the language of publication. A broad search strategy was followed using a combination of free-text words and medical subject heading (MeSH) terms synonymous with 'type 1 diabetes' and 'intensive insulin treatment' and 'glycaemic control'. Searches were restricted to publications between the dates shown above for each of the databases and August 2010. The search strategies together with the filter for RCTs, were tailored appropriately to meet the requirements of each database. The reference lists of the included trials were searched to identify additional trials. Where possible, authors of relevant trials were contacted to obtain further information and additional references that met our inclusion criteria.

2.2.3 Data Extraction and Quality Assessment

Titles and abstracts retrieved from the initial bibliographic searches were scanned and assessed to identify those potentially meeting the inclusion and exclusion criteria. Full reports of those appearing to meet the criteria were obtained to confirm their eligibility, and any disagreement was resolved by discussion amongst the author of this thesis and her supervisors. Assessment of trial quality and data extraction was carried out independently by two of the three reviewers. If data were missing, the authors of the trials were contacted to obtain the information.

For each trial, data were collected for the following: general information (date of data extraction, first author, year of publication, journal and aim of study); study methodology

(study design, randomization procedure, duration of intervention, duration of follow-up); participants (inclusion and exclusion criteria, numbers, gender, mean age, baseline measurements, losses to follow-up); interventions (purpose of intervention, description of intervention and control groups); outcomes (primary and secondary outcomes). Criteria for assessment of trial quality included the reporting of the method of randomisation, blinding of objective measurement of the main trial outcomes and loss to follow-up. Potential scores ranged from zero to a maximum of five (55).

2.2.4 Statistical Analysis

For trials reporting a series of measurements over the intervention period, the change from baseline to the final measurement of the outcomes of interest, which were body weight and HbA1c, was used. For trials using a crossover design, the data provided from baseline to the first intervention period only was used. For each trial, the mean change in each group was calculated by subtracting the final mean from the baseline mean. Where the standard deviation of the change within each group was not provided, it was estimated using the following equation: $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2 - (2r \sigma_1 \sigma_2)}$, where a conservative correlation coefficient (r) value of 0.5 was assumed (56), and σ was the standard deviation of each group.

The mean differences from the trials were pooled in a meta-analysis comparing the effects of the interventions on body weight and HbA1c levels in the intervention and control groups with a p value of 0.05 being considered statistically significant. Review Manager (Version 5_0_23; Update Software, Oxford, UK) was used for the final analyses and STATA 11 for a meta-regression analysis.

2.3 Results

2.3.1 Trial Characteristics and Methodology

The search strategy identified a total of 1399 titles and abstracts from which full publications describing 108 papers were retrieved for more detailed evaluation (Appendix I). From these publications, 21 potentially eligible RCTs were identified, of which seven were excluded for the following reasons: (i) the intervention did not include an intensive insulin regimen defined as \geq three insulin injections per day (57,58); (ii) a high proportion of patients in the intervention group administered $<$ three insulin injections per day (Perry *et al* 52% and Mühlhauser *et al* 40%) (59,60); (iii) participants were pregnant (61); (iv) study centres used different analytical methods of HbA1c measurement (62); or (v) all patients in the intervention group were on pump therapy (63).

The 14 trials that met all the inclusion criteria (20,23,42,45,52,64-72) were systematically reviewed and, where possible, the data were pooled in meta-analyses comparing the effect of interventions on body weight and HbA1c respectively. One trial failing to report weight at baseline (70), four trials not reporting follow-up measures of weight (42,52,65,67), and one trial reporting only body mass index (BMI [kg/m^2]) (64) were excluded from the pooled analysis of the effect on body weight. Three trials that measured HbA1 (52,71,72) were also excluded from the pooled analysis of the effect on HbA1c. One trial (DCCT) (20) included patients on insulin pump therapy, as well as patients on multiple daily injections. On further investigation it was made clear that only a small proportion of participants (13%) were on insulin pumps and it was decided to include the trial in the systematic review.

Appendix II shows the characteristics of the included trials. Six trials had more than 100 participants (20,23,52,66-68) and eight trials followed the patients for up to, or more than, one year (20,23,52,66,67,69,71,72). Three trials included children and/or adolescents

(20,64,68). Where possible the adult data were extracted and analysed (20,68), or the authors confirmed that all study participants were at least 18 years of age (64). The duration of follow-up for all trials ranged from three months to 7.5 years.

In nine trials, the intervention used telecommunication devices for data transmission, insulin dosing advice, blood glucose testing alerts and for communication between patients and healthcare professionals (20,42,45,52,64,66,68,69,72). Three trials had psychological components (65,67,70), five included dietary (20,23,52,67,69) and three had physical activity components (20,67,69). All but five trials (42,52,64,65,71) set pre-defined blood glucose targets for the participants randomised to the intervention group.

Patients in the trial control groups either continued with usual care from the diabetes team or a standardised form of usual care including performing blood glucose self monitoring at least four times daily (68), or keeping a blood glucose diary (64). In five trials, the treatment in the control group consisted of <three insulin injections per day (20,52,69,71,72). In the others, the number of injections used in the control group was not reported in the paper (23,42,45,64-68,70).

Methodological quality varied widely (Appendix II). Attrition rates were modest, with six trials showing dropout rates of <10% (20,64,65,70,71,73). Less than half the trials used intention to treat analyses. If the type of analysis was unclear, or was not reported in the paper, it was assumed that the authors did not follow intention to treat analyses.

2.3.2 Outcome Measures

Impact on body weight

The eight trials reporting baseline and follow-up body weight measures (20,23,45,52,66,68,69,71) showed a significant pooled mean weight gain of 1.59 kg [95% CI 1.20 to 1.97; $p < 0.0001$] following intensification of glycaemic control (Figure 1). When the two trials that reported change in HbA1 rather than HbA1c were excluded (52,71), the pooled mean weight gain of 1.55 kg [95% CI 1.16 to 1.95; $p < 0.001$] was still statistically significant. The largest trial (DCCT) (20) found a significant mean weight gain of 2.10 kg between intervention and control groups following treatment intensification. In this analysis, data for the 1246 DCCT participants who were ≥ 18 years of age at randomization at 1-year follow-up were used. Gender-specific data from this trial showed that the mean increase in BMI was significantly higher among female participants (74). The other trials failed to report gender-specific data on body weight.

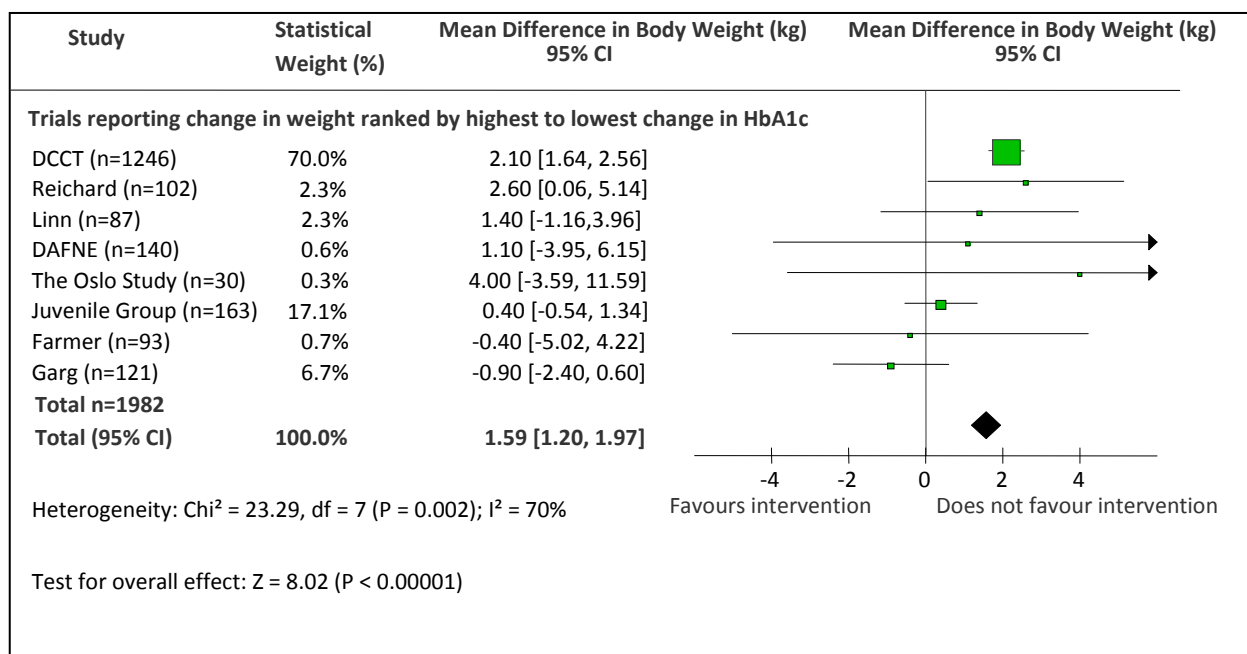


Figure 1: Meta-analysis of changes in body weight (kg) between intervention and control groups

There was significant heterogeneity between the trials, which had wide confidence intervals, varying follow-up duration and sample sizes. To investigate the heterogeneity between the eight trials, sensitivity analyses was carried out including only those trials specifically comparing a basal bolus insulin regimen (\geq three injections) to $<$ three insulin injections/day (20,52,69,71). In this subgroup, there was a significant increase of 2.10 kg [95% CI 1.65 to 2.55; $p<0.00001$] in body weight between intervention and control groups and no heterogeneity ($\text{Chi}^2=0.68$, $\text{df}=3$ ($p=0.88$); $I^2=0\%$).

Impact on HbA_{1c}

A pooled mean decrease of 0.95% [95% CI 0.85 to 1.05; $p<0.00001$] in HbA_{1c} was shown between intervention and control groups, which was statistically significant (Figure 2). In the six trials that reported both changes in weight and HbA_{1c} (20,23,45,66,68,69), the mean decrease was 1.09% [95% CI 0.98 to 1.20]. Ranking the trials in descending order (from the trial showing the largest weight gain (20) to the trial showing the least (66)), with studies failed to report a change in weight ranked alphabetically (42,64,65,67,70), it became apparent that the trials demonstrating the larger weight gain also showed the largest improvement in HbA_{1c}.

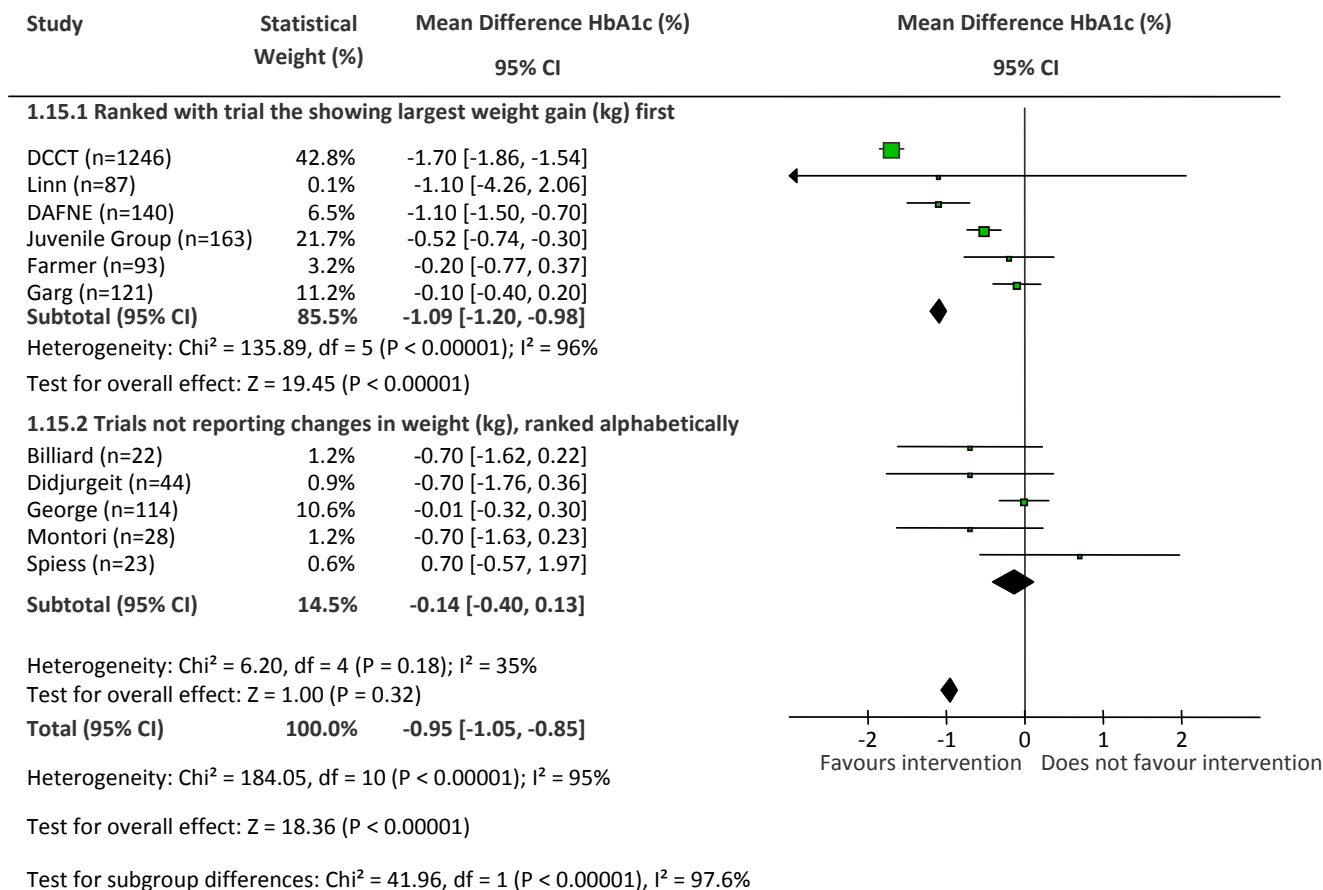


Figure 2: Meta-analysis of changes in HbA1c (%) between intervention and control groups

The DCCT, which was the trial with the largest sample size, had a considerably larger effect size on HbA1c compared to the other trials (20). Excluding this trial from the analysis (20) reduced the number of patients by 66.5% and the pooled mean decrease in HbA1c from 0.95% to 0.39% [95% CI 0.26 to 0.52], although this reduction remained statistically significant ($p < 0.00001$). Heterogeneity amongst the trials was also reduced.

All but one trial (70) reported a decrease in HbA1c in the intervention compared to the control group, and in three trials this reduction was statistically significant (20,23,68), as it was in two (52,72) of the three trials (52,71,72) that measured HbA1. Three trials specifically compared a basal bolus insulin regimen (\geq three injections) with $<$ three injections/day (20,52,72). Another

trial, DAFNE, assessed the effect of a 5-day intensive education course on matching insulin dose to carbohydrate intake on a meal-by-meal basis, compared with usual care (23) whilst a further trial compared continuous glucose monitoring with intensive insulin treatment compared with SMBG (68). Apart from DAFNE (23), the trials that showed a statistically significant decrease in HbA1c had telecommunication components and offered structured follow-up support to patients, in addition to the intensified treatment and educational components (20,52,68).

Meta-regression analysis to investigate the effect of HbA1c on body weight

To assess the relationship between HbA1c and body weight, the trials in Figure 2 were ranked in descending order starting from that showing the largest improvement in HbA1c (20). Visual inspection of the forest plot suggests that the trials that demonstrated the largest improvements in HbA1c also showed the largest increase in body weight (Figure 2). To quantify the effect of HbA1c on body weight, an exploratory meta-regression analysis was performed (Figure 3) which suggested that each 1% improvement in HbA1c is associated with a significant weight gain of 1.63 kg [95% CI 0.68-2.60, $P < 0.005$].

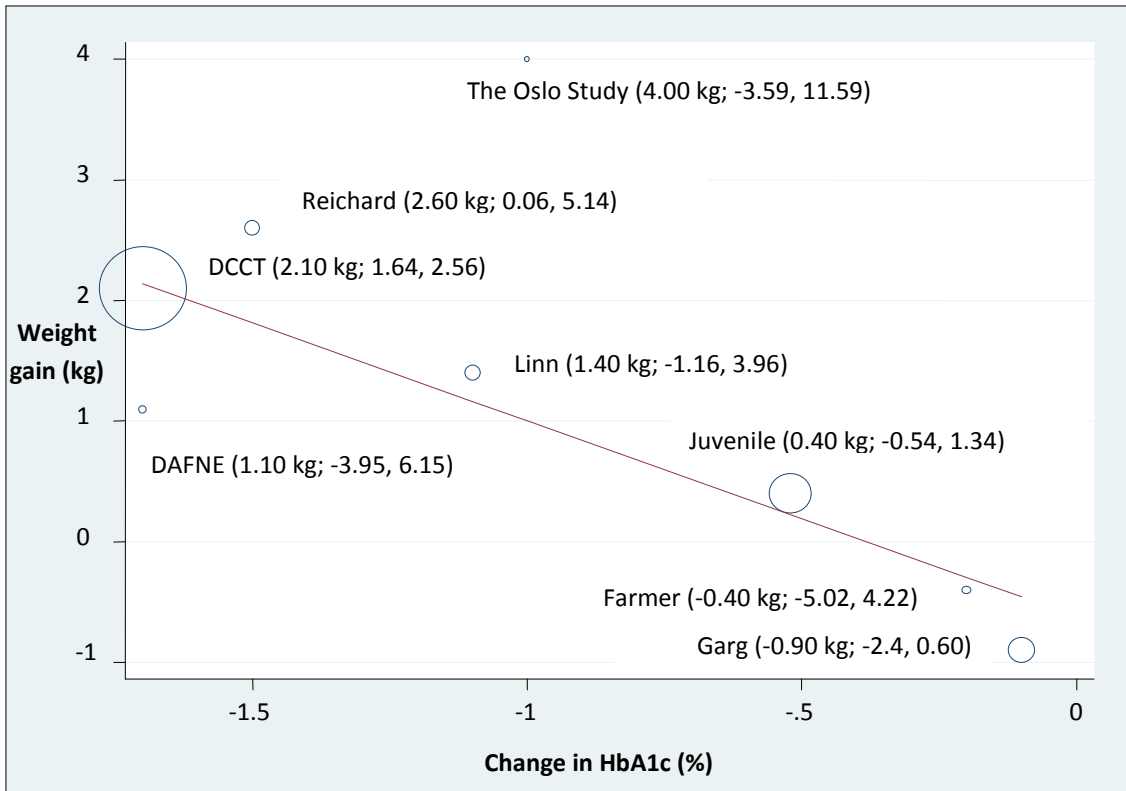


Figure 3: Meta-regression analysis showing changes in body weight (kg) for every 1% change in HbA1c. The size of the circles corresponds to the weight (%) of each study.

2.4 Discussion

This systematic review confirms the clinical observation that intensification of glycaemic control in adults with type 1 diabetes results in weight gain. The meta-analyses found a pooled mean decrease in HbA1c of 1.09% with a corresponding mean increase in weight of 1.59 kg. As far as we are aware, no such systematic review has been conducted previously.

The review has a number of strengths. It included only RCTs as they are methodologically more rigorous and have a lower risk of bias and confounding than observational study designs. The broad search strategy used, allowed identification of trials that aimed at intensifying glycaemic control using a wide range of interventions including dietary, telehealth and psychological strategies, in addition to intensive insulin (\geq three injections per day) and

monitoring regimens. There was no language restriction and an attempt was made to contact the authors to gather any missing data.

The findings are not explained by the inevitable weight gain after diagnosis following initiation of insulin treatment, since only one small trial included in the analysis recruited newly diagnosed patients (70). Nevertheless, the results need to be interpreted with care because there are a number of limitations. Although the exploratory meta-regression analysis suggests that each 1% improvement in HbA1c is associated with a weight gain of about 1.63 kg, an association observed between variables at an aggregate level does not necessarily represent an association that occurs at an individual level. While this is a physiologically plausible association, it could not be assessed more rigorously without conducting an individual patient data meta-analysis, which requires access to the raw data. Some of the trials identified were conducted nearly twenty years ago before HbA1c assays were aligned to the DCCT assay and before the introduction of analogue insulin (20,71). Limited evidence suggests that insulin detemir (75), but not insulin glargine (76) is associated with a reduced energy intake and reduced weight gain compared with NPH insulin. Only eight of the trials provided data for our primary outcome, which was body weight, and durations of interventions varied widely between trials. In addition, it was difficult to assess objectively the methodological quality of several studies (20,52,64,69-72) undertaken prior to the publication of the CONSORT statement that specified detailed reporting standards for RCTs (77). Furthermore, as weight was not defined as an outcome in any of the trials, most publications did not report in detail its method of measurement.

Although the average trial attrition rate was 11.9%, the largest trials (20,68) had attrition rates of only 3% and 1.5% respectively. With the exception of five trials (20,52,69,71,72), most had a short follow-up period and small sample sizes, possibly providing unreliable estimates. However, there was no heterogeneity between trials comparing a basal bolus insulin regimen

(\geq three injections) to <three injections/day, but there was substantial heterogeneity across all trials, which may be due to the clinical and methodological diversity among the trials. As the heterogeneity could not be fully explained, a random effects model for the meta-regression analysis was used (78,79).

The results of this systematic review are consistent with those for type 2 diabetes (47) including the results of the United Kingdom Prospective Diabetes Study (UKPDS) which showed an association between weight gain and intensification of glycaemic control (80). In type 1 diabetes, non-randomised studies (46,81,82) have also reported weight gain with intensive treatment but, unlike RCTs, may be subject to confounding and bias. Surprisingly, none of the published reviews in patients with type 1 diabetes have systematically assessed or commented on body weight following intensification of diabetes treatment (83-85).

The largest effect on body weight was observed in the DCCT, which had the most statistical information, resulted in the largest reduction in HbA1c, and was one of the longest trials (20). Although the rate of weight gain in patients in the intervention group in the DCCT decreased with longer follow-up, the accumulated weight was persistent (74). This was most apparent in adolescent and adult women who on average, continued to gain considerable amounts of weight (approximately 5kg) and had significantly greater waist circumferences (approximately 3cm) compared to the conventionally treated group after an average follow-up of 70 months. However, the distribution of increase in weight was similar in the control and intervention groups during the first seven years of the trial. Patients in the highest quartiles of weight gain in the intensive treatment group also had the highest blood pressure, cholesterol and lipid levels compared to patients in the lowest quartiles (36). These findings are consistent with the results of prospective observational studies showing female patients treated with intensive insulin therapy having significantly greater weight gain than male patients (86,87). A high prevalence of psychiatric symptoms, disordered eating habits and insulin omission (32) which,

in turn, have serious implications for diabetes management, has been observed in overweight young adult female patients (29).

2.5 Conclusion

This systematic review suggests that a range of interventions designed to intensify glycaemic control that specified and administered at least three insulin injections per day and included a variety of educational, telecommunication and psychological strategies, can improve HbA1c levels but may result in weight gain. Surprisingly, only eight trials aiming to intensify glycaemic control reported changes in body weight. The results of the review highlight a gap in the literature and emphasise the importance for future research of developing interventions specifically designed to intensify glycaemic control whilst preventing concurrent weight gain.

Interventions currently focus mainly on intensifying glycaemic control by matching insulin dose to carbohydrate intake, and provide minimum information on energy intake and energy expenditure, which both influence body weight. Areas in which future interventions might be developed include helping patients to recognise the contribution of all macronutrients, not only carbohydrate, to energy intake, and increasing insulin sensitivity through physical activity. Such approaches could potentially prevent weight gain from becoming a barrier to the intensification of glycaemic control in adult patients with type 1 diabetes, and would be the main focus of the proposed intervention.

3. The Effect of Physical Activity on Insulin Sensitivity. A Systematic Review and Meta-Analysis

3.1 Introduction

In type 2 diabetes, physical activity has been shown to improve glycaemic control, cardiorespiratory fitness and to increase insulin sensitivity (88). The effect of physical activity in type 1 diabetes is less clearly defined and the evidence has not been systematically reviewed. Intensive insulin regimens of at least three injections per day can result in undesirable weight gain (20). Insulin-related weight gain may be prevented by increasing insulin sensitivity, which in turn reduces insulin requirements. This chapter systematically reviews the evidence for the effect of physical activity on insulin sensitivity and glycaemic control in adult patients with type 1 diabetes.

3.2 Research Design and Methods

The Cochrane Library (November 2010), MEDLINE (1950), EMBASE (1980), and CINAHL (1980) databases were searched for studies designed to increase physical activity, without any restriction on the language of publication. A broad search strategy was followed using search terms synonymous with "type 1 diabetes" and "physical activity" and "insulin sensitivity" and "insulin dose" or "glycaemic control". The reference lists of the included trials were searched to identify additional studies.

This review was restricted to adults of ≥ 18 years old, with type 1 diabetes as defined by the diagnostic criteria reported in the study publications. Measures of glycaemia and/or insulin sensitivity or insulin dose should be reported as outcomes. In vivo, insulin sensitivity is

assessed using a series of direct and indirect methods, with the euglycaemic clamp technique considered the best available method (89,90)

Physical activity was defined as the act that increases energy expenditure that could be either aerobic, where muscular and cardiorespiratory systems are involved, or anaerobic and resistance training, involving muscular strength only. Non-Randomised and Uncontrolled Clinical Trials (NRUCTs) were included, provided that patients receiving the experimental intervention followed a prescribed exercise program. RCTs were included if the prescribed exercise intervention was compared to no exercise. The included studies were required to stipulate specific recommendations on type, frequency, intensity and duration of exercise (91) with a specific objective, such as to improve insulin sensitivity or to optimise glycaemic control. Duration of follow-up should have been of at least six weeks, since any exercise program of shorter duration would not be long enough to demonstrate changes in glycaemic control and sustained effects on insulin sensitivity.

Studies were excluded if the experimental intervention involved a single exercise session, the recommended increase in exercise was not adequately described or the intervention group was exposed to another intervention (such as dietary alterations) that was not applied to the control group. Studies failing to specify the type of diabetes, or assessed exercise levels using indirect methods (i.e. self-administered questionnaires) and studies including pregnant women were also excluded.

Information was also collected on study design, length of intervention, participant characteristics including diabetes duration, age and weight, and type of exercise including frequency, duration and intensity. The mean changes in reported measures of insulin sensitivity or insulin dose, glycaemia and weight from the beginning to the end of the study were calculated for each study by subtracting the final mean from the baseline mean. Where

the standard deviation of the change within each group was not provided, it was estimated using the equation: $\sigma = \sqrt{[\sigma_1^2 + \sigma_2^2 - (2r \sigma_1 \sigma_2)]}$ (92), where a conservative correlation coefficient (r) value of 0.5 was assumed, and σ was the standard deviation of each group. The between and within-group mean differences were pooled in meta-analysis comparing the effects of physical activity interventions on insulin sensitivity or insulin dose and HbA1c. A p value of 0.05 was considered statistically significant. Review Manager (Version 5_0_23; Update Software, Oxford, UK) was used for the analyses.

3.3 Results

The search strategy identified 1835 articles from which publications describing 238 studies were retrieved for more detailed evaluation (Appendix III). Full text assessment of the eligible studies resulted in the inclusion of ten NRUCTs (93-102) and three RCTs (103-105), with a total of 151 patients receiving an exercise intervention. One of the RCTs reported baseline and follow-up measures for both groups together after receiving the exercise intervention, and for the purposes of this review it was treated as an uncontrolled clinical trial (UCT) (105). The median average age reported in the studies was 32 (range 24.4 to 42) years, with one study including one patient aged 15 (98). The median average insulin dose was 40 (range 32 to 49) units per day and 63% of participants were males.

Of the NRUCTs shown in Appendix IV, four were UCTs with no comparison group (97-99,105) and seven were non-RCTs with the control groups recruited from different population to the intervention group (93-96,100-102). More specifically, controls were either patients with type 1 diabetes, or healthy individuals, or individuals with different activity levels from the intervention group. To minimize heterogeneity, results only from the patients receiving the experimental intervention are presented. The duration of the NRUCTs ranged from six to 24

weeks and exercise prescription ranged from moderate intensity training (93) to endurance training (96,100,101) in shorter studies, whereas longer studies involved training of progressively higher intensity (94,95,97), heavy resistance weight lifting (105), endurance (102) and interval training (98). All NRUCTs provided supervision during training. Follow-up in the RCTs ranged between 10 and 20 weeks; frequency of training ranged from three to seven days/week and training consisted of 30 to 60 minutes supervised running (103) and 20 minutes home cycling (104).

Five NRUCTs showed an improvement in HbA1c (93,96-98,102). In one study the change was significant compared to baseline HbA1c (93) and in the other this change was significant compared to controls (102). Six NRUCTs showed reductions in insulin dose (93,94,96,98,101,105) and three reported improvements in insulin sensitivity, assessed by the euglycaemic clamp technique (99,101) or by modification of the insulin suppression test (97). In four of these studies this change was significant compared to baseline pre-exercise levels (93,94,97,99) and in one compared to controls (101). Two NRUCTs did not report follow-up changes in insulin dose or insulin sensitivity (95,100) and one showed an increase in insulin dose (102). Meta-analysis of the NRUCTs showed a reduction in insulin dose of 1.74 units/day [95% CI -1.40 to 4.89] (Figure 4).

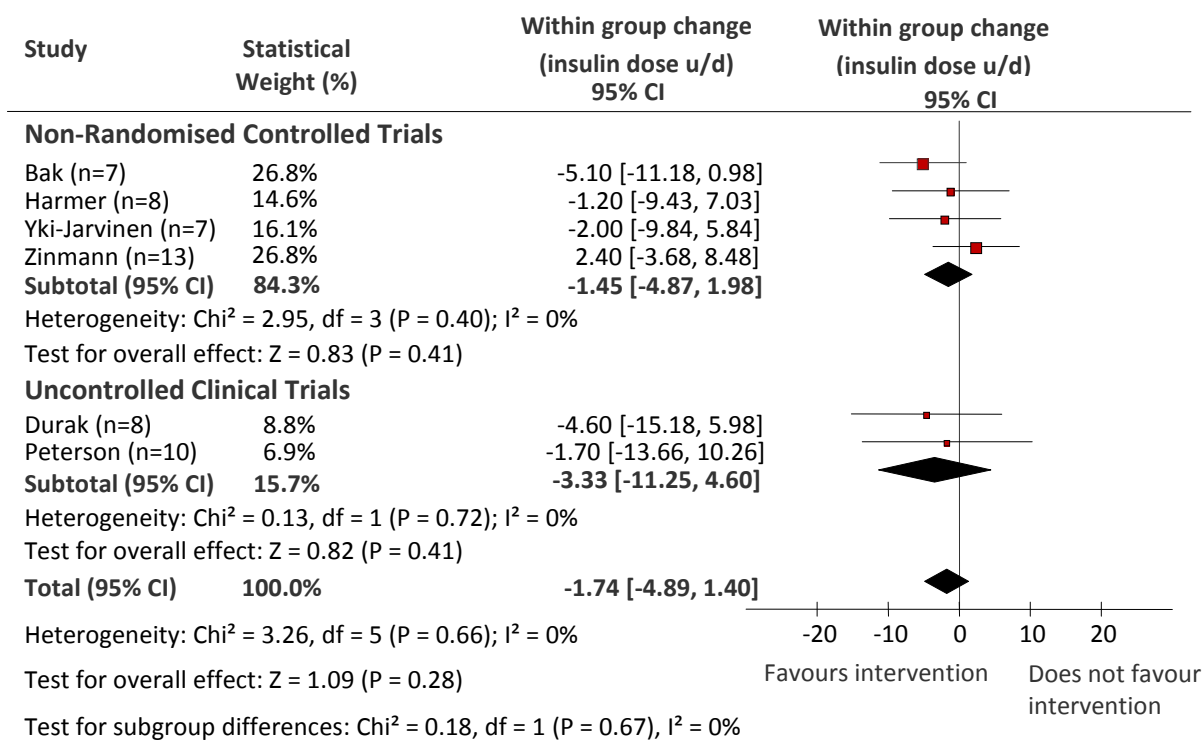


Figure 4: Meta-analysis of changes in insulin dose (u/day) with physical activity

Four NRUCTs showed both an improvement in glycaemic control and a reduction in insulin dose or improvement in insulin sensitivity (96-98,106). Exercise intensity in those four studies ranged from moderate to high intensity. Two of these trials offered additional counselling or teaching (93,97), where patients attended a teaching program on diabetes self-management in relation to exercise, which was followed by a one-week sports camp with high-intensity activities, prior to the training course (97). The other trial required attendance to the outpatient clinic every 2nd week to have blood glucose tests monitored and insulin dose adjusted (93).

One of the two RCTs was restricted only to male (103) and the other to female (104) patients, and only one reported follow-up changes in insulin dose (103). Both reported baseline and follow-up HbA1c. The available data have been pooled in a meta-analysis, which revealed a non-significant improvement in HbA1c of 0.20% [95% CI -0.50 to 0.90] in male and female

patients that received the exercise intervention compared to the control group (Figure 5). There was no heterogeneity between the trials. The trial reporting insulin dose measures found that 30 to 60 minutes of moderate intensity running, 3 to 5 days/week in men, had no effect on insulin dose (103).

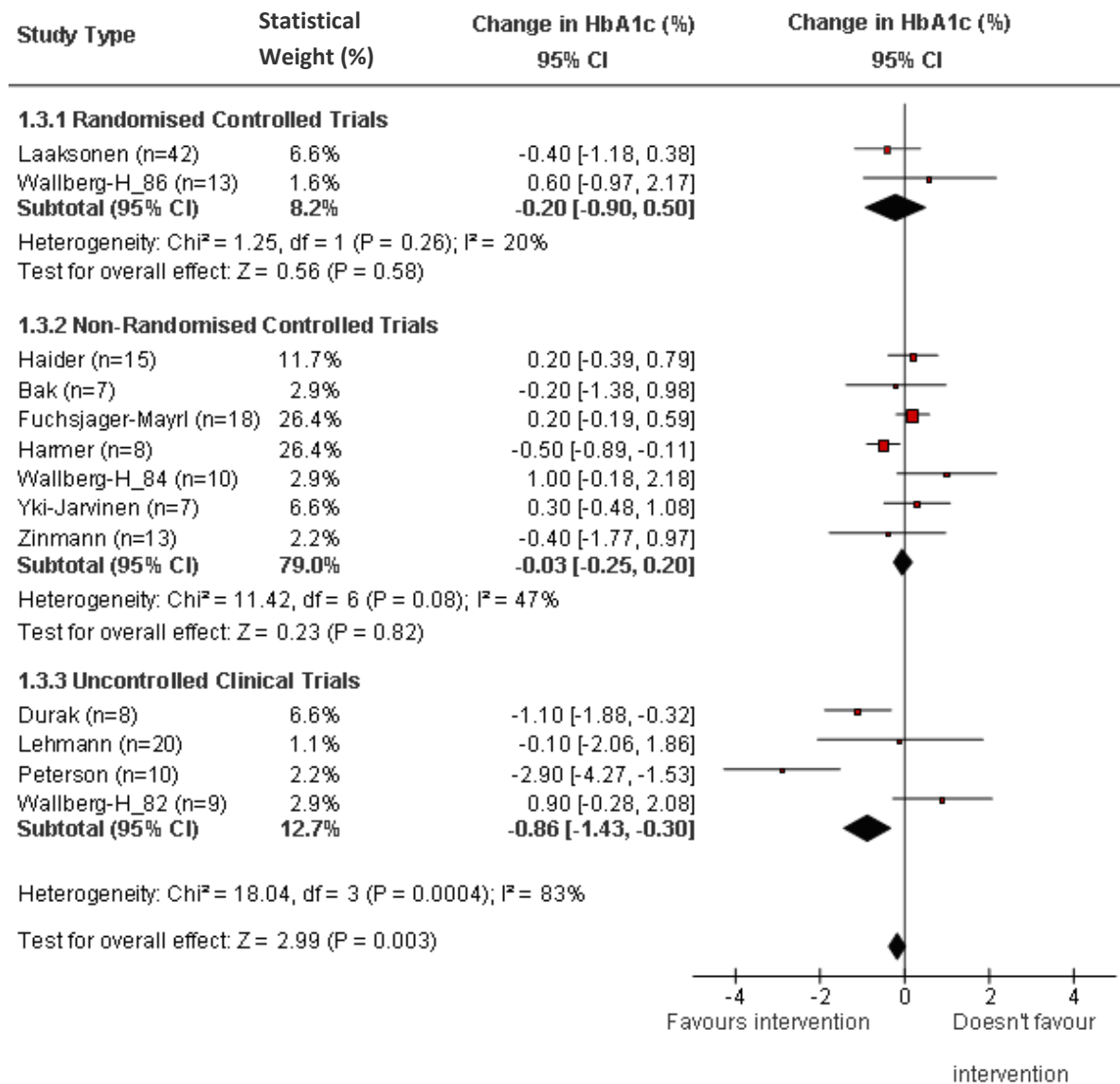


Figure 5: Meta-analysis of changes in HbA1c (%) with physical activity

3.4 Conclusion

The results of this systematic review suggest that physical activity interventions may improve insulin sensitivity (mainly inferred from a reduction in insulin dose) in adults with type 1 diabetes. However, these results do not provide a reliable estimate of the effect size and therefore they should be interpreted with caution. Evidence from RCTs was desirable as they are of higher validity and are less prone to bias. Nevertheless, this review was mainly structured around non-randomised and uncontrolled clinical trials, which are likely to give biased and possibly over-estimated treatment effects. Only one of the RCTs provided baseline and follow-up measures of insulin dose (103).

All studies were of small sample sizes, short follow-up and had weak study designs, giving underpowered results, which could be misleading. The RCTs were published prior to the CONSORT statement of recommendations for reporting RCTs (77) and methodological quality assessment using the Down and Black's tool (Appendix IV) (107) suggested that the included studies were subject to selection bias and confounding. Due to the heterogeneity amongst the trials, it was difficult to draw conclusions as to what type, duration, intensity and frequency of exercise would have the biggest effect on insulin sensitivity and glycaemic control.

This systematic review has a number of strengths. It included studies with a defined exercise intervention and excluded those with multiple intervention components. Consequently, it was possible to assess the effect of exercise per se on insulin sensitivity or insulin dose. Furthermore, this review highlighted a gap in the literature with a near absence of rigorous RCTs designed to increase insulin sensitivity through physical activity. The literature search revealed abundance of studies assessing the effect of a single exercise session on insulin dose or insulin sensitivity (108-111) and of studies meeting this review's inclusion criteria

conducted in children and adolescents (112-114), which unfortunately had to be excluded from the analyses.

The multiple health benefits of physical activity are well established. This systematic review suggests that physical activity could potentially improve insulin sensitivity and reduce insulin requirements. This could in turn prevent the undesirable weight gain that is often observed with intensified insulin regimens designed to optimise glycaemic control. There is need for large, rigorously designed RCTs, using carefully standardised procedures that include components intended at increasing insulin sensitivity through physical activity. Stronger evidence is also required to suggest the type, frequency, intensity and duration of the exercise plan, which would improve insulin sensitivity while preventing the risk of hypoglycaemia, which could be major barrier to physical activity in adults with type 1 diabetes.

The proposed intervention would encourage physical activity as a means of improving insulin sensitivity, reducing insulin requirements and consequently preventing any weight gain associated with treatment intensification.

4. Developing and Evaluating a Complex Intervention to Optimise Glycaemic Control and Prevent Weight Gain in Adults with Type 1 Diabetes

4.1 Introduction

Complex interventions are usually described as interventions that contain several interacting components within the intervention groups. The presence of multiple components makes it hard to precisely define the “active ingredient” that has an impact on the success or failure of the intervention (115-117). Complex interventions can be difficult to develop and reproduce, and RCTs are the optimal study design to minimise the bias and confounding arising from interactions between the intervention components (115). Evaluating complex interventions requires careful development and documentation thus, certain approaches have been developed in an attempt to ensure that the interventions are carefully reproduced and executed (115,117,118). The aim of this chapter is to define the processes followed to develop the proposed intervention taking into consideration the available evidence-base and the results from the two systematic reviews discussed in Chapters 2 and 3. The design of the intervention would be formulated within these processes.

4.2 Framework for the Development of Complex Interventions

4.2.1 The MRC Framework

In 2000, the UK Medical Research Council (MRC) published the “Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health” (115). The aim of this framework was to help researchers and funding bodies to acknowledge and follow the appropriate methods to develop a successful intervention and demonstrate its

effectiveness (Figure 6) (117). The framework provided guidance through a sequential series of five investigation phases by setting out the objectives to be met prior to moving on to the following phase (115). Specifically, in the Pre-clinical phase, a theoretical basis has to be established to inform the potential intervention, while in Phase 1 the intervention components and underlying mechanisms by which they might influence outcomes have to be identified. Phase 2, aims at refining the intervention through an exploratory trial that tests out the feasibility of the intervention components, before moving on to Phase 3, the definitive RCT. The final phase determines the reliability of the long-term implementation of the intervention in uncontrolled settings (116,117).

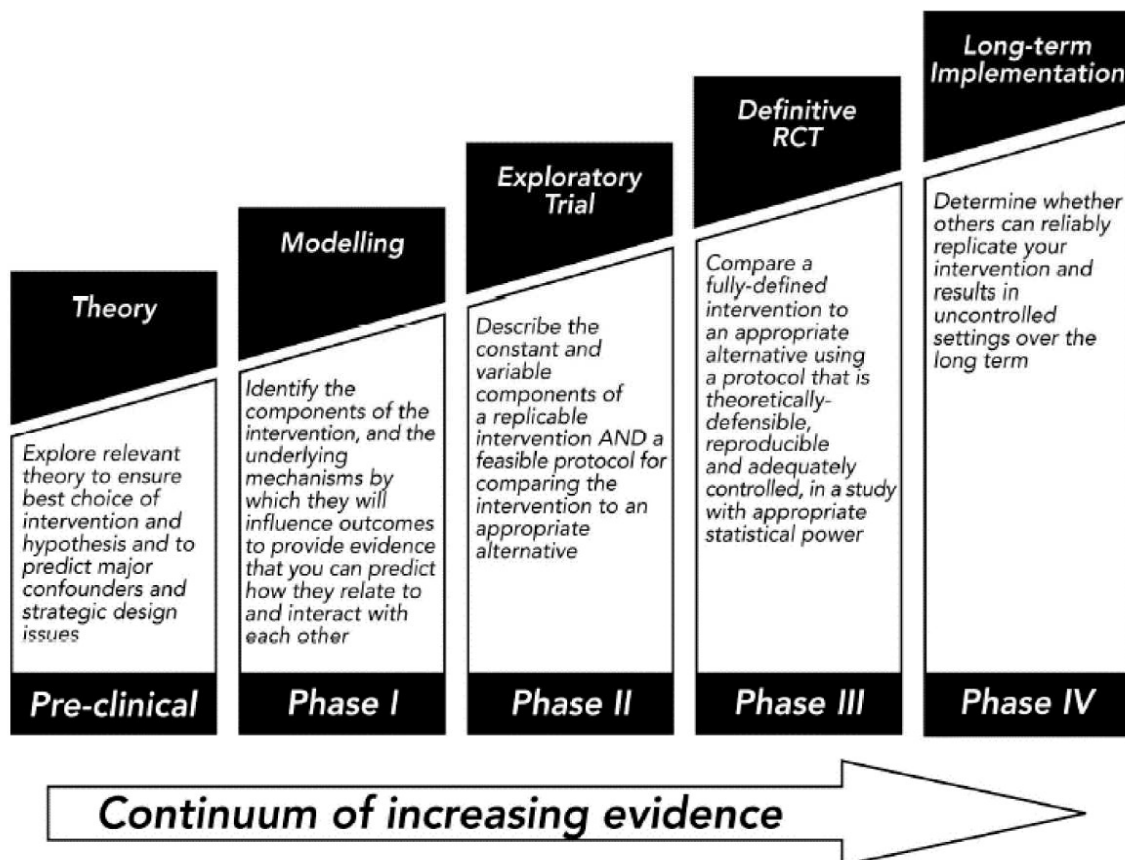


Figure 6: MRC Framework for Development and Evaluation of RCTs for Complex Interventions, 2000

4.2.2 The Upgraded MRC Guidance

Since the development of the MRC Framework, valuable experience has accumulated in evaluating complex interventions, with several publications identifying a number of limitations in the existing framework (116,119,120). A revised and updated guidance was released by the MRC, suggesting that greater focus should be directed to the piloting and development work of a complex intervention. This should be achieved through a more flexible, non-linear process that gives equal importance to the development, implementation and evaluation phases, as shown in Figure 7 (115,116,119).

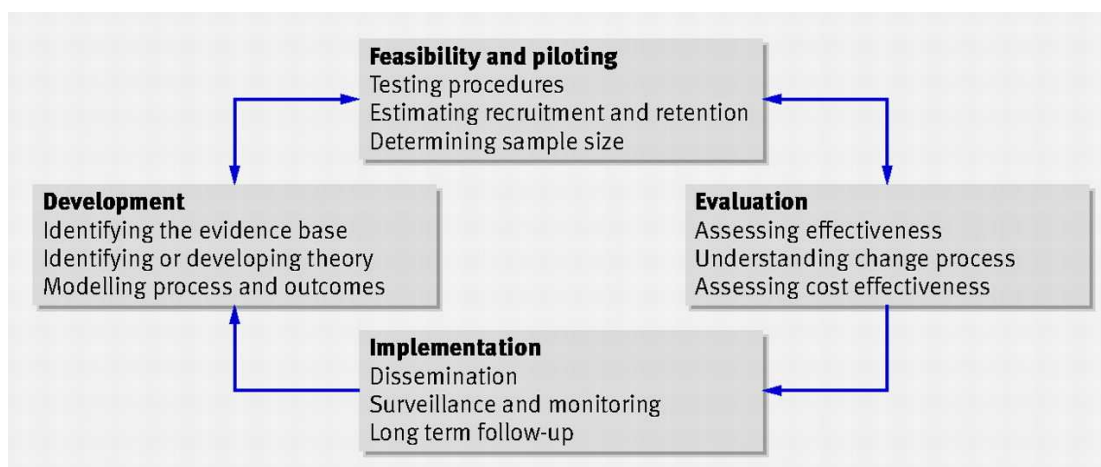


Figure 7: The updated MRC guidance

4.3 Methods

4.3.1 Developing the Complex Intervention

Diabetes programs designed to optimise glycaemic control are multifaceted, complex and involve numerous physiological, psychological and social modifications to improve patient outcomes. What is more, they can be confusing and overwhelming to patients with diabetes (121) who are required to make a range of lifestyle changes, sometimes without even noticing

tangible health improvements (122). This chapter describes the developmental phase of the proposed complex dietary and physical activity intervention to improve glycaemic control and prevent undesirable weight gain, in adults with type 1 diabetes.

In contrast to current programs, the proposed intervention is intended to provide sustainable education and decision support via a mobile phone-based e-health platform, thus encouraging self-management and patient autonomy. The proposed approach draws on the upgraded MRC guidance (117) and defines the intervention at three distinct levels (Table 1).

The first level summarises the theory and evidence underpinning the proposed intervention, in this case, the choice of target population, service provision and the attempt to modify patient behaviour. It deals with trial evidence and the efficacy of the established diabetes management strategies while addressing deficiencies in current service provision and the literature. It also considers the use of the most recent diabetes guidelines (123) and specific psychological models (124), which might be used to facilitate behaviour change. The second level defines the essential tasks and processes required to operationalise level 1, while providing generalisable and sustainable results. The third level defines the people and context within which the intervention will be operationalised (125). This approach provides a structure within which a large number of issues can be systematically addressed whilst retaining a clear view of the overall intervention.

Table 1: Levels of Defining the Intervention

Levels of defining the intervention			
Key issues	Level 1: Theory and Evidence	Level 2: Essential Tasks and Processes	Level 3: People and Context
Target population (Section 4.3.2)	Young adults with type 1 diabetes have poor prognosis with high morbidity and mortality rates (29,87)	Identify potentially eligible patients who might benefit from the intervention.	Young adults seen in secondary care with type 1 diabetes. Recruitment staff.
Service provision (Section 4.3.3)	To intensify glycaemic control and prevent undesirable weight gain in type 1 diabetes		
	Intensive insulin treatment improves glycaemic control and delays or prevents diabetes-related microvascular and macrovascular complications (DCCT) (20).	Assess the effect on glycaemic control of educating patients (both face-to-face and from a distance) on carbohydrate counting, insulin dose adjustment and blood glucose monitoring.	Dietitian, Diabetes Specialist Nurse (DSN), patients. E-health platform to reinforce learning, monitoring and sustainability of intervention.
	Intensification of glycaemic control often results in undesirable weight gain (20; Chapter 2). There is little or no information provision on energy balance and calorie counting in type 1 diabetes management programs (23,126).	Assess the effect on body weight of information provision on energy balance and education on calorie counting and portion control.	
	Physical activity improves insulin sensitivity, reduces insulin requirements (Chapter 3) and could prevent weight gain (127). There is limited or no physical activity promotion in type 1 diabetes management programs (23,126).	Assess the effect on body weight of promoting regular physical activity, while reducing the risk of hypoglycaemia.	
Service delivery (Section 4.3.4)	E-health platforms are acceptable and feasible means of monitoring patients from a distance, demonstrating improved treatment adherence (45,128).	Effectively link patients and diabetes team through a smartphone-based e-health platform.	
Service sustainability (Section 4.3.5)	Intensive long-term interventions have shown sustained improvements in glycaemic control (20). Interventions of shorter duration have failed to show sustained improvements (23,126).	Provision of a short-term, face-to-face intervention, reinforced with an smartphone-based e-health system to provide sustained, long-term improvements to the specified health outcomes.	
Changing behaviour (Section 4.3.6)	Effective ways of behaviour change		
	Introduce specific guidelines (20,129), in line with NICE and Diabetes UK care recommendations (123,130).	Set specific blood glucose targets and daily step goals for patients to aim for and adhere to.	Dietitian, DSN, patients. E-health platform to reinforce learning, monitoring and sustainability of intervention. Diabetes team to review transmitted data and contact patients at pre-agreed intervals.
	To achieve behaviour change and to improve treatment adherence, patients should have a sound knowledge and understanding of their long-term condition (131,132).	Verbal instruction and written material provision explaining symptoms, cause, physical and social impact of illness and its short and long-term complications.	
	Strategies to achieve behaviour change should be linked to specific outcomes (133).	Use of specific tools and prompts to enable carbohydrate and calorie counting and to improve engagement with physical activity.	
	Improving patients' personal control over treatment improves treatment adherence (133).	Provision of (i) the smartphone application to monitor carbohydrate and calorie intake and (ii) pedometer to monitor physical activity levels	
Incorporating appraisal and monitoring into the treatment program improves patient outcomes (134,135).	Provision of real-time graphical feedback for regular monitoring and reviewing of treatment plans		

4.3.2 Target Population: Participant Identification and Recruitment

To determine efficacy, an intervention needs to be evaluated in a specific population. The proposed intervention is specifically directed to young adults with type 1 diabetes. It is hypothesised that this patient group would benefit the most from an educational intervention which involves the use of novel technology and aims at optimising glycaemic control and preventing weight gain (28-30,87).

Level 1: Theory and Evidence

Previous work justifying target population selection

Young adults with type 1 diabetes have a poor prognosis that is associated with poor regimen adherence and metabolic control. Observational study data shows a higher proportion of young adults requiring hospital referral for psychiatric assessments (87). Furthermore, weight gain resulting from intensification of glycaemic control may encourage young adults to intentionally omit insulin injections to induce weight loss and to adopt disordered eating habits (25,28,29). Eating disorders in this patient group have previously been shown to be predictive of poor metabolic control and subsequent complications (136). Additionally, mobile phone use has been shown to be highest in young people, therefore interventions involving mobile phones are likely to benefit this age group the most (137).

Level 2 and Level 3: Essential Tasks and Processes, People and Context

Patient recruitment and retention

Considering the existing evidence-base, the proposed intervention is likely to confer greater benefit on the vulnerable population of young adults who attend their scheduled clinic appointments but have never participated in a structured education program such as DAFNE,

while excluding patients with severe psychological disorders (45). To target this group, a feasible recruitment strategy needs to be established.

Previous work by Farmer et al, involving the use of mobile phone technology in the same patient population, confirmed the feasibility of patient identification from hospital records and recruitment on attendance to routine clinic appointments. This strategy resulted in high recruitment and retention rates with 91% and 83% of patients in the intervention and control group respectively, completing the nine-month intervention (45). The proposed intervention would therefore recruit patients from the same population as Farmer et al, from the Young Adult Clinic in Oxford, using their successful recruitment strategy.

A possible limitation of the strategy could be that it does not capture patients who do not attend their hospital appointments, who may be those who would benefit the most from the proposed intervention.

4.3.3 Service Provision: Defining the Key Objectives of Healthcare within the Proposed Intervention

The various components of the proposed intervention focus on providing patients with the skills to optimise their glycaemic control, without any weight gain. Diabetes education forms a major part of the intervention, with the intention of helping patients gain the knowledge and skills required to achieve the desirable outcomes.

Level 1: Theory and Evidence

Previous work justifying the objectives of the proposed intervention

Chapter 2 provided evidence that intensification of glycaemic control is accompanied by weight gain. To date, no reported intervention has incorporated components specifically directed at preventing weight gain. The main focus was to improve patient awareness of the carbohydrate content of foods, with little or no attention given to energy balance, protein, fat and to the calorific content foods (23,45,67,69).

Additionally, recent qualitative evidence revealed that patients who attended structured education on treatment intensification, developed carbohydrate-avoiding strategies such as preferring foods higher in fat, thus increasing the risk of weight gain and consequently of developing CVD (121). Furthermore, evidence from the DCCT showed that patients in the highest quartiles of weight gain in the intensive treatment group also had the highest blood pressure, cholesterol and lipid levels compared to patients in the lowest quartiles, facing increased risk of developing CVD (36).

In type 2 diabetes, physical activity has been shown to improve cardiorespiratory fitness, glycaemic control and to increase insulin sensitivity (88). The effect of physical activity in type 1 diabetes is less clearly defined, although evidence from small, uncontrolled studies suggests that short bouts of physical activity significantly improve insulin sensitivity in patients with diabetes (108-111). The systematic review reported in Chapter 3 provided evidence that regular physical activity could improve insulin sensitivity and reduce insulin requirements which could, in turn, prevent weight gain in adult patients with type 1 diabetes. Furthermore, the most successful programs for sustained weight control in diabetes involved combinations of physical activity, calorific restriction and behaviour modification (127).

There is strong evidence supporting the need for a dietary, educational intervention, which in line with carbohydrate counting, also incorporates the concept of energy intake and energy expenditure, if glycaemic control is to be optimised without any weight gain.

Level 2: Essential Tasks and Processes

The proposed intervention would incorporate elements of previous structured diabetes education programs (23,126). The education program forming part of the intervention would include components intended to teach patients how to calculate their personal insulin to carbohydrate ratio (insulin sensitivity) and to correct for out-of-target blood glucose levels (correction dose). Patients would be encouraged to monitor their blood glucose levels at least four times per day (pre-prandially and before night sleep) and to keep a record of their blood glucose levels and insulin doses.

Contrary to current diabetes programs, the proposed intervention would provide additional strategies to help avoid undesirable weight gain by exposing patients to the concept of the energy balance equation, while giving equal attention to all macronutrients (carbohydrate, protein and fat) (138) and to how they affect blood glucose levels, insulin requirements and calorie intake. A key component would be the provision of a smartphone-based support package, which includes elements building on the education program, such as an iPhone application that can be used to visually assess the carbohydrate and calorie content of food and drink photographs. This will be discussed in more detail in Chapter 5.

Encouraging physical activity would also be a fundamental part of the proposed intervention not only as an adjunct to weight loss but also for its role in improving insulin sensitivity. Due to the increased risk of exercise-induced hypoglycaemia, many patients with type 1 diabetes may choose not to engage with physical activity. Individualised physical activity plans accompanied

by on-going support and advice on appropriate measures to avoid hypoglycaemia and hyperglycaemia could potentially enhance long-term adherence to physical activity (139-141). Patients would be encouraged to follow the NICE guidelines and the Diabetes UK recommendations for physical activity (123,130) and would be advised to follow their individualised exercise plans, thus supporting approaches to promote safe exercise, while maintaining blood glucose levels within the desired targets.

Attempts to encourage physical activity would be supplemented with movement sensors such as accelerometers and pedometers, which have been shown to reinforce engagement with physical activity and increase patient motivation (142). This will be discussed in more detail later on, in Chapter 7.

Level 3: People and Context

Diabetes specialist nurses, dietitians and clinicians, all remain essential for service provision in the proposed intervention. The e-health platform would assist the team in integrating regular and sustainable education, support and feedback mechanisms for the intervention participants.

4.3.4 Service Delivery

The proposed intervention is intended to provide an effective and efficient method of health care delivery for patients with type 1 diabetes. The use of e-health would provide an innovative platform through which the intervention would be delivered. E-health is defined as the delivery of health services, information and education at a distance enhanced through the Internet and related technologies (143).

Level 1: Theory and Evidence

Previous work justifying the use of the e-health platform

E-health platforms have been shown to be an acceptable and feasible means of monitoring patients from a distance (41), demonstrating reduced number of hospitalised patients, hospitalizations and bed days of care, as well as improved measures of quality of life (144). Contrary to previous evidence (41) recent systematic review evidence showed that e-health interventions using mobile phone technology significantly improved glycaemic control. Nevertheless, this effect was more profound in patients with type 2 diabetes (145) and amongst those receiving personalised advice and support (146).

Level 2 and 3: Essential Tasks and Processes, People and Context

Developing and using the e-health platform

The proposed intervention would require preliminary exploration of the use of an e-health platform in effectively linking patients and the diabetes team, building on previous work (41). All participants would have access to the e-health platform through a smartphone, the Internet and telephone. Each participant would be provided with an Apple iPhone (a smartphone that is also an iPod, a video camera and a mobile internet device with email and

Global Positioning System (GPS) maps), which would be linked to a blood glucose meter via Bluetooth technology. Following a blood glucose test, patients would be able to upload (or manually type) their readings from the meter to the iPhone, thus keeping an electronic blood glucose diary. Through the iPhone, patients would also have access to a carbohydrate and calorie counting application that includes photographs of 1900 common food and drink items of up to six portion sizes, displaying the weight, carbohydrate and calorie content of each portion (Appendix V). This application would provide a visual carbohydrate and calorie-counting guide and would act as a diet and diabetes management diary.

The inputted patient information would be transmitted from the iPhone, through the Internet, onto an NHS secure central server for storage. In the clinic, the diabetes team would have access to each patient's data for monitoring and education purposes and for feedback provision. The healthcare professionals would communicate with patients through the telephone, the Internet (email) or through text messages. Real-time graphical feedback of inputted data would be made available to each patient through their iPhone or through access to their personal individualised website, thus helping patients to identify and recognise trends and to self-manage their condition more effectively. The e-health platform will be discussed in detail in Chapter 5.

4.3.5 Service Sustainability: Improving Treatment Adherence

One of the main aims of the intervention is to provide a means of delivering a sustainable program with long-term treatment adherence. This section will build from current evidence and will describe the means of making the proposed intervention more sustainable.

Level 1: Theory and Evidence

Previous studies have demonstrated that intensive continuous support and long-term follow up are required for sustained improvements in glycaemic control (20,52). Interventions of shorter duration have only shown modest improvements in glycaemic control and short-term sustainability (23), highlighting the importance of continuous support provision in achieving the desirable outcomes.

Level 2: Essential Tasks and Processes

Providing a sustainable service

As discussed in the following sections, one of the main components of the proposed intervention is the provision of sustained education intended to improve patients' diabetes self-management skills. Face-to-face education has the potential to be reinforced through the use of the e-health platform, providing sustained education from a distance. Through the novel iPhone application patients would be supported in adjusting insulin doses to carbohydrate intake and monitoring their energy intake.

The iPhone application would also introduce an optional bolus calculator as a tool to help patients in insulin and correction dose decisions, based on a rational algorithm. Blood glucose levels, inputted dietary data and total insulin doses would be transmitted to the central server, and made available to the diabetes team, in real time, thus providing a sustainable service. To what extent the photographs displayed on the iPhone are safe to be used in clinical practice (147) and whether patients are able to accurately estimate the carbohydrate and calorie content of food from those photographs, would be evaluated prior to embarking to a definite trial. This will be further discussed in Chapter 8.

Level 3: People and Context

The e-health platform is intended to assist the integration of regular long-term education, support and feedback mechanisms to the study participants. Through real-time data transmission patients would have access to their own data and so will the diabetes team thus facilitating active communication and providing a mean with which to deal with possible problems or concerns as they arise. The diabetes team would contact the patients at pre-agreed time intervals, to discuss and adjust treatment plans and to offer further education and support whenever needed.

4.3.6 Effective Ways of Behaviour Change

Although type 1 diabetes is a chronic, long-term condition, it is possible for patients to live a healthy, complication-free life through treatment intensification and sustained support-provision from the diabetes team (20). Effective self-management from the patients themselves is also required, which involves a degree of behaviour change, such as: monitoring blood glucose levels at least four times/day and aiming specific blood glucose ranges; performing carbohydrate counting using a variety of tools and adjusting insulin doses accordingly; engaging with physical activity and following a healthy, calorie controlled diet (148). Such elements need to be introduced into the proposed program as they would inform and guide the intervention development at all levels.

Self-management education programs that incorporate a theoretical framework (154) and include cognitive reframing teaching methods (suggesting alternative self-perceptions) (155) are more likely to improve glycaemic control and have better outcomes, than programs that do not. The Common Self Model of Illness (theory of self-regulation) developed by Leventhal

and colleagues (156,157) is a promising approach to understanding and improving the self-management of a chronic condition like diabetes.

Leventhal's Common Sense Model of Illness focuses on people's response to a perceived health threat. Back in the 1960's, Leventhal and his colleagues investigated how fear (or perceived health threat) influences people into taking health-promoting actions, such as to stop smoking or wearing a seat belt (158). Through this research, Leventhal et al identified that people with long-term conditions actively create a cognitive representation of the experiences and adjust the coping mechanisms according to these representations (159), or simply put, patients' perceptions and beliefs about their condition. These perceptions are summarised into the following five distinct components:

- **Identity:** The patients' knowledge and beliefs on what is their long-term condition, its symptoms and its treatment
- **Cause:** The patients' beliefs on what caused the condition
- **Timeline:** The patients' beliefs about the duration of the condition
- **Consequences:** The patients' beliefs on what the consequences of their long-term condition are, both physical and social
- **Curability:** The patients' beliefs on whether the condition can be cured or kept under control

As patients obtain new information about their condition and evaluate their attempts to deal with its effects and consequences, new representations are formed, with new information adopted or discarded, as patients' judge necessary (158-159). It is therefore important for both healthcare professionals and researchers to understand patients' perceptions of their chronic condition and the expectations they have from their treatment. The proposed

intervention would take into consideration Leventhal's Common Sense Model of Illness and in line with current evidence and practice, it would adapt its various components in an attempt to modify behaviour and achieve the desirable outcomes.

Improve patients understanding of diabetes

Level 1: Theory and Evidence

Many patients with long-term conditions express great concerns about the way their illness affects their ability to live a "normal" life (153). This is especially true for type 1 diabetes as it is a condition primarily managed by the patients themselves. To make informed decisions about diabetes self-management, patients need to have sufficient knowledge of diabetes, its complications and treatment (131), as suggested by Leventhal's Common Sense Model of Illness (158-159). Recent evidence from a cross-sectional study of 151 participants, confirmed that the greater the knowledge on diabetes-related complications (nephropathy, retinopathy, neuropathy and CVD), the better the treatment adherence (132). It is therefore important that the proposed intervention provides patients with the necessary knowledge and skills to self-manage their diabetes, competently and confidently.

Level 2 and Level 3: Essential tasks and Processes, People and Context

The proposed intervention would incorporate face-to-face education courses, which would provide patients with a basic understanding of type 1 diabetes including symptoms, cause, and the physical and social impact of illness. Attention would also be given on the diabetes-related microvascular and macrovascular complications and their prevention mechanisms. These courses would be complemented with written material, the iPhone carbohydrate and calorie counting application and the e-health platform. Through the e-health platform, patients would

have constant, but at the same time discrete access to information about their condition and its effective management, keeping the intrusion into their personal lives to a minimum.

The dietitian and diabetes nurse would be the key people involved in the teaching process and sustained education and support would be provided through the e-health platform.

Guideline Provision

Level 1: Theory and Evidence

Explicit guideline provision has been shown to improve medical practice and clinical outcomes (130). Taking into consideration Leventhal's Common Sense Model of Illness, the provision of specific guidelines and targets could modify patients' perceptions about the consequences and curability of diabetes with the potential of achieving behaviour change.

Taking clinical evidence into consideration, interventions directed at optimising glycaemic control, which advised patients to aim for specific blood glucose ranges, have shown significant improvements in HbA1c (20,23,68,72). Furthermore, studies, which had a step goal, approach to promote physical activity, showed significant improvements in physical activity engagement (149-152). Similarly, interventions that required participants to keep a step diary, demonstrated a significant increase in activity levels, compared to studies that did not require a diary (129).

Level 2: Essential Tasks and Process

To optimise glycaemic control and prevent undesirable weight gain, the proposed intervention would support patients in achieving blood glucose levels within pre-defined target ranges. Using movement sensors such as pedometers and accelerometers, patients would also be

supported in aiming for specific step goals, as well as keeping a step diary and recording their daily step count.

A pragmatic approach would be followed, where individual blood glucose and step targets would be negotiated with each patient. Blood glucose targets would be set by taking into consideration each patient's glycaemic control and insulin sensitivity patterns. Step targets would be informed, by each patient's baseline activity levels and ability to make the appropriate treatment adjustments before, during and after exercise.

Level 3: People and Context

The diabetes team would agree realistic treatment goals (blood glucose targets and step goals) with patients and would monitor adherence through the e-health platform. The team would actively encourage patients to keep up with their individual treatment plans, to remain focused and would intervene if necessary, by making the appropriate alterations to treatment goals, as required.

Linking behavioural strategies to specific outcomes

Level 1: Theory and Evidence

In its "Guidance on the Use of Patient-Education Models for Diabetes" (24), NICE concluded that diabetes teaching sessions should encompass a variety of different methods to help patients learn. At the same time the programs should meet the needs of all participants, taking into consideration any special circumstances, diabetes duration and learning styles.

Level 2: Essential Tasks and Processes, People and Context

Together with solid diabetes knowledge, patients have to implement effective self-management behaviours, such as frequent monitoring of blood glucose levels and symptoms to detect a possible risk for hypo-and-hyperglycaemia. This, in turn informs the need for specific self-management actions such as dietary adjustments and insulin injections to bring blood glucose levels back to normal. The proposed intervention would link behavioural strategies to specific outcomes such as: the frequent monitoring of blood glucose levels and carbohydrate counting to prevent hypo-and-hyperglycaemia; calorie counting to prevent undesirable weight gain and physical activity engagement to improve insulin sensitivity, reduce insulin requirements and prevent weight gain. A variety of tools and prompts would be used to enhance learning, achieve behavioural change and change patients' perceptions about diabetes and its management.

Specifically, to optimise glycaemic control, patients would be exposed to the variety of methods used to assess the carbohydrate content of foods, using a number of practical exercises such as visual aids (food models and food plates), kitchen scales, household measures and food labels, as well as the iPhone carbohydrate and calorie counting application. To prevent weight gain, patients would learn the different methods used to assess the energy density of foods (calorie counting, visual estimation, food models, food labels, weighing foods using scales), and would appreciate the importance of portion control for weight management. To promote adherence to physical activity, patients would be provided with a pedometer to monitor progress, which would also be used as a physical activity motivation tool.

Level 3: People and Context

The dietitian will be the key person in this process. Medical and nursing support could be asked if required or if requested by the patients. The e-health platform would offer sustainable education, monitoring and feedback when needed.

Improving patient personal control over condition

Level 1: Theory and evidence

Evidence suggests that by improving patients' control over their treatment, adherence also improves (133). By improving confidence, illness representations and perceptions could also change, new representations could be created, potentially leading to behaviour modification and improved treatment adherence and outcomes (156-159). It is therefore important for patients with type 1 diabetes to feel confident in developing strategies to manage their symptoms and setting their individual treatment goals.

Level 2 and Level 3: Essential Tasks and Processes, People and Context

The proposed intervention would be designed to improve patients' confidence and to minimise any stress relating to diabetes self-management. The provision of specific tools, such as the iPhone and the pedometer, would potentially help patients feel more in control of their diabetes. The iPhone application would enable patients to reliably estimate the carbohydrate content of their meals at any time. This, would in turn, improve their skills and confidence in matching the appropriate insulin dose to the carbohydrate content of their meals. Similarly, through access to the calorific content of foods, as well as having the pedometer to monitor

their physical activity levels, patients would possibly feel that they are less likely to be in positive energy balance and therefore more likely to avoid undesirable weight gain.

The diabetes team would support patients in feeling more in control of their diabetes, by offering sustainable monitoring and by reviewing the treatment plans and goals regularly.

Incorporating appraisal and monitoring into the treatment program

Level 1: Theory and Evidence

Interventions designed to change parts of the Leventhal's Common Sense Model of Illness, including self-monitoring and self-care behaviours, have been shown to improve diabetes self-management and outcomes (134,135). To make informed decisions about the management of their diabetes, regular feedback mechanisms, appraisal and monitoring should also be incorporated into the treatment program.

Level 2 and Level 3: Essential Tasks and Processes, People and Context

This intervention would incorporate specific appraisal and monitoring methods into the treatment program, such as real-time graphical feedback of patient data (through the iPhone and website), regular monitoring of individual patient data and feedback provision from the diabetes team, through the e-health platform.

4.4 Conclusion

The aim of the proposed intervention is to optimise glycaemic control and prevent undesirable weight gain in young adults with type 1 diabetes. This chapter described the developmental phase of the complex dietary and physical activity intervention, by following the upgraded

MRC guidance and taking into consideration a theoretical framework, namely, the Leventhal's Common Sense Model of Illness. The intervention has been defined using three distinct levels, theory and evidence, tasks and processes and people and context. The evidence and efficacy of the established diabetes management strategies has been summarised, and the way in which the proposed intervention would address the deficiencies in the current service provision and literature have been described. The main components of the intervention have been identified, together with a strong evidence-base that justifies their specific role in the intervention. The following chapters describe the main components of the intervention in detail and identify the mechanisms through which each would contribute to achieving the desired intervention outcomes.

5. The e-Health Platform

5.1 Introduction

A significant proportion of healthcare resources are required to treat a long-term condition like diabetes (160). Nevertheless, treatment adherence has been shown to be sub-optimal, acting as a barrier to the effectiveness of diabetes interventions (161,162). The consequences of non-adherence are primarily felt by the patient (micro-level) in the form of poor glycaemic control resulting in complications, and by the general population (macro-level) in the form of increased society costs (162).

The cost of diabetes is challenging healthcare systems, even in the most affluent countries (163) therefore, the ability to self-manage diabetes should be a priority (164). Each patient spends on average just three hours a year interacting with healthcare professionals. The rest of the time patients deal with the daily challenges of diabetes, themselves (165). The term “self-management” refers to the tasks a patient can perform with or without the support of a healthcare professional, to minimise the impact of the illness on health (166). In the UK, the Department of Health’s policy document recognised the support for self-management as one of the three pillars of the NHS social care for long-term conditions model (167).

The levels of support required by patients with long-term conditions are highlighted by the “Kaiser-Permanente triangle” (Figure 8). This figure was initially used by an American-managed care organisation, to explain their strategy for allocating resources. The diagram is stratifying patients into three groups, based on the level of support they require. The three levels of care are (i) the large majority of patients, who are usually able to self-manage their own condition (70-80% of all cases); (ii) the group requiring more professional care to avoid complications or to slow down disease progression (15-20% of all cases); (iii) the smallest group with complex needs that requires more intensive level of care (3-5% of all cases). The

two levels of care at the top of the triangle would require more healthcare professional support to prevent the condition of patients from deteriorating and requiring an even more intensive level of support (168).

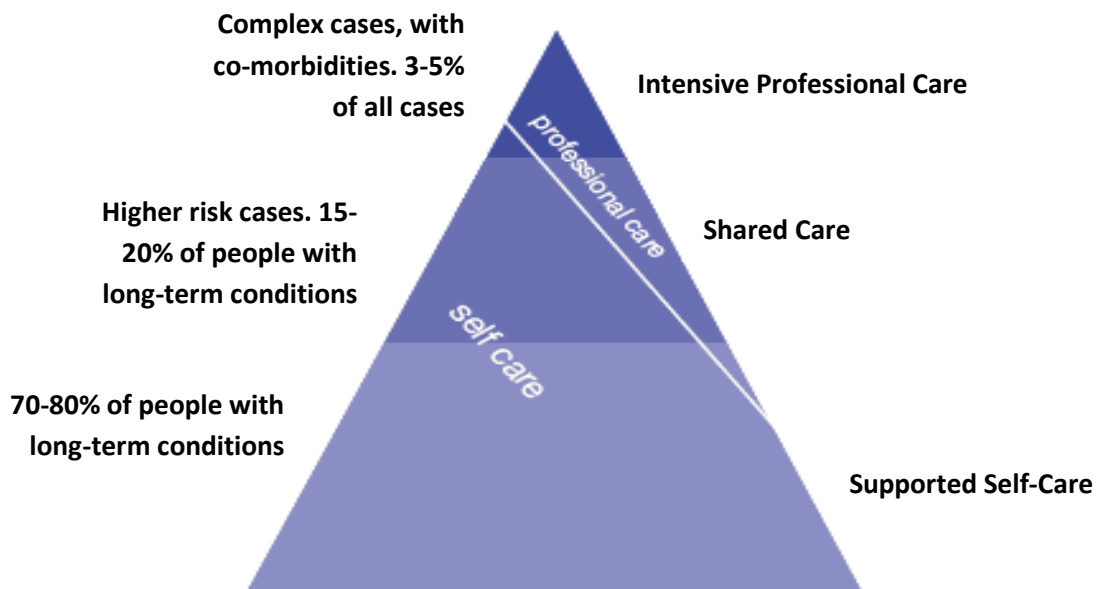


Figure 8: The Kaiser Permanente Triangle: Ratio of Shared Professional Care to Self-Care Across the Long-Term Conditions Population Base (168).

Several patient education programs have been developed to enhance self-management skills with the aim of making information provision more accessible and skills training widely available (23,126,169,170). Nevertheless, as stated in Chapter 1 and Chapter 4, these programs are not without their limitations, such as a lack of demonstrated long-term sustainability of treatment effects (23), lack of evidence for significant improvements in HbA1c (126) and a failure to achieve dietary liberalisation (121).

The challenge is to develop an innovative intervention targeting the patients under the “supported self-care” group of the Kaiser-Permanente triangle (Figure 8), which would improve self-management skills, glycaemic control and prevent undesirable weight gain, while

minimising intrusion into patients' privacy and everyday life. This is especially true for type 1 diabetes where demanding insulin regimens, carbohydrate counting and frequent blood glucose monitoring are required to reduce the mortality, morbidity and healthcare costs (20).

5.2 The role of e-Health Platforms in Healthcare Delivery

To support diabetes self-management, patients and healthcare professionals should work in partnership for education provision, effective monitoring and sustained follow-up of care (171). This can take a number of forms from face-to-face consultations and home visits, to the use of information and communication platforms, like telemedicine and telecare (144,172). Telemedicine is defined as "the delivery of healthcare at a distance using electronic means of communication – usually from one clinician to another". Telecare is defined as "the continuous, automatic and remote monitoring of real-time emergencies and lifestyle changes over time, in order to manage the risks associated with independent living". Usual devices for telecare include personal alarms, movement detectors and falls monitors (143).

Despite the variety of available definitions, these platforms fall under the umbrella term of "e-health" (173), defined as "the delivery of health services, information and education at a distance, enhanced through the Internet and related technologies" (143). E-health offers patients and healthcare professionals additional ways of interaction with the potential of increased and improved access to care. It also helps to overcome a number of barriers to treatment including physical location and busy timetables (174).

From the very beginning, e-health platforms have been utilised in a variety of healthcare fields such as psychiatry (175) and paediatrics (176). Despite those early projects appearing clinically and technically successful, wider interest and enthusiasm among healthcare professionals has only recently become apparent, following the development of more sophisticated technology

(177,178). Nowadays, a growing number of applications relating to healthcare are appearing, offering the potential for reducing costs (178) and increasing the efficiency and effectiveness of healthcare provision (137).

5.2.1 Wireless Applications and Bluetooth Technology

The feasibility of wireless technology in communicating healthcare information, such as vital signs, was demonstrated more than 30 years ago. Historically, wireless monitoring included physiological parameters such as heart rate and blood pressure (179). More recently, practical portable devices and communication networks have become widely available. Wireless communication has led to the development of sensors that enable healthcare professionals to diagnose, monitor and educate patients remotely, through the provision of real-time information, thus making healthcare available anywhere, anytime and in a wide range of settings and medical specialities (44,180).

Additionally, Bluetooth technology, originally proposed by Ericsson in 1994, emerged as a substitute to cables. Bluetooth is wireless technology that allows any electrical device such as mobile phones, headsets and portable computers to communicate and transmit data to each other, without the need for wires or cables to link the devices, thus allowing real-time data transfer (179); for example, the wireless transmission of blood glucose readings from the glucometer to a mobile phone.

5.3 Capacity of e-health Platforms in Delivering a Complex Diabetes Support Program

As discussed previously (Chapter 1 and 4), the DCCT demonstrated that treatment intensification prevents the development and reduces the progression of diabetes

complications (20,21). Apart from treatment intensification, important components of the DCCT success were the frequent clinic visits and the regular telephone support between patients and specialist nurses. Patients in the intensive insulin therapy group visited their study centre weekly until the target blood glucose ranges were achieved, and then monthly thereafter. They also received frequent diabetes-related telephone calls, in addition to two educational calls per year and ad hoc “trouble shooting” calls (20,22).

The DCCT’s intensive support provision showed that treatment intensification could be achieved through education via constant access to information about the disease. E-health platforms could potentially help replicate the DCCT approach by improving and speeding up the communication between healthcare professionals and patients and by providing sustainable education and support provision from a distance (181).

E-health platforms for diabetes care have been shown to be feasible and acceptable (45,128), leading to improved treatment adherence (45), quality of life and patient satisfaction outcomes, reduced number of hospitalised patients, number of hospitalisations and bed days of care (144). Several reviews have emphasised the potential advantages of e-health via telecommunication technologies in the management of diabetes (41,43) and confirmed the benefits of monitoring and communicating with patients from a distance (182-184).

In type 1 diabetes, evidence for the effectiveness of e-health platforms in improving glycaemic control, or reducing healthcare expenditure while maintaining HbA1c levels, is still inadequate (45,128). It has been suggested that to significantly improve glycaemic control, interventions should (a) target a motivated patient population that is contemplating better control (45), and (b) to become more intensive, by providing real-time decision support systems for insulin doses (185) and by incorporating dietary and physical activity components to the intervention (45).

5.4 Developing an e-health Platform with Smartphone Technology for a Complex Diabetes Support Program

5.4.1 Smartphones: an Important Component of e-health Platforms

Towards the end of the 20th century, technological improvements led to advances in the functional capacity and usability of mobile phones. Back in the 1980's mobile phones were bulky, expensive and restricted solely to calls (186). Nowadays, smartphones offer the standard mobile phone services such as voice and text messaging, but also have a wider range of facilities. They offer the potential for advanced computing and communication, such as Internet access and geo-positioning systems. They also have larger screens of higher resolution and incorporate features such as high quality cameras and recording devices (187).

The latest generation of smartphones are viewed as handheld computers, rather than as phones. They have powerful computing capabilities, high capacity memories and open operating systems, allowing the development of applications which are easy to set-up, download and use. An application is defined as software that runs on a mobile device, such as the iPhone, and allows the device to perform specific tasks that are normally restricted to computers. These applications are now widely available on every aspect, allowing connectivity into the world wide web of knowledge, offering the potential for use in education and medicine (187).

Smartphones have the potential for a key role in healthcare: (a) they are of personal nature since each phone has a unique identity and is associated with a specific individual, thus maintaining confidentiality; (b) their owners usually have their phone with them all the time, thus making continuous monitoring and information transfer possible anywhere, any time; (c) they keep users connected, thus enabling communication with healthcare professionals and peers and (d) they are increasingly intelligent. They have been described as small computers

with the potential of offering health applications and containing algorithms that enable them to handle large amounts of data and to identify significant trends and events (180).

Smartphone uses in healthcare do have some limitations such as the incomplete coverage of mobile networks across regions and possible information overload (180). Other factors such as loss or theft of the device may compromise the confidentiality of patients' personal information held on the phone (188). They may also replace personal contact with healthcare professionals and may not be suitable for people suffering from poor manual dexterity or failing vision (187).

Although there are already hundreds of smartphone applications available to support efforts to monitor and improve health, and despite the fact that morbidity increases with age, it is suggested that the most successful applications are currently those targeted towards the younger and healthier populations (189). Evidence shows that mobile phone owners aged 15-24 are spending more time calling or texting than any other age group (137,190). Given the integration of smartphones in young people's lives, they could offer the ideal medium for the delivery of the proposed intervention that is specifically targeted at young adults, through the e-health platform.

5.4.2 Smartphone Applications in Supporting Diabetes Self-Management

The smartphone platforms available today include the Android, Apple iOS, BlackBerry, Symbian and Windows. Some smartphones, such as BlackBerry incorporate small internal keyboards in their design, while more recently, the Apple's iPhone and Google's Android touch screen devices with their "tactile graphical user interfaces and natural gesture control" have made smartphones attractive and increasingly popular (180,187). The subsequent upgrades

have reinforced their popularity and demand over the years and with their prices continuing to fall, they became even more attractive to consumers (186).

Recently, a team consisting of a diabetes specialist dietitian, a photographer and an engineer have developed an iPhone application specifically targeted at patients with diabetes (191). The application guides patients through most of the steps of the insulin dose adjustment process, by providing access to a carbohydrate and calorie content of 1900 food and drink photographs of up to 6 portion sizes. This application could potentially help patients optimise glycaemic control through carbohydrate counting and insulin dose adjustment and prevent undesirable weight gain through portion control and calorie counting.

Table 2 reports the insulin dose adjustment process and maps it to the corresponding functions of the iPhone carbohydrate and calorie counting application:

Table 2: Insulin dose adjustment process mapped to the iPhone carbohydrate and calorie counting application

Insulin Dose Adjustment Process	iPhone Application Processes
Identify the food and drink in a meal that contains carbohydrate	Access to photographs of 1900 popular food and drink items of up to 6 portion sizes
Estimate the carbohydrate content of each meal component Estimate the carbohydrate content of the whole meal	Provision of carbohydrate grams and calories for each portion size Match the food in meal to photograph portion size. Instant calculation of total carbohydrate (and calorie) content of meal
Check pre-prandial blood glucose levels against pre-defined blood glucose targets	Manual input of pre-prandial blood glucose readings into application (does not take into consideration individual blood glucose targets)
Calculate the insulin dose required to cover the grams of carbohydrate of the meal, taking into consideration insulin sensitivity for different times of day (breakfast, lunch, evening meal and snack)	Access to insulin bolus calculator Manual input of insulin sensitivity for breakfast, lunch, evening meal and snacks
Consider factors that could affect blood glucose levels (exercise, illness, alcohol etc). Decide if a correction dose is required	Does not take into consideration the need for correction dose & some of the factors affecting blood glucose levels (exercise, illness, alcohol).
Decide on total insulin dose Inject insulin dose	Suggests total insulin dose based on insulin sensitivity and blood glucose levels For safety purposes the bolus calculator can be switched off
Keep a record of carbohydrate intake, pre-prandial blood glucose levels, correction dose and total insulin dose injected	Automatic diary record keeping of food portion sizes, grams of carbohydrate, insulin sensitivity and total insulin dose injected

The iPhone and its carbohydrate counting application could form the basis of the e-health platform through which the complex dietary and physical activity intervention would be delivered. The aim of this platform would be to help patients in optimising glycaemic control and preventing undesirable weight gain by providing continuous access to portion sizes, the

carbohydrate and calorie content of foods and, by effectively linking patients and the diabetes team. Figure 9 links the individual components of the e-health platform and illustrates how they would communicate with each other. Table 3 describes the processes that take place between the different components of the platform and explains how these would potentially contribute to achieving the desirable outcomes.

Figure 9: The e-health platform

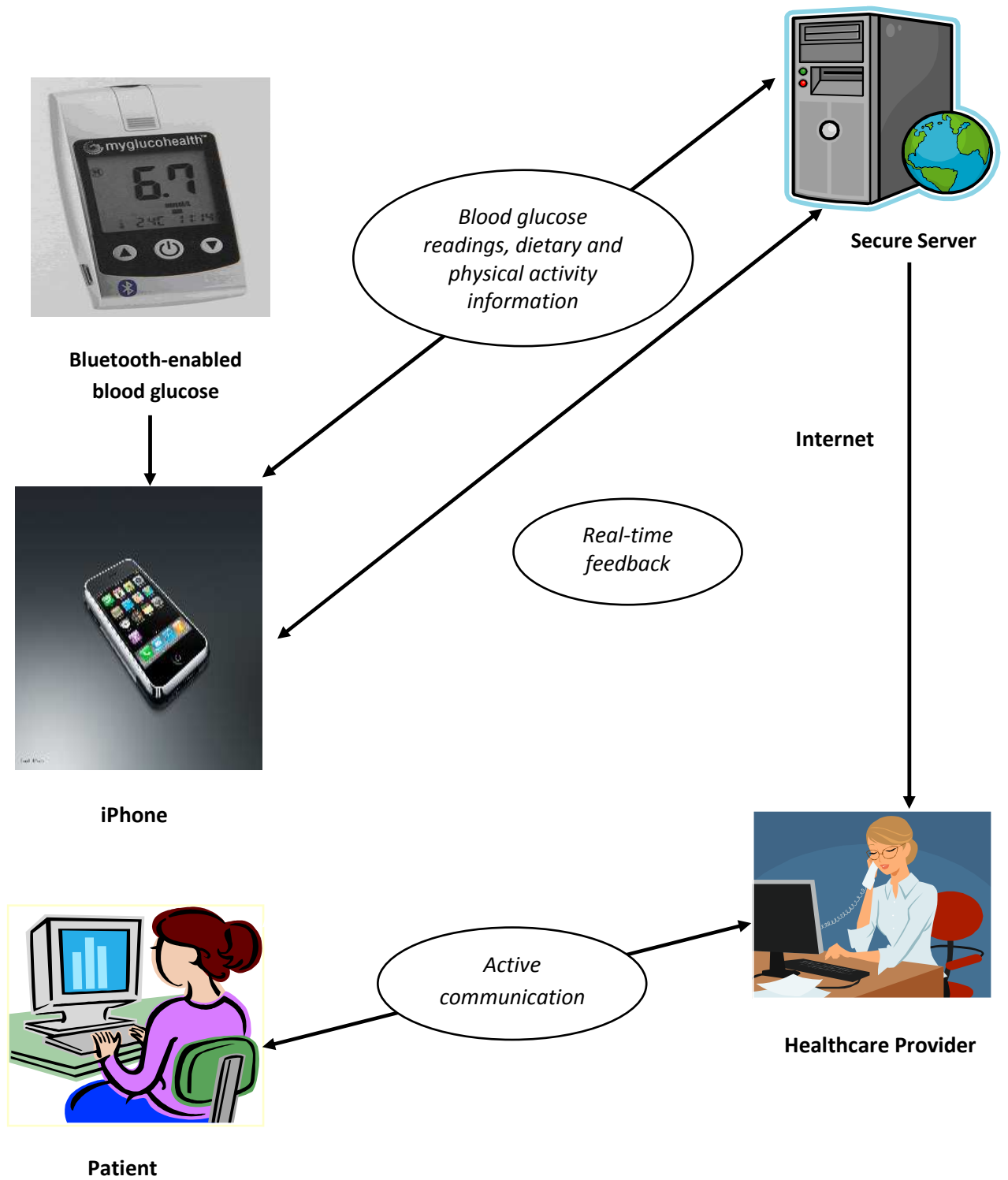


Table 3: The role of the e-health platform in achieving desirable outcomes

Potential components of e-health platform	Process		Contribution to achieving desirable outcomes
Bluetooth-enabled blood glucose meter	Patient	Bluetooth-enabled blood glucose meter	Encourages frequent blood glucose monitoring Blood glucose test results automatically stored on iPhone and central server and can be accessed by patients and healthcare professionals at any time No need to keep a paper-diary
	Perform blood glucose test	Show blood glucose reading	
	Manually type (or transmit via Bluetooth technology) blood glucose result into phone	Transmit blood glucose results from meter to iPhone and central server	
iPhone Carbohydrate and Calorie Counting Application Food pictures	Patient	Phone	Sustained education through continuous access to the carbohydrate and calorie content of foods Informed decision on insulin doses through access to the carbohydrate content of foods
	Select food(s)	Show food portion(s)	
	Select portion size	Show portion Carbohydrates/Calories	
		Show Carbohydrates/Calories content of meal	
iPhone Carbohydrate and Calorie Counting Application Insulin bolus calculator		Show Carbohydrate content of meal	Raised awareness and ability to monitor portion sizes and the calorific content of foods for weight management
	Manually input insulin: Carb ratio for specific meal	Show insulin: Carbohydrate ratio for specific meal	
	Decide on total insulin dose (and correction dose) and manually type into phone	Bolus calculator suggests insulin units required for whole meal (no correction dose included)	
		Real-time data transmission to secure server	
Secure server, Internet	Patient	Healthcare professional	Active communication between patient and healthcare professional Sustained education provision Continuous monitoring, trouble shooting and dealing with problems as they arise
	Real-time electronic graphical feedback (on iPhone or via individual secure website)	Access to patient's transmitted data through website	
	Option to contact healthcare professionals when needed to discuss results, current treatment regimens or for support and feedback	Feedback, support and advice provision to patients via email and other communication means (SMS, telephone)	

5.5 Conclusion

The e-health platform is hoped to offer the potential for sustained education, monitoring and treatment from a distance. The iPhone application would guide patients through the insulin dose adjustment process and enable them to assess food portion sizes and the carbohydrate and calorie content of their meals whenever needed, thus making diabetes self-management possible at any time.

Ideally, diabetes management through the e-health platform should not only be an option for younger people but also for the majority of patients under the Kaiser Permanente's Triangle (Figure 8). Although smartphones and their applications have a higher uptake by the younger age groups, one has to keep in mind that the older people of tomorrow will include the young and middle aged of today, who are more familiar with computers, smartphones and the Internet than previous generations. The adoption of smartphones by older people, including those with a chronic disease such as diabetes, will therefore come with time. With the decreasing cost, with smartphone applications becoming easier to use and with the increased awareness of smartphone potential in healthcare, perhaps patients with type 1 diabetes would move to the next level and incorporate them in the daily management of their condition.

A major goal for patients would be the acquisition of the skills required to make informed decisions about their treatment, instead of relying solely on the iPhone application and on the healthcare professionals for advice. For this reason, diabetes education would be a major component of the proposed intervention and chapters 6 and 7 describe this in greater detail. Particular attention would be given to the different methods of assessing energy intake and energy expenditure and how these, in line with the e-health platform, would form the basis of the proposed intervention.

6. Assessing the Carbohydrate and Calorie Content of Food

6.1 Introduction

Although the management of type 1 diabetes primarily focuses on carbohydrate counting and insulin dose adjustment, attention to diet is also important. Dietary guidelines for people with type 1 diabetes are similar to those recommended for the general population and are based on the healthy eating framework (33). Additional goals of dietary advice specific for type 1 diabetes are to achieve and maintain optimal metabolic and physiological outcomes, including the reduction of risk of microvascular and macrovascular disease, by achieving near-normoglycaemia without hypoglycaemia (40).

The relationship between energy intake, energy expenditure and energy balance should form an integral part of nutritional counselling in the general population as well as in diabetes (40). The Food and Agriculture Organisation (FAO) states that “Energy balance is achieved when input (or dietary energy intake) is equal to output (or energy expenditure), plus the energy cost of growth in childhood and pregnancy, or the energy cost to produce milk during lactation” (192). Positive energy balance represents a gain in energy stores in the form of carbohydrate, protein and fat. Negative energy balance represents the energy mobilization from the body stores as carbohydrate, protein and fat (193). To prevent undesirable weight gain one has to either achieve energy balance, where energy intake matches energy expenditure, or to be at negative energy balance, through a combination of reduced energy intake (primarily by reducing fat consumption) and an increase in physical activity.

This chapter focuses on the “energy intake” part of the energy balance equation, which is important if undesirable weight gain is to be avoided in type 1 diabetes. It discusses the flow of energy through the body and the different methods used to quantify it. The contribution of all macronutrients to energy intake is highlighted, and specific attention is given to

carbohydrate, which the main nutrient affecting the post-prandial rise in blood glucose levels. It gives an overview of the history of carbohydrate counting and describes the variety of methods that can be used to assess the carbohydrate and the calorific content of foods, an element that receives little emphasis in diabetes education courses (23). Finally, it draws from current practice and evidence and describes the dietary component of the education program of the proposed intervention.

6.2 The flow of Energy and its Components

The “maximum” (combustible) energy content of foods can be assessed using bomb calorimetry (33) and Figure 10 gives an overview of the energy flow of food through the body for the maintenance of energy balance (194). It provides an expression of the energy content of food after subtracting several energy losses through heat. The energy that remains is referred to as “net energy for maintenance” which can be used to support human basal metabolism, physical activity and the energy required for growth, pregnancy and lactation (195).

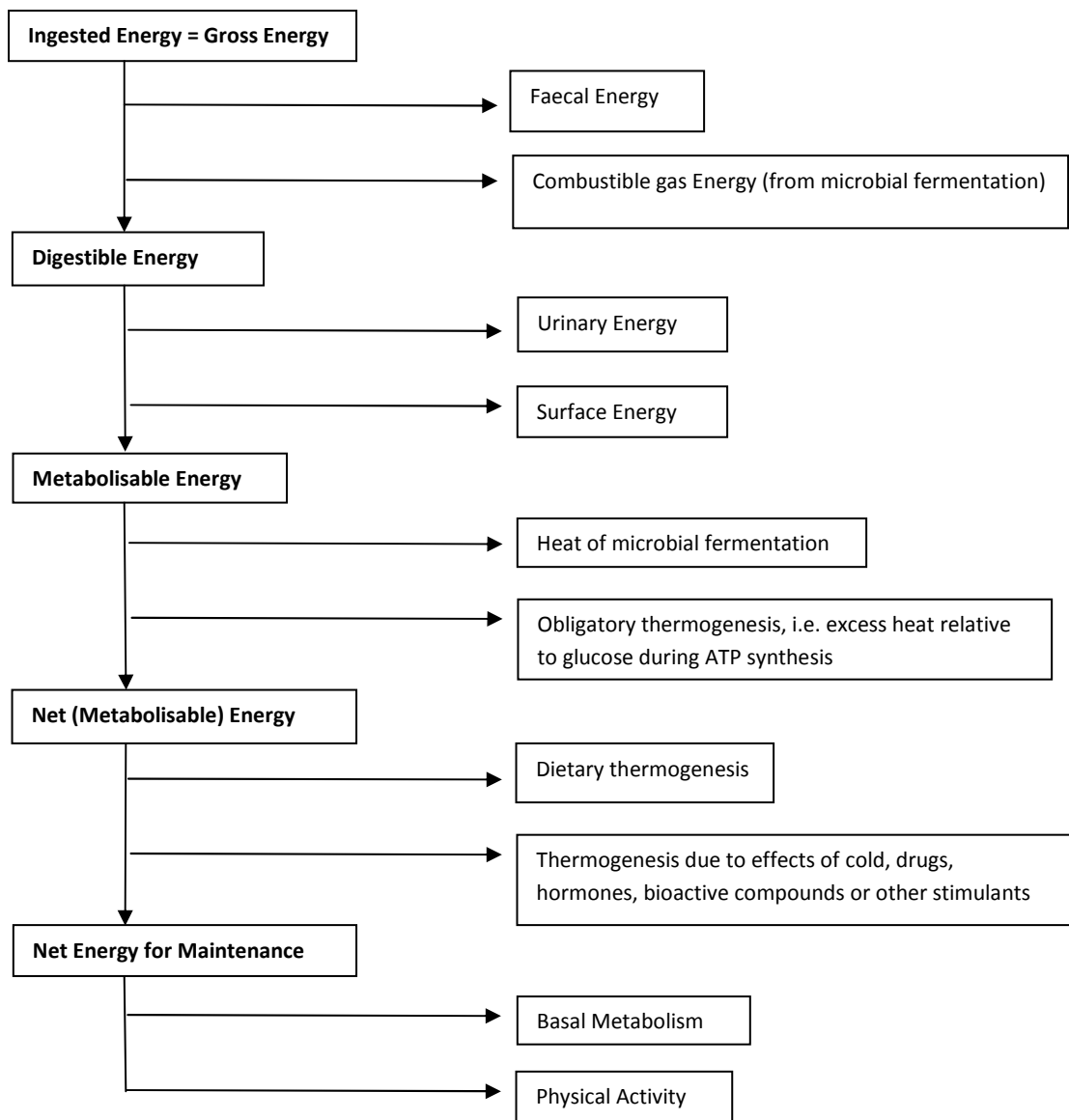


Figure 10: Overview of food energy flow through the body for maintenance of energy balance (194)

The energy content of food is defined by the levels of the three macronutrients protein, carbohydrate and fat, as well as alcohol. Protein is best measured as the sum of individual amino acid residues and when expressed in this way, an energy conversion factor of 4 kcal/g (17 kJ/g) should be used. Carbohydrate is analysed in a way that determines both available carbohydrate and dietary fibre. Direct analysis assesses the available carbohydrate by

difference (total carbohydrate minus dietary fibre) and allows separation of individual mono- and disaccharides and starch. When carbohydrate is determined by direct analysis, an energy conversion factor of 4 kcal/g (17 kJ/g) should be used. When expressed as monosaccharide equivalents, a conversion factor of 3.75 kcal/g (16 kJ/g) should be used (195). The fat content of foods is analysed as fatty acids and expressed as triglycerides (196). This approach excludes any wax esters as well as the phosphate content of phospholipids which cannot be used for energy. For fat, a factor of 9 kcal/g (37 kJ/g) should be used. Alcohol, although not a nutrient (it is a toxicant), contributes to energy intake and the general energy conversion factor recommended is 7 kcal/g (29 kJ/g) (195).

The macronutrients that comprise food, and alcohol, make up the energy intake part of the energy balance equation. Taking into consideration that 1kg body weight equals 7000 calories and that carbohydrate is the main nutrient that affects the post-prandial rise in blood glucose levels (33), it is important for patients with type 1 diabetes to feel confident in assessing both the energy (calorie) and carbohydrate content of their meals.

6.3 Methods of Measuring Energy Intake

Measuring dietary intake influences food choices, which, in turn, determine the nutrient and energy content of the diet and weight status. In diabetes, food choices also affect glycaemic control and the risk of developing complications (197). Over the last few decades, there has been an increasing awareness that measuring dietary intake may in fact be the most challenging problem faced by nutritional epidemiologists (198,199). To date, there is no reference measurement of dietary intake among free-living individuals. In epidemiological studies, habitual or long-term dietary intake is mainly assessed through structured questionnaires which are subject to considerable errors, leading to biased estimates of diet-

disease associations (200) and the difficulty of measuring long-term cumulative individual dietary exposure (201). Measuring diet is therefore subject to important methodological limitations while the most accurate methods are costlier in terms of time, manpower and money (202).

Table 4 describes the various methods for assessing dietary intake and discusses their advantages, limitations and relative cost:

Table 4: Methods for Assessing Dietary Intake (Refers to table on page 81)

Method of Dietary Intake Assessment	Techniques	Principal Uses	Description	Advantages	Limitations
Current Dietary Intake	Weighed food records	When accurate quantified measure of nutrient intake is required	Weighing food and drink prior to consumption, usually for a period of 3-7 days. Accurate description of food and its weight recorded in a booklet. Leftovers also weighed and deducted from original portion weight	Reference method – provides the most reliable quantitative measurement of intake	High respondent burden; Open to misreporting of nutritional intake (conscious and unconscious); Limits its use to some sectors of population – requires certain level of intellectual ability; Follow-up necessary – requires personnel; Costly recording equipment (particularly if electronic)
	Estimated food records: Quantification of food and drink is estimated rather than weighed	When quantification is less important than identifying meal pattern and food choices; When cost and subject uptake is more important than the loss of quantitative accuracy	Respondents are asked to estimate food and drink using: <ul style="list-style-type: none"> Household measures such as cups and spoons Food photographs Food models 	Less invasive, therefore more acceptable; Lower respondent burden than weighed food diaries; Useful tool for clinical practice especially when qualitative, rather than quantitative aspects of diet are assessed	Open to misreporting of nutritional intake (conscious and unconscious); Requires subject cooperation and certain level of literacy skills; Less precise (involves portion size interpretation); Less suitable for large-scale or multicentre trials where different personnel are evaluating portion sizes, introducing bias and error; Expensive
Recalling Past Intake	24 hour recall	A quick baseline assessment of meal pattern and food choices	Trained interviewer asks respondent to recall in detail everything consumed in the previous 24 hours.	Quick, simple; Places a minimal burden on the subject; Suitable for large-scale surveys; Can be administered by telephone; Does not directly influence food choices; Useful tool for clinical practice as a starting point for further dietary exploration	Relies on memory – recalled intake nearly always underestimates actual dietary intake; Fabrication of dietary intake is possible (i.e. to impress the interviewer; bias in recording “good/bad” foods); Assessment confined to short period (single observation) – providing poor measure of variations in daily food intake
Estimating Typical Dietary Intake (Retrospective)	Food Frequency Questionnaire (FFQ)	To identify nutritional deficiencies resulting from food choices; To identify foods consumed infrequently, not captured by short-term food records; To classify individuals into tertiles or quintiles of intake within a population	Consists of a list of foods and a selection of options relating to the frequency of consumption of each of the foods listed (times per day, daily, weekly, fortnightly, monthly)	Low respondent burden; Can be posted or completed over the telephone; Can be self-completed; Suitable for large-scale surveys; Useful in epidemiological studies	Accuracy dependent on portion size evaluation; Possible over-reporting of ‘healthy’ (fruit and veg) and under-reporting of ‘unhealthy’ foods (fat and alcohol); Requires to be validated in relation to reference method; Requires respondent’s ability to think abstractly; Time consuming. 81 May compromise respondent’s cooperation

6.4 Brief History of the “Diabetic Diet”

One of the main aims of current diabetes education programs is to help patients achieve dietary liberalisation. However, this has not always been the case. From the early days of insulin, diet was considered to be the keystone of diabetes treatment. The “diabetic diet” was first described by RD Lawrence in the 1920’s who initially suggested that carbohydrate should be restricted so that “patient’s own insulin could deal with food properly”, and in severe cases “insulin injections should be given to the patient” (203).

Later on, and contrary to the most recent education courses which concentrate only on carbohydrate (23,126), RD Lawrence advised that equal attention should be given to all three macronutrients - carbohydrate, protein and fat. In 1925, during the early days of insulin, the “line ration diet” was recommended to people with type 1 diabetes, which was later developed into the “Lawrence weighed diabetic diet black and red portion/lines”. The aim of this diet was to eat equal amounts of carbohydrate, protein and fat every day, by weighing food at each meal. Foods containing carbohydrate were called the “black portions” and foods containing protein and fat were the “red portions” (204).

With insulin availability and use increasing, patients were “allowed” to consume more black portions (carbohydrate) than red (protein and fat). Black portions should be distributed to balance the action of insulin and should be no more than 100g. More black portions could be consumed if the patient was physically active. Red portions could be consumed “as convenient” and alcohol should only be taken under medical supervision (203). Patients referred to carbohydrate portions as “exchanges”. This type of low carbohydrate diet however, has led to more frequent consumption of protein and fat-containing foods, as they had “no effect on blood sugars”. Additionally, cheese was considered to be a “snack food” and diabetic foods were becoming increasingly popular. During this time of highly prescriptive diets for diabetes, insulin

was administered by a glass syringe and urinalysis was used as a method of monitoring glycaemic control (204).

It was not until 1982 that the then British Diabetic Association (BDA) published the first policy statement on nutrition (204), suggesting that carbohydrate restriction was unnecessary and counter-productive. This policy marked the abandonment of the carbohydrate-restricted diet for patients with diabetes and highlighted the importance of a diet high in complex carbohydrate and dietary fibre and low in fat. In 1992, a second statement of dietary recommendations was published by the BDA reinforcing the previous recommendations. The use of carbohydrate exchange systems was no longer recommended and neither was the use of diabetic foods. Instead, carbohydrate consumption was encouraged at each mealtime and between meals (snacks). Most importantly, fat reduction was emphasised, providing strategies to achieve this, such as consumption of reduced fat products, fruit and vegetables and lean meat (205).

6.5 The Evolution of Analogue Insulin and Carbohydrate Counting

Nowadays, carbohydrate counting and insulin dose adjustment constitute the largest component of diabetes education courses and there is evidence to support their effectiveness in optimising glycaemic control and preventing or delaying complications. During 1963-1966 and after several years of laboratory work, human insulin was chemically synthesised in Germany, China and the United States. In 1978 insulin was successfully produced with the same amino sequence as seen in humans, and in 1980 recombinant DNA “human” insulin was first tested. This technology has now led to the development of human insulin analogues, offering specific and desirable properties such as altered pharmacokinetic characteristics (206), resulting in reproducible action profiles (207). Since 1996, a variety of insulin analogues have been introduced worldwide (207).

Quick acting insulin analogues offer better post-prandial blood glucose control and reduce nocturnal hypoglycaemia compared to conventional short-acting insulins. Furthermore, their

rapid onset of action allows them to be injected immediately before meals, and sometimes even after eating, making them suitable for people with erratic eating habits (207). The long-acting insulin analogues have flatter action profiles providing a more predictable background control.

Despite the lack of evidence confirming any significant improvement in glycaemic control, and the fact that they are more expensive, (208), analogue insulins offer patients the ability to recreate near-physiologic insulin secretion patterns. The basal-bolus insulin regimen has allowed greater flexibility in the timing of meals and when combined with frequent blood glucose monitoring (which has been simplified by the introduction of simpler and faster meters), has also allowed patients to adjust their insulin doses to match carbohydrate intake, thus lowering the perceived burden of dietary restriction (40).

The liberalised approach of matching insulin to carbohydrate on a meal-by-meal basis has been advocated in Düsseldorf, Germany since the 1980's (209) and more recently in the UK through the publication of the DAFNE trial results (23). There are however, patients who lack the ability, confidence and motivation to acquire the necessary skills, usually because they have not received the appropriate education and support required to develop them. It is therefore important for patients to receive proper training which would expose them to the different methods of carbohydrate counting, and would help them to achieve the flexibility to vary their carbohydrate intake at mealtimes and to adjust their insulin doses accordingly.

Educational programs such as DAFNE advocate that dietary liberalisation can be achieved through carbohydrate counting, but provide little or no information on protein and fat, while the calorific content of food is generally neglected from diabetes teaching curriculums. Thus, patients may choose to restrict carbohydrate intake and rely on foods high in protein and fat in an attempt to minimise their insulin requirements, unaware of the undesirable health (and weight) consequences of their food choices (121). The proposed intervention would therefore teach patients to recognise all the macronutrients that constitute food (carbohydrate, protein

and fat) and to estimate both carbohydrates and calories. The following sections will describe the variety of methods that would be used by the proposed intervention, to teach patients how to measure dietary intake, with specific emphasis given to carbohydrate and calorie counting.

6.6 Estimating the Carbohydrate and Calorie Content of Foods

A number of methods would be used to teach patients how to estimate/measure dietary intake, including the carbohydrate, protein, fat and total energy content of foods. The subsequent sections will discuss the following methods:

- Reading food labels
- Weighing food using scales
- Using carbohydrate reference tables or booklets
- Using household measures (like cups and spoons)
- Visual estimation (using portion control tools and food photographs)

6.6.1 Reading Food Labels

Description of method and its application

Reading food labels involves reading and gathering the relevant nutritional information displayed on the food packets. The main objective of the Nutritional Labelling and Education Act (NLEA) of 1990 was to provide consumers with the appropriate information, which would assist them in making and maintaining healthy dietary practices. For the first time since 1973, major changes in food labelling regulations took place, which required standardised nutritional information to appear on almost all food packets manufactured after May 1994 (210-212). In the UK, the Food Labelling Regulations (1996) suggested a format for the nutritional labelling of foods which had to be in accordance with the 1990 EC Directive (213). Nutritional labelling should be voluntary and should comply with the strict rules governing the format (33). The minimum amount of information displayed on food packages should consist of:

- Energy (expressed as kj **and** kcal/100 g or 100 ml)
- Protein (g/100 g or 100 ml)
- Carbohydrate (g/100 g or 100 ml)
- Fat (g/100 g or 100 ml)

Alternatively, more detailed information can be provided:

- Energy (expressed as kj **and** kcal/100 g or 100 ml)
- Protein (g/100 g or 100 ml)
- Carbohydrate (g/100 g or 100 ml)
 - Of which sugars (g/100 g or 100 ml)
- Fat (g/100 g or 100 ml)
 - Of which saturates (g/100 g or 100 ml)
- Fibre (g/100 g or 100 ml)
- Sodium (g/100 g or 100 ml)

Nutrition information is presented per 100g or 100ml, but most manufacturers also present the information per quantified serving (33). A growing number of supermarkets and food manufacturers are also using the traffic light colours labelling system. Along with the grams, the quantity of fat, saturated fat, sugar and salt is also labelled as high (red), medium (amber) and low (green) to help consumers make healthier food choices (214).

Strengths and Limitations

Food label use has been significantly associated with consuming a diet lower in fat (215) and higher in fruit and vegetables (216). For patients with type 1 diabetes, food label information on carbohydrate would be the most relevant for insulin dose adjustment and the information on calories for preventing weight gain. This would potentially improve prognosis and reduce healthcare costs, with the only cost to patients being the time spent to read the food labels (217). One major drawback of food labels is that they can only be used with packaged foods and are not suitable for foods like pasta, rice and potatoes. Furthermore, they involve some degree

of literacy and mathematical ability. People who will not consume the “recommended serving” or the 100g portion reported on the food label will have to weigh the portion size and work out the amount of nutrient of interest, a process that can be considered to be time consuming and possibly unsustainable.

Implications for diabetes management

Nutrition knowledge is an essential component of successful diabetes management and has a significant impact on food label use. Previous research has shown that education has a positive impact on the likelihood of using food labels at home (217), and that targeted consumer education is efficient in improving general health (218). People with diabetes, however, seem to have limited knowledge of how to apply the food label information to meal planning and diabetes management (219,220). Therefore education on reading food labels would form a core component of the proposed intervention, with specific attention given to carbohydrate and calories.

6.6.2 Weighing Food Using Scales

Description of method and its application

Nutritional scales are used to weigh the food portion intended for consumption. Food reference tables, booklets or food labels can be used to gather information per 100g of food and then work out the amount of carbohydrate and total energy in the weighed portion size.

Strengths and Limitations

This system is useful for foods like breakfast cereals, potatoes, pasta and rice, as portion sizes can vary between people. If similar portions of the same food are usually consumed, patients can

weigh the food once and record the relevant information in a diary for future reference. This method however, could be placing significant burden on patients as it can be time consuming and a certain degree of literacy and mathematical ability is required (as with food labels), with the possibility of making it unsustainable.

Implications for diabetes management

It is one of the main methods used in diabetes education programs to teach carbohydrate counting. Unfortunately evidence for the uptake and effectiveness of this method in diabetes outcomes is absent and therefore it is difficult to comment. Weighing food using scales would however be part of the education component of the proposed intervention, in order to conform to the current diabetes education practices.

6.6.3 Using Carbohydrate and Calorie Reference Tables or Booklets

Description of method and its application

Carbohydrate reference tables and booklets contain information on typical portion sizes of the most commonly eaten carbohydrate foods and give the carbohydrate value, either in carbohydrate grams or carbohydrate portions (CPs). One CP contains 10g of carbohydrate. Carbohydrate reference tables also list the 'reference value', which is the same as the information given in food tables as *grams of carbohydrate per 100g*. The same tables and booklets may or may not contain information about calories, protein and fat.

Strengths and Limitations

Patients can carry the booklets with them, making carbohydrate and calorie counting accessible anywhere, at any time. They can also label or highlight the foods they consume more often for easy retrieval and future reference.

Some foods such as rice, pasta, potatoes are difficult to estimate as portion sizes can vary. It may therefore be useful for patients to weigh these foods first to get an accurate assessment of the carbohydrate content of their portion sizes. Similar to the other methods, gathering information from reference tables and booklets requires the ability to work out the nutrient content of a specific portion if only the information per 100g is provided.

Implications for diabetes management

Carbohydrate and calorie reference tables and booklets could be an invaluable learning tool for patients with type 1 diabetes. They are compact and easy to carry around, thus acting as an accessible education tool. Unfortunately, the evidence for their effectiveness in improving diabetes outcomes has yet to be demonstrated. The booklets would be used in the proposed intervention, to conform to current diabetes education practices.

6.6.4 Using Household Measures

Description of method and its application

Several convenient measures such as spoonfuls, cupfuls or bowlfuls can be used to estimate the carbohydrate content of meals of varying portion sizes. For example, one tablespoon of cooked white rice contains 10g carbohydrate or 1 CP.

Strengths and Limitations

This method is useful both when eating at home and out but it requires some degree of practice and good memory. The patients could keep a diary with the necessary information with them for reference and easy access when needed.

Implications for diabetes management

Evidence on the effectiveness of the use of household measures in improving glycaemic control is limited. However, a recent 6-month randomised controlled trial demonstrated the efficacy of a calibrated “diet plate” in inducing weight loss and reducing hypoglycaemic medication requirements in 130 obese patients with type 2 diabetes. The “diet plate” was divided into a number of sections providing a visual guide for portion size assessment (221). The section on the plate account for the carbohydrate, protein and vegetable portions of the meal and it has been calibrated so that a full female and male plate provides 650 and 800 kcals respectively. Nevertheless, its efficacy improving glycaemic control and preventing weight gain in type 1 diabetes has yet to be demonstrated. The diet plate would be used in the proposed intervention as a carbohydrate and calorie counting tool.

6.6.5 Visual estimation

Description of method and its application

It involves estimating the nutrient content of foods and drink using realistic food models and food photographs.

Strengths and Limitations

Visual estimation using food models and food photographs, especially if scaled to real-life sizes, has been widely used in diabetes education courses. Used regularly, they may help patients train

their eye, thus making carbohydrate and calorie counting easy and accessible at any time. Precise measurement however could be prone to error (222,223), usually towards underreporting (224). The tendency of patients to underreport the nutrient content of food and drink items from photographs will be discussed in more detail in Chapter 8.

Implications for diabetes management

Estimated nutrient intakes from photographs have been shown to be on average, with the exception of vitamin C, within $\pm 7\%$ of the nutrient content of the actual amounts of food consumed (225), however in diabetes, the evidence for their effectiveness has yet to be demonstrated. A recent RCT showed no changes in HbA1c or BMI in the intervention group estimating the carbohydrate content of food models (226). In the proposed intervention, the iPhone carbohydrate and calorie counting application would be used as a visual education tool, helping patients with carbohydrate and calorie counting and with insulin dose adjustment.

6.7 Conclusion

Understanding the energy intake component of the energy balance equation is important in type 1 diabetes as it helps patients to appreciate the contribution of all macronutrients, and not only carbohydrate in the calorific content of foods. In line with current education programs, mastering carbohydrate assessment would form a major component of the proposed intervention, which would utilise the variety of methods discussed in this chapter. By incorporating calorie counting into type 1 diabetes education it is hypothesised that the undesirable weight gain that accompanies treatment intensification would be prevented.

Unfortunately, the evidence for the effectiveness of the different methods of carbohydrate and calorie counting in optimising glycaemic control and preventing weight gain is empirical and

limited. Carbohydrate assessment is the main feature of diabetes education courses and the different methods of assessing the carbohydrate content of foods have become the standard practice. However, there is no expectation that patients should use any method religiously, as they may find one fitting their lifestyle better compared to the other. They would, however be encouraged to find the one method (or combination) that works best for them and helps in making informed decisions about management of their diabetes.

The DAFNE trial attempted to establish an evidence-based approach on carbohydrate counting however, it is difficult to know which of its components best works (23). The proposed intervention will go one step further and explore the effectiveness of food photographs from the iPhone carbohydrate and calorie application in optimising glycaemic control and preventing weight gain.

To further support patients in achieving energy balance, the energy expenditure component of the energy balance equation would be taken into account by encouraging physical activity. Physical activity is the most variable component of energy expenditure and the strategies to improve adherence are summarised in the next chapter.

7. Assessing Energy Expenditure

7.1 Introduction

Modern insulin regimens provide patients with type 1 diabetes the flexibility to incorporate physical activity in their everyday lives. In the general population the health benefits of physical activity are well established, with strong scientific evidence demonstrating improvements in several cardiovascular risk-factors including blood pressure, cholesterol and triglyceride levels (227), lower rates of various chronic diseases and improved psychological well-being (228). Regular physical activity should therefore constitute an important component of diabetes management.

Despite the strong recommendation for physical activity, the exact role of prescribed physical activity in weight management is not well defined, with studies showing conflicting outcomes (229). As discussed earlier (Chapter 1 and 3), undesirable weight gain in type 1 diabetes is often accompanied by adverse physiological and psychological consequences, which interfere with diabetes management (29,36,47).

Both weight gain and weight loss are functions of energy balance. Prevention of undesirable weight gain in type 1 diabetes could potentially be achieved by changes in both energy intake (as discussed in Chapter 6) and energy expenditure (229). This chapter discusses the components that constitute energy expenditure, focusing on physical activity, which is the most variable component. It describes the different methods of assessing physical activity through a variety of subjective and objective measures and evaluates their application for use in the proposed intervention that aims to optimise glycaemic control and prevent undesirable weight gain, in young adults with type 1 diabetes.

7.2 The Components Energy Expenditure

The Total Energy Expenditure (TEE) of an individual over a whole day can be determined by its three principal components. These are Basal Metabolic Rate (BMR), Diet-Induced Thermogenesis (DIT) and physical activity (33).

7.2.1 Basal Metabolic Rate (BMR)

BMR is the amount of energy expended at rest, while maintaining the basic physiological functions such as respiration, circulation and thermoregulation (33). It is the largest component of TEE as it constitutes between 45 and 70% of the total energy expended for most adults (192). It is primarily determined by body mass and therefore varies with body weight and composition, age and gender (33).

The most common technique for quantifying BMR in the research setting is by direct or indirect calorimetry, under standard conditions, with the subject in a post-prandial state (fasted for at least 12-14 hours), at complete rest, in a thermoneutral environment (between 26 and 30 degrees centigrade) (192,230-232). Direct calorimetry measures heat output directly, while indirect calorimetry measures oxygen consumption and carbon dioxide production, which are proportional to metabolic heat production (33,230). These methods are expensive and time consuming and therefore not commonly used in clinical practice. Instead, BMR is estimated with reasonable accuracy from a person's weight, age and gender by using predictive equations such as the Schofield, the Harris-Benedict and the Henry equations (230,232-234).

7.2.2 Dietary Induced Thermogenesis (DIT)

A smaller component of energy expenditure, DIT, is the energy required during the processes of digestion, absorption, and during the increase of sympathetic nervous system activity after eating, resulting to an increase in heat production and oxygen consumption. It is estimated that

the metabolic response to food increases total energy expenditure by 10% over a 24-hour period. For practical purposes DIT is considered to be part of BMR and is not taken into consideration when predicting energy expenditure (235).

7.2.3 Physical Activity

Physical activity is the most variable component of energy expenditure in humans and it is defined as body movement produced by skeletal muscles, resulting in energy expenditure (236). Humans perform obligatory and discretionary physical activities. Obligatory activities include daily activities such as going to work and looking after a home and a family. They cannot be avoided within a given setting and are imposed on a person by the economic, cultural and social environment. Discretionary activities include engaging with physical activity regularly for fitness and health and participating in individually and socially desirable activities for personal satisfaction, social interaction and community development (192).

It is estimated that physical activity accounts for 20 – 50% of daily total energy expenditure (33). This can vary between individuals, depending on type, intensity and frequency of activity (237). All forms of physical activity can affect energy balance and there is significant variation in the energy cost of any activity both within and between people due to differences in body size, intensity and duration.

Table 5: Examples of physical activity by intensity (238)

Light Activity⁺ ≤ 3.0 METS* (< 3.5 kcals/minute)	Moderate Activity⁺ 3.0-6.0 METS* (3.5 – 7 kcals/minute)	Vigorous Activity⁺ > 6.0 METS* (>7 kcals/minute)
Casual walking	Brisk walking (4-4.5 mph), walking uphill, hiking	Race walking (more than 4.5 mph), jogging, running
Bicycling < 5mph	Bicycling 5-9 mph, low impact aerobics	Bicycling > 10 mph, high impact aerobics
Sitting	Yoga	Karate, judo, tae kwon do
Light weight training	Weight training	Circuit weight training
Dancing slowly	Moderate dancing	Vigorous dancing
Leisure sports (i.e. table tennis)	Competitive tennis, volleyball, badminton	Competitive basketball, football, rugby, hockey, water polo
Light gardening/house work	Housework that involves intense scrubbing/cleaning	Pushing non-motorized lawnmower
Occupations requiring extended periods of sitting	Occupations that require an extended amount of time standing or walking	Occupations that require heavy lifting or rapid movement

⁺ Intensity level for an average person, defined as 70 kg. The activity intensity levels in this table are most applicable to men aged 30-50 years and women aged 20-40 years. Intensity is a subjective classification.
^{*}The ratio of exercise metabolic rate to resting metabolic rate. One MET is defined as the energy expenditure of sitting quietly, which, for the average adult, approximates 3.5 ml of oxygen uptake per kilogram of body weight per minute (1.2 kcal/min for a 70 kg individual).

Apart from calories, measures of physical activity levels can be expressed as multiples of BMR. This approach was adopted by the Committee on Medical Aspects of Food and Nutrition Policy (COMA) panel on Dietary Reference Values (DRV), which defined two factors, which determine the contribution of physical activity to total energy expenditure the Physical Activity Ratio and the Physical Activity Level (239):

(i) **Physical Activity Ratio (PAR):** The ratio of the energy cost of a specific activity to BMR. PAR's range from 1.0 to 1.4 for sedentary activities like sitting or standing, 2.5 to 3.3 for moderate activity like walking at normal pace, to 6.0 to 9.0 for vigorous activity like jogging or playing tennis.

(ii) **Physical Activity Level (PAL):** The ratio of daily total energy expenditure to BMR. It is the weighted average value of the energy cost of the various activities of varying PAR within a 24-hour period. It indicates 24-hour energy expenditure as a multiple of BMR and includes dietary and other thermogeneses, which increase energy expenditure above the BMR. The FAO identified three levels of activity associated with a population's lifestyle. These categories indicate the habitual physical activity performed by most individuals in a population, over a period of time (192).

Table 6: Physical Activity Level Categories

Activity Lifestyle	Category PAL Value
Sedentary or light	1.4 – 1.69
Active or moderately active	1.70 – 1.99
Vigorous or vigorously active	2.00 – 2.40 (PAL values >2.40 are difficult to sustain over a long period)

The majority of the UK population can be considered to live sedentary lifestyles and the FAO reported that individuals with a “predominantly sedentary Western lifestyle” demonstrate PAL range of 1.55-1.65. Multiplying BMR by the PAL gives an estimate of the daily energy expenditure according to occupational level or recreational activities (33).

7.3 Methods of Assessing Physical Activity

BMR remains fairly constant within and between people and it only varies 5-10% in adult life. It is physical activity that mostly affects the variation in energy expenditure (240). As discussed in Chapter 3, in diabetes, physical activity may improve insulin sensitivity and reduce insulin requirements. Insulin is an anabolic hormone and may lead to weight gain (47). It is therefore important for patients with type 1 diabetes to engage with physical activity monitor their activity levels, to improve their sensitivity to insulin and potentially prevent weight gain. Table 7 provides an overview of the subjective and objective methods that can be used to quantify physical activity:

Table 7: An overview of physical activity assessment methods (241)

Method	Description	Strengths	Limitations
Subjective Measures			
Physical activity questionnaires	Record the type, duration and intensity of physical activity	Inexpensive, non-invasive, low participant burden; Possible to estimate energy expenditure from the synopsis of all activities	Poor reliability and validity; Recall bias, misinterpretation of questions possible; Unsuitable for individuals with literacy problems
Physical activity diaries	Record activity patterns on a daily basis or as activities are happening	Fewer recall problems as recording takes place at the point of activity; More detail than self-report and more accurate; Record details of specific activities	Expensive to administer and analyse; High participant burden. May influence subjects (encourage higher levels of physical activity than usual); Tendency to over-report physical activity
Direct observation	Visual observation by a researcher recording type, duration and intensity of activity.	Can concurrently provide qualitative and quantitative data; Specific physical activity behaviours can be coded	Moderately expensive; Trained observers required; Time and labour intensive; Observer preference may alter behaviour; Can be used over short periods
Objective Measures			
Pedometer	Small unit worn on the waist. It counts the number of steps taken	Inexpensive, non-invasive, can be administered in large groups; Good measure of walking activity and can be used to set goals for promoting behaviour change	Between-instrument variation can occur; Only measures walking type activity; Accuracy can be reduced during an exercise class
Accelerometer	Small unit, usually worn on the waist. It measures duration and intensity of activity through a motor sensor	Non-invasive; Provides an objective measure of body movement; Measures frequency, intensity and duration	Expensive; Less useful for detecting upper body movement or movement on a vertical plane (i.e. cycling); Data analysis requires expertise and specialist software
Heart rate monitoring	Measures heart rate as a proxy measure of activity, intensity and duration	Non-invasive; Provides an indirect physiologic measure of activity; Measures frequency, intensity and duration	Expensive; Monitor can cause occasional discomfort; Heart rate can be affected by gender, fitness and temperature
Geographical positioning systems (GPS)	Measure movement patterns by global positioning technology	Detects movement, speed of movement and distance travelled whilst outdoors; Geographical maps of data can be produced.	Expensive; Does not work indoors and can provide erroneous results; Some participant burden. Poor signal in some areas

7.3.1 Subjective Measures

Until the development of movement monitors (or motion sensors) such as accelerometers and pedometers, the most common method of assessing physical activity was self-report (241), which was not generating objective data (242). Consequently, a large number of subjective measures of physical activity are currently in use, including questionnaires, activity logs and

diaries. These measures are cost-effective when used in population level surveillance and can be useful in providing information on the type and context of physical activity, which is not provided by objective measures (243). Furthermore, they are the most practical choice for public health evaluations on diet and physical activity for weight management interventions (241).

Nevertheless, subjective measures would not be suitable means of measuring physical activity in the proposed intervention. They vary greatly in validity, reliability (243) and in their ability to quantify the frequency, intensity, type, and duration of various activities as they rely on memory recall (241). Error associated with recall techniques is estimated to be between 30 and 50% and is mainly attributed to factors related to recall ability, cognitive development and the tendency to respond in socially desirable ways (244). Furthermore, systematic review evidence reported that subjective measures of physical activity could both be higher and lower than objective measures, adding to the existing concerns regarding reliability (245).

7.3.2 Objective Measures

There is a range of ways of objectively measuring physical activity, including doubly labeled water, calorimetry and heart rate monitoring, which are solely used in the experimental setting. In the free-living setting, advances in physical activity assessment resulted in the proliferation of movement monitors such as pedometers and accelerometers. They are small devices that can be worn on various body locations (ankle, wrist, hip) with the trunk (hip or lower back) being the most common place (242). These offer a potentially important opportunity to incorporate objective measures of energy expenditure into diabetes self-management. The proposed intervention would evaluate the use of movement monitors (pedometers and accelerometers) as motivation tools to promote physical activity and prevent undesirable weight gain in adult patients with type 1 diabetes, and this section will further discuss their application and use.

Pedometers:

Pedometers count the number of steps walked per day and they have emerged as self-monitoring tools that promote physical activity in a variety of populations (142). Despite the lack of convincing evidence for their effectiveness, their validity in measuring physical activity has been confirmed by several studies (246) and their use shows promising results in preventing weight gain and inducing weight loss (129,247). A recent population-based cohort study of 592 adults showed that a higher step count at the end of the five-year follow-up period was associated with a lower BMI, lower waist-to-hip ratio, and higher insulin sensitivity measured by the homeostatic model assessment of insulin sensitivity (HOMA) (248).

Contrary to current physical activity recommendations, which are based on time and intensity (30 minutes per day of moderate-to-vigorous physical activity at least five times a week), pedometers do not record intensity and this is a disadvantage (249). They also only measure movement in the vertical plane, capturing walking or running type movements, missing activities in the horizontal plane such as cycling (250).

Guidelines on the use of pedometers suggest that adults should take 10,000 steps per day which is approximately equivalent to 5 miles (8km) covered on foot (251). It is however still unknown whether this target is realistic in routine clinical practice or associated with any significant improvements in health outcomes (129). It has been suggested that the 10,000-step target is unreasonably high for low-active or sedentary adults, thus contributing to low physical activity adherence (252). Nevertheless, studies which had a step goal as the main predictor of physical activity showed significant improvements in physical activity levels (149-152). Similarly, participants in interventions that required keeping a step diary significantly increased their activity levels, compared to studies that did not require a diary (129). In establishing how many days of data collection are needed to estimate mean pedometer-determined steps/day, a

previous study reported interclass correlations of 0.71 to 0.84 for any two-day recording, and two consecutive days capturing 89% of the variance of a seven day recording period (253).

Accelerometers:

Accelerometers measure step counts and body accelerations per minute (254,255), and unlike pedometers they provide real-time estimates of frequency, intensity and duration of physical activity in free-living individuals (256). With the development of newer, more sophisticated monitors, accelerometry is now viewed as the preferred method for objective physical activity assessment (242). Drawbacks related with accelerometry include the high costs, inconsistencies in calibration and validation literature and the lack of understanding on how to manipulate, analyse and interpret the data produced by the accelerometer output (242,257).

7.4 Implications

The dramatic increase in overweight and obesity in the general population, together with the weight gain that appears to accompany intensification of treatment in type 1 diabetes, focuses attention on the need for patients to increase physical activity levels. Patients with type 1 diabetes may engage in any type of physical activity they wish. However, several potential adverse effects can occur, including exercise-induced hypoglycaemia, hyperglycaemia and ketosis (258). Evidence suggests that individualised physical activity plans, accompanied by on-going support and advice on appropriate measures to avoid hypo- and hyperglycaemia could potentially enhance long-term adherence (48,139,140).

Several strategies to manage diabetes around exercise are available, which enable patients to engage in physical activity, while maintaining adequate control of their diabetes. Such strategies include reducing pre-exercise bolus insulin dose to reduce hypoglycaemia during and following exercise, to take extra carbohydrate which is useful for unplanned or prolonged physical activity,

and to decrease post-exercise basal insulin to reduce nocturnal hypoglycaemia (259). These strategies would form a vital component of the education program of the proposed intervention.

Objective measures of physical activity, such as pedometers and accelerometers, would be used in the proposed intervention as motivational tools and sources of feedback display. A sealed accelerometer would be used to measure baseline physical activity on two weekdays and one weekend day. Baseline physical activity levels would then inform the individualised physical activity plans and daily pedometer step-targets that patients would aim for.

Together with assessing physical activity levels using pedometers and accelerometers, patients should have a sound knowledge on managing their diabetes before, during and after physical activity. All these, in conjunction with the continuing education and provision of decision support and prompts from the e-health platform, could improve adherence and prevent the undesirable weight gain that often accompanies intensification of treatment in type 1 diabetes.

8. The iPhone application – Evaluating its Agreement with the Standard Food Composition Tools and Assessing Patient’s Ability to Estimate the Carbohydrate and Calorie Content of its Food Photographs

8.1 Introduction

The Diabetes Control and Complications Trial has provided conclusive evidence that optimising glycaemic control through intensive insulin treatment regimens reduces the risk and progression of diabetes-related microvascular and macrovascular complications (20). Intensive treatment regimens where insulin doses are matched to carbohydrate intake and blood glucose levels have since been advocated for the treatment of type 1 diabetes (23). Such regimens, however, require a good understanding of, and ability to identify and estimate correctly the carbohydrate content of the diet (23,260). In addition to carbohydrates, the other macronutrients that comprise food (protein and fat), as well as alcohol, should also be taken into consideration. Despite having minimal or no direct effect on blood glucose levels, they contribute to the energy (calorie) intake, and overlooking them, may lead to weight gain (47).

A variety of instruments assessing general diabetes knowledge including diabetes complications and foot care are widely available (261-263). Nevertheless, there are no standardised measures to assess the ability of patients to estimate the carbohydrate and calorie content of food and drink (264). Additionally, systematic bias and large random error may occur in quantifying food and drink consumption (265). Estimates from studies using doubly labelled water have specifically shown caloric intake to be routinely underreported by 20-50% (266-268).

As described in the previous chapters, a variety of tools can be employed to help patients measure the carbohydrate and calorie content of food, such as replicate food models, dietary scales and household measures. Visual aids, such as food photographs have also been used in an

attempt to improve accuracy (269), however, the few studies assessing their usefulness remained inconclusive (225,270-273).

The photographic method of diet evaluation was first described by Elwood and Bird who asked study participants to take pre-and post-meal photographs of the foods and drinks consumed, using a high-quality, high-speed camera. This was reported as being a cost-effective method for gathering dietary information (274,275). Bird and Elwood published correlation coefficients comparing the data gathered from the photographic records with weighed food records. The coefficients ranged from 0.84 to 0.97, showing good correlation. Although no published reliability information could be found (275), since then, food photographs have been used as one of the methods of estimating food portion sizes and nutrients of commonly eaten foods (225,265,276). More recently, Nelson et al showed that estimated nutrient intakes from photographs were on average, with the exception of vitamin C, within $\pm 7\%$ of the nutrient content of the actual amounts of food consumed (225).

The aims of this chapter are (i) to assess the agreement between the carbohydrate and calorie values of the foods on the iPhone carbohydrate and calorie counting application (191), and the corresponding values reported by standard food composition tables (147); (ii) to assess patients' ability to estimate the carbohydrate and calorie content of a selection of commonly eaten food and drink photographs taken from the iPhone application. The results of these two pieces of research would (i) establish whether the iPhone application's photographs are safe to support patients in making informed decisions on their carbohydrate and calorie intake as well as insulin doses; (ii) provide a rationale for the proposed intensive dietary intervention that teaches patients carbohydrate and calorie counting in real-time, through the novel iPhone application.

8.2 Materials and Methods

8.2.1 Assessing the agreement between the carbohydrate and calorie values of the photographs on the iPhone application and the corresponding values reported by standard food composition tables

The iPhone application contains 16 food and drink categories, namely: Biscuits & Crackers; Bread; Breakfast; Cakes & Bakery; Desserts; Drinks; Fruit; Meals; Pasta & Grains; Snacks; Take-Away; and Vegetables & Pulses. Each category contains a variety of food and drink photographs of up to six portion sizes, beginning from the smallest photo to the largest, as shown in Appendix V. Each photograph clearly displays the weight of the food/drink and its carbohydrate and calorie values.

In clinical practice, the standard food composition tables (147) are used as reference for the nutrient content of food and drink. These tables report the nutritional values per 100g for hundreds of food and drink items. The nutrient content of these food/drink items has been derived from an average of different products (i.e. Tesco's, Waitrose, Sainsbury's), or from an average of different recipes.

The food and drink items displayed in the iPhone application's photographs consist of single items, such as a Digestive biscuit, or more complex foods which have been cooked from a recipe, such as Lasagna. For single items, the authors of the book (and iPhone app) used food labels or the standard food composition tables, to derive the carbohydrate and calorie content of the portions displayed in the book. For more complex foods, such as Lasagna, they followed a recipe.

For example, for Digestive biscuits, the standard food composition tables report an average of different types of Digestive biscuits (i.e. Tesco's, Waitrose, Sainsbury's), and show the nutrient content of 100g of Digestive biscuits. For Lasagna, the standard food composition tables report an average of different recipes, and report the nutrient content of 100g of Lasagna, (as well as the individual Lasagna components).

To calculate the carbohydrate and calorie content of the cooked Lasagna, for example, the authors of the book and app weighed each component of the recipe separately (i.e. minced meat, tomato sauce, lasagna sheets etc). They used the standard food composition tables to calculate the carbohydrate and calorie content per 100g of each recipe component. Then, they determined the weight of the whole Lasagna portion (the total amount of Lasagna made from the recipe) and calculated (from the individual recipe components) the carbohydrate and calorie content of 100g of Lasagna.

They then decided the six portion sizes that would be displayed in the book/app, and presented each portion on the plate, beginning from the smallest portion, for Lasagna = 80g, to the largest portion, for Lasagna = 665g. Then, they calculated the carbohydrate and calorie content for each one of the six portions, using the carbohydrate and calorie values per 100g Lasagna.

Even if the picture of a food made from a recipe has values that were derived from the standard food composition table values for each of the recipe component ingredients, the values for the cooked recipe still need to be standardised to reflect the average value from a range of recipes. If the iPhone app is to be used in clinical practice, it is important to establish whether the carbohydrate and calorie values reported in the photos (which are derived from a single product or single recipe) agree with the values reported in the standard food composition tables.

To investigate the relative agreement between the two tools, I carried out the following steps:

- I selected three food photographs from each of the 16 food and drink categories (Appendix VI), to obtain a representative range of foods and drink items.
- I produced an Excel document and I recorded the weight of each food selected and the carbohydrate and calorie values reported for each portion (Appendix VI).
- Then I found each food in the standard food composition tables.

- The standard food composition tables report the carbohydrate and calorie content of foods per 100g.
- I adjusted the carbohydrate and calorie values reported in the standard food composition tables to match the portion size of the food photographs.

Example

- Food category – Biscuits & Crackers
- Number of food: 56
- Food type – Cream Crackers
- Photograph portion size: 8g
- Carbohydrate content as reported in the 8g photograph: 5g
- Calorie content as reported in the 8g photograph: 35 calories
- Carbohydrate content per 100g cream crackers reported in standard food composition tables: 63g. Adjust for an 8g portion: $(63/100) \times 8 = 5.04\text{g}$
- Calorie content per 100g cream crackers reported in standard food composition tables: 414 calories. Adjust for an 8g portion $(414/100) \times 8 = 33.12$ calories

Therefore, for 8g Cream Crackers:

- iPhone photographs report 5g Carbohydrate, 35 calories
- Standard food composition tables report 5g carbohydrate, 33 calories

The same process was carried out for the rest of the food and drink items selected.

Then correlation coefficients were calculated, and the Bland-Altman plots were used to measure the agreement between the two tools, as described in the following sections.

Although perfect agreement between the two sources of information would not be possible, it would be important to establish the extent and nature of any disagreement between them (277). Differences in the carbohydrate and calorie values reported on the iPhone photographs and the standard food composition tables would inform the safety of the use of the new tool in optimising glycaemic control and preventing undesirable weight gain, in routine clinical practice. A systematic underestimation of calorific intake would have an adverse effect on body weight. A systematic underestimation of carbohydrate intake would lead to hyperglycaemia and hypoglycemia respectively.

8.2.2 Data Preparation and Initial Investigations

The first step in assessing the agreement between the two tools was to plot the data showing the carbohydrate and calorie values of the foods selected from the iPhone application (191), against the values of the corresponding foods from the standard food composition tables (147), on the x and y axis respectively. This method helped in the visual assessment of the agreement between the two tools (279). The two tools would agree perfectly if all the points lay along the line of equality. This method, however, provided no information on the between-tool variability in carbohydrate and calorie values (280).

8.2.3 Use of the Correlation Coefficient

The second step in the process of assessing the agreement between the two tools was to calculate the correlation coefficient (r) (277), which would measure the strength of their association. In the case of perfect correlation all the points would lie along the line of equality. However, correlation coefficients are not necessarily informative. Two measures would be expected to be highly correlated if they were both designed to measure the same quantity; however, it is possible for highly correlated measurement tools to have poor agreement (277).

This analysis would therefore provide limited information on how much the carbohydrate and calorie values reported by the iPhone application differ from the values reported on the standard food composition tables.

8.2.4 Measuring Agreement

A more appropriate statistical procedure was therefore used (277) to assess the agreement between the carbohydrate and calorie values reported by the iPhone application (191) and the standard food composition tables (147). The graphical method described by Bland and Altman (277) was followed, where the arithmetic difference in carbohydrates and calories between the two tools was plotted against their mean carbohydrate and calorie values. The plot of difference against the mean, allowed the investigation of a relationship between the measurement error and the true value. As the true value was unknown, the mean difference between the two measurements was estimated, based on the assumption that the differences were normally distributed (279).

8.2.5 Audit assessing the ability of patients with type 1 diabetes to estimate the carbohydrate and calorie content from a sample of food and drink photographs from the iPhone application

Following the assessment of the agreement between the two tools, and after establishing the safety of the iPhone application for use in routine clinical practice, an audit was carried out to investigate the ability of patients with type 1 diabetes to estimate the carbohydrate and calorie content of a selection of food and drink items taken from the 1900 photographs available on the iPhone application. This audit would offer valuable information on the patients' baseline carbohydrate and calorie counting skills and would provide further evidence for the rationale of

the proposed intervention. The recruitment rates would provide information on the feasibility and acceptability of the intervention, while the patients' answers would provide an indication of their ability to estimate the carbohydrate and calorie content of food from photographs. If knowledge was shown to be sub-optimal, this would add to the current evidence-base highlighting the urgent need for structured educational dietary interventions directed at this patient group that specifically aim to improve carbohydrate and calorie counting knowledge, in order to optimise glycaemic control and prevent undesirable weight gain.

(a) Sample Selection and Eligibility

The aim was to recruit half the patients attending the Young Adult Clinic in Oxford. This was considered to be a big enough sample size to enable a number of preliminary analyses to be conducted with reasonable precision, prior to recruiting a larger number of patients, possibly from other centres as well. As this was a small-scale audit there was no power calculation. Patients were eligible for participation if they were aged between 18 and 30 years, had type 1 diabetes for at least six months without any major complications, were on a basal bolus insulin regimen and did not have any other concurrent medical conditions.

(b) Food selection

A variety of commonly eaten food and drink items (n=12) were selected from the photographs available on the iPhone application (191). These photographs were used to assess the patients' ability to distinguish between carbohydrate, protein, fat and energy density (calories) (Table 8). The sample of foods and drinks was selected purposively to include those used to teach carbohydrate counting in current diabetes education programs (23). Baked cod and cheddar cheese were selected as they contain no carbohydrate, while foods such as deep fried chips and

shortbread were selected because they contain carbohydrate and are also are high in fat and therefore energy dense.

Table 8: Food and drink photograph selection for audit.

Food	Plate cm	Portion Size (g)	Carbohydrate	Calories
Mash Potato (no butter)	26	235	40	169
Chips (deep fried)	26	230	70	550
Baked Cod	26	125	0	120
Cheddar Cheese	26	50	0	208
Rice (white)	26	225	70	311
Spaghetti (white)	26	220	70	345
Bread (wholemeal)	20	36	15	78
Bread (white)	20	33	15	72
Shortbread	20	13	10	81
Banana (without skin)	20	85	20	81
Orange Juice	(1/2 pint)	(1/2 pint)	24	95
Semi-skimmed milk	(1/2 pint)	(1/2 pint)	13	132

(c) Preparation of food and food photographs

The food was prepared by Mr Cheyette (diabetes specialist dietitian and author of the Carbs and Cals book which forms the basis of the iPhone application) (191) and the portion sizes were carefully weighed using the Salter 303 Aquatronic Kitchen Scales (281). The photographs were taken Mr Balolia, a professional photographer under controlled conditions of light and presentation (191). For the purpose of the audit, the selected photographs were printed in the landscape orientation, in colour and were blown up to real-size dimensions. The plate diameter was 20 cm for the small and 26 cm for the large.

(d) Assessment procedure

Information on age, gender, duration of diabetes, most recent HbA1c (%) and most recent BMI (kg/m²) were collected from the patients' medical notes. Patients were invited to participate on routine appointment attendance at the Young Adult Clinic in Oxford. The purpose of the audit was explained in detail and those patients agreeing to participate were presented with the 12 food and drink photographs. They were asked to estimate the carbohydrate and calorie content of each photograph and to report their estimated values on the data collection sheet provided (Appendix VII). The patients were also asked if they attended any diabetes education courses (such as DAFNE (23) or InSight (126) and whether they would like their information to be made available to the dietitian. If this was not desirable, and to respect confidentiality, the data collection sheet remained anonymous.

(e) Statistical Analysis

Data were collected and tabulated in a password-protected Microsoft Excel document and was analysed using Excel 2007 and the 'R' statistical package. For each assessment, the actual carbohydrate and calorie content of the food and drink items was subtracted from the estimated values. Thus a positive value indicated an overestimate and a negative value an underestimate. The percentage difference was the difference in grams and calories divided by the actual grams and calories of each food item, multiplied by 100.

For analyses purposes, the food and drink items were ranked in ascending order, starting from those with the lowest carbohydrate or calorie content. The mean and median estimates were calculated, and for carbohydrates the ± 10 g error margin was reported, in accordance with recent evidence suggesting that small errors of ± 10 g in carbohydrate estimation are unlikely to significantly affect post-prandial glycaemic control (282). The proportion of patients under and over reporting was calculated, as well as the proportion of patients within the ± 10 g error

margin. Further analyses were carried out to assess whether the ability of patients to estimate the carbohydrate and calorie content of food and drink items from photographs was associated with HbA1c levels and BMI.

8.3 Results

8.3.1 Assessing the agreement between the iPhone application and the standard food composition tables

Figures 11 and 12 show the correlation of carbohydrate and calorie values from the iPhone application's food and drink photograph selection (Cheyette) (191) against the standard food composition tables (McCance) (147). The null hypothesis here was that the carbohydrate and calorie values reported by the two tools were not linearly related. This hypothesis was rejected since for both carbohydrates and calories, the majority of values lied on the line. The correlation coefficients were $r=0.99$ for carbohydrates and $r=0.96$ for calories ($p<0.01$), suggesting near-perfect association. It could therefore be concluded that the two tools were highly correlated; however, as mentioned earlier, this high correlation does not mean that the two tools are in good agreement.

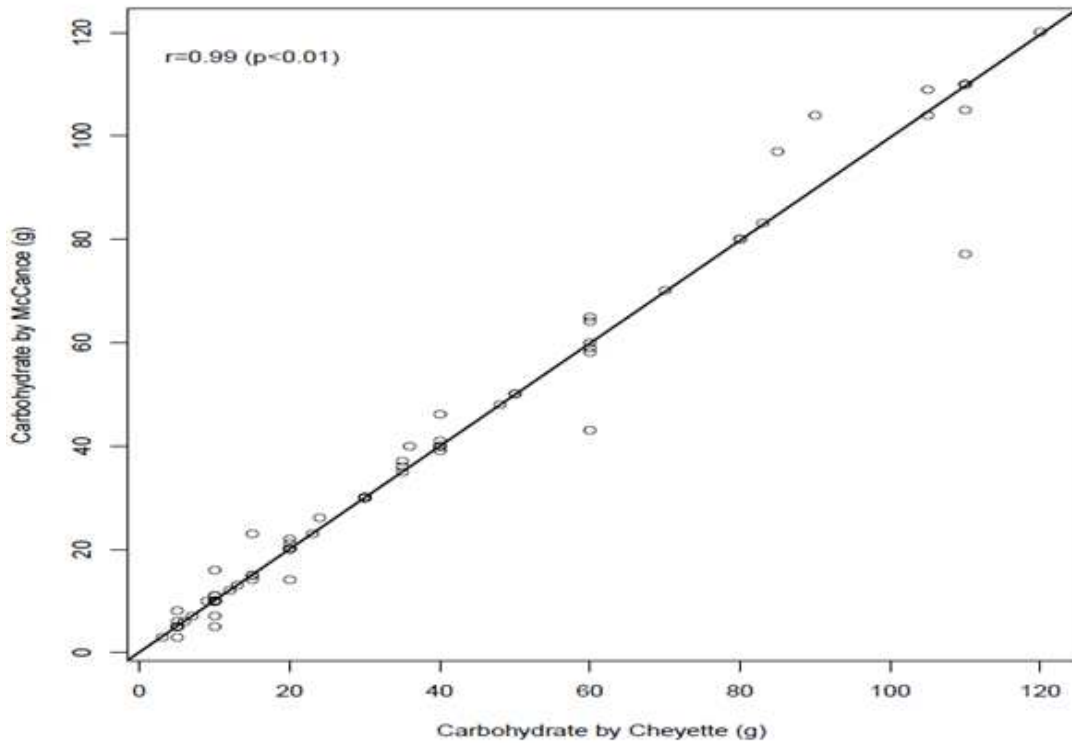


Figure 11: Carbohydrate (g) reported the two tools, with line of equality

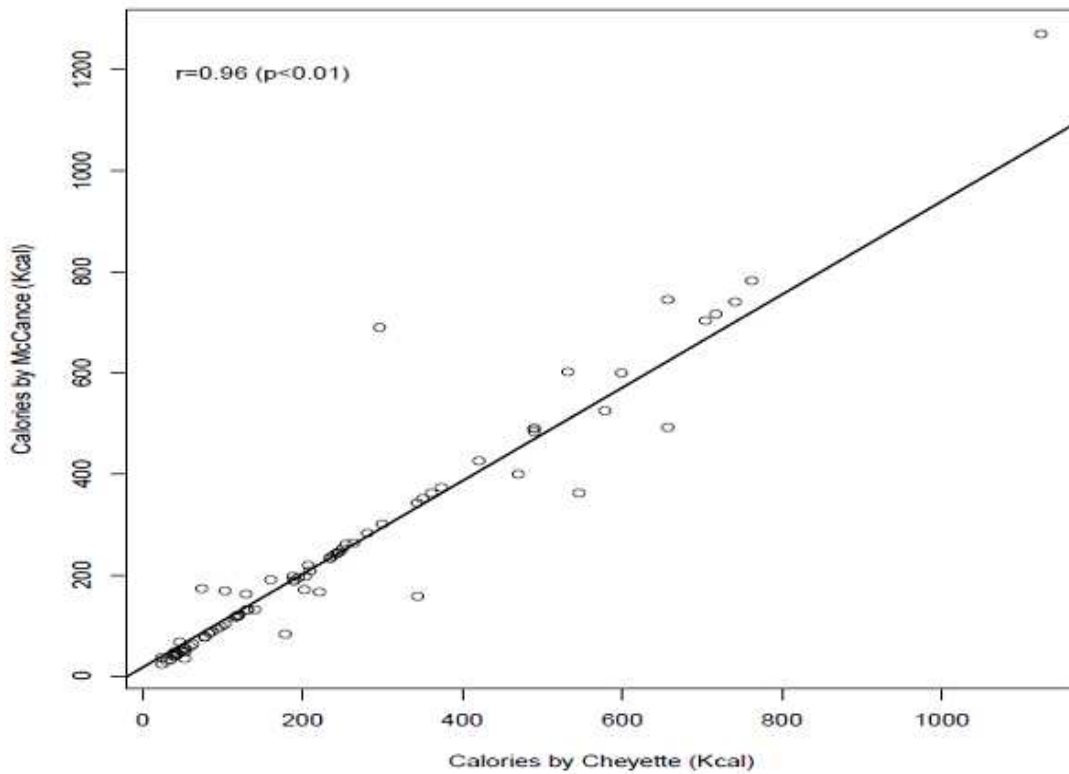


Figure 12: Calories reported by the two tools, with line of equality

Figures 13 and 14 show the Bland Altman Plots comparing the difference between the two measurements against the mean of the two measurements, for carbohydrates (Figure 13) and calories (Figure 14). The mean difference between the two tools for carbohydrate was nearly perfect, at 0.02 [95% CI -1.1 to 1.1] g and the mean difference for calories was 1.55 [95% CI -12.1 to 15.2] kcal. In both cases, the 95% Confidence Intervals included zero suggesting that there is no evidence that the two tools differ in the carbohydrate and calorie values they report (Table 9).

Table 9: Mean difference and limits of agreement between the iPhone application and Standard Food Composition Tables (McCance) for carbohydrates and calories

48 Foods	Mean Difference (McCance-iPhone app)	95% CI for mean difference	Limits of agreement (mean difference \pm 2SD)	
			Lower	Upper
Carbohydrate (g)	0.02g	-1.1 to 1.1	-10.1	10.1
Calories (kcal)	1.55 kcal	-12.1 to 15.2	-127.7	124.8

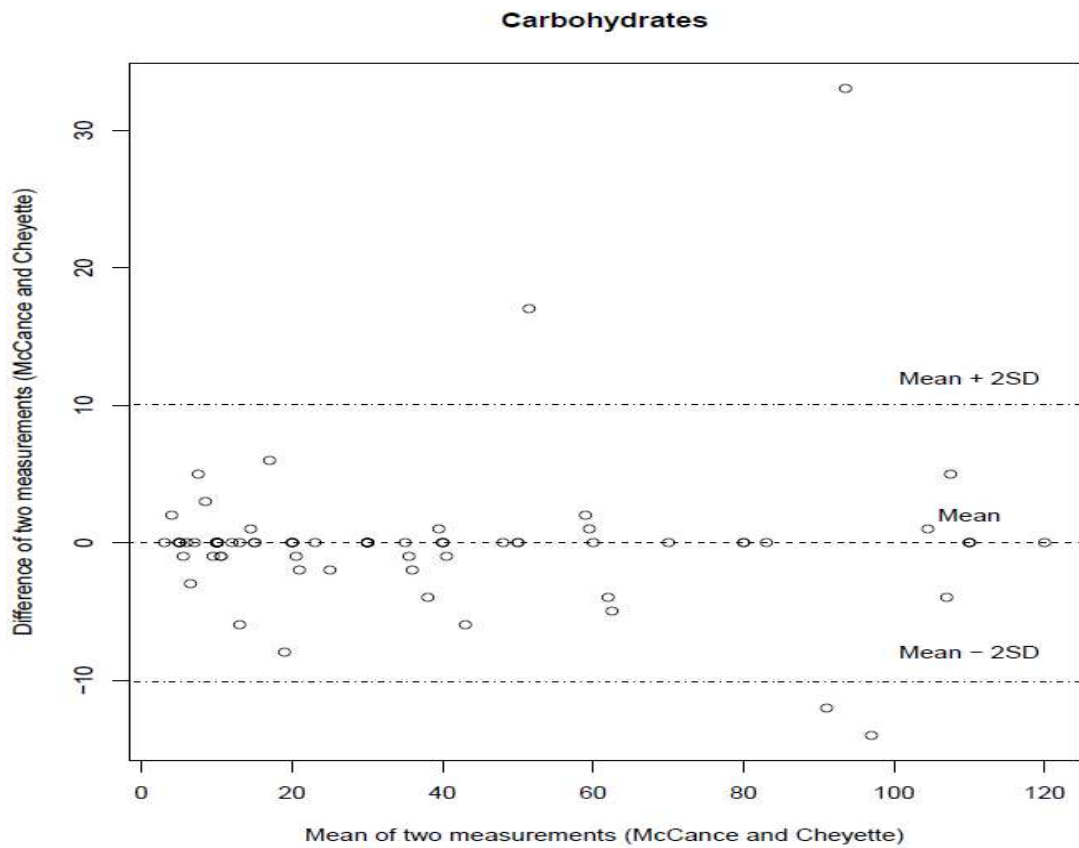


Figure 13: Difference in carbohydrate (g) between the two tools, against the mean carbohydrate (g) of the two tools

For carbohydrate (Figure 13 and Table 9), the limits of agreement (-10.1 to 10.1) are small enough to be confident that the iPhone application photographs could be used in place of the standard food composition tables.

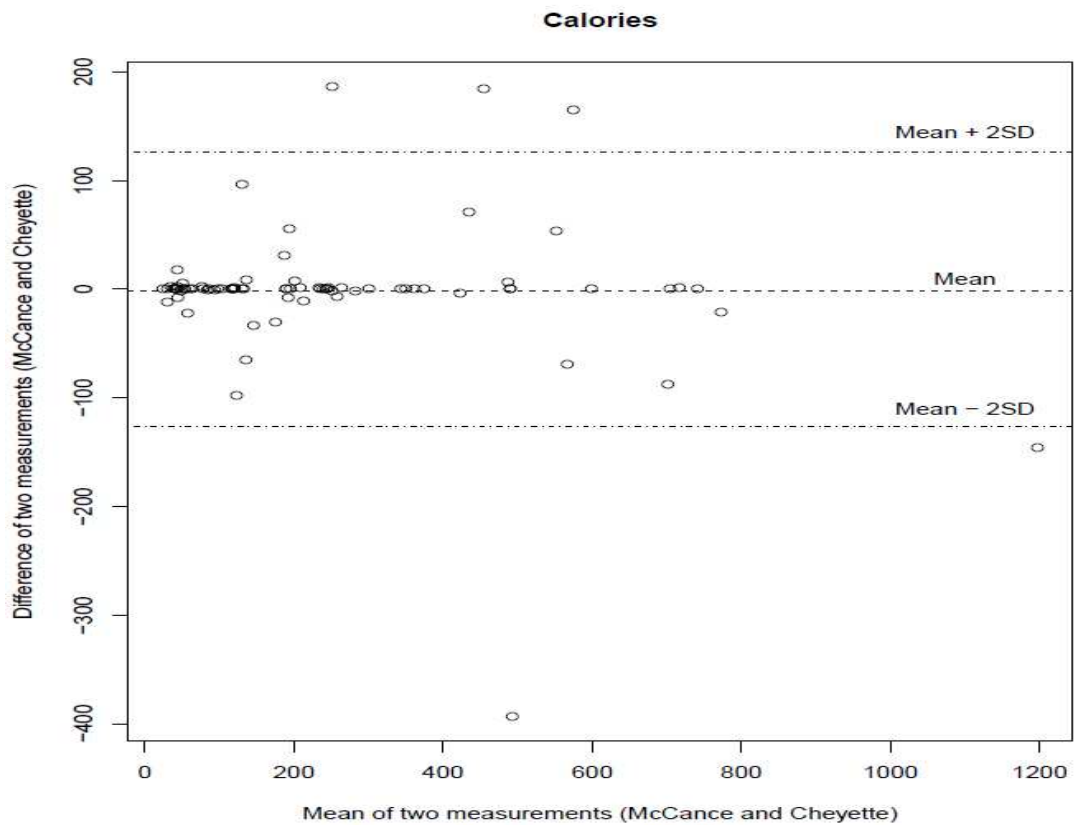


Figure 14: Difference in calories (kcal) between the two tools, against the mean calories (kcal) of the two tools

For calories (Figure 14 and Table 9), the limits of agreement (-127.7 to 124.8) are wider. Nevertheless, closer investigation of the outliers indicated that they represent foods the nutrient content of which can vary depending on method of cooking (Lasagna, spaghetti Bolognese, scampi and Indian samosa), or they include foods cooked by following a specific recipe (black pudding, Indian samosa, scampi), making the discrepancies between the two tools unavoidable, but reasonable.

8.3.2 Audit assessing the ability of patients to estimate the carbohydrate and calorie content of foods from photographs

Of the 105 patients attending the Young Adult Clinic in Oxford, 52 were approached during attendance to a routine clinic appointment. The purpose of the audit was clearly explained and the patients were given the opportunity to ask questions. All patients approached at the clinic agreed to participate. Appendix VIII shows the audit participant characteristics.

Of the 52 participants, 53.8% were males. The mean HbA1c (SD) was 9.0% and the mean BMI (SD) was 25.2 (kg/m²). 13.5% of the participants had attended a diabetes education course and 71% consented to making their answers available to the diabetes dietitian (Table 10). Only 15.4% of participants had an HbA1c <8%.

Table 10: Patient Characteristics

N	Gender (M/F)	Median Age (IQ range)	Median Diabetes Duration Months (IQ range)	Mean HbA1c (%) (SD)	BMI (kg/m ²) Mean (SD)	Inform Dietitian (Yes/No)	N Education
52	28/25	22.7 (18-26)	159 (9-265)	9.0 (1.3)	25.2 (4.5)	37/15 (71%)	7/52 (13.5%)

All 52 participants attempted to estimate the carbohydrate and calorie content of the 12 food and drink photographs presented to them, with the possibility of providing a total of 1248 answers for both carbohydrate and calories. Many were reluctant to estimate the calorific content of the foods, with 17 (32.7%) patients not providing any answer for calories for any of the foods, and seven (13.5%) not providing any answer for carbohydrates. The proportions of answers provided for carbohydrates and calories were 84.1% and 65.9%, respectively. In total,

18% [95% CI 0.02 to 0.35] more answers were given for carbohydrates compared to calories (Figure 15).

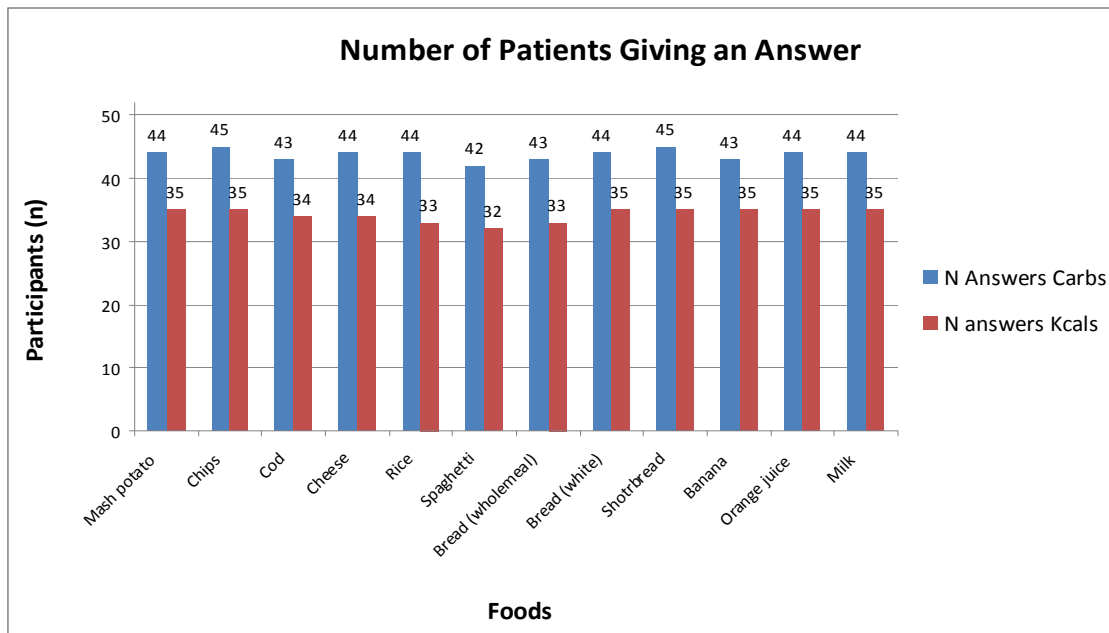


Figure 15: Number of Patients Giving an Answer for Carbohydrates and Calories (out of 52)

Figures 16 and 17 show the carbohydrate and calorie estimates for each photograph. The foods were ranked in ascending order starting with the one with the lowest carbohydrate (Figure 16) or calorie (Figure 17) content.

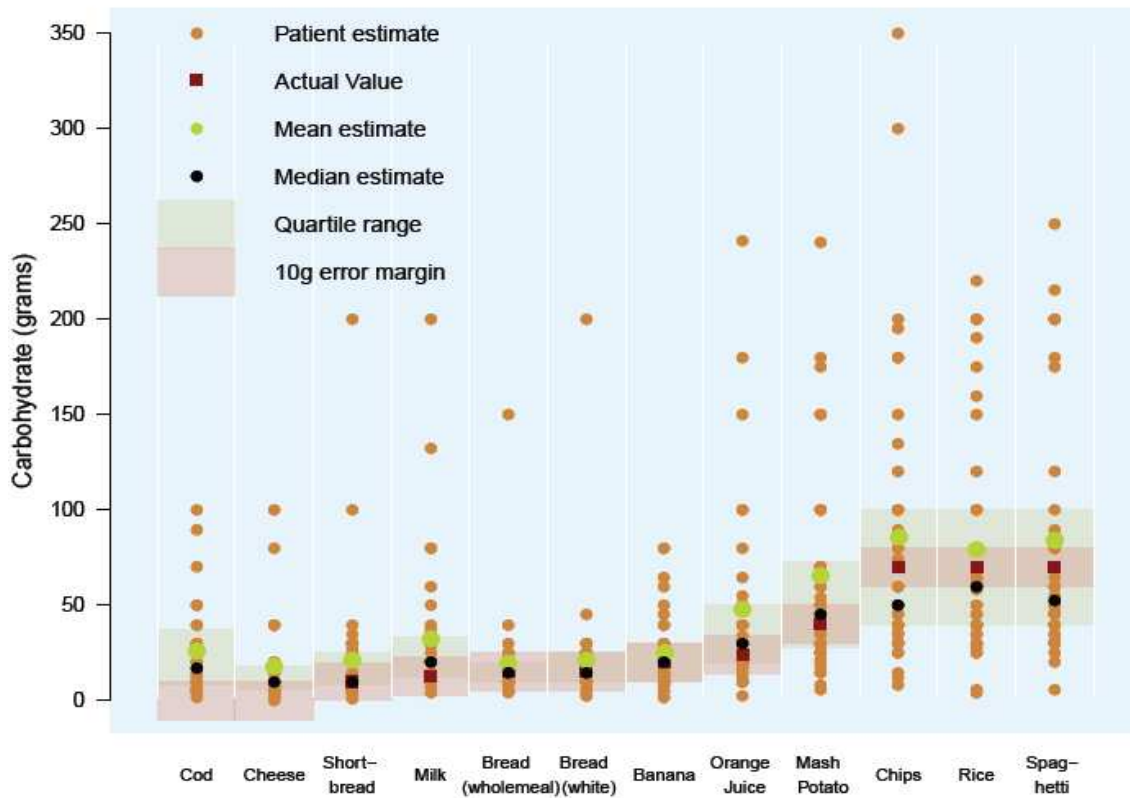


Figure 16: Carbohydrate Estimates from Photographs

There was great variation in the estimated values for carbohydrates. A very small proportion of patients estimated correctly or within the $\pm 10g$ error margin (278) (Table 11). Bread (both white and wholemeal), shortbread, cheese and cod were the foods for which the majority of estimations were within the $\pm 10g$ error margin. However, only half of the patients were aware of the fact that cod and cheddar cheese do not contain any carbohydrate. For bread (both white and wholemeal) and shortbread the mean estimate was closer to the actual value.

Spaghetti, rice and chips were the foods with the highest carbohydrate content and it can be observed that the majority of patients underestimated the carbohydrate content, while for chips, spaghetti and orange juice not a single patient gave a correct answer.

Table 11: Proportion of patients under and overestimating carbohydrates from photographs

Food	Carbohydrates (g)	Proportion of patients within the \pm 10 g margin of error	Proportion of patients answering correctly	Proportion of patients underestimating
Mash potato (Without butter)	40	21.2%	3.8%	55.8%
Chips	70	7.7%	0.0%	65.4%
Breaded Cod	0	53.8%	38.5%	42.3%
Cheddar Cheese	0	53.8%	30.8%	32.7%
White Rice	70	17.3%	5.8%	73.1%
Spaghetti	70	7.7%	0.0%	69.2%
Bread (wholemeal)	15	65.4%	13.5%	61.5%
Bread (white)	15	55.8%	17.3%	61.5%
Shotbread	10	63.5%	19.2%	57.7%
Banana	20	42.3%	13.5%	69.2%
Orange juice	24	34.6%	0.0%	44.2%
Milk (semi skimmed)	13	42.3%	3.8%	40.4%

There was a wider variation in the estimates for calories. As the calorific content of foods increased, so did the tendency of patients to underestimate (Figure 17, Table 12). This was especially true for rice, spaghetti and chips, which were the most calorific foods. Interestingly, out of 624 possible answers for calories, only one correct answer was provided, by one patient, for orange juice. For calories, an arbitrary 10% error margin was set, but this was not based on any evidence and therefore was not further investigated. For bread (both white and wholemeal) and for banana the mean estimate was closer to the actual value.

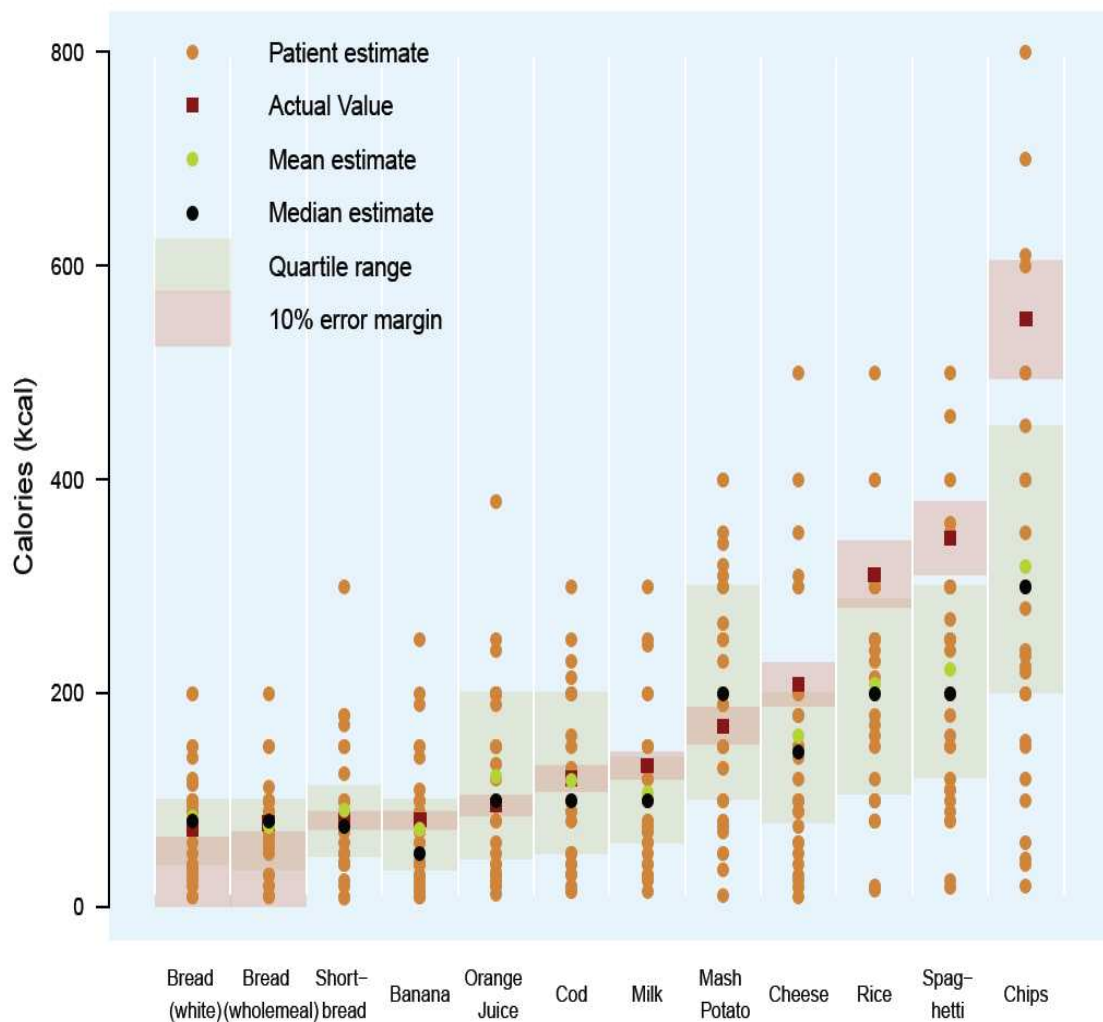


Figure 17: Calorie estimates from photographs

Table 12: Proportion of patients under and overestimating for calories from photographs

Food	Calories	Proportion of patients overestimating	Proportion of patients underestimating
Mash potato (Without butter)	169	41.2%	58.8%
Chips	550	7.8%	92.2%
Breaded Cod	120	29.4%	68.6%
Cheddar Cheese	208	17.6%	82.4%
White Rice	311	9.8%	90.2%
Spaghetti	345	15.7%	84.3%
Bread (wholemeal)	78	37.3%	62.7%
Bread (white)	72	45.1%	54.9%
Shotrbread	81	27.5%	72.5%
Banana	81	21.6%	78.4%
Orange juice	95	41.2%	56.9%
Milk (semi skimmed)	132	17.6%	82.4%

Establishing the Association between HbA1c, BMI and Patient Estimations

The aim of this section was to comment on whether the ability of patients to estimate the carbohydrate and calorie content of food from photographs was associated with HbA1c and BMI. To investigate this, the carbohydrate and calorie estimates for the most calorific food (chips 550 kcals) and least calorific (White Bread 72 kcals) were plotted against HbA1c and BMI.

Figures 18 – 21 give an indication that the ability of patients to estimate the carbohydrate and calorie content of chips from photographs was not related to either HbA1c or BMI. The greater variation in estimations for calories compared to carbohydrates was once again confirmed, and patients with better and worse glycaemic control giving similar estimations. The tendency of

patients to underestimate the calorific content of more energy dense foods was also established, with 92.9% of participants underestimating the calorific content of chips.

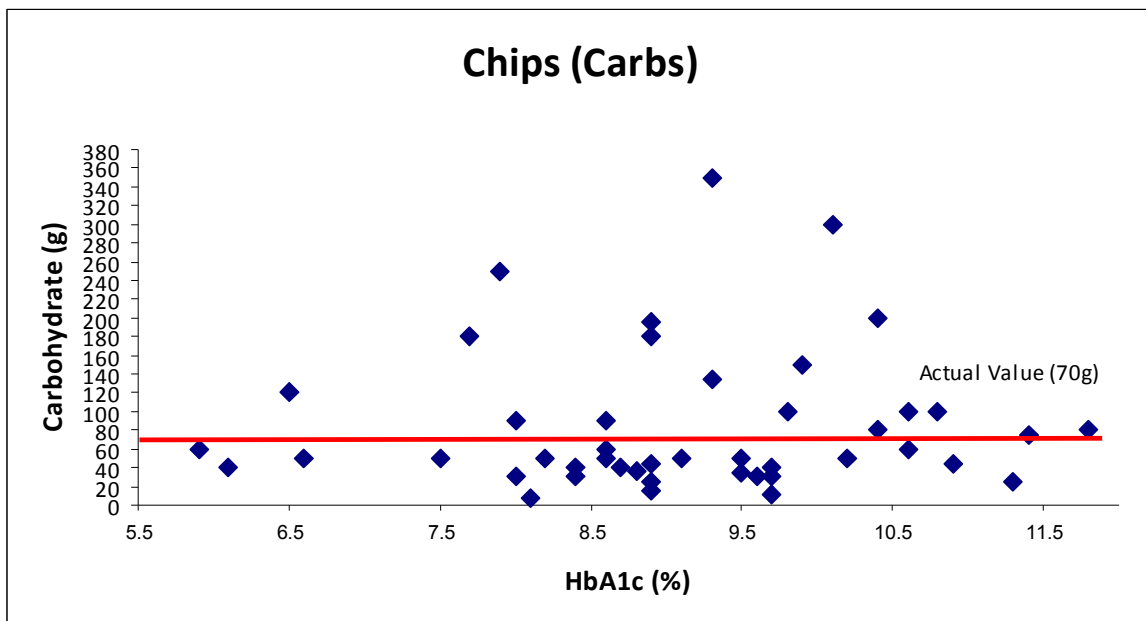


Figure 18: Carbohydrate estimations for Chips plotted against HbA1c (%)

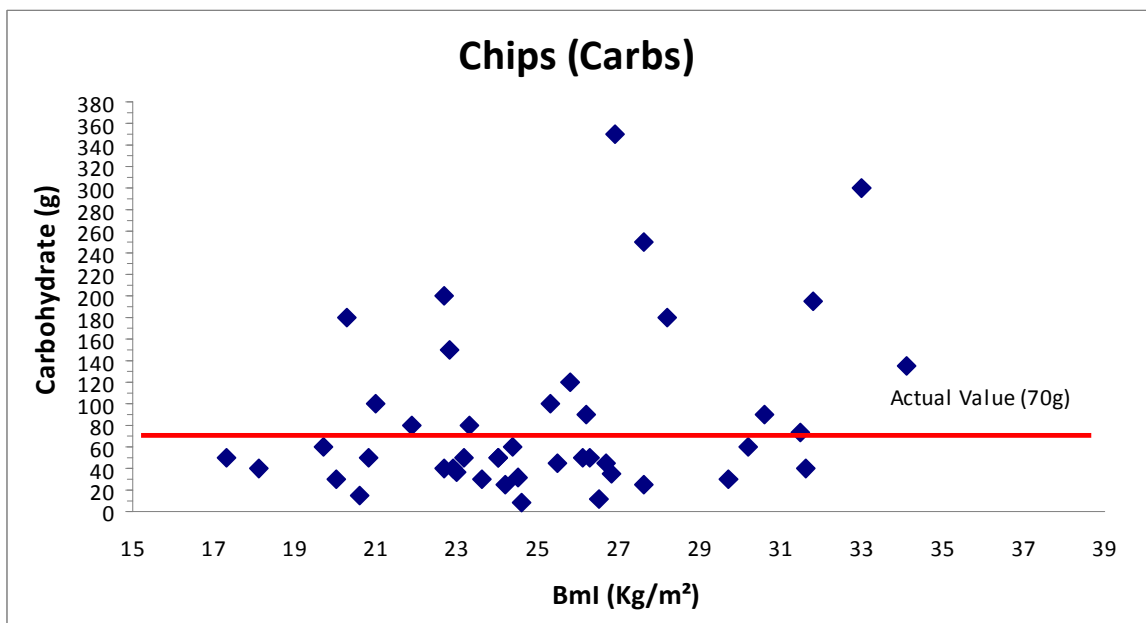


Figure 19: Carbohydrate estimations for Chips plotted against BMI (kg/m²)

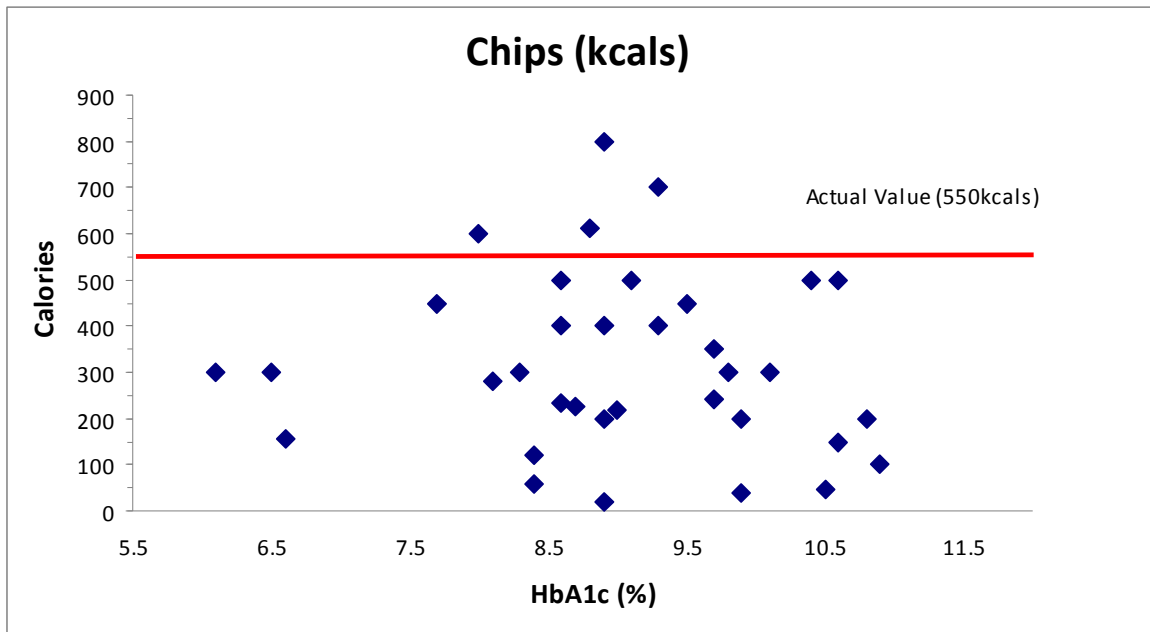


Figure 20: Calorie estimations for Chips plotted against HbA1c (%)

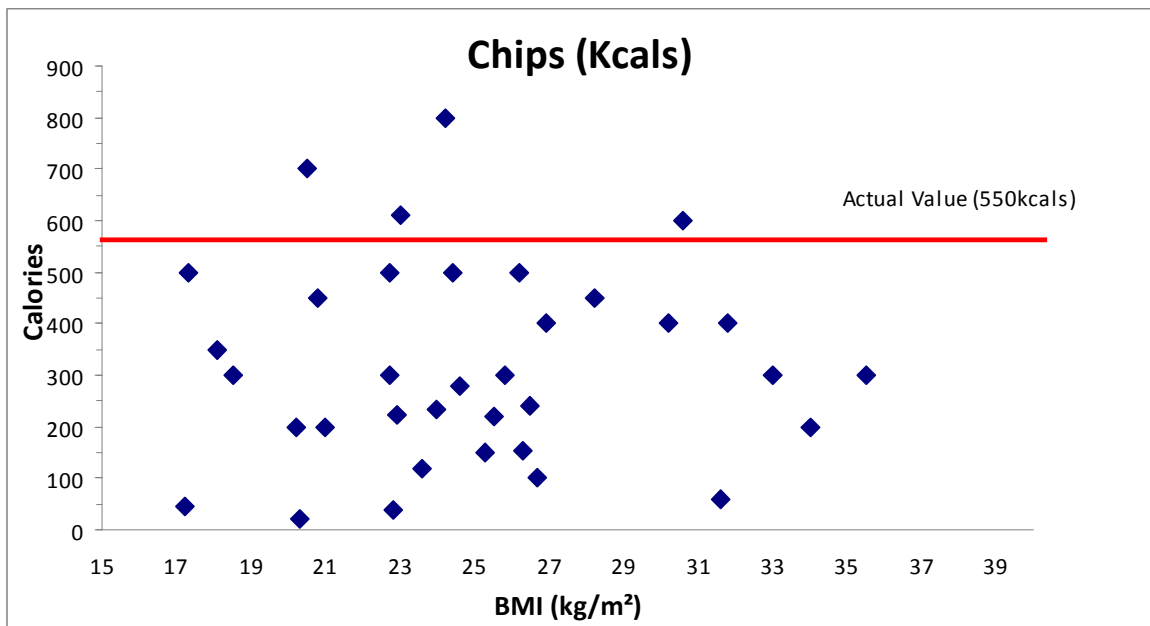


Figure 21: Calorie estimations for Chips plotted against BMI (kg/m²)

To further investigate whether the ability of patients to estimate the carbohydrate and calorie content of food was associated with HbA1c and BMI, the carbohydrate and calorie estimates of the food with the lowest calorific value (white bread, 72 kcals), were plotted against HbA1c and BMI. Once again, the variation in carbohydrate and calorie estimates was not related to HbA1c levels or BMI, with patients with better glycaemic control failing to provide the correct answer.

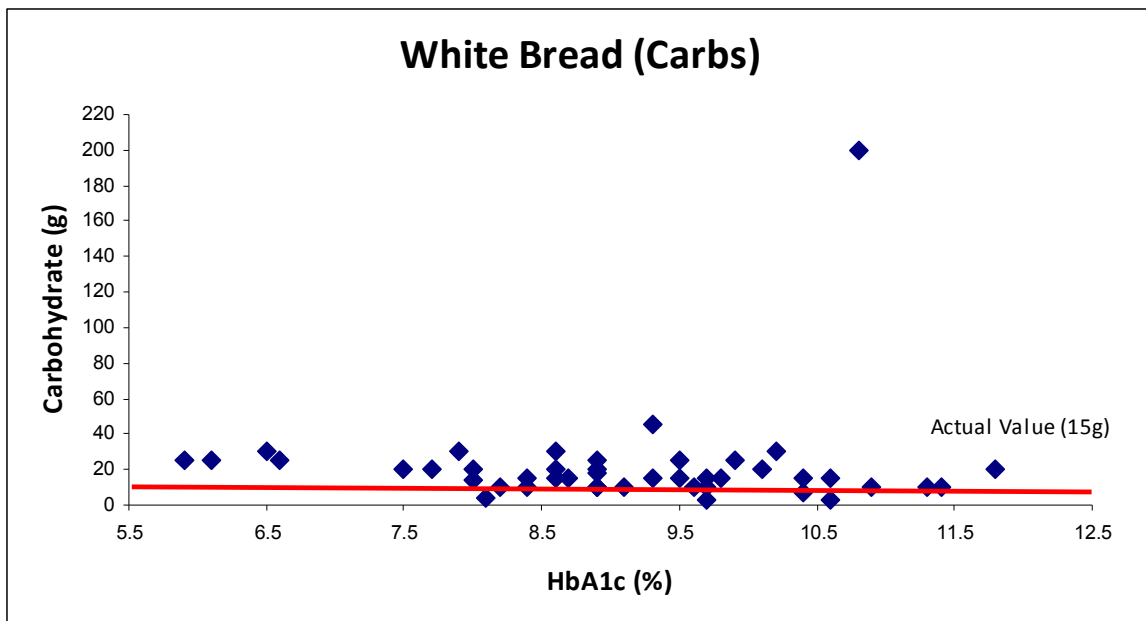


Figure 22: Carbohydrate estimations for white bread plotted against HbA1c (%)

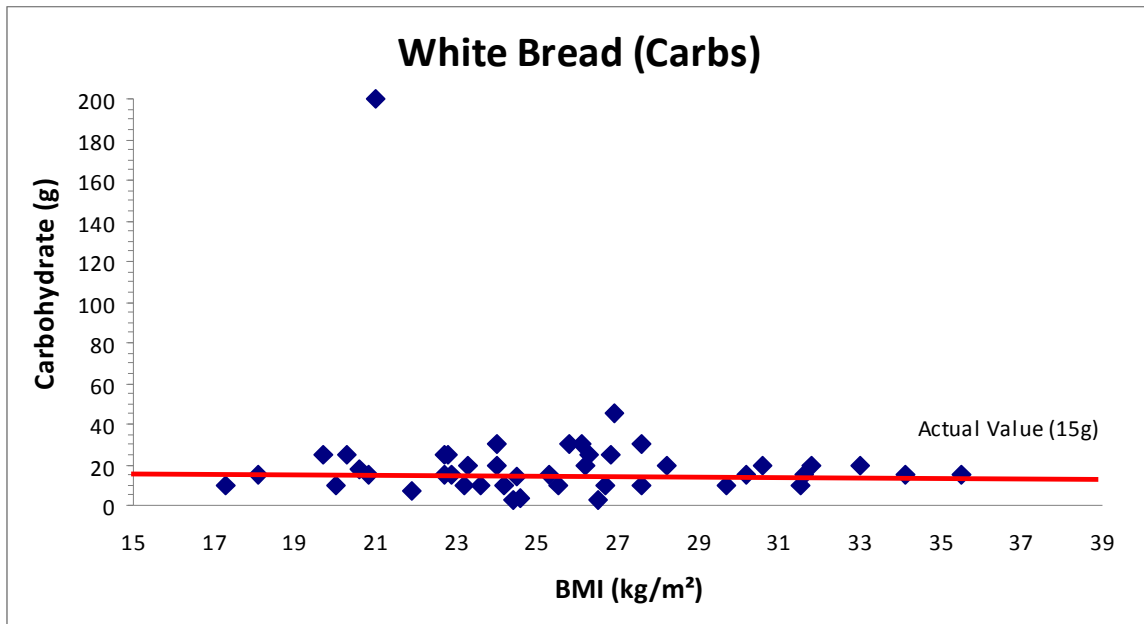


Figure 23: Carbohydrate estimations for white bread plotted against BMI (kg/m²)

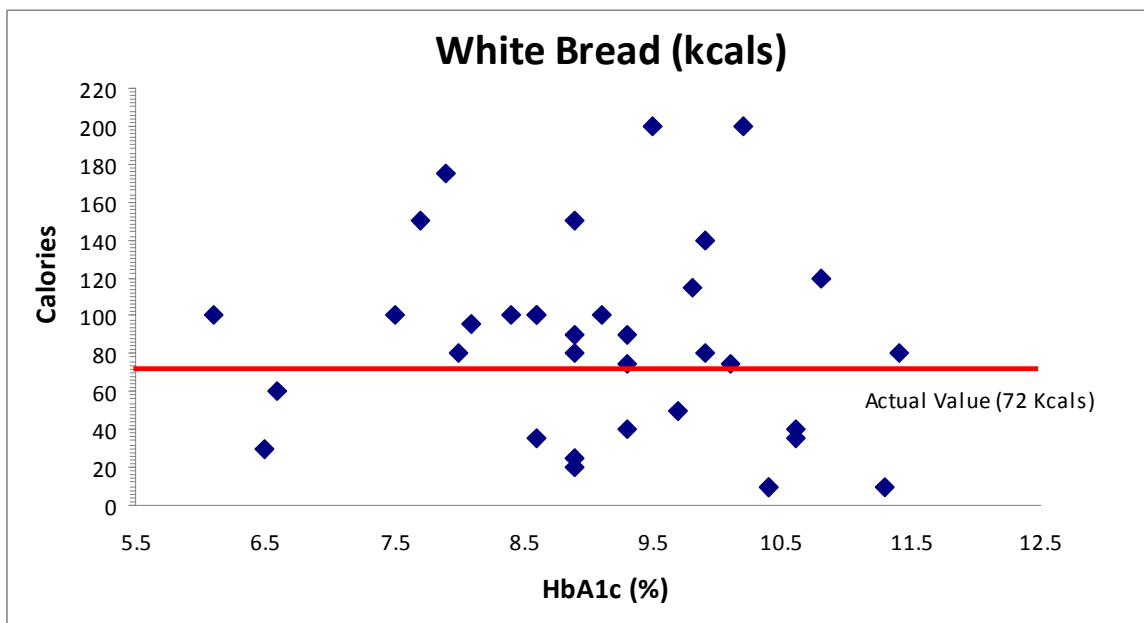


Figure 24: Calorie estimations for white bread plotted against HbA1c (%)

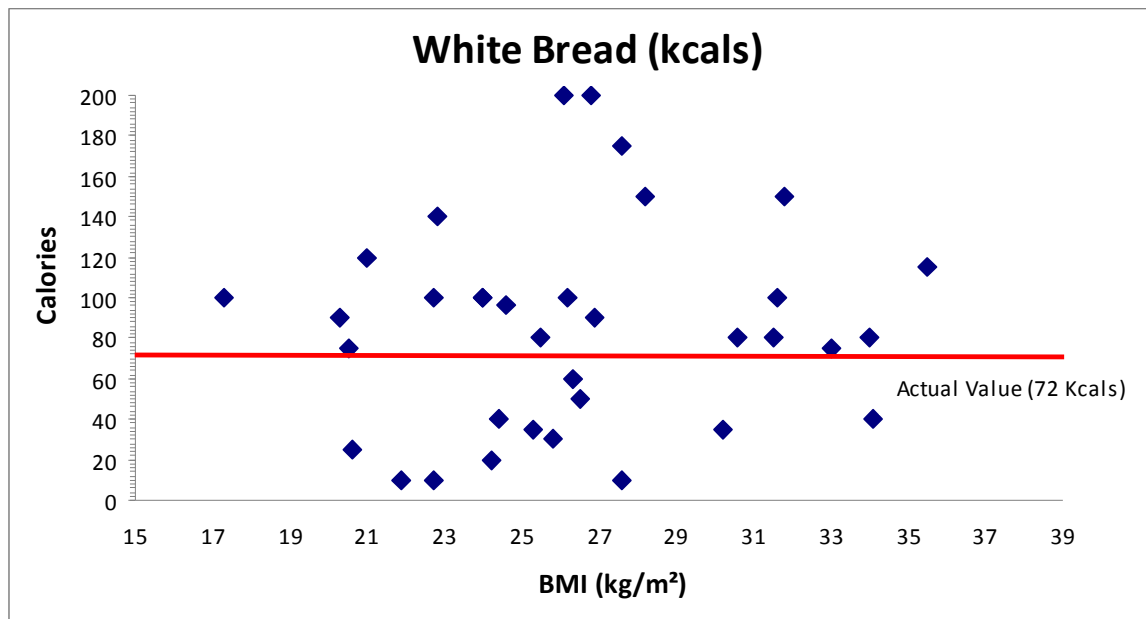


Figure 25: Calorie estimations for white bread plotted against BMI (kg/m²)

8.4 Discussion

8.4.1 Agreement between iPhone Application and Standard Food Composition Tables

The first part of this chapter was set out to investigate the agreement between the carbohydrate and calorie content of the food and drink items linked to the photographs included on the iPhone applications and those reported on the standard food composition tables. It was established that there was excellent agreement between the two tools. The results for carbohydrate suggest that estimation errors from the iPhone photographs would be within the $\pm 10\text{g}$ limits proposed by Smart et al, 2009 (282).

If the iPhone was systematically underestimating the carbohydrate content of foods, the risk of hypoglycaemia would be increased, unless the bias was recognized by the patient (following education) who would make the appropriate insulin dose adjustments. If the iPhone carbohydrate values were imprecise (i.e. if the limits of agreement were wider), again there would be an unpredictable risk for both hyper-and hypoglycaemia as the patient estimate could

be randomly above or below the true value. Taking the ± 10 g estimation margin as safe, this analysis shows that the performance of the iPhone in carbohydrate counting is clinically acceptable in fact, it is excellent.

For calories, a greater variability between the two tools was observed, mainly for foods which were taken from a recipe or when different brands of foods were used between the iPhone and the standard food composition tables. This type of error was expected as food preferences and cooking methods can vary between people. It is therefore important to educate patients on using a variety of tools for the carbohydrate and calorie counting assessment of their meals, as discussed in chapter 6.

The findings of these analyses make it possible for the iPhone application to be used in the proposed intervention for carbohydrate and calorie counting and for offering sustained patient education. The use of the application by patients could potentially improve diabetes knowledge as well their ability and confidence to make informed decisions about their treatment. In line with carbohydrate, the availability of the calorific content of foods on the iPhone application makes it possible for patients to monitor their energy intake and food choices, thus preventing undesirable weight gain.

8.4.2 Audit Assessing Patient Ability to Estimate the Carbohydrate and Calorie Content of Food from Photographs

Optimal glycaemic control still remains a challenge for many people with type 1 diabetes. Although many factors contribute to suboptimal diabetes control, poor adherence to treatment regimen and particularly poor dietary adherence can be predictive of poor control (283,284).

Studies assessing the validity of the use of food photographs in adults have shown them to be useful aids for portion size assessment, but with considerable under- and overestimation of

portion sizes (271,273,285,286). Evidence suggests that for certain foods such as spaghetti and chips, there is a greater tendency to under/overestimate portion sizes (271,287). It is still unknown whether specific food shapes or appearance is related to patterns or errors in portion size estimation (272,276). Studies have shown the flat slope phenomenon and regression to the mean where small portion sizes are overestimated, large portion sizes are underestimated and medium portion sizes usually estimated reasonably well (271).

Although the results of the audit provided important preliminary information on patients' carbohydrate and calorie knowledge from food photographs, they have not been encouraging. The majority of participants displayed limited carbohydrate and calorie counting knowledge. What is more, they failed to recognise even the carbohydrate-free foods. This misperception increases the possibility of administering an insulin dose when consuming those foods and therefore increasing the risk of hypoglycaemia. A small proportion of patients did manage to provide an estimate for carbohydrate within the $\pm 10\text{g}$ error margin (282). Generally, the variability in estimates for carbohydrate was much less than for calories but this was not related to either HbA1c or BMI. There was a tendency to underestimate most foods, and especially spaghetti, rice and chips, which had the highest carbohydrate content.

For calories, there was a wider variation in estimations, with the most energy dense foods being underestimated. This was especially true for chips (550 kcals), spaghetti (345 kcals) and rice (311 kcals), an observation that is in agreement with evidence from the literature (271,287). Similar to carbohydrates, the variability in estimates was not related to HbA1c or BMI. It is however established that 1 kg equals 7000 calories (33) and any underestimation of the true caloric value of foods, if sustained, would most probably lead to positive energy balance and consequently to weight gain.

This audit has a number of limitations. It is a small-scale audit with a limited number of participants and it is possible that a larger sample size could produce more meaningful results

and potentially gives a greater insight to patients' carbohydrate and calorie counting knowledge. There is a possibility that the selection of foods used for the audit was not representative of the foods most commonly consumed by the patients, thus adding to the variability of the answers. Furthermore, it is important to note that the ability to estimate is multidimensional and therefore showing food pictures to patients in isolation might not be enough in helping them estimate correctly. Additionally, the patients were asked to provide estimates without having the opportunity to use the iPhone application and get familiar with the photographs, the food portion sizes and their carbohydrate and calorie values. It would be interesting to re-assess the same patients' ability to estimate the carbohydrate and calorie content of food from photographs after a six-month period of using the iPhone application. Further work is required with a larger sample size and more advanced analyses, possibly controlling for a selection of confounders, such as years since diagnosis, gender and education status, to answer this question in greater detail.

The ability of patients to correctly estimate the carbohydrate and calorie content of foods is not the only determinant of glycaemic control (283,288). There are multiple factors contributing to optimum glycaemic control and behaviour change is one of them. Knowledge is an important but not the only determinant to patient behaviour (261,262). Knowledge however, in the form of health literacy and numeracy in carbohydrate and calorie counting and performing insulin dose calculations is important to treatment adherence and to optimising glycaemic control (289). The proposed intervention would therefore draw from a variety of teaching methods, to enhance carbohydrate and calorie counting knowledge. It would provide face-to-face education and sustainable support through the e-health platform, while ensuring that knowledge has been consolidated, in an attempt to optimise glycaemic control and prevent undesirable weight gain in young adults with type 1 diabetes.

9. Final Discussion

The purpose of this work was to develop a specification and to lay out a process for evaluating a dietary and physical activity intervention that is more effective and less resource-intensive than current interventions and aims to optimise glycaemic control and prevent undesirable weight gain. To assess whether there was sufficient evidence to justify the development of the intervention, two systematic reviews were carried out, which confirmed that intensification of diabetes treatment leads to weight gain and that physical activity could potentially improve insulin sensitivity and reduce insulin requirements, thus preventing undesirable weight gain.

Taking into consideration the results of the reviews and the available evidence-base, a developmental phase of the proposed intervention was initiated following the revised MRC guidance. Through this process, the main components of the intervention have been defined and the processes that need to be followed as well as the people involved to achieve the desired outcomes have been described.

Glycaemic control would be optimised through patient education in acquiring the skills required to make informed decisions about their treatment. Particular attention would be given to carbohydrate counting and insulin dose adjustment. The novel iPhone application providing 1900 photographs of up to six portions of food and drink items would be given to all patients to complement the education process and to help in making carbohydrate counting and insulin dose adjustment possible anytime, anywhere. Weight gain would be avoided through educating patients on calorie counting and portion size assessment. The iPhone application would also contribute to this process. Furthermore, physical activity would be promoted through motion sensors such as pedometers and accelerometer, which would be used as motivation tools, in an attempt to increase energy expenditure and prevent weight gain.

The e-health platform would maintain the active communication between patients and healthcare professionals. Feedback provision (both graphical and through the healthcare

professionals) would help patients in recognising trends and self-managing their diabetes more effectively. The excellent agreement between the iPhone application and the standard food composition tables was established, making the iPhone application a safe option for clinical practice in supporting patients in making informed decisions on their carbohydrate and calorie intake and insulin dose adjustment.

To provide a stronger rationale for the proposed intervention, the ability of patients to estimate the carbohydrate and calorie content of a selection of commonly eaten foods from the iPhone application's photographs was assessed. The results of this audit revealed a wide variation in the estimations, with the majority of patients failing to provide the correct estimates or to recognise the absence of carbohydrate in carbohydrate-free foods. There was a tendency to underreport the true values, which became more profound as the carbohydrate and calorie content of foods increased. The variability in estimates for both carbohydrates and calories was not related to HbA1c or BMI.

10. Conclusion

There is overwhelming evidence that intensification of glycaemic control can improve the poor prognosis of type 1 diabetes. With the development and availability of new healthcare technologies, the quality of diabetes care has improved and non-diabetic insulin profiles have become a possibility. However, achieving sustained improvements in glycaemic control has been proven to be a challenge and consequent weight gain could act as a barrier to treatment compliance.

The proposed intervention would draw from a variety of components in an attempt to optimise glycaemic control, without weight gain. By doing so, it may provide additional functionality in comparison with previous attempts to improve outcomes in this area. Further pilot work would be needed to assess the feasibility and acceptability of each of the proposed components through a variety of quantitative and qualitative tests.

This preliminary work would inform whether educating patients from a distance via the e-health platform supported by an iPhone carbohydrate and calorie counting application is feasible. It would provide an insight on the use of motion sensors in promoting physical activity in order to improve insulin sensitivity and would assess the effectiveness of the e-health platform in reviewing the patients' transmitted information and providing further education, support and feedback from a distance.

Most importantly, this work would offer the opportunity to assess in a randomised controlled trial whether a complete diabetes package, including all the intervention components described in this thesis, would optimise glycaemic control, prevent undesirable weight gain and influence the current provision of care for young adults with type 1 diabetes, in the clinical setting.

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