Effects of a Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health

A thesis submitted to Auckland University of Technology in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD)

By

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Thesis Abstract:

Purpose: To compare the effects of iso-time and quasi iso-effort high-intensity interval training (HIIT), resistance training (RT) or both HIIT and RT (COMBO), all with a low carbohydrate high fat diet (LCHF) in sedentary and overweight individuals. **Methods:** 54 adults (18-60 y, M=24, F=30) were randomised to one of three experimental groups: LCHF+HIIT, LCHF+RT or LCHF+COMBO. For 12 weeks the participants performed their 20 min exercise protocol thrice weekly, while following the LCHF diet (≤100 g CHO, ~1.5g PRO/kg and unrestricted fat intake). Sessions involved 10x1 min of high-intensity effort (~17 RPE on a 6-20 scale) interspersed with 1 min recovery periods. Target heart rate for HIIT was ≥95% HRR whereas for RT, resistance was set @ ~70-80% of maximum, or approximately 2 repetitions short of failure. Outcomes assessed were body composition, blood biomarkers, and performance measures.

Results: Adjusted between group differences were analysed with general or generalised linear models. Improvements in HbA1c were significantly greater for LCHF+HIIT than both LCHF+RT (β= 2.41, p=0.014) and LCHF+COMBO (β= 2.58; p=0.005). Body mass reduction was significantly greater for LCHF+HIIT relative to LCHF+COMBO (β= 1.88, p=0.049). Upper body strength was superior for LCHF+RT relative to LCHF+HIIT (β= 4.18; p=0.024). Resting metabolic rate (RMR) was greater for LCHF+COMBO (β= 896.02; p=0.004) and LCHF+RT (β= 690; p=0.024) both relative to LCHF+HIIT. Otherwise, there were no significant differences between groups observed.

Conclusion: These combinations of LCHF and exercise were similarly effective for improving cardiometabolic risk factors, potentially due to the high-intensity effort elicited in all three conditions, and the LCHF.

Keywords: Metabolic Syndrome, $\dot{V}O_2$peak, VAT, RMR, Weight loss

Novelty bullets: • LCHF+COMBO or LCHF+RT provide an advantage vs LCHF+HIIT for metabolic health because RT spares LBM and increases RMR. • RT, HIIT or COMBO were equally effective for improving aerobic capacity. • RT, HIIT or COMBO + LCHF were equally effective for reducing VAT.

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Attestation of Authorship

“I hereby Abelardo Gil Sotomayor declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.”

Chapters 2 and 3 represent two separate papers that have been submitted to peer-reviewed journals for consideration for publication. My contribution was at least 80% for both of them; co-authors and their contribution are stipulated in the co-author section.

A.Gil Sotomayor

February 2020

Co-Authored Work

2 Gil-**S**otomayor **A**., **H**arris **N.**, **B**orotkanics, **R**., **W**illiden **M.**, **K**ilding, **A**. LCHF and High-Intensity. A Comparison of a Single Session's Acute Effects of HIIT vs RT (In final preparation for submission to Journal of Sports Medicine and Physical Fitness).

G-**S. A.**, 80% Planning, methods selection, data collection, extraction, and analysis. Manuscript writing.

H. N., 10% Guidance on data analysis and interpretation. Review of manuscript.

B. R., 5% Advice and guidance on statistical modelling. Review of manuscript.

W. M., 2.5% Advice on interpretation of findings. Review of manuscript.

K. A., 2.5% Advice and guidance on metabolic assessment. Review of manuscript.

3 Gil-**S**otomayor, **A.**, **W**illiden **M.**, **B**orotkanics, **R**., **P**lank, **L H**arris **N.** Effects of iso-time, quasi iso-effort high-intensity interval training, resistance training or both combined with low-carbohydrate high fat diet. (Submitted to the journal of Applied Physiology Nutrition and Metabolism. Status: Awaiting EIC decision).

G-**S. A.**, 80% Planning, methods selection, data collection, extraction, and analysis. Manuscript writing.

H. N., 10% Guidance on data analysis and interpretation. Review of manuscript.

B. R., 5% Advice and guidance on statistical modelling. Review of manuscript.

W. M., 3% Advice and guidance on nutritional input. Review of manuscript.

P. L., 2% Advice and guidance on body composition assessment. Review of manuscript.

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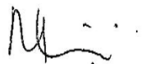
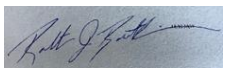
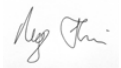
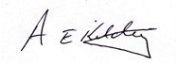
Mikki Williden	18-06-2020	
Robert Borotkanics	18-06-2020	
Nigel Harris	18-06-2020	
Andrew Kilding	18-06-2020	
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Introduction

Pharmacological treatments have historically been used to reduce risk factors associated with metabolic disorders. However, interventions that focus on improving diet and physical activity (exercise) have been identified to be as effective and are considered the initial treatment for metabolic disorders (1-3) such as central obesity, dyslipidaemia (raised triglycerides [TG], lowered high density lipoprotein cholesterol [HDL-C]), raised blood pressure and raised blood glucose (impaired fasting glucose [IFG] to type 2 diabetes mellitus [T2DM]). They are likely to occur simultaneously in what is known as metabolic syndrome (MetS) that is defined as having three or more of these risk factors (4). It is important to acknowledge that MetS is normally used to characterise metabolic health. Metabolic health could be defined as the ideal state of homeostasis (5), the physiological state when all parameters are within acceptable ranges (5); in other words, a state of physical wellbeing.

MetS is a very common condition worldwide (6), and it poses an elevated risk for developing cardiovascular disease (CVD) and T2DM (4). The International Diabetes Federation (IDF) estimated that worldwide the number of prediabetic people was over 374 million in 2019 and it is estimated to reach 578 million by 2030, of which the highest number of adults are in the 30-39 year age group (7). The number of individuals with diabetes worldwide in 2017 was estimated to be 451 million (between 18-99 y) and expected to reach 693 million by 2045 (8).

A feasible explanation for this could be the fact that healthy habits start to decline as we age (9). Modern lifestyles induce people to prioritise work, and in the process, this leads to bad eating habits such as relying on nutrient-poor, energy-dense convenience food and fast food. In addition, physical activity starts to decline, leading to energy imbalances and the appearance of overweight and CVD. These factors may recreate the appropriate stimuli to trigger metabolic disturbances, especially an excess of body fat and with it, inflammation. Over time, this can lead to the risk factors of MetS, including hyperglycaemia, dyslipidaemia, hypertension and increased waist circumference. In addition, in the last two decades obesity has increased 70% in young adults (30-39 y), making them the most increased fattest group (10). The presence of MetS and prediabetes themselves increase the likelihood of CVD, and obviously T2DM, therefore the management of individuals with MetS should be directed to ameliorate cardiometabolic risk factors and prevent the development of CVD and T2DM (4, 11).

Prevention strategies that target lifestyle behaviours have demonstrated that dietary interventions and exercise protocols that lead to a lowered glycaemia, lipid levels, and hypertension, etc., promote a reduction of the relative risk of developing diabetes by 58%, compared to pharmacological treatment where the relative risk reduction approximates between 25% to 30%, with a more pronounced reduction in cardiovascular risk (12). It is necessary to highlight that by reducing the risk of T2DM it also decreases the risk of CVD and as a consequence improves metabolic health (MetS).

Over the years diabetes prevention programmes have demonstrated that non-pharmacological approaches, diet and exercise, should be favoured to reduce and delay drug therapy. The Action for Health in Diabetes trial (Look AHEAD trial) (13), was recently terminated after finding no difference between the pharmacological approach recommended by the American Diabetes Association (ADA) and an intensive lifestyle treatment intervention that used physical activity and a calorie-restricted low fat diet (<30% of total energy [TE]) in a type 2 diabetic population with or without a history of CVD. In alignment with Van Name et al. (14), who also reported a reduction in risk factors after a lifestyle intervention based on the Diabetes Prevention Programme (DPP) that found weight loss as a consequence of an intensive lifestyle intervention (ILI), can reduce the progression of diabetes in adults with prediabetes (15). The Van Name research group conducted a similar programme to that of the DPP and compared it to the usual treatment for 14 weeks, retesting at 1 year. At the end of that period there was a difference of 6% in body mass between the two groups that favoured ILI, in addition to better fasting insulin, and smaller glucose excursions (14). This illustrates the effectiveness of diet and exercise to improve metabolic health outcomes to the same extent as pharmacological treatment.

Although it's acknowledged that any general physical activity will result in positive effects on metabolic health in previously sedentary individuals (16), there are two exercise modalities that have recently attracted specific attention owing to their potential potency. The first, high-intensity interval training (HIIT), comprises of work bouts of 10 s to 4 min at >90% $\dot{V}O_2$max interspersed with low intensity active recovery period of various durations. Though most exercise in the HIIT condition is aerobic, periodic excursions involving anaerobic energy pathways force the mitochondria to greater improvements in exercise capacity, mitochondrial biogenesis (17), enzymatic markers associated with glycolysis (18), aerobic metabolism and beta (β)-oxidation (18). There is agreement that this type of exercise is suitable and effective at improving health markers in people with prediabetes (19). Another exercise modality with proven efficacy is resistance training (RT), which has been found to have clinically and statistically significant effects on MetS risk factors such as obesity, HbA1c levels and systolic blood pressure, and therefore would also be efficacious in the management of type 2 diabetes and metabolic disorders (20). Both exercise modalities typically involve higher effort brief work bouts, with some typically distinctive known responses and adaptations subject to the specifically utilised

approach. Therefore, it is essential to disentangle whether it is the effort involved, or it is the way the muscular fatigue is induced which causes the metabolic improvements in order to underpin effective high-intensity exercise recommendations.

In addition to the training, using a nutritional strategy provides a more effective health strategy than either one used in isolation (21). The traditional approach has been to combine a low calorie diet and aerobic resistance training in both (21). However reducing calories may not necessarily improve metabolic health if carbohydrate content is not considered, which is an influential component in factors such as glycaemic control, lipid profile and body composition (22, 23).

In terms of specific nutritional approaches regarded as healthy, a low-carbohydrate, high-fat diet (LCHF), as defined by Feinman et al.(24), providing no more than 26% of total energy intake of CHO, may be a superior macronutrient distribution to reduce glycaemia and body weight in addition to improving lipids and inflammation markers (22, 24). A LCHF diet usually favours eating food that is minimally processed (or 'whole food') while discouraging consumption of processed food, and typically comprises ≤ 100g of CHO per day (in line with Feinman's definition) a moderate protein intake (15-25% of total energy), and comparatively higher in fat [50-60% of total energy] (22, 23). This diet has been referred to as the default diet to treat metabolic syndrome and diabetes due to its reduced CHO content (24, 25).

Given the known benefits of HIIT, RT, and a combination of these modalities as independently effective options, it is of interest to determine their relative efficacy, in particular when combined with a LCHF diet approach. Hence the purpose of this study was to describe the effect of a combination of a LCHF and HIIT, RT, or combined HIIT and RT (COMBO) in sedentary and overweight individuals at risk of metabolic disease on a range of metabolic health outcomes.

Rationale and Significance of the Study and Thesis Aims

1) It is of paramount importance to contribute to the body of knowledge in preventing rather than treating what is one of the major health issues in public health history worldwide. The MetS is a cluster of cardiometabolic risk factors which raises the likelihood of developing CVD and T2DM and it is estimated that one in every 4-5 adults has it (Canale et al., 2013).

2) Published evidence shows that non-pharmacological preventive strategies are equally, or more effective in the prevention of metabolic disease especially T2DM (12, 13, 26, 27), therefore it is logical to provide a potent and novel strategy based on the combination of high effort/intensity exercise training and diet by means of CHO restriction.

3) HIIT and RT have been identified as two very potent exercise modalities capable of improving health to the same extent or more than aerobic exercise training (AET)(28). HIIT improves cardiorespiratory fitness, glycaemic control, muscular strength, lean body mass, bone mineral density and decreases insulin resistance, therefore preventing sarcopenia and osteoporosis. HIIT comprising 60 s; >90% HRmax of high intensity (HI) followed by an active recovery period of low intensity 50 watts (W) is an exercise strategy that is attainable in contrast to more demanding all-out versions (29). HIIT forces the mitochondria to greater improvements in exercise capacity (30), mitochondrial biogenesis (31, 32), enzymatic markers associated with glycolysis (18), aerobic metabolism and beta (β)-oxidation (18, 33). There is agreement that this type of exercise is suitable and beneficial for inactive individuals with prediabetes, who are overweight, and patients with T2DM (19, 29, 34, 35). RT is considered the preferred choice to preserve and stimulate muscle growth (hypertrophy) and develop strength (36, 37). Also, RT is effective in improving aerobic capacity (38, 39). When RT is combined with aerobic exercise training (AET) the literature indicates that results are even better than any of these modalities in isolation (36, 39). Therefore it makes sense to use HIIT in substitution of aerobic exercise training (AET).

4) In terms of diet, the low carbohydrate high fat diet (LCHF), has recently been defined by Feinman et al. (24, 40), as the default diet for treating and improving MetS and T2DM because the CHO content of the diet is directly responsible for increasing the glycaemic load of any meal. This translates to an increase in postprandial glycaemia to the same extent of CHO intake. Research has shown that it may take a superior macronutrient distribution to reduce

glycaemia and body weight while also being effective in improving lipids and inflammation markers (23, 24, 41-45).

5) Recently, and in agreement with our point of view, it has been hypothesised that combining a LCHF diet and HIIT would be advantageous since both strategies are complementary to each other (43). When RT and LCHF have been used in the same intervention it has resulted in a better body composition, especially preservation of muscle mass (44, 46). These implications make it necessary to characterise the metabolic responses of a LCHF diet combined with high-intensity exercise (HIIT and RT or both).

To our knowledge there have been only a few somewhat recent studies in prediabetic subjects combining RT with HIIT by Álvarez et al. (47-50) showing that intermittent exercise is effective in producing changes in glycaemic control and weight loss and warrant more research exploring the effects of HIIT and RT. Both exercise modalities share similar patterns in administering high intensity anaerobic bouts, but HIIT also includes in some cases an aerobic component which could provide additional stimuli to reduce glycaemia more effectively by stressing the cardiovascular response. By contrast, heavy weights RT presents a unique way to engage muscular fibres when resistance is applied, producing muscular fatigue and a delayed cardiovascular response. Therefore, it is important to understand if it is just the high intensity as the reason for the improvements, or the way the muscular fatigue is induced when performing these exercise modalities. It is important to detect if the combination of HIIT and RT may provide an additive beneficial effect for metabolic health as the combination of AET and RT. Likewise it is very compelling to know if a LCHF diet used concomitantly may potentiate improvements in metabolic parameters involved in the pathogenesis of T2DM and other cardiometabolic diseases.

Consequently, the purpose of this thesis was to compare the efficacy of HIIT vs RT vs HIIT+RT while following a LCHF diet for • improving MetS parameters; fasting glucose, HbA1c, C-peptide, insulin to assess glycaemic responses; • HDL-C, LDL-C and TG to assess lipid control; and • C-reactive protein for assessing inflammation response. • Also, their effect on body mass, lean body mass, fat mass, visceral adipose tissue for assessing body composition using DEXA, and • ultimately their effect on metabolic health as assessed using the simple metabolic syndrome (siMS) score.

Thesis organisation

This thesis was designed to produce a cohesive work of investigation aiming to answer the overall research question. Which combination of exercise training and LCHF diet provides the best effect on maximising metabolic health parameters?

The specific aims are for Chapter 2 to describe the acute effects of a single exercise session of HIIT and RT necessary to provide a better understanding of the findings over the 12-week intervention. The specific aims of Chapter 3 are to identify the additive effects of combining HIIT and RT, and determine which combination of LCHF and high-intensity training is more likely to be continued after the end of supervision.

This manuscript has four sections designed to provide a coherent and cohesive body of work on optimising the health of individuals at risk of metabolic impairment such as Metabolic Syndrome. Its structure of three parts followed first a systematic review of the literature, investigation for comparing the acute effects of HIIT vs RT, and the description of training effects to allow the identification of the best combination of high-intensity training and LCHF diet. The first section (Chapter 1), is a literature review that is the result of a systematic compilation of the current and past research in this area of non-pharmacologic strategies for maximising metabolic health. It provides evidence of what has been produced and informs the gaps in the existing literature which may help the reader to understand the importance of this thesis. It is important to let the reader know why a narrative approach was favoured against a meta-analytic review. After scrutinising the literature, it was not possible to identify a sufficient number of studies using a randomised control trial design nor similar interventions that could be used to quantify the findings using a meta-analytic technique. This also highlights the lack of previous studies addressing the hypothesis of this doctoral research.

The experimental chapters (2 and 3) were prepared as individual stand-alone original papers and are in final preparation for publication to peer reviewed journals. The first experimental section (Chapter 2) presents the comparison of HIIT and RT performed iso-time and quasi iso-effort. These two characteristics and the fact that that was conducted after at least six weeks of a combined training programme and LCHF diet constitutes the novelty of this study. This study was essential to help in understanding and explaining the metabolic improvements of a 12-week intervention. It covers the changes in energy expenditure, carbohydrate (CHO) and fat oxidation hormonal responses after a single session of HIIT and RT.

Chapter 3, the second and final original experimental chapter, presents the comparison of HIIT, RT or both combined with a LCHF diet. It describes and characterises the metabolic effects of these exercise modalities over three months, details diet and exercise adherence, physiological responses (heart rate, aerobic capacity, strength, blood biomarkers and wellbeing) and finishes the results section with its translation to cardiometabolic risk informing the overall impact of the intervention in metabolic health. The final section (Chapter 4), merges both experimental chapters in a cohesive manner, providing an engaging, fluid and immersive discussion that overviews the whole thesis, including a summary of the key findings, the limitations, practical application and areas for future research. Given the great interest that prevails in the scientific world, with both health professionals and the general public, this thesis addresses questions that would allow best practice for the application of HIIT and RT combined with a LCHF diet for improving metabolic health to be optimised in people at risk of developing metabolic disease, e.g. type 2 diabetes.

1 Nutrition and Physical Activity (Exercise) for Metabolic Health

Literature/Past Research Review.

Over recent years, nutritional trends for improving metabolic health are showing an increased demand for the inclusion of the low carbohydrate high-fat diet (LCHF) as a healthy and feasible nutritional approach (24). In this respect, the latest American Diabetes Association (ADA) position stand of 2019 Lifestyle Management of Medical Care (45), for the first time, presents the LCHF diet as an option for treating type 2 diabetes mellitus (T2DM). Conversely, at the same time ADA claims the research is not enough and more is required to establish the benefits of a LCHF diet (51). Despite this claim, there are several published studies that support the utilisation of a LCHF diet for preventing and treating metabolic disease including T2DM. Table 1-1 provides evidence showing the efficacy of a LCHF diet in comparison with a high-carbohydrate low-fat diet (HCLF). From the metabolic markers that are included (body mass, body fat, lean body mass, waist circumference, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides, triglycerides-LDL-C ratio, HbA1c, fasting glucose, insulin, HOMA-IR, systolic and diastolic blood pressure, and C-reactive protein). It is possible to observe that those markers which related to body composition, the improvements were superior with the LCHF diet, however greater LBM loss seem to also be the case. However, with the lipids, glycaemic control seems to favour the LCHF diet.

Weight control, diet and metabolic health

The consumption of high amounts of processed foods containing refined carbohydrates (CHO) may be one of the major factors leading to obesity and metabolic dysfunction (52, 53). This excess leads to elevated insulin secretion, promoting glucose oxidation, impaired fat oxidation, de novo lipogenesis, and storage of fat. Thus, becoming overweight is the main acquired challenge to insulin action according to Ferrannini, Gastaldelli, and Iozzo (54); concomitantly, this leads to inflammation, insulin resistance (55), and oxidative stress (56). The accumulation of visceral fat, also referred to as central obesity, has been established as an underlying reason for MetS caused by obesity-induced chronic inflammation (55). Given this relationship, it is not surprising that 80 to 90% of all cases of T2DM are directly related to overweight or obesity (57, 58). Therefore, if weight loss is achieved it should impact on glycaemia and reverse many of the symptoms associated with MetS. These factors illustrate that weight loss in T2DM prevention is one of the most important goals for metabolic control. This rationale is in line with current guidelines of T2DM treatment (59, 60) that has established weight control as one of the priority goals of medical nutrition therapy (60).

Recently, investigators from the University of Castilla-La Mancha Spain (61) conducted a study with 138 individuals with metabolic syndrome and central obesity. They assessed the relationship between

the changes in cardiorespiratory fitness (CRF) and the components of MetS after 16 weeks of aerobic interval training. Their goal was to confirm or contradict the high association between the cardio-protective effect that confers fitness to overweight-obese individuals, against the CVD risk factors that define MetS, in contrast to those that do not maintain an adequate level of fitness, known as the 'fat but healthy' paradox (62, 63). At the end of the intervention, Mora-Rodríguez et al. (61) found an improvement in body mass, mean arterial blood pressure (MAP) and waist circumference while CRF improved by 16%. This improvement in CRF did not represent a significant predictor of the MetS z-score changes (r= -0.231; β= -0.024; P = 0.788); whereas body mass accounted for the 25% prediction of the MetS z-score improvements (r= 0.508; β= 0.360; p=0.001). The authors concluded that the exercise dependent improvements in CRF were not predictive of the amelioration of the MetS z-score, while a little more than 2% weight loss was found to be a significant contributor for improved metabolic health risk factors. That led them to recommend that exercise training programmes should emphasise the need to target weight loss for individuals with MetS.

Another study that underscores the importance of weight management is the one by Vidigal et al. (64) that explored the prevalence of MetS and its components in a group of 226 health professionals of the municipality of Viçosa, Brazil. Participants were between 20–59 y. A cross-sectional observational multicentre study in the frame of the LATIN America METabolic Syndrome (LATINMETS) was used. They found that the overall prevalence of MetS was 4.5%, and it increased with age (20 to 29 years: 1.3%; 30 to 39 years: 5.6%; ≥ 40 years: 26.3%) ($p < 0.01$). Vidigal et al. were able to observe that the presence of pre-MetS and MetS was associated with several measures of adiposity, total cholesterol/HDL-c and LDL-c/HDL-c ratios and serum complement C3 concentrations. The LATINMETS-Brazil findings were that MetS was more frequent among non-active health professionals and was present only in individuals who were overweight. The combination of physical inactivity and obesity were associated with insulin resistance. Also in the Colombian version of the LATINMETS conducted by González-Zapata et al. (65) in a population of 285 volunteers (20 to 61 y) in Antioquia, Colombia found that the prevalence of MetS in individuals with excess weight was 10 times higher compared to those with a normal BMI and was also more frequent when individuals were not active. These two powerful studies depict robust evidence of the importance of addressing weight loss and fitness to improve metabolic health, as thinner and fitter individuals have the best metabolic outcomes; however, by no means is being a metabolically healthy obese person protective of developing metabolic disease (66).

Diet is perhaps the most important factor in weight loss and control (67). For this reason, it has been the first choice for the prevention and treatment of obesity-related metabolic diseases. Since 1980 when the first dietary guidelines were issued, the maximum recommended upper limit intake of fat for the general public was set at 30% of total energy for total fat and no more than 10% of total energy for

saturated fats with the objective to limit energy intake coming from fat (68). There was the firm belief that it was energy intake coming from the fat and saturated fat in combination with lack of exercise which was the reason behind the exponential growth of obesity and the rise in heart disease (68). However, data obtained in the United States, from 1989-1991 and 1994-1996, reports of the trends of macronutrient intakes in the population indicated that the increased energy intake was caused primarily by a higher CHO intake (69). Data from National Health and Nutrition Examination Survey in the USA (NHANES) for 1971-2000 indicated similar trends, with an increase in energy intake mainly attributable to an increase in CHO intake, being a 62.4 g increase among women ($p< 0.010$) and a 67.7 g increase in men ($p< 0.010$). Total fat intake in g increased in women by 6.5 g ($p< 0.01$) and decreased in men by 5.3 g ($p< 0.010$) (69). This is in line with the public recommendations to reduce fat intake, and increase CHO intake, yet did not slow the rate at which the population became increasingly overweight.

Worldwide, the public health establishment started large nutritional research initiatives to tackle the problem of excess energy intake leading to cardiovascular disease, but continued with the same dietary advice given by ADA (70), advocating a diet that restricted caloric intake while maintaining a high carbohydrate low fat intake (68, 71). Internationally, for more than three decades this has been the preferred and most common approach for weight and metabolic control for individuals with MetS and/or at risk of T2DM. A reduced or restricted calorie low fat diet (20-35% TE, with ≤10% TE of saturated fatty acids [SFA]), high carbohydrate, rich in fibre and moderate protein (PRO) at approximately 15% TE macronutrient distribution is recommended.

This macronutrient distribution was used for the major diabetes prevention trials such as the 6y Malmö feasibility study (72), DaQing IGT and Diabetes Study (73), Finnish Diabetes Prevention (74), and Diabetes Prevention Program (15). These preventive strategies have been successful in delaying T2DM, however, the numbers of people with the condition worldwide are still growing (71); in the US 34% of the adult population has MetS (75) which suggests more potent and effective prevention strategies to contribute to the reduction of newly diagnosed people with T2DM worldwide are needed (76). This is why the Indian National Dietary guidelines in 2011 introduced a modification in the amount of CHO that is lower than previous guidelines as an attempt to reduce the incidence of MetS, T2DM and CVD. In January 2014, the American Diabetes Association (ADA) (60) released the new dietary guidelines for T2DM. The most sensible change was in relation to the appropriate ratio between macronutrients; earlier guidelines had always set a fixed range for the percentage of CHO, PRO and fat, but not this time. The ADA stated that there is no research comparing diets that conclusively allows determining such values, and as for today, these should be tailored according to individual characteristics (60). In addition, the ADA is indicating that there are other options, like the “Mediterranean dietary-style, mono-unsaturated fatty acids (MUFA) rich eating pattern which may

benefit glycaemic control and CVD risk factors and therefore be recommended as an effective alternative to a lower-fat higher CHO eating pattern" (60).

Carbohydrate intake: should it be reduced instead of fat?

Carbohydrate (CHO) is probably the most consumed nutrient by far (52, 69); there are a few reasons for this. Foods containing CHO provide the most ready energy source naturally available and for this it is considered the main energy source by many (77) despite it providing less than half the energy of fat by gram of substrate. Also, unprocessed carbohydrate foods (such as vegetables and fruits) are high in fibre (important for health) and are mineral and vitamin rich foods (78) which also provide phytochemicals that are emerging as potent nutrients that may be essential for optimal health (79, 80). Another aspect for consideration is pre-diabetes, also known as impaired fasting glucose (IFG), or impaired glucose tolerance (IGT) or both (81), which reduces the ability of the body to cope with high glucose levels after having a large carbohydrate intake. As it is largely asymptomatic, it typically goes undiagnosed which poses a greater danger of developing T2DM; the projections are that the number of individuals with prediabetes will reach 398 million by 2030 (81). Worldwide nearly 50% of people with diabetes live unaware of having their disease (76), showing the magnitude of the problem. This does not consider, however, carbohydrate quality, and that an excess of CHO triggers a cascade of metabolic processes that may lead to inflammation (82), the underlying process that leads to metabolic impairment. Experts in the field of clinical nutrition (82) reported that the growing evidence underscores the crucial role of CHO intake involvement especially for individuals with diabetes or metabolic stress, their main conclusions were that excess glucose and fructose exacerbates metabolic complications in skeletal muscle, adipose tissue, and the liver that can result in a negative clinical impact. It is concluded that efforts should be made towards defining optimal plasma glucose targets, to avoid excessive plasma glucose variability and optimising glucose control relative to nutritional support (82). The best way to avoid excessive glucose supply to the body is by CHO restriction (24, 83).

Song, Song and Song (84) examined the period between 2008 and 2012 and found an association of dietary CHO and fat intakes with lipid abnormalities in a sample of 14,301 Korean adults (5715 men and 8586 women) aged 30+ years with no diagnosis and treatment for diabetes, hypertension, or dyslipidaemia. Dietary CHO and fat intakes were estimated from 24-hour recall data and analysed using multivariate logistic regression odds ratios. These were computed for lipid abnormalities; that is, elevated total cholesterol (TC), low HDL-C, high TC to HDL-C ratio, elevated non–HDL-C, elevated LDL-C and elevated triglycerides (TG) across quintiles of dietary CHO and fat intakes. They found that energy from CHO was positively associated with elevated TG and low HDL-C but inversely associated

with elevated TC and elevated LDL-C in both men and women. An energy-adjusted CHO intake also showed a positive association with low HDL-C. Dietary fat intakes had the opposite association with lipid abnormalities. The authors of this study concluded that a high-CHO diet undesirably increased TG and reduced HDL-C which was concerning, despite the benefit for LDL-C. Dietary strategies emphasising appropriate macronutrient intakes from the type of lipid abnormalities are recommended for the prevention of cardiovascular disease in Korean adults. This study is a clear example of the potentially negative outcomes when a higher CHO diet is advocated.

In 2015 the USDA issued the newly reviewed dietary guidelines for Americans, in which saturated fat is no longer a dietary constituent of concern (85); prior to this it was targeted for reduction due to its effects on increasing LDL-C serum levels (and subsequently increasing risk of CVD). More recent analyses of population data suggest this is not a concern (52). Indeed, there is thinking that a low-CHO high fat diet (LCHF) also rich in saturated fat may have a deleterious health effect; however, quite a few studies found no harmful effects despite the increase in LDL-C in healthy adults and diabetic populations following a LCHF diet.

A LCHF diet has recently been defined by Feinman et al. (24) as moderately low CHO 45% of total energy; low CHO 30 to 20% of total energy; and very low CHO intake to less than 50 g CHO per day. The latter have also been termed very low CHO ketogenic high fat diets (VLCKD) as they increase the production of ketone bodies, such as β-hydroxybutyrate (β-OHB) and acetoacetate, a process denominated ketogenesis in the liver (86). A LCHF diet usually favours whole food intake while discouraging consumption of processed food. A LCHF diet typically comprises less than 100 g of CHO per day, supplying a moderate amount of protein intake (15-25% of total energy), with the rest of dietary food intake coming from fat (50-60% of total energy) (22, 23). Research has shown that it may take a superior macronutrient distribution to reduce glycaemia and body weight while also being effective in improving lipids and inflammation markers (22-24), and that a LCHF diet meets these requirements.

Hu et al. (87) conducted a meta-analysis of randomised controlled trials that included 23 trials and accounted for a total of 2788 participants comparing low-CHO (≤45% of energy from CHO) diets and low fat diets (≤30% of energy from fat) and contrasted the effects on metabolic risk factors. They found that individuals following a LCHF diet had a small but significantly lower reduction in total cholesterol weighted mean difference, (WMD) 0.15 $mmol \cdot L^{-1}$ 0.15 $mmol \cdot L^{-1}$ (0.04, 0.26) 95% CI and LDL-C (WMD) 0.21 $mmol \cdot L^{-1}$ (0.06, 0.36) 95% CI, on the other hand did better for increasing HDL-C (WMD) 0.18 $mmol \cdot L^{-1}$ (0.11, 0.26) 95% CI and reducing triglycerides (WMD) -0.78 $mmol \cdot L^{-1}$ (-1.07, -0.48) 95% CI.

Reductions in body mass and waist circumference were similar in both diets. The authors concluded that LCHF diets are a feasible alternative for weight loss for individuals with metabolic abnormalities.

Mansoor et al. (88) conducted a meta-analysis of randomised controlled trials to assess the effects of LCHF vs HCLF diets on weight loss and cardiovascular risk factors. LCHF was defined as having a CHO intake of less than 20% of total energy (20-30 $g \cdot day^{-1}$ of CHO during the first phase of the diet), and a low-fat diet was defined as having less than 30% of total energy of fat intake. Eleven studies, including a total of 1369 participants, were included in this meta-analysis. Compared with participants in the HCLF diet, those assigned to the LCHF diet had greater weight and triglycerides reductions (WMD) -2.17 kg (-3.36, -0.99)95% CI and (WMD) -0.26 $mmol \cdot L^{-1}$ (-0.37, -0.15) 95% CI respectively. However, HDL-C and LDL-C were increased (WMD) $0 \cdot 14$ $mmol \cdot L^{-1}$ (0.09, 0.19) 95% CI and LDL-C (WMD) 0.16mmol·l (0.003, 0.33) 95% CI respectively. While Mansoor et al. (88) concluded that these results were indicative of more beneficial changes for those participants assigned to the LCHF diet, they were cautious to include a warning statement referring to the rise in LDL-C. However, like Hu et al. (87) and Bueno et al. (89), Mansoor et al. referred to the possibility that these LDL-C particles were large-sized particles which are less atherogenic (88, 90).

While LCHF diets may improve metabolic markers associated with both CVD and T2DM, these tend to contain more saturated fat than a HCLF diet. As such, there is much debate on the overall risk of following a LCHF diet, particularly given the aforementioned rise in LDL-C that has been reported. A meta-analysis by Siri-Tarino et al. (91) summarised studies which investigated the association of saturated fat and the risk of coronary heart disease (CHD), stroke and cardiovascular disease (CVD) in prospective epidemiologic studies. This research uses a random effects model design to calculate relative risk estimates for CHD, stroke and CVD. A total of 21 articles including 347,747 individuals were followed between 5 to 23 y. The analysis revealed that 11,006 developed stroke or CHD during the follow-up and, the relative pooled risk estimate that compared a low saturated fat intake to those with the highest saturated fat intake was not significant (RR= 1.07 (0.96, 1.19) 95% CI p= 0.220 for CHD, RR= 0.81 (0.62, 1.05) 95% CI p= 0.110 for stroke, and RR= 1.00 (0.89, 1.11) 95% CI p= 0.950 for CVD). The authors concluded that saturated fat was not implicated in increasing the risk of CHD nor CVD, therefore the recommendation for future research was that more data is required to calculate the implications of the specific nutrients used to replace saturated fat. Since the publication of this meta-analysis in 2010, there have been numerous other studies that have come to a similar conclusion (92-99).

In another more recent meta-analysis in 2016, Cheng et al. (92), investigated the relationship between saturated fat (SFA) intake and stroke that included 15 studies, 476,569 participants and a total of

11,074 suffered strokes. To estimate this relationship, the Log relative risks (RRs) with the associated 95% CI, were obtained for the highest vs the lowest SFA intake, weighed by the inverse of the variance method. A reduced overall stroke risk was related with a higher SFA intake (RR = 0.89 (0.82–0.96) 95 % CI and fatal stroke risk of RR = 0.75 (0.59–0.94) 95% CI). The subgroup analysis demonstrated a positive association with a greater SFA intake and a reduced stroke risk for a follow up duration of ≥ 14 y, and risk of stroke increased with a daily intake of < 25 g•d of SFA. Individuals with longer duration of higher SFA intake and a BMI <24 [RR = 0.75 (95 % CI 0.65–0.87)], seem to have a lower risk of stroke. It was pointed out that this meta-analysis showed the benefit of SFA increasing HDL-C in opposition to the elevation of TG observed with high CHO diets which is associated with an elevation of stroke. The authors concluded that it is difficult to assess the exact type of fat that confers this protection against stroke. However, it was not possible to know the exact stroke-reduction of specific subtypes and specific food sources of SFA (i.e. plant vs. animal) therefore it needed to be clarified in further studies (92, 93).

In a 12-month non-randomised controlled trial, Maekawa et al. (100) looked at the effects of a low CHO diet (<120 $g \cdot day^{-1}$) with no other restrictions versus a conventional (control) HCLF diet on glycaemic control and progression to T2DM. At 12 months the incidence of diabetes was significantly lowered in the experimental versus the control group (0 vs 13.9% p=0.02) while their glucose levels and HbA1c were normalised. There was also a reduction of 33 $mg \bullet dL^{-1}$ in OGTT (p=0.001) and a non-significant reduction of LDL-C (p=0.26). In addition to a significant decrease in the homeostasis model assessment of insulin resistance (HOMA-IR) value, body weight and TG were also reduced at 12 months, and there was a significant increase in HDL-C (p<0.001).

In another study, Tay et al. (101) compared a very low-CHO high-unsaturated fat diet, [14% CHO (50 $g \bullet d^{-1}$), 28%PRO, and 58% FAT (10% saturated fat)] and a high-CHO low fat diet [energy-matched 53% CHO, 17% PRO, 30% FAT (10% saturated fat)] both combined with supervised aerobic and resistance exercise (60 min; 3 $d \bullet wk^{-1}$) for 52 weeks in a population of type 2 diabetic patients. After the 52^{nd} week, both groups had a substantial weight loss and lowered their fasting glucose and HbA1c, however the LCHF group had achieved the greatest reductions in medications, and had more favourable outcomes in both lipid profile and blood glucose control, leading the researchers to recommend this diet for better management of T2DM.

As excess body fat is a risk factor for poor metabolic health, studies that investigate methods to achieve a reduction in body fat are relevant to the current research. In a meta-regression looking at the effects of the variation in PRO and CHO intake on body composition, Krieger et al. (102) found that diets, irrespective of energy intake and exercise participation but lower in CHO content, had better

weight (fat) loss effects and those richer in PRO had better lean body mass preservation contrary to the HCLF diet. However, LCHF diets were associated with the loss of fat-free mass; Krieger et al. proclaimed that it was probably because a lower CHO intake may cause ketosis and the latter increases water excretion; or maybe because there is lower insulin secretion as the result of reduced CHO, since insulin inhibits proteolysis (102). This turn down or disadvantage may be an indication that protein intake should be higher during a LCHF diet and even higher during energy deficit on a weight loss LCHF diet. In this respect Soenen et al. (103) compared a normal protein [0.8 g of PRT per kg body weight $(BW)^{-1}$] low fat vs a high protein diet (1.2 g·kg BW^{-1}) and concluded that during weight loss a higher protein intake is required to preserve initial REE and more pronounced sparing effect of LBM (103). For this reason, the PRO intake in the present research was set to 1.5 g•kg LBM.

Tobias et al. (104) conducted a systematic literature review and meta-analysis to summarise a very large body of randomised controlled trials to examine the effectiveness of long term low fat diets vs usual diet, low CHO diets and other higher fat diets on reducing excess body fat. The long-term effect was defined as being at least a duration of one year or longer. The meta-analysis included a total of 53 studies consisting of a sample of 68,128 participants. For weight loss trials, a LCHF diet led to greater significant results WMD 1.15 kg (0.52, 1.79), whereas the low fat interventions did not obtain any greater significant difference when compared with any other higher fat intake diet obtaining a WMD of 0.36 kg (-0.66, 1.37) 95% CI but led only to a greater weight difference when compared to a usual diet and the calculated WMD was -5.41 kg (-7.29, -3.54) 95% CI. Comparisons for weight maintenance and no weight loss studies only included a low fat diet vs higher fat group comparisons; low fat and higher fat diets obtained a similar weight loss and in the only case where low fat had greater weight loss results was when compared to a usual diet. When there was a difference of more than 5% of the caloric intake coming from fat, and when the difference in triglycerides was at least 0.06 mmol·L^{-1} at follow-up in weight loss interventions, higher fat diets led to greater significant results in weight loss with a WMD 1.04 kg (0.06, 2.03) 95% CI and 1.38 kg (0.50, 2.25) 95% CI respectively. After obtaining these results, Tobias el al. (104) stated that the long-term effects of a low fat diet on body mass depends on the intensity of the intervention in the comparison group. When the comparison was made with a similar intensity intervention the low fat diet was inferior. In this light, Tobias et al. (104) were not able to identify any clear evidence that indicated any superiority of following a HCLF diet over LCHF diets. They concluded that because there is no evidence justifying the recommendation of a HCLF diet, nutritional guidelines should cease recommending HCLF diets for weight loss.

From a practical point of view, dietary compliance is essential for the success of any dietary intervention (57), satiety being one of the main factors to promote adherence. Studies using ad libitum

LCHF diets have confirmed that these diets induced spontaneous calorie intake reduction (41) while intakes of CHO and PRO were restricted and increased respectively.

The PREDIMED (105) (or in Spanish “Prevención con Dieta Mediterránea study”) participants were randomised to one of two Mediterranean diets, supplemented with either free virgin olive oil (1 litre·wk^{-1}) or nuts (30 g·day^{-1}), or an education group on a low fat diet (control group). Diets were ad libitum and no advice on physical activity was provided. The main outcome was the 52% reduction of diabetes incidence. What is important to highlight is that there was a higher level of fat in the nuts and olive oil groups and, despite the fact that the diets were ad libitum, these two supplemented diets were superior to a HCLF diet, and do not follow current guidelines rationale that still recommends a HCLF diet.

Not long ago, the research group headed by Dr Yusuf presented the first findings of the Prospective Urban Rural Epidemiological (PURE) study, which is an observational, prospective study that analysed 150,000 individuals in 18 countries from five continents whose objective was to examine the impact of urbanisation on the development of primordial risk factors (for example: physical activity and nutrition changes), primary risk factors (for example: obesity, hypertension, dysglycaemia and dyslipidaemia, smoking), and CVD. The full findings were revealed a few months after the publication (18). In this study it was demonstrated that with an increased CHO intake there was also an increase in the risk of cardiovascular disease. This study supports the notion that eating a low CHO (< 50% of energy intake) diet is not only better for weight loss but for reducing the risk of suffering CVD. This type of study, after large well conducted randomised controlled trials, is the most powerful tool (17) to provide medical evidence of the best practices for improving health and reducing the likelihood of disease.

Ha, Joung and Song (106), analysed the population of 16,349 participants aged 30 years and older from the fifth and sixth Korea National Health and Nutrition Examination Survey that used a comprehensive 24 h food frequency questionnaire to obtain food intake data. It used a low CHO score, which is a measure of the proportion of CHO provided by the diet, going from 0 to 10; 10 being the lowest CHO intake, and 0 being the highest. The other macronutrients were also given a score out of 10 for a total score of 30. When the researchers analysed the data using multiple regression, they did not find any association between a low CHO intake with a MetS score, nor its components (waist circumference, blood pressure, and triglyceride levels). On the other hand, women in the highest decile of both the low CHO intake that included animal products and a plant-based (vegan style) low CHO diet score had higher HDL-C levels. Men in the top decile of the animal-based low CHO diet score also had higher HDL-C levels compared to those in the lowest decile of the low CHO diet score.

The authors (106) of this study concluded that Koreans following a LCHF diet are less likely to have low HDL-C and did not increase the risk of developing MetS for both male and female.

Kwon, Lee, and Lee (107) investigated the role of CHO and fat intake in MetS in Korea using a population-based, cross-sectional design study that included 15,582 individuals (6737 males and 8845 females). Participants were divided into nine groups based on CHO and fat intake proportion; multiple logistic regression analysis was performed after adjusting for confounding variables. In males, a higher proportion of total energy intake, regardless of fat intake, significantly increased the risk of MetS. Whereas the female risk of MetS was only elevated in those cases with the highest CHO proportion and the lowest fat intake. Researchers concluded that for reducing the prevalence of MetS it was necessary to reduce the excess of CHO intake paired with adequate fat levels.

In summary, a low CHO diet may be the best choice as it could lead to a greater reduction of CVD risk, being able to normalise glucose along with other metabolic parameters while promoting weight loss. In terms of TE, these CHO restricted diets also have an advantage compared to restricted calorie diets as they are more successful in reducing body weight, potentially due to the higher protein energy intake (102). The higher protein intake that commonly is a feature of a CHO restricted diet seems to boost the thermic effect of food and provide also an advantage in weight loss while minimising loss of muscle mass (41). Despite the evidence of the superiority of these diets over HCLF diets for improving glycaemic control, metabolic markers, and weight loss outcomes, there is reluctance to recommend CHO restricted diets because in some cases it has raised LDL-C levels. However, these increments may correspond to a less harmful particle size lipoprotein as it has been shown on various occasions (41, 108). There are fewer studies in populations who have cardiometabolic risk factors associated with MetS that address the use of CHO restricted diets. It is important to highlight that CHO restricted diets are able to reduce all MetS components hyperglycaemia, dyslipidaemia, high blood pressure and obesity at the same time, and in a better way than a HCLF diet. In addition, experts who advocate the LCHF diet as the nutritional strategy of choice regard the imbalances in metabolic control is due to a high CHO intake (24) and various reviews have pointed out that a LCHF diet is a viable option to prevent diabetes (24, 109) and perhaps the best approach to reduce MetS (24, 25, 44, 110, 111). That is why this evidence warrants more research that applies this nutritional approach to establish if they are as effective as (or better than) the Mediterranean diet to counteract pre-diabetes. If these studies confirmed earlier findings, this would therefore warrant the LCHF diet to be recommended as the dietary model for preventing and reducing MetS worldwide.

Carbohydrates may not always need to be low

While it has been demonstrated above that LCHF may be an effective tool for improving parameters associated with MetS, higher CHO intake have not always been implicated in metabolic dysregulations. This has been a point of serious debate and disagreement and there is reluctance to fully accept the necessity of a LCHF diet because higher CHO diets have been found effective for improving body composition and metabolic control as it was in the case in the Look Ahead Study (112, 113).

Korsmo-Haugen et al. (114) performed a systematic review and meta-analysis comparing the effects of LCHF diets and HCLF diets for at least 12 weeks on body weight, glycaemic control, lipid profile and blood pressure in adults with T2DM. This study included 23 investigations that involved 2178 participants. Participants that followed a LCHF diet had a slightly greater reduction in HbA1c (-1.0 $mmol \cdot mol^{-1}$ (-1.9, -0.1) 95% CI [-0.09% (-0.17, -0.01)] and triglycerides, [-0.13 $mmol \cdot L^{-1}$ (-0.24, -0.02). Changes in weight, HDL-C, LDL-C and TC were similar between the two diets. Subgroup analyses suggested that the difference between HbA1c was only evident in studies that lasted at least 6-months and with a high risk of bias. Authors concluded that the energy provided by CHO was not an important determinant of response to dietary management, especially considering long-term studies. The authors also identified that the studies included dietary patterns as high as 60% of total energy derived from CHO and it was observed that these CHO quantities were manageable for participants without deleterious effects to metabolic health. CHO restriction was effective for reducing HbA1c when this was accompanied by weight loss. For most of those studies that used CHO restriction, the objective was weight loss. In the absence of weight loss, the improvement in metabolic parameters was not observed. From this meta-analysis it can be interpreted that weight loss seems to be a necessity for observing improvements in glycaemic control, thus, it may be caloric restriction that is most important.

Sartorius et al. (113) assessed the association between obesity and CHO intake by performing a systematic review and a meta-analysis to estimate attributability, and identified the determinants of obesity including the effect of the association of consuming a HCLF versus LCHF diets (stratum 1), as well as the percentage of CHO in total energy intake (stratum 2) using odds ratio and 95% CI for the analysis of both strata. Twenty-two papers were meta-analysed, which included a total of 200,075 participants. Strata 1 and 2 OR were non-significant 1.043 (0.933, 1.154) 95% CI, and 0.984 (0.926, 1.042) respectively. The authors concluded that it was not possible to make a link between a high-CHO diet or the percentage of total energy derived from CHO, and an increased odds risk ratio of obesity. Despite this conclusion, there were indications that high levels of inactivity and high CHO intake coming from refined grains were linked to obesity that was the case for a Sri Lankan study. Due to the lack of standardised reporting this research did not have adequate information to draw robust

conclusions. However, there was evidence that metabolic disease is highly influenced by these two factors (inactivity and high-CHO intake) (115). In this regard, the literature shows that the hepatic manifestation of MetS is the non-alcoholic fatty liver disease (NAFLD) (116) which is both a consequence of and aggravated by insulin resistance. This is a key component of the metabolic disease and its presence is an indication of impaired metabolism (117) and likely manifested as a result of excessive CHO intake that contributes to increased triglyceride levels and fat accumulation in the liver (116).

Kang et al. (116) observed that MetS was present in 34% of a total of 91 individuals with NAFLD, in the ATPIII clinical scale, and had a higher HOMA-IR (7.66 vs 4.45, p=0.040); interestingly the block food frequency questionnaire revealed that these individuals also had a higher CHO intake (51% vs 45%, p=0.030) and a lower fat intake (34% vs 40%, p=0.010). To note, the PRO intake, the total energy intake and even physical activity levels, were similar to those individuals with NAFLD but without metabolic syndrome. Kang et al. concluded that the restriction of CHO intake deserves more attention and more research in this area is warranted.

Snorgaard et al. (83) conducted a meta-analysis attempting to clarify if there is a reason to opt for a LCHF diet instead of a HCLF diet for managing T2DM. Their final analysis included 10 randomised controlled trials with a total of 1376 participants and assessed the following outcomes at three months, six months and end of one year of intervention: HbA1c, BMI, body mass, LDL-C, quality of life (QoL), and attrition. HbA1c showed more improvement in the LCHF diets at intervals of three and six months, having a greater glucose-lowering effect with higher CHO restriction. But this effect (difference) was no longer present (equally improved for both diets) after one year of intervention. Consequently, BMI, body mass, LDL-C, quality of life (QoL), and attrition were similar across all time points. The authors (83) did not however find any difference between the two diets, the lower CHO intake having the better glucose-lowering effect, and the LCHF diets being better for glycaemic control within one year of treatment.

Finally, there are also other factors that support the case for maintaining a high percentage of total energy intake coming from CHO and these are the CHO quality and the glycaemic index (GI). Factors that can modulate the increase in the blood glucose concentration following eating, the glycaemic response (GR), and in consequence can influence metabolic health (118). CHO quality is given by the amount of fibre present in a given food containing CHO, with more fibre content, means more quality (118). Briefly the GI was developed to allow individuals with diabetes a greater glycaemic control. It provides an estimation of the increase in the glycaemia following eating of a portion of food containing a fixed amount of carbohydrate (usually 50 g) is calculated by GI= (iAUC test food/iAUC reference

food) × 100, where iAUCtest = incremental area under the curve of 2-h of a test food (the desired food's GI); iAUC = incremental area under the curve of 2-h of a reference food, usually a glucose solution or white bread). While the glycaemic load is expressed by GL = GI x (available carbohydrate in a given amount of food) for the purpose of predicting the GR.

In the Netherlands, Sluijs et al. (119) conducted the European Prospective Investigation into Cancer and Nutrition–Netherlands (EPIC-NL) to assess the relationship between CHO quantity and quality in the development of T2DM investigating the associations of dietary glycaemic load (GL), glycaemic index (GI), carbohydrate, and fibre intake a 10 y prospective cohort study conducted in 37,846 participants aged 21-70 at baseline and free of T2DM. Dietary intake was assessed with a validated food-frequency questionnaire. A total of 915 incident T2DM was documented, after adjustment for sex, age and established T2DM risk factors, dietary factors, hazard ratios (HR) per standard deviation (SD) were calculated. Dietary glycaemic load (GL) was associated with increased T2DM risk [1.32; (1.14, 1.54) 95% CI; p<0.001]. GI tended to increase diabetes risk [HR: 1.08, (1.00, 1.17) 95% CI; p= 0.05]. Dietary fibre intake was inversely associated with T2DM risk (HR: 0.92; (0.85, 0.99) 95% CI p< 0.05), whereas carbohydrate intake was associated with increased diabetes risk [HR: 1.15; (1.01,1.32) 95% CI; p< 0.05]. Of the carbohydrate subtypes, only starch was related to increased diabetes risk [HR: 1.25 (1.07, 1.46) 95% CI, p< 0.05]. After the exclusion of misreports, all associations became slightly stronger. According to Sluijs et al. (119), both carbohydrate quantity and quality seem to be important factors in T2DM prevention.

As mentioned before, fibre can confer a protective effect against disease, foods containing more fibre are advocated. For this reason, one of the aspects that is used for measuring CHO quality, and therefore the means to assess this, is using the carbohydrate-to-fibre ratio. With this in mind, Alessa et al. (118) investigated its relation to the incidence of coronary heart disease (CHD). They analysed a sample of 75,020 women and 42,865 men and detected 7,320 cases of incident CHD in a prospective cohort study. Concluding that dietary cereal fibre appears to be an important component of carbohydrate quality. While the carbohydrate-to–cereal fibre ratio and the starch to cereal fibre ratio was associated with an increased risk for incident CHD, of 20% [pooled-RR = 1.20; (1.11, 1.29) 95% CI; p-trend < 0.0001], and 17% [pooled-RR = 1.17;(1.09, 1.27) 95%CI; p-trend < 0.0001], respectively. Whereas the carbohydrate-to-fibre ratio D (pooled-RR=1.04; (0.96, 1.13) 95% CI; p-trend=0.46), was not. The authors concluded that dietary cereal fibre appears to be an important component of CHO quality. The CHO-to–cereal fibre ratio and the starch to cereal fibre ratio, were associated with an increased risk for incident CHD but not the CHO to fibre ratio.

Another study previously conducted by Alessa et al. (120) also used CHO quality to assess the incidence of T2DM in a prospective cohort study including a sample of 70,035 women free of T2DM, CVD and cancer at baseline from the Nurses' Health Study (1984–2008). The Cox regression methodology evaluated this relationship. Participants were followed for 14 y, in that time 6934 incidents of T2DM were detected. Multivariate analysis did not find any risk when comparing the largest extreme quintiles, higher carbohydrate intake was not associated with T2DM (RR = 0.98; (0.89, 1.08) 95% CI; *p*-trend = 0.840), whereas starch was associated with a higher risk (RR = 1.23, (1.12, 1.35) 95%CI; *p*-trend <0.0001). Total fibre (RR= 0.80, (0.72, 0.89) 95% CI; *p*-trend < 0.0001), cereal fibre (RR= 0.71, (0.65, 0.78) 95% CI; *p*-trend < 0.0001), and fruit fibre (RR = 0.79, (0.72, 0.85) 95% CI; *p*-trend < 0.0001) were associated with a lower T2DM risk. The ratio of CHO to total fibre intake was marginally associated with a higher risk of T2D (RR = 1.09, (1.00, 1.20) 95% CI; *p*-trend = 0.04). On the other hand, positive associations were found between the ratios of carbohydrate to cereal fibre (RR= 1.28, (1.17, 1.39) 95% CI; *p*-trend <0.0001), starch to total fibre (RR = 1.12, (1.02,1.23) 95% CI *p*-trend = 0.03), and starch to cereal fibre (RR= 1.39; (1.27, 1.53) 95% CI, *p*-trend < 0.0001) and T2DM. It was concluded that diets with high starch, low fibre, and a high starch to-cereal fibre ratio were related with a higher risk of T2DM.

In summary, there is an ongoing debate whether having a high-CHO or a low-CHO diet is better; there is consensus therefore that choosing a low glycaemic index diet can be favoured for addressing metabolic disorders. This prevents having a large glycaemic response which makes it more difficult to manage. It seems that by using the same logic to decide the total CHO amount is an idea not welcome just yet (83, 113, 114) despite one meta-analysis demonstrating that it is the amount in fact that regulates the glucose lowering effect (83), which adds up to other existing evidence that the amount of CHO intake matters (24, 52), even if there is no difference in any other aspect.

In this sense, a low CHO approach should be considered a preferred option for those at metabolic risk. Indeed, evidence supports that CHO restriction may be the most effective possible way to achieve metabolic health and weight loss, and should be the preferred modality for T2DM and cardiometabolic syndrome prevention and treatment (24, 53). When CHO has been restricted (25 to 45% of TE coming from CHO) it has been found to be effective in promoting an adequate glucose control (121-123), improved lipid profile, weight loss in those at risk and diabetic populations (123). These outcomes have obvious implications for reducing CVD risk, with reductions in risk factors such as decreased TG, systolic blood pressure and improved HDL-C (41, 124, 125). Table 1-1 presents summarised results of interventions comparing the effects of either a LCHF diet or a HCLF diet on different metabolic markers. The superiority of the LCHF diet can be seen, or at least an equal effect between the two diets where a negative sign represents a better outcome for a LCHF diet and a positive outcome for

the HCLF diet, except for those variables that they are expected to augment, i.e. HDL-C where a positive sign would indicate a better outcome for a LCHF diet (23, 125-157).

Table 1-1 Body composition parameters difference LCHF vs LFD. (Part 1)

Body mass (weight loss)

year	Author	Duration	Difference LCHF − LFD	LCHF Baseline MEAN±SD	LCHF Change kg	LFD Baseline MEAN±SD	LFD Change kg
1992	Garg et al. (125)	3 weeks	0.2	89±4.5	-1.2	89±4.5	-1.4
2003	Brehm et al. (127)	26 weeks	-4.6	91.2±8.4	-8.5	92.3±6	-3.9
2003	Foster et al. (128)	52 weeks	-1.89	98.7±19.5	-4.34	98.3±16.4	-2.46
2003	Samaha et al. (129)	26 weeks	-3.9	130±22.7	-5.8	131.8±27.3	-1.9
2003	Volek et al. (130)	4 weeks	-0.4	59.8±4.6	-1.2	58.6±0.5	-0.8
2004	Meckling et al. (131)	10 weeks	-0.2	91±4.5	-7	92.3±3	-6.8
2004	Sharman et al. (132)	6 weeks	-2.8	109.1±17.8	-6.2	102.9±2.9	-3.4
2004	Stern et al. (133)	0-52 weeks	-2	132±23	-5.1	129±20	-3.1
2004	Volek et al. (134)	50 d ♂/30 d ♂	0	2±2	0	0±0	0
2004	Volek et al. (135)	4 weeks	-1.9	76.2±12.9	-2.96	76.2±12.9	-1.06
2004	Yancy et al. (136)	24 weeks	-5.5	97.8±15	-12	96.8±19.2	-6.5
2005	Dansinger et al. (137)	0-8 weeks	0	100±14	-3.6	100±15	-3.6
2005	Dansinger et al. (137)	0-26 weeks	0.4	100±14	-3.2	100±15	-3.6
2005	Dansinger et al. (137)	0-52 weeks	1.2	100±14	-2.1	100±15	-3.3
2005	McAuley et al. (138)	0-26 weeks	-8	97.2±10.4	-8.5	97.6±16.4	-0.5
2005	McAuley et al. (138)	0-52 weeks	-1	97.2±10.4	-5.4	97.6±16.4	-4.4
2005	Nielsen et al. (139)	26 weeks	-9.6	100.6±14.7	-11.4	101.5±15.5	-1.8
2005	Yancy et al. (140)	16 weeks	-8.7	131.4±18.1	-8.7	0±0	0
2006	Nielsen JV and Joensson E. (23)	12 weeks	-8.7	100.6±14.7	-8.7	0±0	0
2006	Nielsen JV and Joensson E. (23)	12-26 weeks	-2.7	91.9±14.7	-2.7	0±0	0
2006	Nielsen JV and Joensson E. (23)	26-102 weeks	2.8	89.2±14.3	2.8	0±0	0
2006	Noakes et al. (125)	12 weeks	1.3	33.3±3.1	-4.1	34.8±2.1	-5.4
2006	Truby et al. (141)	0-8 weeks	-0.5	90.3±12.7	-5.2	88.8±13.3	-4.7
2006	Truby et al. (141)	0-26 weeks	0.6	90.3±12.7	-6	88.8±3	-6.6
2006	Truby et al. (141)	8-26 weeks	0.9	85.1±4.4	-1.3	84.1±3.2	-2.2
2007	Gardner et al. (142)	0-52 weeks	-2.5	86±13	-4.7	86±10	-2.2
2007	LeCheminant et al. (143)	0-12 weeks	-1.2	109.6±17.3	-20.4	105.5±15.9	-19.2
2007	LeCheminant et al. (143)	12-32 weeks	0.4	89.2±14.4	0.1	86.3±11.9	-0.3
2008	Pérez-Guisado et al. (144)	12 weeks	-13.52	108±3.18	-13.52	-	-
2008	Shai et al. (145)	104 weeks	-1.8	91.4±14.3	-4.7	91.3±12.3	-2.9
2009	Brinkworth et al. (146)	52 weeks	0.1	93.9±15.5	-11.5	94.5±12.7	-11.6
2009	Davis et al. (147)	0-12 weeks	-2	93.6±18	-5.2	101±19	-3.2
2009	Davis et al. (147)	0-26 weeks	-0.4	93.6±18	-4.8	101±19	-4.4
2009	Davis et al. (147)	0-52 weeks	0	93.6±18	-3.1	101±19	-3.1
2009	Volek et al. (148)	12 weeks	-4.9	96.5±13.7	-10.1	94.4±15.2	-5.2
2010	Foster et al. (149)	12 weeks	-1.12	103.3±15.5	-9.49	103.5±14.4	-8.37
2010	Foster et al. (149)	26 weeks	-0.84	103.3±0	-12.18	103.5±14.4	-11.34
2010	Foster et al. (149)	52 weeks	-0.06	103.3±0	-10.87	103.5±14.4	-10.81
2010	Foster et al. (149)	104 weeks	1.03	103.3±0	-6.34	103.5±14.4	-7.37
2010	Iqbal et al. (150)	0-26 weeks	-0.8	118.3±21.3	-2.8	115.5±16.7	-2
2010	Iqbal et al. (150)	0-52 weeks	-0.1	118.3±21.3	-1.3	115.5±16.7	-1.2
2010	Iqbal et al. (150)	0-104 weeks	-1.3	118.3±21.3	-1.5	115.5±16.7	-0.2
2010	Yancy et al. (151)	48 weeks	-1.9	124±25.7	-11.4	119±26.8	-9.5
2011	Paoli et al. (152)	6 weeks	-6.8	86.2±16.4	-6.8	0±0	0
2013	Gu et al. (153)	0-4 weeks	-6	96.1±2.7 SE	-6	-	-
2013	Gu et al. (153)	4-8 weeks	-2.7	90.1±2.6	-2.7	-	-
2013	Liu et al. (154)	12 weeks	0.5	64.8±6.5	-5.3	67±11.33	-5.8
2014	Bazzano et al. (155)	52 weeks	-3.5	96.3±12.7	-5.3	97.9±13.5	-1.8
2017	Saslow et al. (156)	32 weeks	-9.7	109±24.9	-12.7	90.9±16.4	-3
2018	Gardner et al. (157)	52 weeks	-1.8	96.3±15.7	-8.3	97.5±14.7	-6.5

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Body composition parameters difference LCHF vs HCLF. (Part 2)

Body fat (kg)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change kg	Baseline MEAN±SD	Change kg
2003	Brehm et al. (127)	0-12 weeks	-1.77	37.33±4.79	-4.29	37.83±2.65	-2.52
2003	Brehm et al. (127)	0-26 weeks	-1.8	37.33±4.79	-3.77	37.83±2.65	-1.97
2004	Meckling et al. (131)	10 weeks	1.3	33.3±3.1	-4.1	34.8±2.1	-5.4
2005	McAuley et al. (138)	0-26 weeks	-1.4	44.8±6.8	-5.5	45.9±11	-4.1
2005	McAuley et al. (138)	0-52 weeks	0.1	44.8±6.8	-3.4	45.9±11	-3.5
2006	Noakes et al. (125)	12 weeks	-0.5	37.6±1.3	-4.5	37.9±2.2	-4
2006	Truby et al. (141)	0-8 weeks	-0.4	35.7±6	-3.5	34.2±6.9	-3.1
2006	Truby et al. (141)	8-26 weeks	0.8	32.2±3	-1.2	31.1±2.4	-2
2006	Truby et al. (141)	0-26 weeks	0.4	35.7±6	-4.6	34.2±6.9	-5
2009	Volek et al. (148)	12 weeks	-1.9	38.7±7.7	-5.6	37.1±10	-3.7
2010	Foster et al. (149)	26 weeks	-0.49	40±7.6	-8.65	40.4±7.8	-8.16
2010	Foster et al. (149)	52 weeks	-0.54	40±7.6	-7.83	40.4±7.8	-7.29
2010	Foster et al. (149)	104 weeks	-0.15	40±7.6	-3.99	40.4±7.8	-3.84

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Lean body mass (kg)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change kg	Baseline MEAN±SD	Change kg
2003	Brehm et al. (127)	0-12 weeks	-1.98	50±6	-2.8	51±5	-0.8
2003	Brehm et al. (127)	0-26 weeks	-1.24	50±6	-2	51±5	-0.7
2004	Meckling et al. (131)	10 weeks	-0.9	58±3	-1.9	57±3	-1
2006	Noakes et al. (125)	12 weeks	-0.6	47±2	-2.6	49±3	-2
2009	Volek et al. (148)	12 weeks	-2.4	54±12	-3.4	55±11	-1
2010	Foster et al. (149)	26 weeks	-0.35	61±13	-3.5	61±12	-3.2
2010	Foster et al. (149)	52 weeks	-0.3	61±13	-3	61±12	-2.7
2010	Foster et al. (149)	104 weeks	-0.21	61±13	-2.4	61±12	-2.1

Note: Diff. Between groups, (−) sign denotes better outcome for LFD.

Waist circumference (cm)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change cm	Baseline MEAN±SD	Change cm
2005	Dansinger et al. (137)	0-8 weeks	-0.6	109±11	-3.3	111±13	-2.7
2005	Dansinger et al. (137)	0-26 weeks	-0.7	109±11	-3.2	111±13	-2.5
2005	Dansinger et al. (137)	0-52 weeks	-0.3	109±11	-2.5	111±13	-2.2
2005	McAuley et al. (138)	0-26 weeks	-2.2	110±9.9	-9.9	109.2±12.5	-7.7
2005	McAuley et al. (138)	0-52 weeks	-1.1	110±9.9	-5.4	109.2±12.5	-4.3
2005	Yancy et al. (140)	16 weeks	-	130±10.5	-6.7	-	-
2006	Truby et al. (141)	0-8 weeks	-1.2	102±10.6	-6.7	100±10.3	-5.5
2006	Truby et al. (141)	8-26 weeks	0.6	95±6.1	-2.4	94.5±5.1	-3
2006	Truby et al. (141)	0-26 weeks	0.2	102±10.6	-8.1	100±10.3	-8.3
2007	LeCheminant et al. (143)	32 weeks	-1	111±10.1	-14.2	106.6±9.6	-13.2
2011	Paoli et al. (152)	6 weeks	-9.5	107±15.4	-9.5	-	-
2013	Gu et al. (153)	0-4 weeks	-	105±1.7	-3.8	-	-
2013	Gu et al. (153)	4-8 weeks	-2.1	101±1.5	-2.1	-	-
2013	Liu et al. (154)	12 weeks	-1	90±5.5	-7.8	91±1.1	-6.8
2014	Bazzano et al. (155)	51 weeks	-1.7	108.4±9.3	-6.7	111±10.7	-5
2018	Gardner et al. (157)	52 weeks	-1.4	106.7±11.4	-5.5	107.2±10.9	-4.1

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Lipids: total cholesterol difference LCHF vs HCLF (Part 3)

Total cholesterol (mmol·L^{-1})							
year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change mmol/l	Baseline MEAN±SD	Change mmol/l
1992	Garg et al. (125)	3 weeks	-2.57	6.1±0.62	-3.59	6.1±0.6	-1.02
2003	Brehm et al. (127)	0-12 weeks	-0.32	5.3±6.63	-0.53	4.8±0.2	-0.21
2003	Brehm et al. (127)	0-26 weeks	0.02	5.3±0.17	-0.02	4.8±0.2	-0.04
2003	Samaha et al. (129)	26 weeks	0.08	4.7±1.34	0.08	5±0.8	0
2003	Volek et al. (130)	4 weeks	0.98	4.6±0.02	0.73	4.8±4.5	-0.25
2004	Meckling et al. (131)	10 weeks	1.66	5.9±0.03	0.05	5.9±0.4	-1.6
2004	Sharman et. al. (132)	6 weeks	-0.35	5±0.83	-0.54	4.4±1	-0.19
2004	Stern et al. (133)	0-52 weeks	0.35	4.7±1.24	0.16	5±0.8	-0.19
2004	Volek et al. (134)	4 weeks	0.39	4.7±0.88	0.05	4.7±0.9	-0.34
2004	Yancy et al. (140)	24 weeks	0.14	6.3±0	-0.21	6.2±0	-0.35
2005	McAuley et al. (138)	0-26 weeks	0.3	5.8±1.1	-0.3	6±0.9	-0.6
2005	McAuley et al. (138)	0-52 weeks	0.2	5.8±1.1	-0.2	6±0.9	-0.4
2005	Yancy et al. (140)	16 weeks	-0.07	4.6±1.4	-0.07	-	-
2005	Dansinger et al. (137)	0-8 weeks	0.44	5.5±0.8	-0.05	5.5±0.9	-0.49
2005	Dansinger et al. (137)	0-26 weeks	0.27	5.5±0.8	-0.02	5.5±0.9	-0.29
2005	Dansinger et al. (137)	0-52 weeks	0.17	5.5±0.8	-0.11	5.5±0.9	-0.28
2006	Nielsen JV and Joensson E. (23)	12 weeks	0.2	5.6±1.2	0.2	-	-
2006	Nielsen JV and Joensson E. (23)	12-26 weeks	0.3	5.8±1.1	0.3	-	-
2006	Nielsen JV and Joensson E. (23)	26-102 weeks	-0.4	6.1±1.1	-0.4	-	-
2006	Noakes et al. (125)	12 weeks	0.39	5.8±0.21	-0.1	5.6±0.2	-0.49
2006	Truby et al. (141)	0-8 weeks	0.44	5.8±0.9	0	5.6±1.1	-0.44
2006	Truby et al. (141)	8-26 weeks	0	5.7±0.7	0	5.1±0.6	0
2006	Truby et al. (141)	0-26 weeks	0.01	5.8±0.9	-0.01	5.6±1.1	-0.01
2008	Pérez-Guisado et al. (144)	12 weeks	-0.56	5.4±0.15	-0.56	-	-
2009	Davis et al. (147)	0-26 weeks	0.01	4.4±0.83	0	4.3±0.9	-0.01
2009	Davis et al. (147)	0-52 weeks	0.01	4.4±0.83	0	4.3±0.9	0
2009	Volek et al. (148)	12 weeks	-0.05	5.4±0.67	-0.28	5.3±0.8	-0.23
2010	Foster et al. (149)	104 weeks	0.1	4.9±0.78	-4.88	5±0.9	-4.98
2010	Iqbal et al. (150)	0-26 weeks	0.05	4.7±1.2	0.03	4.7±1.1	-0.02
2010	Iqbal et al. (150)	0-52 weeks	0.2	4.7±1.2	-0.02	4.7±1.1	-0.21
2010	Iqbal et al. (150)	0-104 weeks	0.03	4.7±1.2	-0.31	4.7±1.1	-0.34
2010	Yancy et al. (151)	48 weeks	0.13	4.7±0.87	-0.1	4.8±0.9	-0.23
2011	Paoli et al. (152)	6 weeks	-0.6	5.3±1.03	-0.6	0±0	0
2013	Gu et al. (153)	0-4 weeks	-0.52	5.1±0.12	-0.52	-	-
2013	Liu et al. (154)	12 weeks	0.59	5±1.05	-0.01	5.2±0.2	-0.6
2014	Bazzano et al. (155)	52 weeks	0.02	5.1±1.1	0.05	5.3±1.1	0.03

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Lipids: low density lipoprotein cholesterol difference LCHF vs HCLF (Part 4)

Low density lipoprotein cholesterol (mmol·L^{-1})							
			Difference	Baseline	Change	Baseline	Change
year	Author	Duration	LCHF - LFD	MEAN±SD	mmol·L^{-1}	MEAN±SD	mmol·L^{-1}
1992	Garg et al. (125)	3 weeks	0	3.68±0.57	-0.67	3.68±0.57	-0.67
2003	Brehm et al. (127)	0-12 weeks	-0.08	3.23±0.14	-0.31	2.94±6.36	-0.23
2003	Brehm et al. (127)	0-26 weeks	0.13	3.23±0.14	-0.02	2.94±6.36	-0.16
2003	Samaha et al. (129)	26 weeks	-0.03	2.95±0.93	0.1	3.05±0.75	0.08
2003	Volek et al. (130)	4 weeks	0.58	2.94±0.66	0.43	3.11±0.72	-0.15
2004	Meckling et al. (131)	10 weeks	1.37	4.37±0.28	0.03	4.27±0.34	-1.34
2004	Sharman et. al. (132)	6 weeks	0.17	3.25±0.73	-0.2	3.05±2.07	-0.37
2004	Stern et al. (133)	0-52 weeks	0.28	2.9±0.83	0.21	3.13±0.73	-0.07
2004	Volek et al. (134)	4 weeks	0.31	2.92±0.78	0.16	2.92±0.78	-0.16
2004	Yancy et al. (136)	24 weeks	0.23	4.07±0	0.04	3.83±0	-0.19
2005	Dansinger et al. (137)	0-8 weeks	0	0±0	0	0±0	0
2005	Dansinger et al. (137)	0-26 weeks	0	0±0	0	0±0	0
2005	McAuley et al. (138)	0-26 weeks	0.3	3.8±0.9	0	3.9±0.8	-0.3
2005	McAuley et al. (138)	0-52 weeks	0	3.8±0.9	-0.1	3.9±0.8	-0.1
2005	Yancy et al. (136)	16 weeks	0.26	2.51±0.64	0.26	0±0	0
2006	Noakes et al. (125)	12 weeks	0.58	3.83±0.18	0.18	3.65±0.22	-0.4
2007	Gardner et al. (142)	0-8 weeks	0.32	2.82±0.75	0.06	2.87±0.7	-0.26
2007	Gardner et al. (142)	0-26 weeks	0.13	2.82±0.75	0.04	2.87±0.7	-0.08
2007	Gardner et al. (142)	0-52 weeks	0.12	2.82±0.75	0.02	2.87±0.7	-0.1
2008	Pérez-Guisado et al. (144)	12 weeks	-0.22	2.96±0.16	-0.22	-	-
2008	Shai et al. (145)	104 weeks	0.07	3.03±0.89	-0.08	3.03±0.92	-0.14
2009	Davis et al. (147)	0-26 weeks	0.15	2.5±0.69	-0.1	2.4±0.74	-0.25
2009	Davis et al. (147)	0-52 weeks	0.14	2.5±0.69	-0.04	2.4±0.74	-0.18
2009	Volek et al. (148)	12 weeks	0.18	3.36±0.57	0.13	3.31±0.8	-0.05
2010	Foster et al. (149)	12 weeks	-0.02	3.11±0.66	-0.19	3.21±0.76	-0.16
2010	Foster et al. (149)	26 weeks	0.26	3.11±0.66	0.01	3.21±0.76	-0.25
2010	Foster et al. (149)	52 weeks	0	3.11±0.66	-0.22	3.21±0.76	-0.22
2010	Foster et al. (149)	104 weeks	0.08	3.11±0.66	-0.12	3.21±0.76	-0.21
2010	Iqbal et al. (150)	0-26 weeks	0.85	2.83±1.02	0.9	2.79±0.96	0.05
2010	Iqbal et al. (150)	0-52 weeks	-4.49	2.83±1.02	-4.7	2.79±0.96	-0.21
2010	Iqbal et al. (150)	0-104 weeks	-8.045	2.83±1.02	-8.2	2.79±0.96	-0.16
2010	Yancy et al. (151)	48 weeks	-1.68	2.99±0.81	-1.91	3.04±0.84	-0.23
2011	Paoli et al. (152)	6 weeks	-	3.87±0.75	-0.36	-	-
2013	Gu et al. (153)	0-4 weeks	-	3.09±0.12	-0.08	-	-
2014	Bazzano et al. (155)	52 weeks	-0.03	3.2±0.9	-0.08	3.2±1	-0.05
2017	Saslow et al. (156)	32 weeks	0.15	2.51±0.79	-0.01	2.34±0.75	-0.16
2018	Gardner et al. (157)	52 weeks	0.24	2.94±0.68	0.16	2.89±0.79	-0.08

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Lipids: high density lipoprotein cholesterol difference LCHF vs HCLF **(Part 5)**

High density lipoprotein cholesterol (mmol·L^{-1})							
			Difference	Baseline	Change	Baseline	Change
year	Author	Duration	LCHF - LFD	MEAN±SD	mmol·L^{-1}	MEAN±SD	mmol·L^{-1}
1992	Garg et al. (125)	3 weeks	0.01	0.75±0.06	0.01	0.75±0.06	-0.07
2003	Brehm et al. (127)	0-12 weeks	0.06	1.34±0.07	0.06	1.26±2.23	0.06
2003	Brehm et al. (127)	0-26 weeks	0.18	1.34±0.07	0.18	1.26±2.23	0.11
2003	Foster et al. (128)	52 weeks	-1.21	1.21±0.29	NA	1.28±0.32	NA
2003	Samaha et al. (129)	26 weeks	0	1.06±0.28	0	1.06±0.26	-0.03
2003	Volek et al. (130)	4 weeks	0.41	1.28±0.01	0.41	1.3±0.28	-0.1
2004	Meckling et al. (131)	10 weeks	0.37	1.27±0.05	0.16	1.34±0.08	-0.21
2004	Sharman et. al. (132)	6 weeks	0.01	1.02±0	-0.03	0.99±0.2	-0.04
2004	Stern et al. (133)	0-52 weeks	-0.11	1.06±0.26	-0.02	1.06±0.23	-0.13
2004	Volek et al. (130)	4 weeks	0.13	1.34±0.36	0.03	1.34±0.36	-0.1
2004	Yancy et al. (136)	24 weeks	0.18	1.43±0	0.14	1.4±0	-0.04
2005	McAuley et al. (138)	0-26 weeks	0.19	1.14±0.29	0.14	1.16±0.24	-0.05
2005	McAuley et al. (138)	0-52 weeks	0.14	1.14±0.29	0.12	1.16±0.24	-0.02
2005	Yancy et al. (136)	16 weeks	0.07	0.92±0.2	0.07	-	-
2006	Noakes et al. (125)	12 weeks	0.12	1.26±0.05	0.06	1.31±0.07	-0.06
2007	Gardner et al. (142)	0-8 weeks	0.13	1.37±0.36	-0.01	1.29±0.28	-0.14
2007	Gardner et al. (142)	0-26 weeks	0.13	1.37±0.36	0.13	1.29±0.28	0
2007	Gardner et al. (142)	0-52 weeks	0.13	1.37±0.36	0.13	1.29±0.28	0
2008	Pérez-Guisado et al. (144)	12 weeks	0.12	1.3±1.69	0.12	1±0.03	0
2008	Shai et al. (145)	104 weeks	0.05	0.97±0.87	0.22	1±0.25	0.17
2009	Davis et al. (147)	0-26 weeks	0.17	1.3±0.24	0.16	1.2±0.29	-0.01
2009	Davis et al. (147)	0-52 weeks	0.1	1.3±0.24	0.16	1.2±0.29	0.06
2009	Volek et al. (148)	12 weeks	0.13	0.93±0.7	0.1	1.01±0.16	-0.03
2010	Foster et al. (149)	12 weeks	0.06	1.19±0.35	0.06	1.17±0.3	-0.01
2010	Foster et al. (149)	26 weeks	0.14	1.19±0.35	0.16	1.17±0.3	0.02
2010	Foster et al. (149)	52 weeks	0.11	1.19±0.35	0.21	1.17±0.3	0.1
2010	Foster et al. (149)	104 weeks	0.2	1.19±0.35	0.2	1.17±0.3	0.12
2010	Iqbal et al. (150)	0-26 weeks	-0.06	1.06±0.33	0.01	1.05±0.33	0.07
2010	Iqbal et al. (150)	0-52 weeks	0.07	1.06±0.33	0.07	1.05±0.33	0.03
2010	Iqbal et al. (150)	0-104 weeks	0.02	1.06±0.33	0.02	1.05±0.33	0.02
2010	Yancy et al. (151)	48 weeks	0.1	0.95±0.81	0.1	1.02±0.32	0.09
2011	Paoli et al. (152)	6 weeks	-	1.19±0.19	0.15	-	-
2013	Gu et al. (153)	0-4 weeks	-	1.15±0.04	-0.06	-	-
2013	Liu et al. (154)	12 weeks	0.28	1.3±0.35	0.15	1.44±0.08	-0.13
2014	Bazzano et al. (155)	52 weeks	0.18	1.4±0.3	0.24	1.5±0.3	0.06
2017	Saslow et al. (156)	32 weeks	0.11	1.18±0.39	0.1	1.39±0.33	-0.01
2018	Gardner et al. (157)	52 weeks	0.08	1.29±0.24	0.08	1.28±0.23	0

Note: Diff. Between groups, (−) sign denotes better outcome for LFD.

Table 1-1 Lipids triglycerides and TG/HDL-ratio difference between LCHF and LFD (Part 6)

Triglycerides (mmol·L^{-1})

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change mmol·L^{-1}	Baseline MEAN±SD	Change mmol·L^{-1}
1992	Garg et al. (125)	3 weeks	-0.7	4.01±0.68	-1.46	4.01±0.68	-0.76
2003	Brehm et al. (127)	0-12 weeks	-0.56	1.68±0.15	-0.64	1.23±0.11	-0.08
2003	Brehm et al. (127)	0-26 weeks	-0.41	1.68±0.15	-0.39	1.23±0.11	0.02
2003	Samaha et al. (129)	26 weeks	-0.35	2.12±1.99	-0.43	1.991.35	-0.08
2003	Volek et al. (130)	4 weeks	-0.29	0.86±0.32	-0.26	0.79±0.6	0.03
2004	Meckling et al. (131)	10 weeks	-0.07	1.54±0.25	-0.45	1.51±0.27	-0.38
2004	Sharman et. al. (132)	6 weeks	-1.13	1.55±0.49	-0.68	0.87±0.24	0.45
2004	Stern et al. (133)	0-52 weeks	1.17	2.27±2.31	-0.64	1.83±0.88	-1.81
2004	Volek et al. (135)	4 weeks	-0.12	1±0.38	-0.23	1±0.38	-0.11
2004	Yancy et al. (136)	24 weeks	0.1	1.78±0	-0.21	2.15±0	-0.31
2005	Dansinger et al. (137)	0-8 weeks	-0.36	1.72±1.11	-0.36	1.96±1.47	0
2005	Dansinger et al. (137)	0-26 weeks	-0.09	1.72±1.12	-0.12	1.96±1.47	-0.03
2005	Dansinger et al. (137)	0-52 weeks	-0.07	1.72±1.13	-0.01	1.96±1.47	0.06
2005	McAuley et al. (138)	0-26 weeks	-0.49	1.87±0.82	-0.83	1.88±0.57	-0.34
2005	McAuley et al. (138)	0-52 weeks	-0.16	1.87±0.82	-0.47	1.88±0.57	-0.31
2005	Yancy et al. (140)	16 weeks	-1.12	2.69±2.87	-1.12	0±0	0
2006	Nielsen JV and Joensson E. (23)	12 weeks	-0.2	1.4±1.8	-0.2	1±1	0
2006	Nielsen JV and Joensson E. (23)	12-26 weeks	0.2	1.2±0.8	0.2	1±1	0
2006	Nielsen JV and Joensson E. (23)	26-102 weeks	0	1.4±0.9	0	0±0	0
2006	Noakes et al. (125)	12 weeks	-0.65	1.83±0.19	-0.72	1.51±0.13	-0.07
2007	Gardner et al. (142)	0-8 weeks	-0.71	1.41±0.88	-0.59	1.33±0.7	0.12
2007	Gardner et al. (142)	0-26 weeks	-0.31	1.41±0.88	-0.4	1.33±0.7	-0.09
2007	Gardner et al. (142)	0-52 weeks	-0.16	1.41±0.88	-0.33	1.33±0.7	-0.17
2008	Shai et al. (145)	104 weeks	-0.24	5.6±1.7	-0.27	5.2±1.4	-0.03
2009	Davis et al. (147)	0-26 weeks	-0.06	1.4±0.84	-0.02	1.4±0.67	0.04
2009	Davis et al. (147)	0-52 weeks	-0.14	1.4±0.84	-0.15	1.4±0.67	-0.01
2009	Volek et al. (148)	12 weeks	-0.8	2.38±0.65	-1.21	2.11±0.65	-0.41
2010	Foster et al. (149)	12 weeks	-0.25	1.28±0.62	-0.45	1.4±0.83	-0.2
2010	Foster et al. (149)	26 weeks	-0.18	1.28±0.62	-0.45	1.4±0.83	-0.27
2010	Foster et al. (149)	52 weeks	-0.16	1.28±0.62	-0.36	1.4±0.83	-0.2
2010	Foster et al. (149)	104 weeks	0.02	1.28±0.62	-0.14	1.4±0.83	-0.16
2010	Iqbal et al. (150)	0-26 weeks	0.09	1.75±1.22	-0.01	1.89±1.08	-0.1
2010	Iqbal et al. (150)	0-52 weeks	0.01	1.75±1.22	-0.14	1.89±1.08	-0.15
2010	Iqbal et al. (150)	0-104 weeks	-0.14	1.75±1.22	-0.29	1.89±1.08	-0.15
2010	Yancy et al. (151)	48 weeks	-0.09	1.72±0.84	-0.33	1.54±0.84	-0.24
2011	Paoli et al. (152)	6 weeks	-0.28	1.34±0.68	-0.28	1±1	0
2013	Gu et al. (153)	0-4 weeks	-	1.98±0.23	-0.87	-	-
2013	Liu et al. (154)	12 weeks	-0.47	1.69±1.3	-0.9	1.33±0.12	-0.43
2014	Bazzano et al. (155)	52 weeks	-0.16	1.3±0.6	-0.23	1.4±0.9	-0.07
2017	Saslow et al. (156)	32 weeks	-0.61	1.97±0.90	-0.68	1.71±0.98	-0.07
2018	Gardner et al. (157)	52 weeks	-0.2	1.45±0.13	-0.31	1.45±0.80	-0.11

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

TG/HDL-C ratio

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change	Baseline MEAN±SD	Change
2004	Meckling et al. (131)	10 weeks	-0.5	1.2±0	-0.5	1.1±0	-0.1
2004	Sharman et. al. (129)	6 weeks	-0.66	1.56±0.58	-0.66	0.9±0.27	0.53
2004	Volek et al. (130)	4 weeks	-0.54	1.91±1.03	-0.54	1.91±1.03	-0.08
2005	Dansinger et al. (137)	0-8 weeks	0	0±0	0	0	0
2006	Nielsen JV and Joensson E. (23)	12 weeks	-0.4	1.4±0.9	-0.4	-	-
2006	Nielsen JV and Joensson E. (23)	12-26 weeks	-	1±0.6	0	-	-
2006	Nielsen JV and Joensson E. (23)	26-102 weeks	-	1±0.7	0.3	-	-
2006	Noakes et al. (125)	12 weeks	0	0±0	0	0	0
2009	Volek et al. (148)	12 weeks	-3.3	6.2±2.2	-3.3	5±2	-1
2010	Yancy et al. (151)	48 weeks	-1	4.5±2.7	-1	3.9±2.6	-0.77

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Fasting glucose difference between LCHF and LFD (Part 7)

			Fasting glucose (mmol·L^{-1})				
			Difference	Baseline	Change	Baseline	Change
year	Author	Duration	LCHF - LFD	MEAN±SD	mmol·L^{-1}	MEAN±SD	mmol·L^{-1}
1992	Garg et al. (126)	3 weeks	-2.6	36.7±3.8	-1.6	35.4±3.5	1
2003	Brehm et al. (127)	0-12 weeks	-0.26	5.51±0.14	-0.29	5.06±0.12	-0.03
2003	Brehm et al. (127)	0-26 weeks	-0.3	5.51±0.14	-0.5	5.06±0.12	-0.2
2003	Samaha et al. (129)	26 weeks	-0.5	7.11±2.94	-0.61	6.89±2.61	-0.11
2003	Samaha et al. (129)	26 weeks	-0.17	5.67±0.78	-0.11	5.72±0.78	0.06
2003	Samaha et al. (129)	26 weeks	-1.17	9.33±3.5	-1.44	8.78±3.39	-0.28
2004	Meckling et al. (131)	10 weeks	0.06	6.28±0.67	-0.5	5.44±0.44	-0.56
2004	Sharman et. al. (132)	6 weeks	-0.4	5.23±0.35	-0.3	4.93±0.41	0.1
2004	Stern et al. (133)	0-52 weeks	-0.01	5.61±0.72	0.05	5.66±0.72	0.06
2004	Stern et al. (133)	0-52 weeks	-0.44	9.21±3.66	-1.55	8.55±2.78	-1.11
2004	Volek et al. (134)	4 weeks	-0.28	4.78±0.22	-0.17	4.78±0.22	0.11
2005	Dansinger et al. (137)	0-8 weeks	-0.37	7.06±3.44	-0.54	6.72±3.06	-0.17
2005	Dansinger et al. (137)	0-26 weeks	-7.52	7.06±3.44	-7.8	6.72±3.06	-0.28
2005	Dansinger et al. (137)	0-52 weeks	0.15	7.06±3.44	-0.08	6.72±3.06	-0.23
2005	McAuley et al. (138)	0-26 weeks	0.1	5.1±0.6	-0.3	5±0.6	-0.4
2005	McAuley et al. (138)	0-52 weeks	-0.1	5.1±0.6	-0.2	5±0.6	-0.1
2005	Nielsen et al. (139)	26 weeks	-2.9	11±2.8	-4.1	12.3±1.8	-1.2
2005	Yancy et al. (140)	16 weeks	-1.51	9.08±4.09	-1.51	0	0
2006	Noakes et al. (125)	12 weeks	0	5.3±0.1	0	5.3±0.1	0
2006	Truby et al. (141)	0-8 weeks	0.1	5.47±0.5	-0.04	5.46±0.5	-0.14
2006	Truby et al. (141)	8-26 weeks	0.16	5.43±0.4	-0.13	5.32±0.5	-0.29
2006	Truby et al. (141)	0-26 weeks	0.27	5.47±0.5	-0.19	5.46±0.5	-0.46
2007	Gardner et al. (142)	0-8 weeks	-0.32	5.11±9	-0.4	5.17±0.72	-0.08
2007	Gardner et al. (142)	0-26 weeks	-0.17	5.11±9	-0.2	5.17±0.72	-0.03
2007	Gardner et al. (142)	0-52 weeks	-0.06	5.11±9	-0.1	5.17±0.72	-0.04
2008	Pérez-Guisado et al. (144)	12 weeks	-0.92	6.1±2.22	-0.92	0	0
2008	Shai et al. (145)	104 weeks	-0.32	5.14±1.58	-5.14	4.83±1.44	-4.83
2009	Volek et al. (148)	12 weeks	-0.56	5.61±0.72	-0.67	5.33±0.67	-0.11
2010	Iqbal et al. (150)	0-26 weeks	-0.12	8.77±3.46	-0.53	8.07±2.82	-0.41
2010	Iqbal et al. (150)	0-52 weeks	-0.07	8.77±3.46	-0.79	8.07±2.82	-0.72
2010	Iqbal et al. (150)	0-104 weeks	0.14	8.77±3.46	-0.1	8.07±2.82	-0.24
2010	Yancy et al. (151)	48 weeks	0	2±2	0	1±1	0
2011	Paoli et al. (152)	6 weeks	-	5.33±0.67	-0.28	-	-
2013	Gu et al. (143)	0-4 weeks	-	5.3±0.1	-0.3	-	-
2013	Liu et al. (154)	12 weeks	0.39	6.01±0.9	0.1	6.15±2.09	-0.29
2014	Bazzano et al. (155)	52 weeks	0.12	5.2±0.6	0.02	5.2±0.5	-0.1
2018	Gardner et al. (148)	52 weeks	0	5.5±0.5	-0.2	5.5±0.5	-0.2

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 HbA1c and fasting insulin difference between LCHF and LFD (Part 8)

HbA1c (%)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change %	Baseline MEAN±SD	Change %
1992	Garg et al. (126)	3 weeks	-0.7	8.7±1.1	-1.6	8.7±1.1	-0.9
2003	Samaha et al. (129)	26 weeks	-0.6	7.8±1.2	-0.6	7.4±1.5	0
2004	Stern et al. (133)	0-52 weeks	-0.7	7.4±1.6	-0.8	7.3±1.1	-0.1
2005	Yancy et al. (136)	16 weeks	-	7.5±1.4	-1.2	-	-
2009	Davis et al. (147)	0-12 weeks	-0.38	7.5±1.5	-0.64	7.4±1.4	-0.26
2009	Davis et al. (147)	0-26 weeks	-0.14	7.5±1.5	-0.29	7.4±1.4	-0.15
2009	Davis et al. (147)	0-52 weeks	-0.26	7.5±1.5	-0.02	7.4±1.4	0.24
2010	Iqbal et al. (150)	0-26 weeks	-0.2	7.9±1.7	-0.5	7.6±1.3	-0.3
2010	Iqbal et al. (150)	0-52 weeks	0.2	7.9±1.7	-0.1	7.6±1.3	-0.3
2010	Yancy et al. (151)	48 weeks	1.2	6.2±1	-4.2	6.4±1.4	-5.4
2017	Saslow et al. (156)	32 weeks	-0.5	7.1±0.4	-0.8	7.2 ±0.3	-0.3

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Fasting insulin (pmol·L^{-1})

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change pmol·L^{-1}	Baseline MEAN±SD	Change pmol·L^{-1}
1992	Garg et al. (126)	3 weeks	-200	2470±594	198	2390±528	398
2003	Brehm et al. (127)	0-12 weeks	-116.5	101.4±1.8	-31.8	23.9±2.34	84.7
2003	Brehm et al. (127)	0-26 weeks	18	101.4±1.8	-15	143.4±2.34	-33
2003	Samaha et al. (129)	26 weeks	-122	132±120	-116	108±10	6
2003	Samaha et al. (129)	26 weeks	-48	240±252	-48	216±26	0
2004	Meckling et al. (131)	10 weeks	-36.6	142.2±2.7	-40.8	125.4±1.3	-4.2
2004	Sharman et. al. (132)	6 weeks	-42.3	77.1±32.7	-32	45.1±27.5	10.3
2004	Stern et al. (133)	0-52 weeks	-63	153±139	-49	160±299	14
2004	Stern et al. (133)	0-52 weeks	-7	292±333	-35	229±174	-28
2004	Volek et al. (135)	4 weeks	-13.1	41±21.6	-3.6	41±21.6	9.5
2005	Dansinger et al. (137)	0-8 weeks	-20.4	132±16	-30.6	180±18	-10.2
2005	Dansinger et al. (137)	0-26 weeks	13.8	132±16	-13.8	180±18	-27.6
2005	Dansinger et al. (137)	0-52 weeks	199.8	132±16	-7.2	180±18	-207
2005	McAuley et al. (138)	0-26 weeks	-3.4	83.5±0	-28.5	87.8±0	-25.1
2005	McAuley et al. (138)	0-52 weeks	10	83.5±0	-21.7	87.8±0	-31.7
2006	Noakes et al. (125)	12 weeks	-29.4	64.2±1.1	-21.6	51.6±0.7	7.8
2007	Gardner et al. (142)	0-8 weeks	-11.4	60±7	-18	60±5	-6.6
2007	Gardner et al. (142)	0-26 weeks	-24	60±7	-24.6	60±5	-0.6
2007	Gardner et al. (142)	0-52 weeks	-27.6	60±7	-28.8	60±5	-1.2
2008	Shai et al. (145)	104 weeks	-84.6	84.6±10.2	-84.6	0	0
2009	Volek et al. (148)	12 weeks	-40	107±87	-53	70±47	-13
2009	Volek et al. (148)	12 weeks	-467	1032±901	-503	609±306	-36
2013	Gu et al. (153)	0-4 weeks	-73.8	135±4	-73.8	-	-
2014	Bazzano et al. (155)	52 weeks	10.4	102.8±63.9	-13.9	105.6±54.9	-24.3
2018	Gardner et al. (157)	52 weeks	-0.2	15.5±8.0	-2.9	15.9±13.5	-2.7

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 HOMA-IR & systolic blood pressure difference between LCHF and LFD (Part 9)

HOMA-IR

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change	Baseline MEAN±SD	Change
2004	Sharman et. al. (132)	6 weeks	-1.08	2.49±1.05	-1.08	1.41±0.97	0.33
2004	Volek et al. (130)	4 weeks	-0.18	1.28±0.68	-0.18	1.28±0.68	0.35
2008	Pérez-Guisado et al. (144)	12 weeks	0	0±0	0	0	0
2008	Shai et al. (145)	104 weeks	-3.2	3.2±2.9	-3.2	2.9±1.8	-2.9
2009	Volek et al. (148)	12 weeks	-1.6	2.9±2.5	-1.6	1.7±1.1	-0.3
2013	Gu et al. (153)	0-4 weeks	-	6.1±1.5	-3.8	-	-
2013	Gu et al. (153)	4-8 weeks	-	2.3±0.2	0.5	-	-

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Systolic blood pressure (mm Hg)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change mmHg	Baseline MEAN±SD	Change mmHg
2003	Brehm et al. (127)	0-12 weeks	-5	116±3	-4	115±2	1
2003	Brehm et al. (127)	0-26 weeks	0	116±3	-2	115±2	-2
2004	Meckling et al. (131)	10 weeks	1	125±3	-10	121±2	-11
2004	Stern et al. (133)	0-52 weeks	-2	133±16	1	139±16	3
2005	Dansinger et al. (137)	0-8 weeks	-2.9	129±17	-4	133±17	-1
2005	Dansinger et al. (137)	0-26 weeks	-3.4	129±17	-4	133±17	-1
2005	Dansinger et al. (137)	0-52 weeks	-0.9	129±17	-1	133±17	-1
2005	Yancy et al. (140)	16 weeks	-	135±15	0	-	-
2006	Truby et al. (141)	0-8 weeks	-2.2	135±15	-6	127±15	-4
2006	Truby et al. (141)	8-26 weeks	-0.4	129±13	-1	124±10	-1
2006	Truby et al. (141)	0-26 weeks	-3.1	135±15	-7	127±15	-4
2007	Gardner et al. (142)	0-8 weeks	-5.2	118±11	-7	116±10	-2
2007	Gardner et al. (142)	0-26 weeks	-4.7	118±11	-6	116±10	-2
2007	Gardner et al. (142)	0-52 weeks	-5.7	118±11	-8	116±10	-2
2008	Pérez-Guisado et al. (144)	12 weeks	-15.66	126±5	-17	1±1	-1
2008	Shai et al. (145)	104 weeks	1	131±15	-4	130±2	-5
2009	Davis et al. (147)	0-12 weeks	-4.82	125±18	-6	130±17	-1
2009	Davis et al. (147)	0-26 weeks	36.22	125±18	-1	130±17	-37
2009	Davis et al. (147)	0-52 weeks	3.8	125±18	2	130±17	-2
2010	Foster et al. (149)	12 weeks	-2.54	124±14	-8	125±16	-5
2010	Foster et al. (149)	26 weeks	-0.39	124±14	-7	125±16	-7
2010	Foster et al. (149)	52 weeks	-1.58	124±14	-6	125±16	-4
2010	Foster et al. (149)	104 weeks	-0.09	124±14	-3	125±16	-3
2010	Iqbal et al. (150)	0-26 weeks	-1.2	140±20	-3	140±20	-2
2010	Iqbal et al. (150)	0-52 weeks	6	140±20	-4	140±20	-10
2010	Iqbal et al. (150)	0-104 weeks	-6.7	140±20	-11	140±20	-5
2010	Yancy et al. (151)	48 weeks	-4.44	135±16	-6	129±16	-2
2013	Gu et al. (153)	0-4 weeks	-11.1	135±3	-11	0	0
2013	Liu et al. (154)	12 weeks	-5.3	134±17	-20	131±17	-15
2014	Bazzano et al. (155)	52 weeks	0	120±13	-0.2	125±14	-0.2
2018	Gardner et al. (157)	52 weeks	-1.1	123±12.4	-4	123±13	-2.9

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

Table 1-1 Diastolic blood pressure & C-reactive protein difference between LCHF and LFD (Part 10)

Diastolic blood pressure (mm Hg)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change mmHg	Baseline MEAN±SD	Change mmHg
2003	Brehm et al. (127)	12 weeks	-7	79±3	-7	75±2	0
2003	Brehm et al. (127)	26 weeks	-4	79±3	-5	75±2	-1
2004	Meckling et al. (131)	10 weeks	-1.1	78±4	-6	78±3	-5
2004	Stern et al. (133)	0-52 weeks	2	77±11	3	82±9	1
2005	Yancy et al. (140)	16 weeks	-5.1	79±15	-5	1±1	0
2006	Truby et al. (141)	0-8 weeks	0.5	83±11	-3.6	80±11	-4
2006	Truby et al. (141)	8-26 weeks	-0.3	79±8	-1.1	76±7	-1
2006	Truby et al. (141)	0-26 weeks	-0.5	83±11	-4.9	80±11	-4
2007	Gardner et al. (142)	0-8 weeks	-2.5	75±8	-2.9	75±8	0
2007	Gardner et al. (142)	0-26 weeks	-2.3	75±8	-3.3	75±8	-1
2007	Gardner et al. (142)	0-52 weeks	-3.7	75±8	-4.4	75±8	-1
2008	Pérez-Guisado et al. (144)	12 weeks	-9.28	85±3	-9.3	-	-
2008	Shai et al. (145)	104 weeks	0.1	79±9	-0.8	79±9	-1
2009	Davis et al. (147)	0-12 weeks	-1.8	73±9	-2.2	77±10	0
2009	Davis et al. (147)	0-26 weeks	-1.88	73±9	-0.9	77±10	1
2009	Davis et al. (147)	0-52 weeks	-0.7	73±9	-2.9	77±10	-2
2010	Iqbal et al. (150)	0-26 weeks	3.5	79±10	1	80±12	-3
2010	Iqbal et al. (150)	0-52 weeks	3.8	79±10	-1.2	80±12	-5
2010	Iqbal et al. (150)	0-104 weeks	0.5	79±10	-3.8	80±12	-4
2013	Gu et al. (153)	0-4 weeks	-6	83±2	-6	-	-
2013	Liu et al. (154)	12 weeks	-3	87±8	-10.8	86±10	-8
2014	Bazzano et al. (155)	52 weeks	-0.7	78±9	-0.5	79±8	0.2
2018	Gardner et al. (157)	52 weeks	-1	81±8	-3	81±7	-2

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

C-reactive protein ($mg \cdot L^{-1}$)

year	Author	Duration	Difference LCHF - LFD	Baseline MEAN±SD	Change $mg \cdot L^{-1}$	Baseline MEAN±SD	Change $mg \cdot L^{-1}$
2005	Dansinger et al. (137)	0-8 weeks	0.28	4.4±3.8	-0.33	4.4±3.5	-0.61
2005	Dansinger et al. (137)	0-26 weeks	-0.01	4.4±3.8	-0.71	4.4±3.5	-0.7
2005	Dansinger et al. (137)	0-52 weeks	0.18	4.4±3.8	-0.7	4.4±3.5	-0.88
2006	Noakes et al. (125)	12 weeks	0.34	5.27±0.71	-0.76	4.52±0.78	-1.1
2008	Shai et al. (145)	104 weeks	2.66	4.5±3.3	-0.95	3.6±2.9	-3.6
2014	Bazzano et al. (155)	52 weeks	1.8	46.7±40	-6.7	46.7±48.6	-8.5

Note: Diff. Between groups, (−) sign denotes better outcome for LCHF.

LCHF= Low CHO diet / LFD= Low fat diet / SD= Standard deviation / LCHF-LFD= difference between intervention / Change= difference between post intervention result and baseline (+) indicates weight gain, (-) indicates weight loss and so forth / kg= kilograms / cm= centimetres / mmol·L-1l millimoles per litre / % = percent / pmol·L-1= picomole per litre / mmHg = millimetres of mercury / mg·L-1 = milligrams per litre.

Exercise and the prevention of type 2 diabetes and obesity, therefore metabolic syndrome

Physical activity plays a very crucial role in improving aerobic fitness (36), glycaemic control and insulin sensitivity, and the maintenance of fat-free mass during energy restriction for weight loss (158). Nevertheless, exercise has been underutilised in this regard (159) perhaps for two main reasons: the first being high levels of attrition on exercise interventions (160) due to a patients' persistent excuse of lack of time (36, 159), fatigue, and the idea of not being in control of the situation, regardless of their ability to perform the exercise or not (161); and the second is the physicians' limited knowledge of how to use it effectively (162, 163). Hence, most are not willing to prescribe exercise to people with T2DM (164). Physical activity guidelines indicate that most adults will respond positively to accumulating at least 150 min of aerobic exercise of moderate activity or 75 min of vigorous intensity exercise and at least two sessions of resistance exercise per week, though smaller amounts of activity still provide some health benefits (36, 165).

Diabetes Canada's 2018 Clinical Practice Guidelines for Physical Activity for Diabetes (36) dedicates a predominant amount of its recommendations to HIIT and RT, while the latest American College of Sport Medicine and the American Diabetes Association Position Statement recommendations for Diabetes, and Exercise and Sports Science Australia (159, 166) specifically tailored for type 2 diabetes, has shown evidence that identifies RT and HIIT are very potent exercise modalities that promote glycaemic and metabolic control (167-169).

The metabolic effects of exercise are divided into acute (which are immediate and transient) effects, and a succession of new iterations of a similar stimulus which can create chronic effects. These may not last any longer than 48-72 h unless another repetition is produced within that period; if that happens these effects could extend beyond that time. Commonly named as training effects, these are more durable physiological adaptations that may last or eventually diminish if not continued to be carried out up to the level of maintenance (physical activity) that is provided. These adaptations cannot be understood without one another (170).

Acute effect of exercise for metabolic health

There is evidence demonstrating that a single exercise session of aerobic or resistance training can reduce glycaemia in individuals with or without a metabolic disease (37, 171, 172), and that is important because the cumulative effect is responsible for its long-term effect (training effect). For this reason, it is essential to assess its acute effect and have adequate information to plan and implement training programmes for maintaining and improving metabolic health. The acute effect of a single

exercise session is also responsible for the effect on energy expenditure and lipid oxidation in the long term. As it happens with most performance, after some time the improvements may be of a small magnitude, but knowing the acute effect is going to be beneficial is helpful for developing training strategies.

Acute effect of exercise and glycaemic control

Aguiar et al. (173) tested the hypoglycaemic effect of a single RT session in 89 normoglycaemic adults with at least 6 months RT experience, BMI< 30 $kg \cdot m^{-2}$ and an average age of 29.1±3.4 years, separated into six groups that completed RT protocols consisting of 8 exercises on the following exercise machines: (bench press, leg press 45°, seated row, leg extension, shoulder press, leg curl, triceps pulley, barbell curls): Group1, control session (n = 12); Group 2, circuit (2 × 18 at 50% of 1RM; n = 12); Group 3, 2 sets of 18 repetitions (2 × 18 at 50% of 1-repetition maximum (1RM); n = 19); Group 4, 3 sets of 12 repetitions (3 × 12 at 70% of 1RM; n = 14); Group 5, 4 sets of 9 repetitions (4 × 9 at 80% of 1RM; n = 13); and Group 6, 6 sets of 6 repetitions (6× 6 at 90% of 1RM; n = 19). At the end of the exercise a 75g oral glucose tolerance test was conducted with metabolic measurements every 15 min starting immediately after each RT protocol until 120 min of recovery was reached. All groups had significantly lower values ($p < 0.05$) in the glucose area under the curve (AUC) when compared with the control over a 120 min monitoring period. The 6 × 6 protocol (Group 6) showed a significantly lower glucose AUC vs 3 × 12 protocol (Group 4) and 4 × 9 protocol (Group 5) ($p = 0.004$; $p = 0.001$, respectively). As for blood lactate, the control (Group 1) and 6 × 6 protocol (Group 6) exhibited lower AUC values versus all other groups ($p < 0.05$), and AUC for glucose and lactate concentration showed a negative and significant correlation ($r = –0.46$; $p < 0.001$). The authors concluded that it appears a combination of 9-12 repetitions per set and 3-4 sets per muscle group might be optimal for acute postprandial glucose control (See Table 1-2 part 1).

Parker et al. (171) attempted to clarify if HIIT had the same acute hypoglycaemic response as moderate intensity continuous training (MICT), as the effects of intensity have not been fully elucidated. They compared a HIIT protocol consisting of a 5 min warm-up, 8 × 1- min cycling bouts at 100% of Wmax (175 ± 19 W), interspersed with 1-min active recovery periods cycling at 50 W. A 3-min cooldown was instigated at 50% of Wmax (total workout session 24 min) vs a MICT that consisted of 38 min (79 ± 9 W) of continuous cycling at 50% of Wmax. Continuous glucose monitoring was conducted the previous and following day of the exercise session. Standard breakfast, lunch and dinner were provided during the four days that testing lasted; meals were based on sex, height and weight, and consisted of approximately 55% CHO, 30% fat and 15% protein. Twenty-seven inactive, overweight participants were randomly divided between the two exercise modalities, and their characteristics were similar between interventions. Acute exercise significantly decreased postprandial

glycaemia in whole blood (−6 ± 5%, $p< 0.01$), irrespective of the exercise protocol. Acute exercise provided a similar significant improvement in 24-h average glucose levels (−5 ± 2%, $p< 0.01$), and hyperglycaemic excursions (−37 ± 60%, $p< 0.01$). The authors concluded that given its time-efficient nature, HIIT might be an effective exercise mode to incorporate into exercise programmes for the improvement of 24-h glycaemic control in inactive, overweight and obese adults (See Table 1-2 part 2).

Francois et al. (174) studied the effects of brief intense exercise, denominated as 'exercise snacks', 6x1 min intense (90% of maximal heart rate [HRmax]) incline walking interspersed with one min rest, compared to the control of 30 min of incline walking (60% HRmax). The exercise snacks attenuated by 1.4±1.5 mmol/l, $p= 0.02$, the mean 3-h postprandial glucose concentration following breakfast and dinner by a difference of 0.7 ± 1.5 mmol·L^{-1} $p= 0.04$, but not lunch (0.4±1.0 mmol·L^{-1}, $p= 0.22$). After 24-h, the exercise snacks also improved the 24-h mean glucose concentration by 0.7 ± 0.6 mmol/l ($p= 0.010$) vs control. The authors concluded the ‘exercise snacks’ before main meals were a time-efficient and effective approach to improve glycaemic control, this way confirming the hypothesis that small doses of brief, intense exercise before each main meal (‘exercise snacks’) would result in better blood glucose control than a single bout of prolonged, continuous, moderate-intensity exercise in individuals with insulin resistance (174) (See Table 1-2 part 2).

Gillen et al. (175) investigated the acute effects of the first exercise session of Little et al. (167) that comprised a HIIT protocol of 10 x 60 s cycling bouts at 90% HRmax, interspersed with 60 s of recovery at 50 watts, a less demanding HIIT session they referred to as low volume HIIT; ideal for unfit individuals (see High-intensity interval training; the new time efficient aerobic training section). Seven T2 diabetic participants underwent CGM on a non-exercise day (control; CTRL) and an exercise day under standardised conditions. It was found HIIT reduced hyperglycaemia, measured as a proportion of time spent above 10 mmol/l ($p=0.040$). Postprandial hyperglycaemia, measured as the sum of post-meal areas under the glucose curve (AUC), was also lower after HIIT vs CTRL ($p=0.010$). It was concluded that HIIT had potential to improve glycaemic control in T2DM. (See Table 1-2 part 1).

Finally, Little et al. (17) used the same HIIT protocol (Little et al. 2011, Gillen et al. 2012) (167, 175) and compared the acute effects of HIIT vs moderate intensity continuous training (MICT) which consisted of 30 min at approximately 65% peak heart rate (HRpeak). Postprandial glucose (PPG) responses to lunch did not change, but performing both HIIT and MICT in the morning significantly ($p<0.050$) reduced the PPG incremental AUC following dinner when compared with the control day. All meals were standardised, given prepacked and preweighed with instructions detailing the timing for their ingestion, covering the 48 h period of the testing period. The PPG AUC and the PPG spike

following breakfast on the following day were all significantly lower following HIIT compared with both MICT and the control. Little et al. (17) concluded that a single session of HIIT has greater and more lasting effect on reducing incremental PPG when compared with MICT (See Table 1-2 part 1). Together, this collection of studies (17, 167, 175) indicates that HIIT seems to be effective for glucose control because it may produce a greater glucose uptake post exercise and this is evident when using CGM to measure postprandial glycaemia and it has greater and more lasting effects when compared to MICT after having a standardised meal and despite the exercise HIIT duration being shorter. This is important because endothelial function is affected by postprandial hyperglycaemia. Glucose excursions can also promote oxidative stress directly, impairing flow-mediated dilation which measures endothelial function; reducing nitric oxide bioavailability and activate inflammatory pathways. Due to this, endothelial dysfunction plays a pivotal role in the development, progression, and clinical complications of atherosclerosis.

Acute effect of exercise and energy expenditure

Rozenek et al. (176) investigated and compared the acute cardiorespiratory and metabolic responses to four HIIT protocols consisting of 1 min x 10 work phases interspersed with 1 min recovery phases that differed in work to rest intensity ratios (a) 80% - 0% peak power output (PPO); (b) 80% - 50% PPO; (c) 100% - 0% PPO; and (d) 100% - 50% PPO. Eleven healthy adults volunteered to perform the four HIIT sessions on separate occasions. It was hypothesised that HIIT interval training protocols incorporating the 100% PPO work interval intensities would produce the highest observed average, peak, and nadir cardiorespiratory and metabolic responses. The researchers found that compared to the other protocols the 100% - 50% PPO produced the highest peak average and nadir % $\dot{V}O_2$peak ($p<0.050$). All trials except the 80% - 0% PPO (that obtained the lowest % $\dot{V}O_2$peak), obtained nadir values that were between the recommended ACSM intensities to improve cardiorespiratory fitness (45-90% $\dot{V}O_2$max; 65-90% HRmax). Similarly, average HR and peak HR, RPE, blood lactate, and % $\dot{V}O_2$peak values were produced by 80% - 50% PPO and 100% - 0% PPO protocols. However, even if the intensity was lower, the average %$\dot{V}O_2$peak was significantly higher (9.3% absolute) in 80/50. According to the researchers, it appeared that using the 80% - 0% PPO, 80% - 50% PPO, and 100% - 0% PPO protocols might be for individuals who are at the low to moderate end of the cardiorespiratory fitness spectrum. Given the close and direct relationship of energy expenditure with oxygen utilisation it can be implied that exercise protocols that exerted the greater $\dot{V}O_2$peak are those that can provide a greater energy expenditure, therefore it is why this study was included in this this section of this review (See Table 1-2 part 4).

Schaun et al. (177) compared the acute effects during and after a single session of HIIT vs aerobic exercise training (AET) on energy expenditure (EE), in 26 male adults between 18-35 y. Participants were randomised to either HIIT (n=14) that consisted of 8x20 s at 130% of the velocity associated with the maximal oxygen consumption on a treadmill with 10 s of passive rest, or AET (n = 12) which consisted of 30 min running on a treadmill at a submaximal velocity equivalent to 90-95% of the heart rate associated with the anaerobic threshold. At baseline, both groups had similar $\dot{V}O_2$. During exercise, absolute EE (total kcal) (HIIT=52.78±7.5 kcal min^{-1} vs AET=390.45±65.15 kcal min^{-1}) and $\dot{V}O_2$ (HIIT=10.45±1.48 vs AET=80.5±13.43 L·O_2) were higher for AET. When this was expressed in terms of kcal min^{-1} and L·O2·min^{-1}, both exercise modalities had similar values (HIIT= 14.36 ± 2.34 kcal·min^{-1} vs AET= 13.21 ± 2.08 kcal·min^{-1}), mean $\dot{V}O_2$ for HIIT= 2.84±0.46 L·min^{-1}; vs AET= 2.72±0.43 L·min^{-1}during exercise. At the end of the session during the early phase of recovery, things were different; the total EE and $\dot{V}O_2$ now were significantly greater for HIIT, (HIIT=69.31±10.88 kcal vs AET=55.99±10.20 kcal) and (HIIT=14.29±2.25 L O_2 vs AET=11.55±2.10 L O_2) respectively. These differences remained significant when expressed regarding time $\dot{V}O_2$: (HIIT=0.48±0.08 L·min^{-1} vs AET=0.39±0.07 L·min^{-1}) and also for EE: (HIIT 2.31±0.36 kcal·min^{-1} vs AET=1.87±0.34 kcal·min^{-1}). For the excess post-exercise oxygen consumption (EPOC) EE and $\dot{V}O_2$ were also significantly greater for HIIT (HIIT=26.27±6.28 kcal vs AET=13.43±10.45 kcal), (HIIT= 5.41±1.30 L O_2 vs AET=2.77±2.15 L O_2) respectively. The authors concluded that this data suggested supramaximal HIIT had a higher impact on EE and EPOC in the early phase of recovery when compared to AET (See Table 1-2 part 4).

Likewise Paoli et al. (178) observed that intensity plays an important part when it comes to EE, after a session of either high-intensity interval resistance training (HIIRT) or traditional RT despite traditional RT requiring more time. When participants performed HIIRT, resting energy expenditure (REE) was significantly greater within and in relation to traditional RT whose REE was significantly greater between baseline and 22 h after the exercise session. The RQ was lower for HIIRT ($p< 0.001$). and significantly greater than RT that did not show any difference within the group. From their study it can be concluded that RT is an effective modality to increase REE while HIIRT can improve RQ as well as intensity being a decisive factor for these changes to occur (See Table 1-2 part 3).

Using a randomised crossover design, Steele et al. (179) evaluated the effects of high-intensity interval aerobic exercise and RT on $\dot{V}O_2$, respiratory exchange ratio (RER), blood lactate, energy expenditure, muscle swelling, and electromyography in a sample of nine healthy males and ordinarily active adults, under approximate iso-time and iso-intensity conditions. Exercise regimes were as

follows: RT consisted of a leg press exercise (4×60 s sets of 12-RM) using a tempo of 2 s concentric and 3 s eccentric phases of each repetition. A metronome controlled the tempo of the repetitions. High-intensity aerobic exercise used a recumbent cycle ergometry; 4x60 s intervals with a resistance that was barely allowed to culminate the allotted duration, had at least a cadence of 80 rpm. Both modalities work intervals had 240 s passive breaks interspersed. Perceived effort was similar, and no significant effects of condition were noted in any of the physiological responses assessed (all $p>0.050$). Authors concluded that when high-intensity aerobic exercise and RT are performed under the same conditions and the same muscle mass is involved, both exercise modalities produced similar responses; therefore, it is sensible to suggest that both may offer a similar stimulus to produce chronic physiological adaptations in outcomes such as cardiorespiratory fitness, strength, and hypertrophy. Also, the authors recommended that future research should look to both replicate this study assessing the same and additional physiological measures, and rigorously test the comparative efficacy of effort and duration matched exercise of differing modalities concerning training improvements in physiological fitness (See Table 1-2 part 5).

In summary this research suggest that high-intensity interval training and RT are both effective means to increase energy expenditure after a single exercise session, while higher effort/intensity due to a heavier load can enhance REE to a greater extent and even reduce RQ post RT. When effort and duration are matched for HIIT and RT and the same muscle mass is involved, it is possible that both exercise modalities may elicit similar physiological responses in $\dot{V}O_2$, RER, blood lactate, energy expenditure and may offer similar cardiorespiratory fitness, strength and hypertrophy.

Acute effect of exercise and blood pressure

Blood pressure is another parameter that is directly related to cardiovascular health, both aerobic and resistance exercises have been found effective in reducing systolic and diastolic blood pressure with a more accentuated effect in systolic blood pressure. A recent example is a study performed by Viana et al. (28) where eleven participants with T2DM (age= 52.3 ± 3y) participated in a randomised crossover design to assess the effectiveness of self-prescribed HIIT vs MICT, having blood pressure as one of the variables of interest. Participants underwent a HIIT session in a randomised order (7x1 min interspersed with 2 min active recovery RPE 16-17 or 85% 5 bpm heart rate reserve (HRR), recovery periods at 9-11 RPE or 50% 5bpm HRR) prescribed and self-regulated by RPE, HIIE prescribed and regulated by HR, MICT (26 min jogging RPE 11-14) prescribed and regulated by RPE and a control. Ambulatory 24-h BP was measured after each intervention. Researchers found that only HIIT self-

regulated with RPE showed a reduction in 24-h ambulatory blood pressure (6.7±2.2 mmHg p<0.050) and tendency towards a reduction in daytime systolic blood pressure (7.0±2.5 mmHg p= 0.060). The authors (28) concluded that HIIT was effective in reducing systolic blood pressure and that it was feasible prescribing HIIT based on RPE (See Table 1-2 part 5).

Another example that shows the acute effects of exercise on reducing blood pressure is a study by Morais et al. (180) that demonstrated that RT was more effective than aerobic exercise in improving this parameter in the subsequent 24-h after a single session of either aerobic exercise [20 min cycling @90% of lactate threshold (LT)] vs RT (3 x a circuit with 6 exercises, 8 reps @ 70% 1-RM interspersed with 40 s of recovery) and a non-exercise control session. Ten participants with T2DM participated (age: 55.8±7.7 years; weight: 79.4±14.0 kg; fasting glucose: 7.38±2.04 mmol·L^{-1}). Apart from BP, researchers also assessed HR, mean arterial (MAP) and pulse (PP) BP, as well as lactataemia (Lac), $\dot{V}O_2$, respiratory exchange ratio (RER) and RPE measured at rest, during exercise and control (CON) periods, and 60 min after interventions. BP was also monitored over a 24 h period after each session. Only RT registered a post-exercise BP reduction compared to control, that lasted 8-h after exercise. Comparing pre-exercise rest BP, the BP dip during sleep was greater for RT ($p < 0.050$). Morais et al. (180) concluded that RT was more effective for improving BP after a single bout for individuals with T2DM than aerobic exercise (see Table 1-2 part 6).

Table 1-2 Acute effect of exercise, part 1 glycaemic control

Study characteristics	Primary findings				
Gillen et al. 2012 (175) DESIGN: Experimental controlled trial n= 7 individuals with T2DM that acted as as their own controls. Duration: 2 days Sessions: 1 CTRL: non exercise session Exercise HIIT= 10 x 60-s cycling bouts ~90% HRmax interspersed with 60 s rest. Std. Diet: E: 1704 ± 226 kcal CHO 52±5% PRO: 18 ± 3% FAT: 30 ± 7%	*Average post-meal peak glucose concentration (mmol•L^{-1})				
		HIIT	CTRL	DIFFERENCE HIIT – CTRL	
		9.1 ± 1.9	10.8 ± 2.5	-1.7	p <0.001
	**Average blood glucose 60–120 min following meals (mmol•L^{-1})				
		8.0 ± 1.6	9.3 ± 2.3	-1.3	p <0.001
	***Average time spent in hyperglycaemia (%)				
		4.5 ± 4.4	15.2 ± 12.3	-10.7	p =0.040
	24-h average blood glucose (mmol•L^{-1})				
		7.2 ± 1.2	7.8 ± 1.1	-0.6	p =0.160

*Average 3-h post-meal (lunch, dinner and breakfast) glucose area under the curve (AUC).
*Post-meal peak glucose concentration and average post-meal glucose calculated from 24-h CGM dat
***Average time spent in hyperglycaemia (≥10 mmol·L^{-1}) over 24-h. T2DM= type 2 diabetes mellitus;
= high-intensity interval training; CTRL= control; HRmax= maximal heart rate; E= energy; kcal= kilocalo
PRO= protein; CHO= carbohydrate; FAT= lipids; mmol•L^{-1}= millimoles per litre.
Difference between HIIT and CTRL, a negative sign indicates better outcome for HIIT

Little et al. 2014 (17) n= 10 overweight or obese individuals that acted as well as controls Duration: 3 days Sessions: 1 per type of exercise CTRL= no exercise Exercise HIIT= 10 x 60-s cycling bouts ~90% HRpeak interspersed with 60 s rest. MICT: 30 min at ~65% HR_{peak} Diet E=29 kcal•kg^{-1} CHO= 66±4% PRO=11±2% FAT=23±2% All meals were standardised, prepacked preweighed with instructions detailing the timing for each of the meals provided covering the. 48 h period of the experimeal trial.					DIFFERENCE HIIT - MICT	
		CTRL	HIIT	MICT		
	PPG incremental AUC to dinner after exercise morning mmol•L^{-1}× 2 h					
		162 ± 46	110 ± 35	125 ± 34	-15	(all p<0.050)
	PPG AUC breakfast one day after exercise mmol•L^{-1}× 2 h					
		194 ± 96	125 ± 53	186 ± 55	-61	
	PPG spike (mmol•L^{-1})					
		3.0 ± 1.5	2.1 ± 0.9	3.0 ± 0.9	-0.9	(all p< 0.050)

Difference between HIIT and MICT, a negative sign indicates better outcome for HIIT
PPG= postprandial glycaemia AUC= area under the curve; HIIT= high-intensity interval exercise;
MICT= moderate intensity continuous exercise; CTRL= control. HRpeak=
peak heart rate; h= hours; s= seconds; E= daily energy intake; kcal= kilocalories;
CHO= carbohydrate; PRO= protein; FAT= lipids; mmol•L-1= millimoles per litre.

Table 1-2 Acute effect of exercise part 2 glycaemic control

Francois et al. 2014 (174)
DESIGN: Experimental within-participants randomised cross over design (MICT, RT based interval exercise, and walking-RT based interval exercise)

n= 7♂, 2♀ T2DM adults

Exercise
MICT: Incline walking @60% HRmax
Total exercise: 30-min. When: 30 min before evening meal.

HIIT: 6x60-s intense walking @ 90% HRmax interspersed with 60-s of light walking.
Total Exercise: 12 min.
When: 30 min before breakfast, lunch & dinner.

Combined: HIIT + alternating betweer walking and resistance based exercise.

Total exercise: 12 min. When: 30 min before evening meal & dinner

Exercise regime Blood glucose concentration (mmol•L^{-1})
mean ± SD of variation within participants
Glycaemia across each day over the intervention

	HIIT	MICT	COMBINED	DIFFERENCE HIIT - MICT	DIFFERENCE COMBINED - MICT
Baseline day	6.55±1.13	6.37±0.87	6.63±1.11	0.18	0.26
Exercise day	6.04±0.84*†	6.74±1.17	5.95±0.87	-0.7	-0.79
Day after exercise	6.07±0.73†	6.48±1.03	6.28±0.91	-0.41	-0.2

*p <0.050 for HIIT vs MICTon exercise day (main effect)
† p<0.050 for HIIT vs MICT compared with baseline day (interaction effect)
T2DM= type 2 diabetes mellitus; HIIT= high-intensity interval exercise; MICT= moderate intensity continuous exercise; HRmax= maximal heart rate; s= seconds; mmol•L^{-1}= millimol per litre.

Differences are between HIIT or COMBINED vs MICT a negative result indicates a better outcome for HIIT or COMBINED

Parker et al. 2017 (171)
DESIGN: Experimental randomised trial
n=27
LV-HIIT n=14 9♀, 5♂
MICT n= 13 8♀, 5♂
Sedentary at risk of T2DM, ♀ with or without PCOS
Duration: 1 session

Exercise
LV-HIIT:
8 x 1 min @100% Wmax (175±19 W)
interspersed 60-s @50 W
Total exercise 24 min.
MICT:
38±1 min @50% Wmax (79±9 W)
Exercise performed after a standardised breakfast (55%CHO, 15%PRO, 30% FAT).

CGM (mmol·L^{-1})	LV-HIIT Ex day	MICT Ex day	DIFFERENCE LV-HIIT - MICT
Breakfast	5.3 ± 0.3	5.4 ± 0.4*	-0.1
Breakfast (1st h) before exercise	5.4 ± 0.2	5.8 ± 0.4	-0.4
Breakfast (2nd h) after exercise	4.5 ± 0.2*	5.0 ± 0.4*	-0.5
Lunch	5.1 ± 0.1	5.7 ± 0.3	-0.6
Dinner	4.6 ± 0.2*	5.7 ± 0.3*	-1.1

*p < 0.050 significantly different from the rest of the day
LV-HIIT= low volume high-intensity interval exercise; MICT= modrate intensity continuous exercise; T2DM= type 2 diabetes mellitus; PCOS= polycystic ovary syndrome; W= watts; continuous glucose monitoring; CHO= carbohydrate; PRO= protein; FAT= lipids; mmol•L^{-1}= millimol per litre; s= seconds; h= hours.
Difference are between LV-HIIT and MICT a negative sign indicates a better outcome for LV-HIIT

Table 1-2 Acute effect of exercise part 3 energy expenditure

Aguiar et al. 2018 (173)

DESIGN: Experimental crossover design
n= 89
A) Control = 12
B) Circuit = 12
C) 2x18 = 19
D) 3x12 = 14
E) 4x9 = 13
F) 6x6 = 19

Healthy young adult individuals physically

active with 6 months RT experience
Duration: 1 session
Exercise

RT exercises same for all protocols:
Bench press,seated row,
shoulder press, triceps pulley,
barbell curls, leg press 45°,
leg extension, and leg curl.

Control A= No exercise

Circuit B= 2x18 @ 50% 1-RM no rest

Circuit C= 2x18 50% 1-RM rest=10-15 between each exercise and 30 s between each set.

Circuit D= 3x12= 70% 1-RM rest=10-15 s between each exercise and 60 s between each set.

Circuit E= 4x9=80% 1-RM rest=10-15 s between each exercise and 90 s between each set.

Circuit F= 6x6= 90% 1-RM rest=10-15 s between each exercise and 120 s between each set.

Resistance exercise protocols with 9 — 12 repetitions with 3—4 sets per muscle group

appear to be optimal for postprandial glycaemic control.

Clinical application

It is possible to improve metabolic health with the utilisation of

acute resistance exercise protocols that involve circuit like training exercises at an intensity

of 70 - 80% 1RM that can improve glucose uptake by increasing the glycolytic energy system

leading to decrease postprandial insulin levels; these protocols may be ideal.

RT= resistance training; 1RM= one repetition maximum.

Paoli et al. 2012 (178)

DESIGN: Experimental crossover design
HIRT vs RT
n= 17 ♂

Healthy young adult individuals
physically active with
6 months RT experience

1 session 1 wk appart between exercise modality

HIIRT=
2 sets bench press, 2 sets lat pull and 3 sets leg press
Each set consisted of:
6 reps, 20-s rest
2-3 reps, with 20-s rest,
Intensity: 6RM (~ 80-85% 1RM)

RT
4 sets bench press, 4 sets dorsal machine
4 sets military press, 4 sets bicep curls
4 sets triceps extensions, 4 sets leg pre
4 sets leg curls and 4 sets leg curls.
Each set:
8-12 reps with 60-120-s rest
Intensity: 12 RM (~ 65–70% 1RM)

REE and RQ was measured via indirect calorimetry at baseline and 22 h after exercise session

		HIRT	RT	DIFFERENCE
Baseline				HIIRT - RT
	REE (kcal•24 h	1910 ± 90	1901 ± 93*	9
	RQ	0.83 ± 0.01	0.83 ± 0.01	0
22 h				
	RMR (kcal•24 h	2362 ± 118	1999 ± 89*	363**
	RQ	0.80 ± 0.01	0.82 ± 0.01*	-0.02**

Significance within groups *$p < 0.001$; between groups **$p < 0.001$
HIIRT= high-intensity interval resistance training; RT= resistance training; reps= repetitions; s=seconds; h= hours; 1RM=one repetition maximum; RMR= resting energy expenditure; RQ= respiratory quotient; kcal= kilocalories. Difference HIIRT - RT a negative sign for REE indicates a better outcome for RT; whereas a negative sign for RQ indicates a better outcome for HIIRT

Table 1-2 Acute effect of exercise part 4 energy expenditure

Rozenek et al. 2016 (176)

DESIGN: Experimental randomised cross over design
n= 6♂, 5♀ healthy recreationally active adults
Duration: 1 session

–50% and 100%–0% PPO had similar responses for average HR and peak HR, RPE, blood lactate, and %V̇O2

80%–50% protocol ~ 9.3 higher %V̇O2peak.

Clinical application

These intensities may allow low to moderately fit individuals to gain the benefits of HIIT.
Higher %V̇O2peak may also translate a greater EE during exercise.

Exercise
HIIT
Active Phase | Rest phase
10 60-s | 10 60-s
.@. PPO
a) 80% 0%
b) 80% 50%
c)100% 0%
d)100% 50%

PPO= peak power output, HIIT= high-intensity interval exercise, HR= heart rate, RPE rate of perceived exertion
%$\dot{V}O_2$peak= percentage of peak oxygen uptake

Schaun et al. 2017 (177)
DESIGN: Experimental randomised trial
n= 26♂ healthy currently participating in an aerobic exercise training programmes
HIIT n=14
vs
CTRL n=12
Duration: 1 session

Exercise
HIIT
8 x 20-s @ 130% of maximal velocity associated with $\dot{V}O_2$max
Interspersed with 10-s of passive rest
(treadmill)
Total exercise: 4 min.

vs

CTRL
30 min. running at a submaximal velocity equivalent to 90-95% heart rate associated with ventilatory threshold
Total exercise: 30 min

	HIIT	CTRL	DIFFERENCE HIIT - CTRL
EE during exercise	*52.78 ± 7.50	390.45 ± 65.15	-337.67
EE during post exercise	*69.31 ± 10.88	55.99 ± 10.20	13.32
$\dot{V}O_2$ post (L O_2)	*14.29 ± 2.25	11.55 ± 2.10	2.74
$\dot{V}O_2$ post (L O2•min−1)	*0.48 ± 0.08	0.39 ± 0.07	0.09
EPOC (L O_2)	*5.41 ± 1.30	2.77 ± 2.15	-2.64
EPOC (kcal)	*26.27 ± 6.28	13.43 ± 10.45	-12.84

(*Significant difference between protocols $p < 0.005$)

HIIT= high-intensity interval exercise, HICT= high-intensity continuous exercise,
CTRL= control; $\dot{V}O_2$max= maximal oxygen consumption; $\dot{V}O_2$= oxygen consumption
EE= energy expenditure; EPOC= excess post-exercise oxygen consumption;
L= litres; kcal= kilocalories; s= seconds.
Difference between HIIT and CTRL, a negative sign indicates a better outcome for HIIT

Table 1-2 Acute effect of exercise part 5 energy expenditure and blood pressure

Steele et al. 2018 (179)		RT	AET	DIFFERENCE	
DESIGN: Experimental randomised cross over design		Leg-press	Recumbent bike		
(~ iso time - iso effort)	Mean $\dot{V}O_2$ (ml•kg^{-1}•min^{-1})			RT - AET	
n=9 ♂ healthy adults	Active phase	19.37 ± 6.50	27.33 ± 7.97	-7.96	
HighEffort-RT n=9	Recovery phase	16.00 ± 3.38	17.72 ± 2.78	-1.72	
HighEffort-AET n= 9					
Recreationally active but not involved in	$\dot{V}O_2$ peak (ml•kg^{-1}•min^{-1})				
structured exercise, past 6 months	Active phase	34.75 ± 11.66	39.64 ± 10.79	-4.89	
Duration: 1 session	Recovery phase	34.93 ± 6.81	37.41 ± 8.76	-2.48	
Exercise					
High effort RT:	Mean RER				
Leg-press	Active phase	0.92 ± 0.02	0.99 ± 0.11	-0.07	p =0.014
4 x 1 min @12 RM (2-s concentric, 3-s	Recovery phase	1.10 ± 0.10	1.22 ± 0.13	-0.12	
eccentric) interspersed 240-s of rest					
Total exercise: 240-s min.	Peak RER				
	Active phase	1.12 ± 0.05	1.25 ± 0.13	-0.13	
High-effort AET:	Recovery phase	1.40 ± 0.18	1.53 ± 0.16	-0.13	
Recumbent cycling					
4x60-s sprints @ resistance that allowed	Blood lactate				
no more cycling after 60-s using a minimum cadence of 80 rpm	Active phase	9.68 ± 3.39	9.88 ± 2.88	-0.2	
	Total energy expenditure (EE) (kcal)				
Interspersed with 240-s rest periods					
Total Exercise:	Active phase	68.85 ± 30.80	68.21 ± 35.46	0.64	
240-s	Recovery phase	105.93 ± 26.49	115.57 ± 9.70	-9.64	p =0.022
	Sum of total EE (kcal)	176.59 ± 58.67	95.15 ± 21.53	-18.56	p <0.001
	Muscle thickness				
	Qt (cm) POST	5.66 ± 0.98	5.66 ± 1.04	0	

AET= aerobic exercise; RER= respiratory exchange ratio; EE= energy expenditure; Qt= quadriceps thickness. RT= resistance training; rpm= revolutions per minute; $\dot{V}O2$ peak= peak oxygen uptake; RER= respiratory exchange ratio; s= seconds; ml= millilitres; kg= kilograms; kcal= kilocalories. All mean ± SD.

Viana et al. 2018 (28)							
DESIGN: Experimental randomised cross over design							
n=11 (2 ♂ 9♀)							
sedentary adults withT2DM							
Duration: 1 session							
Exercise		$HIIT_{RPE}$	$HIIT_{HR}$	$MICT_{RPE}$	CTRL	DIFFERENCE	
$HIIT_{RPE}$:						$HIIE_{RPE}$ - $MICE_{RPE}$	
7 x 1 60-s		SBP (mmHg)				$HIIE_{HR}$ - $MICE_{RPE}$	
prescribed and self-regulated	BASELINE	114 ± 13	115 ± 17	116 ± 14	110 ± 14		
@ RPE 16-17 interspersed with 120 s	POST	7*	6*	5*	5*	2	1
active recovery periods	RECOVERY	-1†	1†	0†	3	-1	1
@ RPE 9-11							
Total Exercise:		DBP (mmHg)					
1260-s	BASELINE	75 ± 12	77 ± 12	78 ± 3.5	76 ± 11		
$HIIT_{HR}$:	POST	4	4	3	2	2	1
7 x 1 60-s	RECOVERY	3	0	0	2	-1	1
@ 85% ±5 bpm HRR							
Interspersed with 120-s recovery @ 50%	*: p < 0.05 significant difference vs baseline. †: p < 0.05 significant difference vs post						
±5 bpm HRR prescribed and self-regulated by HR,	T2DM= type 2 diabetes mellitus; RPE= rate of percieved exertion; HRR= heart rate reserve; HR= heart rate; $HIIT_{RPE}$= high-intensity interval exercise self-regulated by RPE; $HIIT_{HR}$= high-intensity interval exercise self regulated by HR; $MICT_{RPE}$= moderate intensity continuous exercise self regulated by RPE; CTRL= consisted of no exercise. SBP= systolic blood pressure; DBP= diastolic blood pressure; mm Hg= millimetres of mercury; bpm= beats per minute; s= seconds.						
Total Exercise: 1260-s	Difference between $HIIT_{RPE}$ and $MICT_{RPE}$, $HIIT_{HR}$ and $MICT_{RPE}$, a negative sign indicates the direction of the HIIT groups.						
$MICT_{RPE}$							
26 min jogging prescribed and regulated							
by RPE 11-14							
Total Exercise: 1560-s							
CTRL							
30 min of rest							

Table 1-2 Acute effect of exercise part 6 blood pressure

Morais et al. 2018 (180)		AE	RT	CTRL	
DESIGN: Experimental randomised cross over design n=10 (3 ♂ 7♀) sedentary adults withT2DM Duration: 1 session	SBP (mmHg)				DIFFERENCE AE – RT
	Resting	129±10.5	129.2±7.7	130.8±8.4	
	24-h	-2	-5*	-2	3
	Walking	0.7	-3.4*	5.8	4.1
	Sleeping	-7.5	-10 †	-6.2	2.5
Exercise RT: 3 x Circuit: Exercises & order leg extensions; bench press; leg press; seated pulley; leg curls; and rowing. 8 reps @12-RM (1-s concentric, 1-s eccentric @ 70% 1-RM) interspersed 40-s of rest between exercises and 60-s between circuits Total exercise: 288-s. (work)	DBP (mmHg)				
	Resting	80.3±8.8	80.5±6.6	79.7±10.1	
	24-h	-1.4	-3.3*	2.5	1.9
	Walking	0.1	-2.4*	4.2	2.5
	Sleeping	-6.7	-7.8†	4.2	1.1
	MAP (mmHg)				
	Resting	101.0±8.4	100.9±6.8	101.3±9.3	
	24-h	-2.8	-4.3*	1.2	1.5
	Walking	-0.8	-2.9*	3.5	2.1
	Sleeping	-9.4	-9.3†	-5.5	-0.1

AE:
Cycling @ 90% LT
Total Exercise:
1200-s (work)

CTRL:
No exercise

T2DM= type 2 diabetes mellitus; AE= aerobic exercise; RT= resistance exercise; CTRL= control, .T= lactate threshold; SBP= Systolic blood pressure; DBP= diastolic blood pressure; MAP= mean arteri blood pressure; 1-RM= one repetition maximum; Resting blood pressure expressed as means (± SD); s= seconds; h= hours; mm Hg= millimetres of mercury. *p < 0.05 vs CTRL; †p < 0.05 vs pre-exercise rest in the same session (-) decrement (no sign) increment. Difference between AE and RT, a (-) negative sign indicates a better outcome for AE

In summary, published evidence of the acute effect of both HIIT and RT, suggests it has the potential to improve glycaemic control, increase EE and reduce blood pressure, which may be as beneficial as aerobic exercise if not better in individuals at risk of developing a metabolic disease. It appears that higher intensities provide a more pronounced improvement in these parameters; however it is not possible to establish yet as to which is the ideal combination. This calls for more research exploring different combinations using high intensities which are achievable when exercise uses various high intensity intervals interspersed with active or passive recovery phases of lighter effort.

Chronic (training) effect of exercise for metabolic control

Resistance training

Resistance training (RT) is a brief, repetitive exercise using body weight (e.g. push-ups), free weights, weight machines, or resistance bands to increase muscle strength and/or endurance. It is useful because it can improve glycaemic control (as reflected in a reduced A1C), decrease insulin resistance, increase muscular strength, lean muscle mass and bone mineral density, leading to enhanced functional status and prevention of sarcopenia and osteoporosis (37). The ideal resistance training

programme has not yet clearly been developed. Ishiguro et al. (37) conducted a meta-analysis with the intention of elucidating what would be an ideal resistance training programme that could maximise glycaemic control that might benefit the most individuals with type 2 diabetes. Studies included were: 1) clinical trials consisting of two groups with and without RT exercise intervention; 2) those with an intervention period of at least 5 weeks; 3) those that clarified that all patients had T2DM; and 4) those that reported or made it possible to estimate the effect size. Results were stratified according to the key characteristics of the participants of the different studies to make it as comprehensive as possible (i.e. mean baseline age, body mass index (BMI), and HbA1c levels) and exercise characteristics (total sets per week, entire sets per bout of exercise, frequency, and intensity). Results integrated 23 studies into the analysis, which comprised of 954 participants; the pooled effect size was -0.34% (-0.53, -0.16) 95% CI. The linear correlation between the number of sets per session that were associated with a larger effect size to programmes with more than 21 sets per session and the opposite to those with less than 21 (p=0.030), by contrast, the number of sets and effect size was not significant (p=0.560). Individuals at baseline who had a shorter diabetes duration (<6 y), (high HbA1c at baseline >58mmol·mol^{-1}), and with a lower BMI <32 kg·m^2 had better outcomes. The authors of the study concluded that RT could be recommended for glycaemic control for individuals with a recent diagnosis, with poor HbA1c,because individuals with advanced T2DM seem to be low-responders to RT and could be more beneficial for those individuals with a BMI between 22.3 and 38.8 kg·m^2.

Hameed et al. (2012) (169) tested an 8-wk progressive resistance training (PRT) protocol on health outcomes compared to a control group (n=24; Table 1), both with T2DM. The intervention group undertook 10-min warm up and five resistive exercises using machines at 65-70% of their predicted 1-repetition maximum (1-RM), 8-wk of PRT led to clinically meaningful improvements in glycaemic control, HDL-C, muscle strength and waist circumference (all p≤0.008). The rest of the parameters did not show any significant modification. Table 1-3 part 1 presents Hameed's results comparing PRT to a control group after 8 weeks of training.

In another study Hansen et al. (181) compared maximal resistance training (MRT) vs endurance resistance training (ERT) on improvements in insulin levels and glucose tolerance (fasting and 2-hour test), insulin and C-peptide measurements in two groups of pre-diabetic individuals (see Table 1-3 part 2). MRT led to reduced blood levels of 2-h glucose (p=0.044), and fasting C-peptide (p=0,023). Insulin resistance measured by HOMA-2 yielded a significant reduction (p=0.040), whereas ERT caused a significant reduction in blood insulin levels (p=0.023), and positive effects on percentage insulin sensitivity (p=0.054) and beta-cell function (p=0.020). These findings led the authors to conclude that both MRT and ERT lead to decreased insulin resistance in people at risk of developing type 2

diabetes; MRT led to a greater increase in glucose uptake capacity (in muscles), whereas ERT led to greater insulin sensitivity.

RT has also been identified to lower T2DM risk; Grøntved et al. (182) after following a cohort of health professionals biennially for 18 years found that 150 min of weight training per week was associated with a decrease of 34% (7%, 54%) 95% CI incidence of T2DM in men. Whereas in the same study, RT was performed in combination with aerobic training (AET), the incidence was reduced by 59% (39%, 73%) 95% CI (182) (See Table 1-3 part 1).

Almenning et al. (183) assessed the effects of HIIT and RT on a range of metabolic, cardiovascular and hormonal parameters in women with polycystic ovary syndrome. Polycystic ovary syndrome is a common endocrinopathy that is associated with insulin resistance that is also present in MetS (184). Exercise also plays an essential role in the treatment of PCOS. As it happens with type 2 diabetes and MetS itself, there is little knowledge regarding the optimal exercise regime (184). Using a three-armed parallel randomised controlled trial, 31 females with PCOS (age 27.2±5.5 years; body mass index 26.7±6.0 kg•m^2) were randomly assigned to HIIT, RT, or a control group. After ten weeks of training three times a week, the HIIT group improved HOMA-IR (17% p=0.014), endothelial function (p=0.080), and HDL-C (p=0.040), whereas with RT the anti-Müllarian hormone was significantly reduced. Both groups had significant changes in their percentage of fat, but that happened without body mass modifications, due to a parallel increase of lean body mass that was significant only for RT. Other markers that were assessed but did not show any significant change were high-sensitivity C-reactive protein, adiponectin and leptin. Researchers concluded that HIIT and RT were able to improve the cardiometabolic profile in polycystic ovary syndrome in the absence of weight loss (see Table 1-3 part 5) (183).

High intensity interval training; the new time efficient aerobic training

More recently HIIT training has been found to be beneficial as a tool for a prediabetic population (34). Earnest et al. (34) measured the effects of three months of eucaloric energy expenditure exercise training (AET vs HIIT) to test the hypothesis that HIIT would provide a more potent exercise stimulus for improving a number of metabolic factors in male individuals at risk of insulin resistance. Primary outcomes were a 24 and 72 hour oral glucose tolerance test (OGTT) to determine both acute (24h OGTT) and chronic (72h OGTT) effects of exercise on glucose control and a homeostasis model assessment of insulin (HOMA-IR) (185). Statistically, significant improvements were found for both the HIIT and AET interventions in the 24-h OGTT values but did not persist at 72-h analyses for either

group. HOMA-IR significantly improved for the HIIT intervention at both 24 and 72-h determinations. While the $\dot{V}O_2$max score improved similarly in both groups, changes in body mass and percentage of body fat were only significant for the HIIT condition (see Table 14). Metabolic syndrome expressed as a summed z-score (zMS) was similar when examined as a full cohort, but when stratified according to the HOMA-IR, individuals that had a high HOMA-IR in the AET condition showed significant improvements, while both low and high HOMA-IR for the participants of HIIT condition recorded significant reductions (p<0.050). It was concluded that either eucaloric AET or HIIT had an impact on fasting glucose, OGTT and $\dot{V}O_2$max values, but HIIT seems to have a greater impact on HOMA-IR and zMS. Earnest et al. results are presented in Table 1-3 part 3.

Little et al. (167) investigated the two-week effects of a low volume HIIT protocol consisting of 10 x 1-min intervals at approximately 90% maximal heart rate (HRmax) with 1-min recovery periods on glucose regulation and skeletal muscle metabolic capacity in patients with type 2 diabetes (see Table 1-3 part 3). The average 24-h blood glucose concentration measured by continuous glucose monitoring (CGM) was found to be reduced after training (7.6±1.0 vs. 6.6±0.7 mmol·L^{-1}). The sum of the 3-h postprandial area under the glucose curve for breakfast, lunch, and dinner was also reduced (both p<0.05). Muscle mitochondrial capacity increased due to the training, as a higher citrate synthase maximal activity was observed. The protein content of Complex II 70 kDa subunit, Complex III Core 2 protein, Complex IV subunit IV, Mitofusin 2 and GLUT4 were all also higher (all p<0.050). This demonstrates that HIIT is capable of improving glucose control and inducing metabolic adaptations in muscle mitochondrial capacity linked to improved metabolic control in patients with T2DM after a relatively short period of time. The acute effects, of the first session of this study were further investigated by Gillen et al. (175) (see Acute effects of exercise and glycaemic control).

In another study, Hood et al. (186) also conducted a two-week practical low volume submaximal constant load HIIT programme (10 x 60 s @~60% of peak power output, that elicited ~80% - 95% of HR reserve with 1 min of recovery between intervals) in seven sedentary yet otherwise healthy individuals. After six sessions of HIIT, the participants significantly enhanced muscle mitochondrial capacity. This was demonstrated by higher protein content of citrate synthase and cytochrome C oxidase subunit IV by (~35%) while the transcriptional corepressor receptor-interacting protein 140 did not change, the transcriptional coactivator peroxisome proliferator-activated receptor γ coactivator α was increased by (~56%). The glucose transporter protein content also was increased by (~260%). The authors concluded constant load may be a practical time-efficient strategy to reduce metabolic risk related disorders, by inducing metabolic adaptations in previously sedentary middle-aged adults. These results are in line with Gillen et al. (187) who found that when overweight women performed 18 sessions over 6 weeks of a low volume (10 x 60 s cycling efforts at approximately 90% maximal heart rate, 60 s recovery) HIIT protocol, a training-induced enhancement in mitochondrial capacity was

achieved. This was shown by increased maximal activities of CS and beta-hydroxyacyl-CoA dehydrogenase ($p \leq 0.050$), as measured in muscle biopsies.

Recently Liu et al. (188) conducted a meta-analysis of randomised controlled trials to quantify the effect of HIIT on body composition, glycaemic control and cardiorespiratory fitness (CRF) compared with MICT and no training at all, in 342 patients with T2D (13 trials). They found that HIIT obtained significant reductions in BMI, body mass, HbA1c, fasting insulin, and $\dot{V}O_2$peak in patients with T2D. HIIT showed a great improvement in body weight; a mean difference (MD) of -1.22 kg (-2.23, -0.18) 95% CI, $p = 0.020$ and BMI MD -0.40 kg/m2, (-0.78, -0.02), $p = 0.040$) vs MICT. Similar outcomes were found for HbA1c MD -0.37 (-0.55, -0.19), $p < 0.001$; relative $\dot{V}O_2$peak MD 3.37 $ml \cdot kg^{-1} \cdot min^{-1}$, (1.88, 4.87), $p<0.001$; absolute $\dot{V}O_2$peak MD 0.37 L/min, (0.28, 0.45), $p<0.001$. These outcomes show that HIIT may be preferred over MICT, as it induced more favourable effects in CRF and weight loss than MICT, in T2D patients, however, when glycaemic control was assessed between MICT and HIIT both were equally effective (188).

HIIT also has been identified as an effective modality to increase fat oxidation; this was reported by Tremblay et al. (189) who compared a 15-week HIIT programme with a 20-week aerobic exercise training (AET) programme. This consisted of uninterrupted cycling 4 times a week, increased to 5 times a week with a duration of 30 min at the beginning that progressively increased to 45 min sessions. The initial intensity was 60% which was increased to 85% of HRR to a 15-wk HIIT consisting of the same number of sessions of continuous exercise at 70% HRR with 19 short- (10-30 s bouts at 60% PPO) and 16 long interval sessions (4-5 bouts of 60 s that increased to 90 at 70% PPO) sessions additional to 5 min of AET at 70% HRR in 27 healthy young adults. The estimated total energy cost of the AET was 120.4 MJ; meanwhile the corresponding value for the HIIT programme was 57.9 MJ. Despite the lower energy cost and a shorter duration, HIIT was found to enhance fat oxidation and produced a more pronounced loss of subcutaneous adiposity. When matched to the energy cost, the decrease of the sum of six subcutaneous skinfolds induced by the HIIT programme was nine-fold greater than AET. Muscle biopsies taken pre- and post-exercise interventions showed significantly greater activity for muscle 3-hydroxyacyl coenzyme-A dehydrogenase (HADH); a marker of beta-oxidation. Their conclusions were that for a given level of energy expenditure, vigorous exercise favours negative energy and lipid balance to a greater extent than exercise of low to moderate intensity; and that a HIIT exercise programme appears to favour the process of skeletal muscle lipid oxidation (See Table 1-3 part 2).

Costa et al. (190) conducted a meta-analysis of randomised controlled trials that lasted between 4-16 weeks to elucidate if HIIT vs MICT can elicit a greater blood pressure reduction in individuals with pre-

to established hypertension. This study compared the chronic effects on blood pressure in participants with resting systolic BP ≥130 mmHg and/or with diastolic blood pressure ≥85 mmHg with or without taking antihypertensive drugs and reported the changes in blood pressure and $\dot{V}O_2$max. This meta-analysis included nine studies with a total of 245 participants. Resting systolic and diastolic blood pressure were similar (MD) -0.22 mmHg (-5.36, 4.92)95% CI, p= 0.930 and (MD) - 0.38 mmHg (-3.31, 2.54), p= 0.740 respectively (seven studies; 164 participants). For $\dot{V}O_2$max, HIIT had significantly greater improvement than MICT with a (MD) of 2.13 ml·kg^{-1}·min^{-1} (1.00, 3.27), p< 0.010 (9 studies; 245 participants). The conclusion was that both exercise modalities were effective for reducing both systolic and diastolic blood pressures. The authors concluded that not enough data was available to calculate ambulatory blood pressure, which reflects with more precision the risk of a stroke or cardiovascular event in this population as it has a stronger correlation with these events than doctor's office detected blood pressure, calling for randomised controlled trials exploring ambulatory blood pressure. Also, they detected that parameters of the peripheral vascular function are improved with HIIT a greater magnitude than MICT, and it is an essential determinant in hypertension. Their data supports the notion that exercise recommendations should include HIIT for the management of BP in adults with pre- to established hypertension (190).

Supporting all this evidence, recently after conducting a meta-review that included 33 systematic reviews (25 were meta-analyses) Martland et al. (191) reported that HIIT is an effective strategy to improve cardiorespiratory fitness, cardiovascular function, body composition, exercise capacity (muscular structure and function), blood glucose, glycaemic control, some inflammatory markers, and anxiety and depression severity in healthy individuals and those with physical health disorders. They also concluded that it is not associated with serious cardiovascular events and acute injuries while it appears to be safe. RT also have been found beneficial to health, as it improves body composition by preserving muscle mass thus energy expenditure, and strength that contributes better metabolic health (37). Despite the benefits of aerobic-based and resistance-based exercise when they are used independently, research also points out that a combination may provide a more potent metabolic effect (192).

HIIT and RT; twice as strong

The literature shows that AET and RT are complementary to each other (193, 194); AET increases aerobic capacity, enhancing cardiovascular adaptation to training while RT triggers an increase in strength by improving neuromuscular adaptations to strength training (193, 194). There is evidence also available that HIIT can replace AET and improve health with a sensibly reduced time commitment

(195). This section presents proof of the utility of these modalities to improve health and attempt to establish if we should recommend either one or both.

Álvarez et al. (196) compared the effects of combined sprint interval training (SIT a form of HIIT) and RT vs either condition alone on a number of health outcomes over a 12-wk period. Forty-three prediabetic female participants were divided into four groups; 12 performed SIT, eight RT, 10 SIT+RT and 13 performed their habitual physical activity as a control group. BMI, waist circumference (WC), body fat percentage by bioelectrical impedance (%BF), fasting blood glucose, HOMA-IR, blood pressure and fitness were assessed pre- and post-intervention. The SIT consisted of 7 x 20 s sprint intervals of >85% as calculated by the HR_{max} that was increased by 2 s every second week followed by resting 120 s intervals that were raised by 5 s each two weeks performed twice a wk. The RT consisted of three sets of five exercises performed until exhaustion. The SIT+RT programme was the combination of these two programmes and were performed over 5 days; two for RT and three for SIT. There was a significant change in the cardiorespiratory test (2-km walking test) for the SIT and SIT+RT groups only (p<0.001). Though there were no significant changes in body composition variables, fasting glucose was significantly reduced in the SIT and RT 24-h post intervention. At 72-h, there were also significant reductions in glycaemic, insulin and HOMA-IR (all p≤0.050) (see Table 1-3 part 6).

The same group investigated the effects of 8 weeks of combined HIIT and RT on insulin resistance (IR), lipid control, body composition, and aerobic fitness in 38 women; 10 healthy women, 9 with hyperglycaemia, 10 with hypercholesterolemia, and 9 with hyperglycaemia/hypercholesterolemia (48) (see Table 16). The HIIT protocol, consisting of 8-14 intervals corresponding to 80-100% of HRR followed by 75-120 s active recovery pedalling at <70% HRR. The RT consisted of performing 3 sets of exercises (each with 1-min in duration) until muscular exhaustion with a 1-min walking recovery break between exercises targeting four upper body (arm) muscle groups. Fasting glycaemia was reduced by 12% in the hyperglycaemic and 14% in hyperglycaemic/hypercholesterolaemic participants, (both p<0.050). Serum insulin and HOMA-IR decreased in all groups from 27 to 37% (all p±0.050). TC and TG had statistically significant reductions; -18% and -27% (both p=0.010) in hyperglycaemic/hypercholesterolaemic individuals only. These studies suggest that it is feasible to combine both HIIT and RT for improving metabolic health in women with metabolic and behavioural imbalances including pre-diabetes and inactivity. This evidence also provides support to designing combined strategies to improve hyperglycaemia, and dyslipidaemia (Table 1-3 part 4).

Another study performed in prediabetic individuals, by Rowan et al. (197) investigated the effectiveness of HIIT (n=11) [4x4 @90% heart rate reserve (HRR)], separated by 3 min of active recovery at 50% - 60%HRR] vs MICT (n=10) (28 min of jogging @60%–70% HRR) iso-time plus RT immediately after two of the three exercise AET sessions per week (total 36 sessions). RT was a circuit comprised of 1-2 sets per exercise of full-body exercises targeting large muscles (marching on the spot with high knees, squats with an overhead kettlebell press, push-ups or modified wall push-ups, forearm plank, step-ups with a medicine ball shoulder press, quadruped bird-dog, wall sit with isometric medicine ball front hold, and stair climb). After 12 weeks both interventions had similar significant improvements in HbA1c, pooled mean= [-0.5%(0.3% - 0.7%) p<0.001]; fasting glucose [-0.4 (-0.7, -0.1) p=0.010]; waist circumference mean reduction of -4.5 cm (-6.8,-2.2) (p< 0.001); aerobic capacity was enhanced by 20% (p< 0.001); HOMA %β function increased by 28.9% (16.5, 39.2) p<0.001. It was concluded that HIIT and MICT have similar effects and were successful in improving aerobic capacity, glycaemic control and waist circumference (See Table 1-3 part 6). From this evidence it is only possible to establish that either one alone or by combining different modalities they are effective in attenuating MetS dysregulations. In terms of the use of exercise to improve metabolic health, the evidence suggests that RT combined with AET work better if both integrate a non-pharmacological strategy (192, 194). Additionally, when exercise and nutrition are also combined into one intervention, this programme or strategy becomes more powerful like those discussed in previous sections, calling to advocate nutrition and exercise together (see Table 1-3 part 8). However, it hasn't been established which strategy is best practice.

Therefore, the question remains, as it is important to establish which strategy provides people with the most potent effect against MetS and all metabolic dysregulations. It is essential to promote research which fine tunes the exercise stimuli required to achieve the most potent effect, by comparing which exercise type on its own has the highest potency to affect MetS risk factors, as precursors of a wide array of metabolic diseases that lead to CVD, the number one cause of death worldwide.

HIIT, RT and LCHF together may be a stronger combination

In the last two decades (198-200) and in recent years (24, 41, 52, 106, 113, 201) the scientific community has been investigating whether CHO restriction or fat restriction is a better approach to combine with exercise. A LCHF diet (discussed and justified from different perspectives in a previous section), combined with exercise, specially one that is intermittent in nature to allow an exposure to a sufficiently high-intensity like RT and HIIT, may be the best approach. In this scenario such a combination would work in synergy (in line with Francois et al.) (43). This proposition implies that LCHF diet provides CHO restriction, less glucose availability and therefore no postprandial hyperglycaemia, limiting the potential detrimental metabolic and cardiovascular consequences of

excessive glucose availability, combined with HIIT and RT they provide an effect of improved aerobic capacity and fat metabolism; improved strength and muscle mass preservation, respectively and both augmented energy expenditure at rest and during physical activity.

Examples of this proposition are those by Volek et al. (44) and Jabekk et al. (46) who pointed out that RT when combined with a VLCKD, improves body composition in overweight individuals with metabolic syndrome or diabetes while improving the majority of markers of impaired metabolism found in these populations. But recently Francois, Gillen and Little (43) published a review stating a similar hypothesis including HIIT and CHO restriction as the two elements that, if combined, could produce a very potent stimuli that reverses the odds of developing and improving metabolic diseases, especially type 2 diabetes. As Feinman et al. (24), Volek (110, 111), and Westman et al. (25, 111, 202) point out, the most effective way to control glycaemia and the rise of insulinaemia is by manipulating CHO intake as if it was a medicine. Indeed Francois, Gillen and Little (43) agreed, saying that this lifestyle strategy represents an optimal intervention to treat metabolic disease; however, further research is warranted in order to harness the potential benefits of CHO-restriction and HIIT for improving cardiometabolic health.

Combining LCHF diet, HIIT, and RT makes sense because they are complementary to each other. Recently, a proof of this combination was investigated in the study by Dahlgren and Gibas (203) who reported an interesting case study that combines a calorie restricted VLCKD, HIIT, and memory training to attenuate memory loss and improve metabolic markers in a patient with comorbid mild cognitive impairment and metabolic syndrome (MetS). This combination has a potent effect on glycaemic control and the production of ketone bodies that ameliorate mitochondrial function, reduce the expression of apoptotic and inflammatory mediators and provide neuroprotection to cells (203). After 12 weeks of CHO restriction and participating in 6 sessions of HIIT every other week, they found an improvement in fasting insulin, blood lipids, blood ketones and risk ratios: HOMA-IR and the triglyceride/HDL. Metabolic syndrome improved, despite it not being certain which was the major contributor to reduce metabolic markers, it is important to acknowledge that having a low-CHO intake did not compromise HIIT and can be combined (Table 1-3 part 8).

The latest research published online first by Ramírez-Vélez et al. (2020) (204) shows the potential of combining HIIT, RT or both with a low calorie diet (1300- 1500 $kcal \bullet d^{-1}$). In their study, the metabolic outcomes of HIIT vs RT vs HIIT-RT vs only nutritional guidance was investigated. They used a 4x4 min at 85-95% HRmax interspersed with 4 min of active recovery HIIT protocol that was match by an energy expenditure of 400-500 kcal per session with RT that consisted of a 6 exercise routine targeting large muscle mass (abdominal, dorsal, upper and lower limb muscles) 12-15 rep with 1-min

rest between exercises at 40-80 1-RM that were performed until participants have spent 250 kcal. The combined group, performed HIIT to spend 250 kcal per session followed by RT also directed to achieve a similar energy expenditure. Participants trained 3 times per week for 12 weeks. The authors observed significant gains in CRF being HIIT with greater gains. While RT obtained the best improvements in vascular outcomes, and concluded that these improvements were the reason that the rest of metabolic risk factors improved which was reflected by the reductions in the MetS z score (See Table 1-3 part 9).

Table 1-3 Chronic effect of exercise, RT part 1

Study characteristics	Primary findings
Grøntved et al. 2012 (182) DESIGN: prospective cohort study n= 32,002 ♂ healthy health professionals Objective At baseline and biennially follow up using questionnaires: to observe from 1990 - 2008 the weekly time spent on RT and AET.	RT for 150 min•wk^{-1} or more lowers the risk of T2DM by 34% (7%-54%) AET for 150 min•wk^{-1} or more lowers the risk of T2DM by 52% (45%-58%) RT and AET for for 150 min•wk-1 or more lowers the risk of T2DM by 59% (39%-73%) Clinical application Both AET and RT, may be effective for improving metabolic health Combining RT and AET may be more potent for improving metabolic health and reduce the risk of developing T2DM. RT= resistance training; AET= aerobic exercise training. %Risk (95% Confidence interval) significant if zero is not within CI.

Hameed et al. 2012 (169)			BASELINE	AFTER	DIFFERENCE PRT – CONTROL	
	HbA1c (%)					
DESIGN: randomised controlled trial		PRT	8.68 ± 0.9	8.06 ± 0.7	-0.24	*p* <0.001
n= 48 (35♂, 13♀)		CTRL	8.29 ± 0.7	8.30 ± 0.7		
PRT=24 CONTROL= 24 individuals						
with T2DM	HDL-C (mmol•L^{-1})					
Duration: 8-wk		PRT	1.26 ± 0.2	1.37 ± 0.2	-0.12	*p* =0.004
Sessions/wk: 3		CTRL	1.43 ± 0.2	1.39 ± 0.3		
Exercise						
	Upper body strength					
PRT group						
Equipment: Resistance machines	Bench press 1-RM (kg)					
		PRT	49.37 ± 9.2	54.98 ± 10	4.69	*p* <0.001
Exercises: Bench press; leg press; lateral		CTRL	50.29 ± 9.4	51.75 ± 9.33		
pull; leg extension; biceps curl.						
	Lower body strength					
Intensity: 65-70% 1-RM						
Rest: 2-3min between sets	Leg press 1-RM (kg)					
Frequency: 3 d•wk^{-1}		PRT	143.14 ± 19.9	159.22 ± 20.1	14.06	*p* <0.001
		CTRL	139.69 ± 21.6	145.16 ± 21.5		
CONTROL group						
Equipment: Cyclergometry	Waist circumference (cm)					
		PRT	91.36 ± 12.1	89.52 ± 12.5	-2.87	*p*= 0.008
Exercise: Cycling and static stretching		CTRL	92.18 ± 11.4	92.39 ± 11		
exercises.						
Intensity: No work load	PRT=progressive resistance training; T2DM= type 2 diabetes mellitus; 1RM one repetition maximum; HbA1c= Glycated hemoglobin A1c; HDL-C= high density lipoprotein cholesterol; mmol•L-1= millimoles per litre; wk= week(s); d= day(s); kg= kilogram; cm= centimetre					
Frequency: 3 d•wk^{-1}	All expressed as means ± SD. Difference between PRT and Control, a negative (-) sign indicates a better outcome for PRT.					

Table 1-3 Chronic effect of exercise, RT part 2

Hansen et al 2012 (181)

DESIGN: randomised controlled trial

n= 18 (4 ♂ 14♀)
Pre-diabetic individuals (IGT)
Duration: 16 wk
Sessions/wk: 3

Exercise
MRT
Duration:
8 exercises
Intensity: 60-85% 1RM
5 sets x 3-4 reps / exercise
No rest between sets.
Frequency: 3 d•wk^{-1}

ERT
Duration:
8 exercises
3 sets x 12-15 reps /exercise
Intensity:
45-65% 1RM
Rest between sets 30-60-s
Frequency:
3 d•wk^{-1}

		Baseline	Post		DIFFERENCE MRT – ERT
ɹcose (mmol•L^{-1}) mean±SD					
	MRT	8.11 ± 2.26	7.24 ± 2.50	p= 0.044	
	ERT	6.91 ± 1.17	6.31 ± 1.21	NS	-0.27
Insulin (pmol•L^{-1}) mean±SD					
	MRT	60 ± 54	52 ± 46	NS	
	ERT	53 ± 34	32 ± 19	*p* = 0.023	13
C-peptide (pmol•L^{-1}) mean±SD					
	MRT	842 ± 349	769 ± 369	NS	
	ERT	804 ± 330	746 ± 304	NS	15
HOMA IR (median)					
	MRT	0.78	0.53	*p* = 0.040	
	ERT	0.72	0.48	*p* = 0.030	-0.01
Insulin sensitivity %S (median)					
	MRT	128	190	NS	
	ERT	137	207	*p* = 0.050	-8
β-cell insulin production %β (median)					
	MRT	67	69	NS	
	ERT	79	56	*p* = 0.020	25

IGT= Impaired glucose tolerance; ERT=Endurance resistance training; MRT= Maximal intensity resistance training; 1RM= One repetition maximum / reps= repetitions; IGT= Impaired glucose tolerance; IR= insulin resistance; HOMA-IR= Homeostasis model of assessment of insulin; %S= Insulin sensitivity; %β= Beta-cells function; pmol•L-1= picomoles per litre. s= seconds; d= days; wk= week. Difference between MRT and ERT, a negative sign indicates a better outcome for MRT

Tremblay et al. 1994 (189)

DESIGN: quasi-experimental

n= 27 (13 ♂ 14♀)
HIIT n=10
MICT n=17

Exercise
AET
4- 5 for 20 wk
Cycling @ ~60 - 85% HRR
Duration 30- 45 min

HIIT
Twice a wk, for 15 wk
AET for 5 min @ 70% HRR plus
short or long interval
sessions for a total of 35
Short int= 10-15x 15s - 30s,
@ 60% PPO in 10s
Long int= 4- 5x 60s - 90s
@ 70% in 90s
Interspersed with recovery periods
until HR= 120-130 bpm
5% increases every 3 weeks

	20 wk of AET= 28,757 ± 7,404 kcal	vs	15 wk of HIIT= 13,829±3,439 kcal	
V̇O2max	↑ **	=	↑ **	

However HIIT produced the most pronounced loss of subcutaneous adipose tissue (9-fold).
Vastus lateralis byopsies baseline vs post exercise:

	AET	HIIT
HK	↓*	↑ **‡
PFK	↓	↑ *†
MDH	↑ **	↑ **
HADH	↑	↑ **‡

AET≈ HIIT for citric acid enzymatic marker

Activity of muscle glycolytic enzymes activity was increased for HIIT
β-oxidation, was significantly greater after HIIT as shown by the overexpression of HADH

AET= aerobic exercise training; HIIT= high-intensity interval training; wk= week; HRR= heart rate reserve; HR= heart rate; bpm= beats per minute; kcal= kilocalories; V̇O2max maximal oxygen consumption hexokinase (HK); phosphofrutokinase (PFK) malate dehydrogenase (MDH). and 3-hydroxyacyl co-A dehydrogenase (HADH). ↑ = increase/upregulation; ↓ = decrease/downregulation; * *p* <0.05 significance within group; ** *p* < 0.01; †= *p* <0.05 between groups; ‡= *p* <0.01 between groups.

Table 1-3 Chronic effect of exercise, HIIT part 3

Earnest et al 2013 (34) DESIGN: randomised controlled trial n= HIIT=21 /AET= 21 pre-diabetic individuals (42 ♂) Duration: 12 wk Sessions/wk: 3-4 Exercise HIIT vs AET 3min warm up ~40% $\dot{V}O_2$max 3-5 min cool down. 6 wk preparatory phase: 6 kcal•kg^{-1}•wk^{-1} adding 2 intervals/wk until reaching 8 intervals in wk 9 and continue until finishing ↑ 2kcal•kg^{-1}•wk^{-1} until 12 kcal•kg^{-1}•wk^{-1} HIIT From wk 6-9 2 intervals adding 2/wk until reaching 8 in wk 9 and continue until finishing 2 min 90-95% $\dot{V}O_2$max 2 min 50% $\dot{V}O_2$max vs AET (CTRL) Steady state of 50-70% $\dot{V}O_2$max	24 hours after last exercise session		DIFFERENCE HIIT − AET
	OGTT mmol•L^{-1} (95% CI)		
	HIIT	−0.79 (−1.38, −0.20)	
	AET	−0.71 (−1.37, −0.06)	-0.08
	HOMA-IR IR (95% CI)		
	HIIT	−0.51 (−0.99, −0.03)	
	AET	−0.23 (−0.77, 0.31)	-0.28
	Metabolic syndrome zMS score ± SD		
	HIIT	− 1.14 ± 1.15*	
	AET	− 1.03 ± 1.68*	-0.11
	*Significant within-group changes from baseline to post-test (zero not within the 95% CI) or p <0.05(		
	HIIT= High intensity interval training; AET= Aerobic exercise training; OGTT= Oral glucose tolerance test; h= hours; HOMA-IR= Homeostasis model assessment of insulin resistance; mmol•L-1= millimol per litre; CI= confidence interval; kcal= kilocalories; kg=kilograms; wk= week(s); zMS score= z Metabolic syndrome score.		
	Difference between HIIT and AET, a negative sign indicates a better outcome for HIIT		

Little et al. 2011 (167)	Blood glucose mean ± SD (mmol•L^{-1})	
	Before	72h after last bout of HIIT
	7.6 ± 1.0	6.6 ± 0.7
DESIGN: Experimental n= 9 individuals with T2DM Duration: 2 wk Sessions/wk: 3 Exercise HIIT 10 x 60-s cycling bouts ~90% HR_{max} interspersed with 60 s rest.	Muscle mitochondrial capacity Citrate Synthase maximal activity ↑ ~20% p =0.040 Protein Complex II 70 kDa subunit ↑ ~37% p =0.030 Complex III Core 2 protein ↑ ~51% p =0.040 Protein Complex COX subunit IV ↑ ~68% p =0.020 Mitofusin 2 ↑ ~ 71% p =0.020 GLUT4 protein content ↑ ~369% p =0.003	
	T2DM= type 2 diabetes mellitus; HIIT= high-intensity interval traning; wk= week(s)HRmax= maximal heart rate; s= seconds; mmol•L-1= millimol per litre.	

Table 1-3 Chronic effect of exercise, HIIT and RT part 4

Álvarez et al. 2014 (48)				
		Glycaemia (mmol•L^{-1})		DIFFERENCE
DESIGN: quasi-experimental				^{1} or ^{2} or ^{3} – ^{H}
n=38♀ classified as:	HG	5.88 ± 0.33	5.16 ± 0.22*	0.22
HG¹= 9	HC	5.22 ± 0.44	4.94 ± 0.27	0
HC²= 10	HGHC	5.94 ± 0.28	5.11 ± 0.33*	0.17
HGHC³= 9	CTRL^{H}	5.16 ± 0.33	4.94 ± 0.28	
CTRL^{H} = 10				
		Cholesterolaemia (mmol•L^{-1})		
Duration: 8 wk	HG	4.61 ± 0.41	4.61 ± 0.63	0.21
Sessions/wk: 3	HC	5.85 ± 0.54	4.79 ± 0.44*	0.39
	HGHC	5.85 ± 0.44	5.57 ± 0.65	1.17
Exercise	CTRL^{H}	4.43 ± 0.62	4.40 ± 0.85	
HIIT:				
60-s x 8-14 80-100% HRR	High density lipoprotein cholesterol (mmol•L^{-1})			
interspersed with	HG	1.32 ± 0.26	1.53 ± 0.36	-0.02
12-s 1-2 wk	HC	1.24 ± 0.26	1.50 ± 0.23*	-0.05
105-s 3-4 wk	HGHC	1.24 ± 0.23	1.47 ± 0.36	-0.08
90-s 5-6 wk	CTRL^{H}	1.37±0.18	1.55 ± 0.18	
75-s 7-8 wk				
active recovery <70%HRR	Low density lipoprotein cholesterol (mmol•L^{-1})			
	HG	2.80 ± 0.54	2.77 ± 0.62	0.31
RT	HC	3.24 ± 0.54	2.85 ± 0.44	0.39
3 setsx60-s x 4 exercises using free	HGHC	3.52 ± 0.72	3.39 ± 0.62	0.93
weights to muscular exhaustion	CTRL^{H}	2.49 ± 0.57	2.46 ± 0.75	
recovery periods of 60-s rest	Triglycerides (mmol•L^{-1})			
between sets, standing	HG	1.14 ± 0.37	1.03 ± 0.29	0.06
position	HC	1.57 ± 0.36	1.12 ± 0.26*	0.15
	HGHC	1.97 ± 0.91	1.65 ± 0.85	0.68
	CTRL^{H}	1.19 ± 0.46	0.97 ± 0.17	

*Significant within-group changes p <0.050

HG= hyperglycaemic; HC= hypercholesterolaemic; HGHC= Hyperglycaemic & Hypercholesterolaemic, HIIT= high-intensity interval training, CTRL^{H} = Healthy Control RT= resistance training, HRR= heart rate reserve. All expressed as means ± SD; mmol•L-1= millimol per litre; wk= week. Difference between ^{1} or ^{2} or ^{3} - H (healthy control), a negative (-) sign indicates a better outcome for for any of the exercise groups vs control.

Table 1-3 Chronic effect of exercise, HIIT and RT part 5

Almenning et al. 2015 (183)		BASELINE	10 wks	DIFFERENCE ^{1} or ^{2} – CTRL
DESIGN: randomised controlled trial	Glucose, (mmol•L^{-1})			
	RT	5.1 ± 0.2	5.1 ± 0.4	0.1
n= 31♀ with PCOS and overweight	HIIT	5.0 ± 0.3	4.9 ± 0.2	-0.1
HIIT¹ n=10	CTRL	5.0 ± 0.4	5.0 ± 0.4	
RT² n=11				
CTRL n=10	Insulin (µIU•mL^{-1})			
	RT	14.9 ± 6.2	13.6 ± 6.3	-4.7
Duration: 3 sessions per wk	HIIT	21.8 ± 7.1	18.8 ± 6.7*	0.5
for 10 wk	CTRL	15.8 ± 8.1	18.3 ± 11.1	
Exercise	HOMA-IR			
HIIT	RT	3.3 ± 1.3	3.1 ± 1.5	0.5
Twice a wk,	HIIT	4.9 ± 1.7	4.1 ± 1.4*	-0.5
4 x 240-s @ 90-95% HRmax $\dot{V}O_2$max	CTRL	3.6 ± 2.1	4.3 ± 2.8	
Interspersed with 180-s of active rest				
@ ~70% HRmax	HDL-C, (mmol•L^{-1})			
Total exercise: 25 min.	RT	1.6 ± 0.5	1.6 ± 0.4	0
and once a wk	HIIT	1.7 ± 0.4	2.0 ± 0.5*	0.4
10x 60-s all out	CTRL	1.6 ± 0.4	1.6 ± 0.4	
interspersed with 60-s rest				
of very low activity	Fat mass (kg)			
	RT	27.1 ± 15.4	26.1 ± 14.7	5.7
RT	HIIT	21.6 ± 9.4	21.0 ± 9.4*	-4.9
8 dynamic strength drills with 10 rep	CTRL	26.2 ± 11.3	25.9 ± 11.4	
@ 75% 1-RM and three sets				
(per exercise) separated by 60-s	Fat mass (%)			
of rest	RT	33.1 ± 9.7	31.6 ± 9.4*	-1.3
CTRL	HIIT	30.2 ± 8.1	29.3 ± 11.4*	-3.6
Participants were advised to stick	CTRL	33.6 ± 7.0	32.9 ± 7.3	
with the recommended ≥150 min of				
moderate intensity exercise.	Visceral fat,(cm³)			
	RT	106.6 ± 52.4	105.5 ± 48.4	-4.2
	HIIT	85.7 ± 39.3	82.4 ± 38.7	-27.3
	CTRL	109.9 ± 40.8	109.7 ± 41.0	
	Fat-free mass, (kg)			
	RT	27.7 ± 4.0	28.9 ± 4.1*	1.5
	HIIT	25.8 ± 3.4	26.3 ± 3.2	-1.1
	CTRL	27.0 ± 3.6	27.4 ± 3.8	
	$\dot{V}O_2$max, (mL•kg^{-1}•min^{-1})			
	RT	39.3 ± 10.2	40.2 ± 8.5	4.2
	HIIT	37.4 ± 4.7	41.1 ± 3.8	5.1
	CTRL	36.8 ± 7.8	36.0 ± 6.9	
	AMH, (pmol•L^{-1})			
	RT	48.5 ± 30.5	33.7 ± 16.5*	-18.3
	HIIT	78.5 ± 56.0	67.1 ± 31.3	15.1
	CTRL	57.4 ± 38.9	52.0 ± 28.2	
	FMD, (%)			
	RT	5.8 ± 2.4	6.2 ± 1.4	1.3
	HIIT	4.0 ± 1.3	5.0 ± 0.3*	0.1
	CTRL	6.1 ± 2.0	4.9 ± 1.9	

*Significant within-group changes p <0.050

PCOS= polycystic ovary syndrome; HIIT= high-intensity interval training; RT= resistance training; $\dot{V}$O2max= maximum oxygen uptake; AMH = Antimüllarian HormoneFMD = flow mediated dilatation; HDL-C= high density lipoprotein cholesterol; mmol•L^{-1}= millimol per litre; pmol•L^{-1}= picomoles per litre; µIU•mL-1= micro international units per1 is equal to 6 pmol•L^{-1} of insulin. Difference between ^{1} or ^{2} – CTRL, a negative of sign indicates the direction the change, that favours the exercise groups. Except for variables that are expected to increase such as HDL-C.

Table 1-3 Chronic effect of exercise, HIIT and RT part 6

Álvarez et al 2012 (196)		BASELINE	24h post Ex	DIFFERENCE [1] or [2] or [3] – H	72h post Ex	DIFFERENCE [1] or [2] or [3] – H
	Glycaemia (mmol•L^{-1})					
DESIGN: randomised controlled trial	SIT	5.66 ± 0.51	5.28 ± 0.71*	-0.44	5.36 ± 0.70*	-0.38
	RT	5.57 ± 0.71	5.15 ± 0.53*	-0.57	5.21 ± .0.31*	-0.53
n: SIT[1]= 12; RT[2]= 8; SIT + RT[3]= 10;	SIT + RT	5.62 ± 0.29	5.38 ± 0.24	-0.34	5.39 ± 0.34	-0.35
CTRLH= 13	CTRL	5.68 ± 0.48	5.72 ± 0.52		5.74 ± 0.49	
individuals with prediabetes (43♀)						
Duration: 12 wk	Insulin (mU•mL^{-1})					
Sessions/wk:	SIT	4.67 ± 3.1	4.03 ± 5.1	0.33	3.80 ± 2*	0.05
	RT	4.86 ± 4.6	4.28 ± 4.1	0.58	2.75 ± 0.9*	-1
SIT= 3	SIT + RT	4.53 ± 4.8	4.30 ± 5.0	0.58	4.01 ± 4.1	0.26
RT= 2	CTRL	3.60 ± 1.6	3.70 ± 1.7		3.75 ± 1.6	
SIT+RT =5						
SIT: 20-s x 7 sprints, >80% HRmax	HOMA-IR					
work int. ↑ 2-s every 2wk	SIT	1.20± 0.8	1.09 ± 1.2	0.17	0.91 ± 0.7	-0.02
interspersed with 120-s rest	RT	1.28± 1.4	1.01 ± 1.1	0.09	0.57 ± 0.2	-0.36
rest int. ↓ 5-s each 2 wk	SIT + RT	1.12 ± 1.2	1.06 ± 1.0	0.14	0.99 ± 1.1	0.06
	CTRL	0.88 ± 0.4	0.92 ± 0.4		0.93 ± 0.4	
RT						
3 sets with 2 min rest x 5 exercises to exhaustion						

*Significance was set ($p \leq 0.050$) for differences between baseline, and 24hpost Exercise, and 72h post Ex; SIT= sprint interval training, RT= resistance training, CTRL= control, int= interval, HOMA-IR= homeostasis model assessment-insulin resistance. wk= week(s); s= seconds; HRmax= maximal heart rate; int= interval; mmol•L-1= millimol per litre; mU•mL^{-1}= milliunits per millilitre; All expressed as means ± SD. Difference between control and each of the experimental group, a negative of sign indicates the direction the change, that favours the exercise groups.

Rowan et al. 2017 (197)		Within group differences		DIFFERENCE
DESIGN: randomised controlled trial				
n= 21 with Pre-T2DM and overweight	HbA1c (mmol•mol^{-1})			HIIT vs MICT
HIIT + RT n=3♂, 8♀	HIIT	−6.5*	(−8.7, −3.3)	-1.1
vs	MICT	−5.4*	(−8.7, −2.2)	
MICT + RT n=3♂, 7♀				
Exercise:				
HIIT				
Thrice a wk	Fasting glucose (mmol•L^{-1})			
4 x 240-s @ 90-95% HRR	HIIT	−0.5*	(−1.0, −0.1)	-0.2
Interspersed with 180-s of active rest	MICT	−0.3	(−0.7, 0.2)	
@ 50~0% HRR				
Total exercise: 21 min.				
and RT twice a wk				
1-3 sets of 8 exercises	Fasting insulin (mmol•L^{-1})			
	HIIT	2.2*	(0.4, 4.0)	3.4
vs	MICT	1.2	(−12.1, 9.8)	
MICT				
Thrice a wk				
28 min				
@ 60-70% HRR	2 h glucose (mmol•L^{-1})			
and RT twice a wk	HIIT	0.2	(−1.3, 1.6)	0.8
1-3 sets of 8 exercises	MICT	−0.6	(−1.9, 0.7)	
RT:				
Full body exercises	2 h insulin (pmol•L^{-1})			
8-15 rep x 3 sets:	HIIT	−19.4	(−22.0, 11.8)	-7.4
marching on the spot with high knees, squats with an overhead kettlebell press, push-ups (or modified wall push-ups), forearm plank, step-ups with a medicine ball shoulder press, quadra-ped (aka Bird-Dog), wall sit with isometric medicine ball front hold, and stair climb directed to engage large muscle groups and multiple joints to maximise mobility.	MICT	−12.0	(−45.4, 6.6)	
	HOMA-%β			
	HIIT	35.0*	(13.7, 56.3)	12.3
	MICT	22.7*	(4.9, 40.5)	
	HOMA -%S			
	HIIT	−35.1*	(−70.3 −0.1)	0.4
	MICT	−35.5*	(−60.2 −10.8)	

*Significant within-group changes from baseline to post-test (zero not within the 95% CI)
T2DM= type 2 diabetes mellitus; HIIT= high-intensity interval training; MICT= moderate intensity continuous training; RT= resistance training; HRR= heart rate reserve; training; mmol•mol^{-1}= millimoles per mole; mmol•L-1= millimol per litre; pmol•L-1= picomoles per litre; HOMA-%β= beta cell function; HOMA -%S= insulin sensitivity. Difference between HIIT and MICT, a negative sign indicates a better outcome for HIIT

Table 1-3 Chronic effect of exercise, HIIT or RT and LCHF part 8

Jabekk et al. 2010 (46)		Within groups difference		DIFFERENCE VLCKD+RT – HCLF+RT
DESIGN: experimental randomised trial n= 16♀ overweight or obese and sedentary female. Duration: 10 wk Study, session: 30 to 50 min VLCKD +RT n=8 vs HCLF + RT n=8 Exercise: RT Both groups included the following exercises: Supine leg press, seated leg extension, seated leg curl, seated chest press, seated rowing, seated shoulder press, seated pull down and standing biceps curl Diet VLCKD: CHO 20-50 g·d^{-1} to induce ketosis and unlimited meats and fats (En%) CHO= 6; FAT= 66; and PRO= 22 and Regular diet (En%) CHO= 41; FAT= 34; and PRO= 17	weight (kg)	VLCKD + RT	-5.6 ± 2.6**†	-6.4
		HCLF + RT	0.8 ± 1.5	
	LBM (kg)	VLCKD + RT	0.1 ± 1.7	-1.5
		HCLF + RT	1.6 ± 1.8†	
	Fat mass (kg)	VLCKD + RT	-5.6 ± 2.9*†	-5
		HCLF + RT	-0.6 ± 0.8	
	Fat %	VLCKD + RT	-3.6 ± 2.5*†	-2.3
		HCLF + RT	-1.3 ± 1.3†	
	BMI	VLCKD + RT	-1.9 ± 0.8**†	-2.2
		HCLF + RT	0.3 ± 0.5	
	Glucose (mmol•L^{-1})	VLCKD + RT	0.1 ± 0.3	0
		HCLF + RT	0.1 ± 0.4	
	Total Cholesterol (mmol•L^{-1})	VLCKD + RT	0.1 ± 1.0	0.3
		HCLF + RT	-0.2 ± 0.6	
	HDL-C (mmol•L^{-1})	VLCKD + RT	0.2 ± 0.9	0.3
		HCLF + RT	-0.1 ± 0.4	
	LDL-C (mmol•L^{-1})	VLCKD + RT	-0.1 ± 0.2	-0.2
		HCLF + RT	0.1 ± 0.2	
	TG (mmol•L^{-1})	VLCKD + RT	-0.3 ± 0.6*	-0.2
		HCLF + RT	-0.1 ± 0.3	

Significant difference VLCHF vs HCLF. *$p \leq 0.050$ **$p \leq 0.001$. †Significant change from baseline $p \leq 0.050$. VLCKD= very low-carbohydrate high fat ketogenic diet HCLF= high carbohydrate low fat diet, RT= resistance training, LBM= lean body mass, g= grams; d= day; kg= kilograms; CHO= carbohydrate; FAT= lipids; PRO= protein; En%= percentage of total energy; mmol•L-1= millimol per litre; HDL-C high density lipoprotein cholestrol; LDL-C low density lipoprotein cholesterol; TG= triglycerides. All expressed as means ± SD. Difference between VLCKD+RT – HCLF+RT, a negative sign indicates that the change variables that are favours VLCKD+RT, except for variables expected to increase such as LBM, and HDL-C, where the opposite applies.

Dahlgren, and Gibas 2018 (203)	Lipid profile improvements	
DESIGN: Case study n= 1 ♀ with MetS and memory loss Duration: 6 sessions in total one session every other wk for 12 wk HIIT + VLCKD Intervention: HIIT protocol Not disclosed. VLCKD protocol Not disclosed.	Lipids	% improvement
	TG	56%
	HDL-C	26%
	TG/HDL ratio	51%
	VLDL-C	37%

MetS= metabolic syndrome, HIIT= high-intensity interval training
VLCKD= very low carbohydrate ketogenic high fat diet; wk= week(s)
TG= triglycerides; HDL

Table 1-3 Chronic effect of exercise, HIIT or RT and LCHF part 9

Ramírez-Vélez et al 2020 (204)

DESIGN: Experimental
randomised single blind factorial 2x2
n=72 (23♂, 49♀)
Completed study as follows:
NG[1]= 16
HIIT[2]= 15
RT[3]= 12
HIIT-RT[4] = 13
Duration: 12 wk
Sessions/wk: 3

NG
AHA and Colombian guidelines
Counseling to change quality of diet
Prescription: exchange list
Reduction of ~250 kcal
induce ~5-10% BW•wk-1
CHO 45–65%; FAT, 20–35%;
PRO10–35% E=1300-1500 kcal•d^{-1}
Individualised and dietitian controlled

HIIT:
4-min warm-up @ 65% HRmax
4-min x 4 85-95% HRmax
interspersed with 4-min active
recovery @ 65% HRmax
Exercise delivery: running on treadmil
4-min cool @ 65% HRmax until
total EE= 400-500 kcal per session.
equivalent to ~12-kcal•kg^{-1}•wk^{-1}
Diet same as NG

RT
Six exercises targetting major muscle
groups: (abdominal, dorsal, upper
and lower limb muscles) using
full ROM Intensity: 40–80% of 1-RM,
12–15 repetitions per set
and 1-min rest between exercises
Duration: 30–40 min to spend
400-500 kcal per session
Exercise delivery: BB squats,
db squats, adductor split squats,
lateral adductor squat, DB biceps
curls, db lateral shoulder raises,
DB military shoulder press and DB
triceps curls. Warm-up and
Cool-down, 10-min each, gradual
exercises including walking and light,
static stretching
Diet same as NG

CT
Split session to spend between
200–250 kcal for
each modality: HIIT and RT.
~400–500 kcal/session.
Diet same as NG

	NG	HIIT	RT	CT
CRF (ml•kg^{-1}•min^{-1})	-0.5	+8.3**	+4.1*	+6.3*
MetS z score	-3.01*	-3.50*	-2.7*	-3.00*
FMD(%)	+2.6	+2.7	+10.5**	+5.3
MAP (mm Hg)	-1	-4	-6	-3
GLU (mmol•L^{-1})	-0.11	-0.17	+0.01	-0.08
HbA1c %	-3.0	-3.5	-8.0	-3.0
TG	-0.40**	-0.06	+0.09	-0.17

HIIT was more effective for improving CRF and RT was more effective to improve the vascular profile which may explain the reduction of MetS score

* p <0.001within groups ** between groups

NG= nutritional guidance; HIIT= high-intensity interval training; RT: resistance training; CT= HIIT-RT; AHA= American Heart Association; Hrmax= maximal heart rate; CRF= cardiorespiratory fitness; MetS= metabolic syndrome; FMD= flow mediated-dilation; MAP= mean arterial blood pressure; GLU= glucose; HbA1c= glicated hemoglobin A1c; TG= triglycerides, ROM= range of motion; BB= barbell; DB= dumbbell kcal= kilocalories, kg= kilogram;1-RM= one repetition maximum; CHO= carbohydrate; FAT= lipids; PRO= protein E= energy intake per day; mm Hg= millimetres of mercury

Wrapping up, from this evidence it is possible to imply that combining a nutritional strategy to an exercise programme is desired, especially if as little as 2% of weight loss can predict a 25% metabolic health improvement (61) in the presence of MetS which suggests that weight loss during an exercise programme has more influence than an increase in aerobic capacity during an exercise programme directed to improve $\dot{V}O_2$ max (61). The addition of a LCHF diet to either HIIT, RT or both seems that it may potentiate metabolic improvements, while HIIT improves aerobic fitness and RT to a lesser extent; RT favours a better body composition by protecting participants from lean body mass loss (44, 46). However, there are at least two concerns of following a LCHF diet and HIIT combined; these relate to the potential of exaggerated responses that might take place in healthy individuals.

The first consideration is due to the fact that a LCHF diet is higher in fat, and that in some individuals, even healthy ones, it may trigger insulin resistance. This has been observed during short studies (up to 5 weeks), that a high intake of fat has led to insulin resistance (205). There was an accumulation of intramyocellular fat (206) (diacylglycerol and ceramides) which therefore increased insulin resistance that lead to hyperglycaemia and dyslipidaemia. Nevertheless, similar effects are observed with the intake of diets high in refined carbohydrates and the potential to include HIIT or RT may protect against this (43). However, evidence is limited (203, 207) that combining HIIT and carbohydrate restriction is effective and minimises unwanted metabolic syndrome risk factors (203), insulin resistance (as a result of carbohydrate restriction); fat oxidation, body composition, fitness improved significantly as well after only two weeks of this combination of LCHF and HIIT. Unfortunately, there are no studies testing both HIIT and RT but there is substantial evidence that HIIT (188) and RT (208) can individually enhance insulin sensitivity and improve body composition. HIIT and RT are known to reduce insulin resistance (205, 209) and improve cardiometabolic risk factors.

The second concern is the exaggerated responses to exercise that may be present in some individuals with metabolic disease (T2DM) (hypertension due to exercise blood pressure, [SBP] 250 mm Hg or [DBP], 115 mm Hg exercise-induced angina, exercise-induced musculoskeletal strain) along with post-exercise exaggerated responses (hypoglycaemia [<3.5 mmol/L or feeling symptoms of hypoglycaemia] or PEH [≤90 mm Hg SBP or ≤60 mm Hg DBP]) (210), that in fact can be present in response to any type of exercise but those of high intensity might pose a greater risk. Therefore, close supervision, especially at the beginning of any HIIT of RT programme, is required to minimise any risk of such exaggerated responses, with exercise exposition and increases in fitness, these events can be minimised (210, 211).

Another consideration and attractive effect of consuming a low-CHO intake is that it causes a reduction of glycogen stores. This in turn increases the maximal mitochondrial enzyme activities and/or mitochondrial content, and increased rates of lipid oxidation (212). These responses are likely regulated by enhanced activation of key cell signalling kinases (e.g. AMPK, p38, MAPK), transcription factors (e.g. p53, PPARδ) and transcriptional co-activators (e.g. PGC-1α), such that a co-ordinated up-regulation of both the nuclear and mitochondrial genomes occurs (212, 213). However, exercising with a low glycogen availability may also increase muscular protein breakdown (214). The latter may require an additional protein intake and an adequate energy intake to avoid muscle catabolism (215-217).

In summary, HIIT (as a substitution of AET) and RT have been found to be an effective and potent tool for improving cardiometabolic risk factor control in overweight, obese, pre-diabetic, and type 2 diabetic individuals that characterise MetS. Exercise programmes are no longer designed to only affect energy expenditure but to modulate several metabolic pathways. In this review, a few examples are given as an indication of their effectiveness in ameliorating cardiometabolic risk factors.

In addition, the synergistic effects of diet plus exercise (particularly a low-CHO high-fat diet [LCHF]) has been seen to improve these health outcomes and plays an important role in the prevention of T2DM (23, 139, 199) and it is an irrefutable fact that nutrition plays a very important role in the prevention of T2DM and any other risk factor of MetS. Finally, energy intake in a LCHF diet (even if ad libitum), due to its higher protein and fat intake, has this satiety effect that limits spontaneous energy intake close to energy requirements (24, 218). This is an additional advantage of lowering the CHO intake (218) producing a greater impact on body weight, while both HIIT and RT maintain an elevated metabolic rate (219) and protect from lean body mass loss (especially RT) (46). For this reason, investigating the effects of combining HIIT and RT with a LCHF is warranted (43, 203, 207) as it may provide a more potent non-pharmacological strategy to avoid MetS, T2DM and CVD.

2 Iso-time and Quasi Iso-Effort, Comparison of the Acute Effects of HIIT and RT Combined with a LCHF diet

Prelude.

The purpose of this thesis was conceived as a whole to investigate which type of exercise combined with a reduction in carbohydrate intake would be a better option to improve the metabolic status of individuals at risk with metabolic disease, whether that is type 2 diabetes, dyslipidaemia, hypertension or any other condition that shares the same metabolic markers that are investigated here.

Characterising the acute responses of a single session of HIIT and RT equated by time and effort was necessary to have the elements to describe the chronic (training) effects of these two exercise modalities while following a low-carbohydrate, high fat (LCHF) diet. This study informs the reader of the acute responses to a single session of either HIIT or RT and provides the elements that would otherwise be missing to fully understand the results of the 12-week intervention. Chronologically, it took place after the sixth week of training, because the demanding nature of the exercise sessions, a period of at least 6 weeks was necessary to allow for adaptation and to assure that every participant was going to be performing at the desired resistance and was able to finish the full session.

ABSTRACT

Currently, there is paucity of research comparing the acute physiological responses of high-intensity interval training (HIIT) with full body circuit type resistance training (RT). The aim of this study was to compare the acute physiological responses to these modalities when performed iso-time and quasi-iso-effort, in a sample of individuals at risk of metabolic disease examining endocrine and metabolic responses. Additionally, all participants were following a low carbohydrate high fat (LCHF) diet.

METHOD: Using a cross-over design, eight participants performed both modalities in a random order. Each session consisted of a 10 x 60 s @ ≥95% HRR (HIIT) or the maximum possible weight (≥ 70% 1RM) to perform 15 reps (2 s concentric, 2 s eccentric) using compound exercises (RT) interspersed with 60 s of recovery. Gas exchange and heart rate were continuously monitored with a metabolic cart. Blood pressure and blood samples that included glucose, interleukin-6, testosterone, cortisol, and human growth hormone, were drawn pre- and post-exercise.

RESULTS: Energy expenditure, $\dot{V}O_2$peak, and heart rate were greater during HIIT (all $p \leq 0.05$) than RT, while cortisol, glucose, growth hormone, interleukin-6, testosterone, and were not significantly different ($p > 0.05$) between groups post-exercise.

CONCLUSION: HIIT may provide a more favourable stimuli for weight control and aerobic capacity enhancement than RT. LCHF did not impair high intensity exercise performance in this population.

Introduction

In recent years, high-intensity interval training (HIIT) and resistance training (RT) have been receiving more public interest given their known metabolic and physiological effects (220, 221). Performing these modalities at high-intensity bursts interspersed with brief passive or active resting periods of equal or dissimilar duration, allows individuals to effect metabolic pathways with potency [i.e. testosterone, cortisol, interleukin-6 [IL-6] (222)] resulting in improved body composition, glycaemic control, fat oxidation and disease risk. Early HIIT protocols were very demanding, because of the effort involved (223). A solution for this situation is a submaximal, safe and enjoyable (224, 225) and effective (175) protocol that uses ten intervals of 60 s, typically at 90%-95% of HRmax (17, 225), interspersed with 60-s of active (light intensity) or passive rest. This protocol has been effective for improving fitness, glycaemic control, body composition (187) and blood pressure (226).

Likewise, full body RT has been recommended as a potent stimuli to metabolic health for individuals at risk of metabolic disease (221). Research has linked RT practice with a reduction in the risk of developing MetS (227). Low strength levels are inversely associated with the risk of MetS and T2DM (228). RT now has a good reputation for improving glycaemic control and it is believed that this effect can be attributed to the repetitive effect of each training session (37). Energy expenditure has been found to improve after a single session of three exercises of 6 repetitions and 2 min rest between sets, using an intensity of 80% of 1 RM. Resting energy expenditure (REE) remained higher 24 h afterwards compared to the same protocol performed at 40% of 1 RM (229). Hence, effort plays an important role in improving REE which can then influence energy balance and fat loss, known to improve risk of metabolic disease. RT can also increase lean body mass (LBM) and has a protective effect on lean body mass during energy restriction (221, 230) making RT an ideal complement to any exercise programme for improving metabolic health.

It is well established that the cumulative effect derived from the systematic repetition of a single exercise session, provides the body with the stimuli (the exercise effect) to induce metabolic changes according to the interplay of the duration, intensity and modality of the exercise session (173). It has been observed that two exercise sessions with the same volume can lead to different outcomes (37, 173, 231). Rozenek et al. (176) tested the acute responses to a low volume HIIT (10 x 1 min interspersed with 1 min of active recovery) in a group of healthy adults by altering the intensity in the work to rest ratio (a) 80% peak power output PPO/0% PPO (80/0); (b) (80/50); (c) (100/0); and (d) (100/50). They found that HR, HRpeak, RPE, blood lactate, and % $\dot{V}O_2$peak values were produced by 80/50 and 100/0 protocols. However, the average % $\dot{V}O_2$peak was significantly higher in 80/50, that was contrary to their initial hypothesis, hence the necessity to assess the acute response to be in the position to provide the public with better and more efficient exercise recommendations.

Recently Steele et al. (179), published a comparison of a matched leg press (4 × 12RM using a 2 s concentric and 3 s eccentric repetition duration controlled with a metronome, thus each set lasted 60 s) and recumbent cycling (4 × 60 s bouts using a resistance level permitting 80–100 rpm), these tasks were approximately matched for duration and effort. They observed similar responses in $\dot{V}O_2$, RER, energy expenditure, muscle swelling and electromyography. Suggesting that when these conditions are met (time, effort and muscle mass involved) it is possible to provide the same stimuli. Therefore, it is feasible that two exercise sessions with the same volume and same work-to-rest ratio, but performed with different exercise modalities exerting quasi-iso effort, may lead to different outcomes. Indeed, research is expanding the knowledge of what we know regarding these two exercise modalities, however there is paucity regarding the acute effects of a 10x1 min HIIT protocol (176, 225, 232) and full body circuit type RT. No direct comparison has been published contrasting HIIT and RT with iso-time and quasi-iso-effort in a sample of individuals at risk of metabolic disease examining endocrine and metabolic responses.

Potentially, this research would contribute to detailing key exercise-induced mechanisms to improve exercise prescriptions for these two exercise modalities. It could also provide information to determine if RT might potentially induce clinically meaningful improvements in cardiorespiratory fitness. Therefore, we sought to quantify and compare energy expenditure (EE), heart rate (HR) CHO and fat oxidation. Also the responses in the glucose, testosterone, cortisol, growth hormone, and interleukin-6 when HIIT and RT are performed iso-time and iso-effort.

Materials and Methods

A randomised crossover design was used to compare the effects of a single exercise session of HIIT and RT. Participants were already participating in a 12-wk study comparing the effects of HIIT, RT or a combination (COMBO), all inclusive of a low carbohydrate, high fat diet (LCHF). Participants in the COMBO group were invited to participate in this study between weeks 6−12 of the 12-wk intervention study, to ensure sufficient familiarisation with the exercise and dietary demands of this acute study, and were required to have attended at least 90% of all previous exercise sessions. See chapter 3 for complete description. Testing sessions were all incorporated within the 12-wk training programme, and were separated by one and two weeks.

Participants

The inclusion criteria were: 18-60 years and 6 weeks of training in both HIIT and RT. The stated exclusion criteria were: pre-diagnosed with a medical condition limiting their ability to participate in the intervention; taking any medication with a direct effect on the outcome measures, including systolic blood pressure (BP) > 180 mmHg and/or diastolic BP > 110mmHg; type 1 diabetes; history of myocardial infarction, angioplasty, coronary artery bypass or cerebrovascular ischemia/stroke; symptomatic congestive heart failure; atrial flutter; unstable angina; unstable pulmonary disease; third degree heart block; recent history of alcoholism, drug abuse; pacemaker; unstable metabolic disease; and orthopaedic or rheumatologic problems that could impair the ability to exercise.

A total of eight individuals (n=8) which included five males and three females (47±6 years and BMI =27.2±2.9 kg•m^2) accepted to participate from the larger training study cohort.

Ethics

All participants were provided with an information sheet describing the details of the study including the benefits and risks of participation. Participants were provided with and signed institutionally approved informed consent documents. The study was approved by the AUT Ethics committee.

Testing session's protocol

Participants were required to refrain from any kind of physical activity regarded as moderate intensity (3−6 METs) (233) or above for the previous 48 hours before the testing day. They were also required to come in to the laboratory in a fasted state, their last LCHF meal eaten at least 8 hours before testing commenced. Participants were advised to duplicate as close as possible the same meal the day before for both the HIIT and the RT exercise sessions to replicate similar conditions for this study. The testing of each exercise modality was conducted 1-2 wk apart and performed at approximately the same time of day. Figure 2-1 provides an overview schematic of the study.

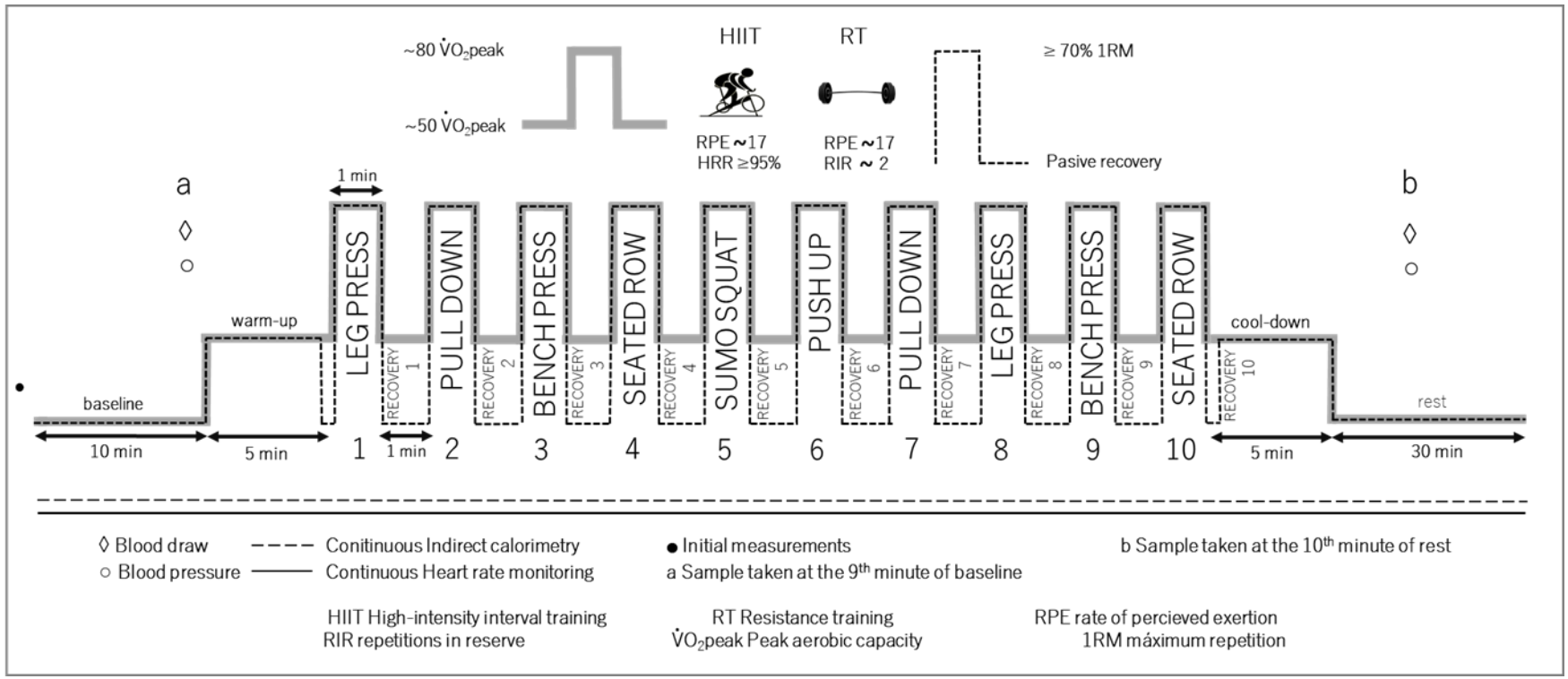

Figure 2-1 Acute study diagram.

Procedures:

Functional testing

Without shoes and in light clothing, height (wall stadiometer to nearest 0.1 cm, baseline only) and weight (to nearest 0.01 kg) were recorded. A Polar Heart Rate Monitor (Polar Electro Oy Kempele, Finland), and Hans Rudolph face-mask (Hans Rudolph Inc. Shawnee, KS. USA) were fitted. Participants sat still on a bed with upper body inclined about 10 min before gas collection began to allow enough time for resting heart rate to be achieved. The gas collection began along with the recording of heart rate, (this continued until the study finished), using a previously calibrated and clean metabolic cart (ParvoMedics TrueOne 2400. East Sandy, UT. USA) following manufacturer guidelines. The gas measurements were taken continuously and averaged every 15 s throughout the whole study. Blood pressure was measured from the non-dominant arm using an automated and certified sphygmomanometer (OMRON Model HEM-7321-E, Omron Corporation, Kyoto, Japan) at three time points: after 10 min of rest, then 15 min after the end of exercise. The average of three consecutive readings was used (234).

Blood was taken from an antecubital vein using BD Vacutainer system (Becton, Dickinson and Company, Franklin Lakes, USA) by a certified phlebotomist. The sample serum was isolated by centrifugation (1500 rpm at 4°C for 10 min) and frozen at -80°C, for later analysis. Samples were analysed for cortisol (nmol/L), glucose (mmol/L), human growth hormone (HGH, ng/mL), insulin (pmol/L), testosterone (nmol/L), and interleukin-6 (IL-6 pg/mL) using specific assays on a Roche Modular E170 at AUT Roche Diagnostic Laboratory

After the 10 min rest period at the start of the session, participants took their position to begin a 5-min warm-up, on a cycle ergometer (Lode Excalibur Sport, Lode BV The Netherlands). The RT session started using Life Fitness 95C Inspire cycle ergometer (Life Fitness USA). Both exercise sessions used the same warm-up intensity, a comfortable self-selected cadence between ~60-65 rpm that was producing an output of ~50 watts (175). An intensity that was considered an easy pace enough to elevate heart rate without exerting the participants. For this reason it was also used for the recovery periods for the HIIT session with the intention of minimising venous pooling (235).

Testing protocol: HIIT session

Prior to each test, the resistance (intensity) was adjusted to meet each participant's required intensity and to ensure HR target was met. Close to the end of the warm-up, participants were made aware that interval number one was about to begin, and 5 s before the Lode Excalibur Sport started to increase the resistance, participants increased the pedal cadence to 100 rpm when

prompted verbally by the person assisting the test. This instruction took place for each of the nine remaining intervals. The ergometer adjusted the resistance of the pedals according to the cadence to regulate the required wattage output throughout the session and meet the work output requirements. In all of the cases exercise resistance was three to five times the resistance of the resting bouts of 50 watts.

After each work period, and during the last 10 s, participants were asked to report the RPE during the first 5 s of the resting period by pointing to the RPE 6-20 scale, which was recorded in the computer software along with the HR reached. This part was essential for the study as effort along with the time were the two factors to be equated. If the RPE or the target heart rate wasn't met after the second work interval, the resistance of the ergometer was increased at the beginning of the third interval by 20 to 50 watts. RPE was asked as if further adjustment was not necessary, so changes were applied to the remaining of the work intervals. After the end of the last work interval, participants continued cycling at 50 watts (60-65 rpm) for 5 min, then lay down and completed 30 min (at least) to capture early full term first EPOC. Ten min into the recovery, a blood sample and blood pressure were taken. The following morning (24-h after) participants returned (8-12 h fast) for the last blood sample and blood pressure measurements.

Testing protocol: RT session

Participants started the RT session with cycling for five min, (as per HIIT), at which time the participants transitioned to the starting position of the RT session. The RT session included 6 compound exercises, switching from upper to lower body exercises. The order was as follows: 1) pull down, 2) leg press, 3) bench press, 4) seated dumbbell row, 5) sumo squat, and 6) push-up. These exercises were executed in this order and repeated until a maximum of 10 sets were completed. That is, participants, performed exercises 1−4 twice, and 5−6 only once.

For each station, the participants had a pre-recorded audio instructing them when to begin the exercise for each repetition. This controlled the tempo of the exercise so the participants knew when to start lifting and when to start lowering the weight. The tempo was 2 s concentric, 2 s eccentric for each phase of the lift. This equated to 15 repetitions per min, and matched the total time of work conducted in the HIIT session. Throughout, until after the end of each work interval, they were asked to indicate how hard they felt the exercise was (RPE) using the 6-20 Borg scale. Heart rate was recorded using the metabolic cart computer software and by hand using a control slip that (see Appendix G) indicated each interval with boxes designated for that purpose during the first few seconds of each resting interval. The participants were also asked about how many reps in reserve (RIR) they felt they had left at the end of each set (236). This is a measure of their

perception of how many repetitions they might be able to perform if they were required to continue with the exercise with the current load. Once the last work interval finished, the participant was instructed to take their position on the cycle ergometer and begin cool-down. When cool-down ended, participants were prompted to return to the bed and sat at least 30 min to record the first period of EPOC. Ten min into the recovery period (15 min after the end of the last work interval), blood pressure was taken, followed by the post-exercise blood collection. After this, participants completed the recovery period and the testing session was finished.

Exercise metabolic cost computation

Energy expenditure was calculated in two ways: For the total energy expenditure for the work intervals including recovery stages, we used energy per task as proposed by Scott (237); total energy expenditure (per task) for the work and recovery sets was calculated by multiplying absolute $\dot{V}O_2$ L/min x 5.05. To calculate CHO and fat oxidation rates, Ferrannini (238) equations and Romijn (239) correction were used to obtain the PRO contribution to energy expenditure. Gases were collected through the duration of the study using a mixing chamber system, $\dot{V}O_2$ and $\dot{V}CO_2$. Metabolic cart was set to average data every 15 s (ParvoMedics TrueOne 2400, East Sandy, UT. USA).

Average energy expenditure, CHO, fat and protein oxidation per min was calculated using stochiometric equations proposed by Ferrannini (238) and is presented in $kcal \cdot kg^{-1}$:

$$PRO = 6.25 \times \dot{N}$$

$$CHO = 4.55 \times \dot{V}CO_2 - 3.21 \times \dot{V}O_2 - 2.87 \times \dot{N}$$

$$FAT = 1.67 (\dot{V}O_2 - \dot{V}CO_2) - 1.92 \times \dot{N}$$

$$EE\ kcal \bullet min = CHO(g) \times 3.72\ kcal \bullet g^{-1} + FAT(g) \times 9.44\ kcal \bullet g^{-1} + PRO(g) \times 4.70\ kcal \bullet g^{-1}$$

Statistics

Statistical Analyses were conducted using IBM-SPSS Statistics (version 24, IBM Corporation. Chicago, Illinois, USA), Stata (version 15, StataCorp LLC Texas, USA) and Excel (version 16, Microsoft Corporation Redmond, WA, USA). Normality was assessed using the Shapiro – Wilks test for normality, and visually confirmed using QQ plots and Histograms. For assessing the difference

between exercise modalities, energy expenditure and substrate oxidation generalised general equations (GEE) were used for normally and non-normally distributed data.

Blood pressure and blood biomarkers differences between groups were assessed using a generalised linear mixed model with restricted maximum likelihood (REML) which provides group differences, time interaction and group•time interaction. ANOVA test was used to assess within group differences and post-hoc tests using student t–test with Bonferroni correction were performed to detect significant results. Hedges g effect sizes were calculated as it uses a correction for small sample sizes (the case of the present study) to quantify the magnitude of the effect with its associated 95% confidence intervals (CI)s. Data are reported as means ± standard deviation or median and interquartile range for non-normally distributed data.

Results

The main findings of this study are that HIIT and RT of iso-time and quasi iso-effort produced significantly different $\dot{V}O_2$peak, HR, energy expenditure, CHO and fat oxidation (Table 2-1), while blood pressure and blood markers were similar except for testosterone (Table 2-2). Table 2-1 reports the between group differences that show the results of the GEE represented by the β coefficient, the SE, the t statistic, probability and 95% CI per condition. Table 2-2 show the between group differences given by the *β* coefficient, the SE, the t statistic, probability and 95% CI of the GLM with REML. Figures 2-2 – 2-3 display mean differences between groups (horizontal lines), and means per interval.

Exercise intensity

Exercise intensity expressed in terms of $\dot{V}O_2$peak of β= -8.005 p<0.001 HIIT (22.2±3.5 ml•kg^{-1}•min^{-1}) vs RT (12.4±1.1 ml•kg^{-1}•min^{-1}) (See Table 2-1). In consequence HR was significantly different (β= -19.306 p=0.017) mean HR for HIIT: 138±16 bpm than RT: 114±19 bpm. (See Figure 2-2 and Table 2-1). MRPE of 16.9±0.9 (HIIT) vs 17.0±0.9 (RT), [β= 0.425 p=0.454] and was similar between HIIT and RT (See Figure 2-3 and Table 2-1).

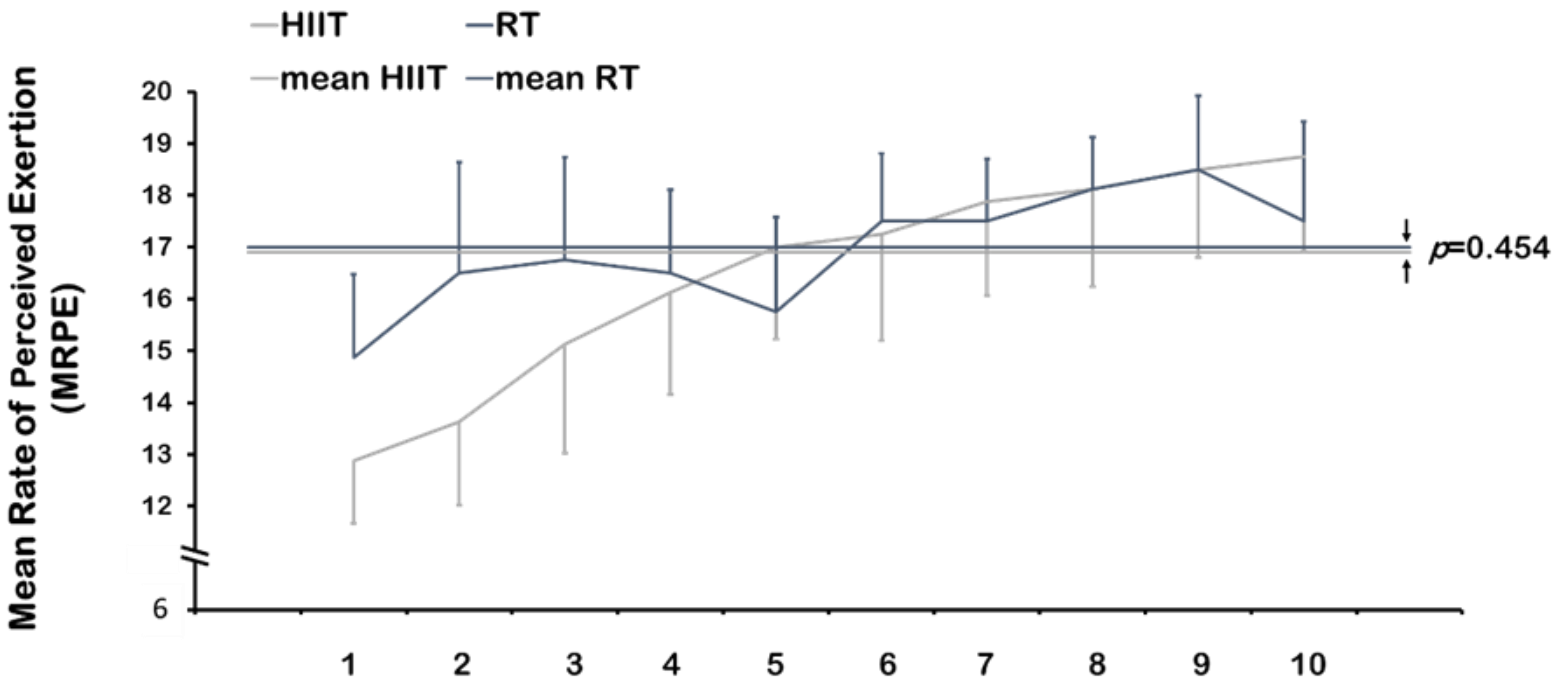

Figure 2-2 Mean rate of perceived exertion

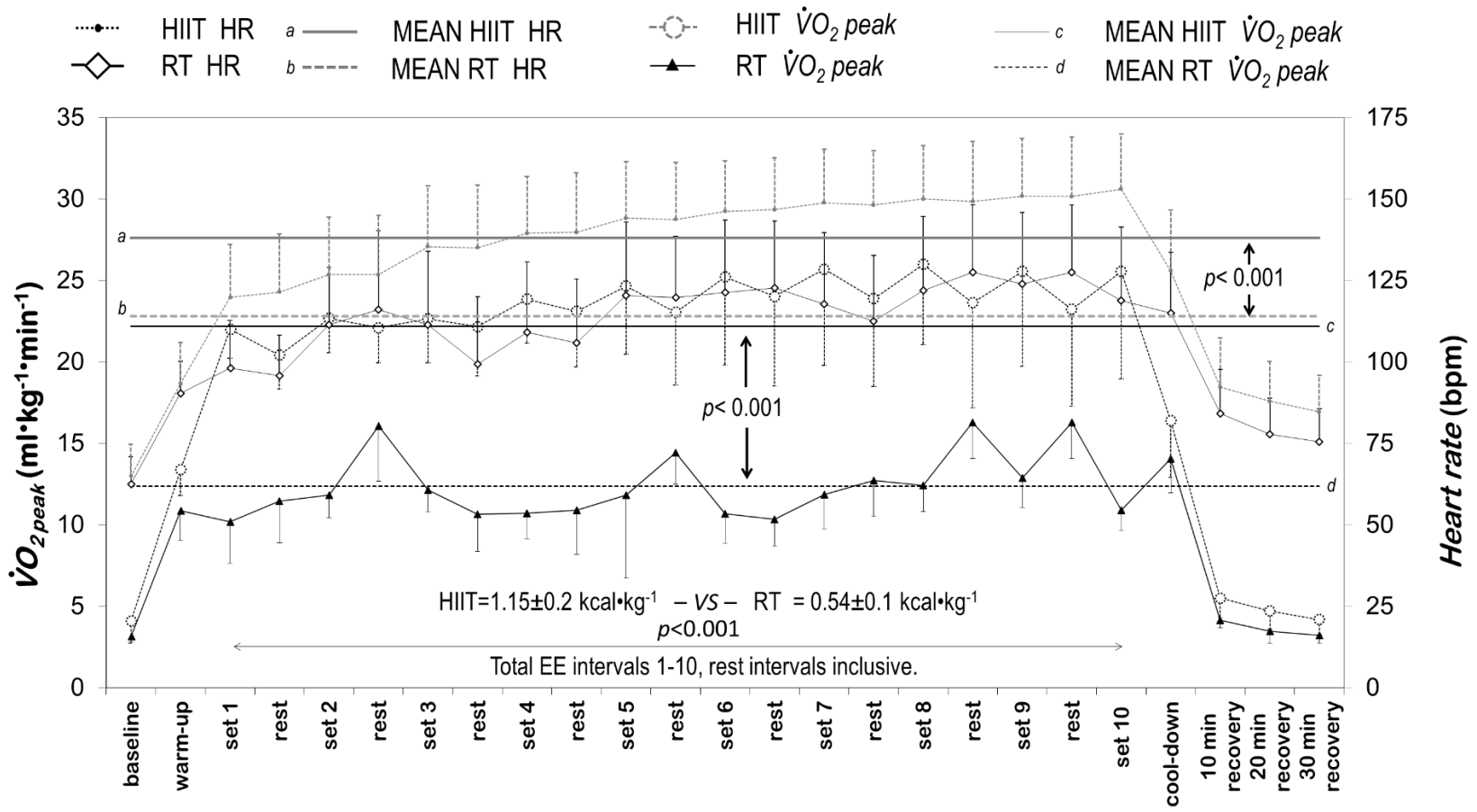

Figure 2-3 Mean $\dot{V}O_2$peak and HR HIIT vs RT across the exercise session

Exercise metabolic cost

Respiratory exchange ratio (RER) was also similar between HIIT (0.97±0.01) and RT (0.98±0.02) [β= 0.003 *p*=0.810] (HIIT-RT). However, the total energy expenditure was greater for HIIT (*β*= -0.040 *p*<0.001), of 1.15±0.2 for HIIT and 0.54±0.1 kcal•kg^{-1}•min^{-1} for RT. Whereas the metabolic cost from CHO oxidation was greater for HIIT 0.10±0.02 kcal·kg^{-1}·min^{-1} vs 0.05±0.01 kcal•kg^{-1}•min^{-1} for RT [*β*= -0.036 *p*<0.001] (See Table 2-1). Fat oxidation for HIIT was significantly greater than RT [*β*= -0.651 *p*=0.002], when this difference was compared kcal•min^{-1}, but when this was computed in terms of BW it was no longer significant; (*β*= -0.004 *p*=0.170; 0.006 (0.002,0.011) kcal•kg^{-1}•min^{-1} and 0.001 (0.000, 0.002) kcal•kg^{-1}•min^{-1}) respectively.

Blood biomarkers

After HIIT and RT there was no difference in the 15-min glucose, IL-6, and cortisol and growth hormone did not show difference between groups (see Table 2-2). Whereas the hormone testosterone was the only significantly different biomarker after 15 min of the last bout of exercise. Showing a greater increase for RT as demonstrated by the group x time interaction (*β*= 0.723, *p*=0.004) (See Table 2-2).

Table 2-1 Aerobic capacity, Energy expenditure, substrate oxidation and aerobic capacity comparison within both HIIT and RT exercise sessions

	Between groups difference RT - HIIT					
	β	LOWER	UPPER	SE	t	p
Exercise parameters						
HR	-19.306	-35.098	-3.514	8.057	-2.396	0.017
$\dot{V}O_2$peak $ml \cdot kg^{-1} \cdot min^{-1}$	-8.005	-10.024	-5.986	1.030	-7.770	< 0.001
RER	0.003	-0.018	0.024	0.011	0.240	0.810
RPE	0.425	-0.688	1.538	0.568	0.749	0.454
Energy expenditure						
tEE $kcal \cdot kg^{-1} \cdot min^{-1}$	-0.040	-0.050	-0.030	0.005	-7.827	< 0.001
Substrate oxidation						
CHOox $kcal \cdot kg^{-1} \cdot min^{-1}$	-0.036	-0.046	-0.026	0.005	-7.144	< 0.001
FATox $kcal \cdot kg^{-1} \cdot min^{-1}$	-0.004	-0.010	0.002	0.003	-1.374	0.170

HIIT= high-intensity interval training, RT= resistance training, *β*=beta coeficient, t= t-statistic, (95% confidence intervals) Total EE= total energy expenditure (calculations comprised the 10 work intervals plus rest intervals 1-9 using Generalised estimating equations), CHOox=carbohydrate oxidation, FATox=fat oxidation, $\dot{V}O_2$peak= peak oxygen uptake, HR= heart rate, RPE= mean rate of perceived exertion Borg scale 6-20.

Table 2-2 Blood pressure, glucose, IL-6, cortisol, testosterone and growth hormone responses at 15 minutes post exercise: differences between sessions

	Between group differences Group-time interaction RT-HIIT					
		β CI 95%				
	β	lower	upper	SE	z	p
SYSTOLIC BLOOD PRESSURE (mm Hg)						
DIFFERENCE at 15min	6.125	-0.960	13.210	3.615	1.690	0.090
DIASTOLIC BLOOD PRESSURE (mm Hg)						
DIFFERENCE at 15min	-3.250	-8.552	2.052	2.705	-1.200	0.230
GLUCOSE ($mmol \cdot L^{-1}$)						
DIFFERENCE at 15min	-0.313	-0.975	0.350	0.338	-0.920	0.355
INTERLEUKIN-6 ($pg \cdot mL^{-1}$)						
DIFFERENCE at 15min	-0.189	-0.994	0.616	0.411	-0.460	0.646
CORTISOL ($nmol \cdot L^{-1}$)						
DIFFERENCE at 15min	13.475	-65.825	92.775	40.460	0.330	0.739
TESTOSTERONE (ng·mL-1)						
DIFFERENCE at 15min	0.723	0.229	1.218	0.252	2.870	0.004
GROWTH HORMONE (ng·mL-1)						
DIFFERENCE at 15min	0.222	-0.810	1.254	0.527	0.420	0.674

Generalised Linear Model using repeated measures with restricted maximum likelihood ratio (REML)
β= regresion coefficient SE= standard error z= z statistic p= probability CI= confidence interval

Discussion

The novel approach of this study was the comparison of HIIT and RT iso-time and (quasi) iso-effort in participants who were on a LCHF diet. The purpose of this study was to compare these two exercise modalities in their acute responses in energy expenditure, substrate oxidation during and after a single session for 30 min (early EPOC) and hormonal responses after 15 min after a session of 10 x 60 s interspersed with 9 x 60 s recovery, before and after a 5-min warm-up and cool-down performed in a cycle ergometer. The study took place once participants were adapted to the LCHF diet and were able to sustain and maintain the same effort through all exercise sessions.

Energy expenditure, aerobic capacity, heart rate responses and effort

The main findings were that energy expenditure (EE) for HIIT was twice as much the energy expended by RT. Consequently, peak oxygen uptake ($\dot{V}O_2$peak) was also two-times greater for HIIT despite the same duration and effort that was confirmed by a similar RPE and also the RER was similar. This could be explained by the extent of muscle mass that was exercised during each modality. The HIIT exercise utilised in the present study was cycling solely performed with the legs, that together represented the largest muscle mass of the body. Lyons et al. (240) found that excess post-exercise consumption (EPOC) lasted longer after lower body exercise than upper body exercise (cycling) when exercise was matched by energy expenditure, indicating that the larger the muscle mass the greater the effect on oxygen uptake as a result of greater energy demand to fuel the work being performed. In the present study RT utilised leg exercises only 30% of the time, and 70% of the time utilised upper body exercises which could have been the reason why energy expenditure was lower for RT since it used a smaller muscle mass for longer. Another possibility that may explain the greater EE was the speed of muscular contraction. It seems that the type of contraction that involved HIIT is similar to the explosive contraction described by Mazzetti et al. (241) who found that explosive contractions during the leg press exercise produced a greater energy expenditure than a leg press exercise using 2 s x 2 s for concentric and eccentric phases respectively. This was exactly the same tempo used in the present study, and was in line with the study by Roberson et al. (242) who tested three circuit training full body RT protocols that used different speeds and loads. The first one used high loads and controlled speed (2 s concentric and 2 s eccentric), the second used a moderated, but explosive concentric and controlled eccentric load (2 s), and the third used a high and explosive concentric and controlled eccentric load (2 s). The rate of energy expenditure was significantly greater for the third protocol. These studies support the hypothesis that contraction speed was a determinant for producing a higher energy expenditure in the present study. Another study that supports this rationale was conducted by Francois et al. (243) who compared upper and lower body sprint interval training (SIT) (5x30 s all-out sprints, interspersed with 4.5 min recovery). They found that both upper and lower body sprints with a

resistance proportional to arms and legs' muscle mass produced a similar metabolic response, including HR.

The heart rate in our study was significantly greater for HIIT, which was in line with EE, denoting a greater oxygen demand during working periods and greater muscle mass involved during exercise at all time. This may be due to the speed and the total number of contractions of each exercise for RT, which was significantly lower than HIIT (15 rep•min^{-1} vs ~100 rpm). Kaikkonen et al. (244) controlled the heart rate during a RT programme by setting the speed of movement, this way it is possible to regulate oxygen demand and therefore EE.

Blood pressure responses

In the present study, BP responses were similar between exercise modalities, after exercise. No adverse effects were detected, indicative of the safety of both modalities. A limitation was the absence of BP measurements during exercise to detect any possible changes in BP during exercise, however it wasn't considered necessary as all participants were normotensive. The absence of any difference in BP between time points is not unusual; La Scala-Texeira et al. (245) compared the acute effects of manual RT and free weights RT in a group of normotensive and hypertensive individuals. Both protocols were matched by time and intensity. BP was measured pre-, during and after 15 min, 30 min, 45 min and 60 min post-training. Normotensive individuals did not show any difference between pre- and at any time point post-training. This could be explained by saying that exercise intensity was insufficient to potentiate post-exercise hypotension in this cohort. The other possible explanation is that for reaching that point when the post-exercise hypotensive (PEH) effect was present it may require a longer time. Zeigel and Swan (246) investigated the acute effects of whole body vibration and RT vs RT alone in a group of pre-hypertensive individuals; PEH did not take place until 45 min after the cessation of exercise. Therefore, there is a possibility that in our study, despite normotensive participants, the PEH effect might have occurred happening well after the BP measurement that was taken at post-15-min post-exercise only.

Glucose and hormonal responses

As expected, glycaemia was similar within and between groups as an indication that both exercise modalities had the same influence. To note, all individuals were on a low carbohydrate high fat diet (LCHF) nutritional approach and had been training for the previous 6 weeks (at least), perhaps then were consequentially normoglycemic at baseline. This may have an influence on the non-significant rise in glycemia after exercise (15 min time point). The magnitude of change measured by Hedges

g was greater for HIIT, which might show a slightly better glycaemic response after HIIT than RT when both modalities are iso-time and iso-effort. Supporting the above statement when individuals are normoglycemic before exercise, Koopman et al. (247) also found a similar result after 24 h of a single resistance exercise session. Little et al. (167) however, observed that a similar 10 x 10 HIIT protocol reduced the 24 h glycaemic response measured by continuous glucose monitoring CGM most likely due to ability to analyse glycaemia over the whole 24 h period which increases the sensitivity of this method over only one sample in our study.

Interleukin-6 is a cytokine with pro- and anti-inflammatory properties and is produced by several sources. During exercise the contractile muscle synthesises and releases it in high concentrations representing the largest release into the bloodstream during exercise when glycogen levels are low and it is supressed with CHO availability (248). Muscle derived IL-6 is the anti-inflammatory kind (248) influencing the adipose tissue and the liver, inducing lipolysis and maintenance of glucose homeostasis (249). In the present study the observed significant increase after exercise, (without any difference between exercise modality), was in line with other studies involving either high intensity aerobic (250) or RT (251) activity. It is considered that duration of exercise plays a far more important role in producing the stimuli (252). In the present study this was probably compensated for by the likely reduced muscular glycogen after participants being on a LCHF diet with no more than 100 g of CHO per day and performing these exercise modalities for over 6 weeks, which could have reduced muscle glycogen. Phinney et al. (253) observed a reduced muscular glycogen content to ~50% of its capacity after 4 weeks of following a ketogenic LCHF diet. In another study, Harber et al. (254) noted one week of a LCHF diet with 5% CHO, ·35% PRO and 60% fat despite restriction of physical activity and a significant reduction in CHO oxidation, intramuscular glycogen stores were reduced by 20%. Following this logic, it is quite possible that in the case of the present study, muscle glycogen depots may have been lower than their full capacity, which favoured IL-6 synthesis. Keller et al. (255) compared two trials of two-legged dynamic knee extensor exercises with two different glycogen concentrations (high and low) to determine which of these conditions influenced the regulation of IL-6 expression. After exercise in both cases, IL-6 concentrations were determined. Their findings were that when there were low glycogen reserves, the expression of IL-6 was greater than when the glycogen depots were greater.

Cortisol was significantly elevated during both conditions, most likely as a consequence of both the intensity exerted during exercise and as a result of the IL-6 increase. Together, cortisol and IL-6 constitute the expected response to high exertion, serving as a signal for the liver to increase glucose output to provide enough energy for the working muscle and to recover from exercise (248). Steensberg et al. (256) demonstrated that, by infusing recombinant human IL-6 in doses simulating the rise in IL-6 during strenuous exercise, this increased the expression of two anti-

inflammatory cytokines (IL-1 receptor agonist and IL-10). Furthermore, it also stimulated the rise of cortisol. All of this happens without any effect on the heart rate, mean arterial pressure, or increasing plasma catecholamines, plasma TNF-α, and temperature, maybe as an indication that IL-6 plays an important role in limiting potentially harmful effects of sustained inflammation (256). Also it is believed that IL-6 stimulation is highly dependent on exercise duration (248). Whereas the IL-6 expression is stimulated when glycogen levels are low (257), LCHF diet is known to reduce glycogen levels (258). This let us think that both HIIT and RT intensity effect combined with the low glycogen originated with the LCHF were able to increase IL-6, that potentially, it may confer an anti-inflammatory effect if it is systematically repeated as part of an exercise programme.

Growth hormone was also significantly increased for both conditions, as has been previously reported when cortisol and lactate are also significantly elevated. Increases are highly dependent on training status and meeting the threshold between volume and intensity (259). Our programme was designed to exert the highest possible hormonal response by choosing compound exercises; 15 repetitions per set with controlled movements and lifting weights close to failure. These consisted of a pull and push, interspersed with either a pull or a push lower body exercise, two to three sets per exercise (see Figure 1). Four sets of 15 repetitions with 1 min recovery periods between sets of four exercises using 60% of 1RM was found effective for producing a significant increase in GH (260).

Previous studies have shown that heavy RT induced greater concentrations of this hormone, as mentioned prior, this programme was structured to induce the greatest hormonal response by reproducing load patterns in previous studies. Since both interventions were successful in increasing GH, it is possible to say it was effective; Benini et al. (261) used a similar RT session (3x8-10 RM) composed of 10 exercises with rest periods of 90-120 s between sets. Since HIIT was equated with time and effort, that was the probable reason that it was also successful in increasing GH momentarily after exercise. Our findings support the notion that GH effect is due to the sum of its acute effect rather than a training effect.

Testosterone was also observed to reach a significantly increased difference from baseline for the RT group, but not for HIIT, but the difference between groups was insignificant. According to the literature, a combination of duration, intensity and volume is required to produce changes in the hormonal anabolic response (259). It seems that the combination of heavy loads and the order of upper and lower body exercises in RT was important for testosterone to reach that level after exercise. Budnar et al. (262) had much shorter duration; sessions of 12 rounds of 30 s kettlebell swings (16 kg) resulted in significant increases in testosterone, growth hormone, and cortisol; the

last two reached the greatest level at 15 min post exercise, whereas testosterone reached its maximum level immediately after exercise (262). In another study, Raymond, Renshaw and Duncan (263) provided evidence to reinforce the role of total load as the key stimulus to potentiate the increase in testosterone, cortisol and growth hormone; comparing 12 swing cycles of 30 s of 8 kg vs 16 kg kettlebell. The 16 kg kettlebell swings provided the greatest increases in these hormones. Regardless of the differences in muscle engagement (i.e. ballistic movements to controlled 2 s concentric, 2 s eccentric), what is noticed is that short duration exercise with the adequate ratio of work to resting periods, is able to generate a significant hormonal response. In the present study, there were no significant increases in testosterone levels in the HIIT condition, potentially because the overload generated was not as great as that in the RT condition. Comparing our study to that of Velasco-Orjuela et al. (264) which used HIIT vs RT equated to energy expenditure, significant reductions in cortisol and non-significant reductions in testosterone were observed, while cortisol to testosterone ratio was increased due to cortisol reductions. Their intervention compared HIIT (85-95% HRR 4x4min intervals with 4 min active rest 75-85 HRR between work intervals with a 5-min warm-up and ended with a 4-min cool down at 65% heart rate reserve until the expenditure of 400 to 500 kcal) and RT (50-70% 1RM, one set 12-15 rep of five upper body exercises including the bicep screw curl, triceps extension, dumbbell side lateral raise, dumbbell front raise and military press. Three lower body exercises included dumbbell squat, dumbbell front lunge, and dumbbell side lunge repeated until reaching 400-500 kcal) or a combination of both. Their participants were sedentary and because of that, they could have lifted less weight than ours and achieved their maximal upper exercise intensity tolerance which may have been lower than our participants' exercise tolerance, who had already trained for at least 6 weeks. That may have allowed our participants to use a greater load and speed in both exercise regimes. Because by the time they participated in the present study their intensity had increased at least twice prior to the exercise testing session. Therefore, it was quite likely that a greater resistance applied in our study for both HIIT and RT elicited the difference.

Results in the present study should be used with caution as this is (to the best of the author's knowledge) the first time this combination of a LCHF diet and HIIT and/or RT is reported. However, it shows the potential of the regime for metabolic manipulation if this exercise designed specifically for an exercise programme was directed to improve metabolic health.

Limitations

Limitations of this study were not including a glycogen measurement, only allowing for speculation of muscle glycogen levels, however, depletion has been observed in diet-only trials lasting just one week (42). A body composition analysis using DXA, magnetic resonance or bioimpedance analysis, limits the calculations to extrapolate results only per kg of body mass reducing the accuracy at the moment to compare it with other studies. A real strength of the present study included the high methodological rigour that was used, providing certainty of the validity of all measurements. Future research may include some of the additional measurements described above and may consider having additional time point measurements for blood sampling immediately after exercise which may allow a better picture for IL-6 and testosterone that may have their peaks at different time points than was measured. Also, continuous glucose monitoring with real time estimation of plasma insulin concentration (265), along with ketone bodies and ambulatory blood pressure monitoring would certainly be an advantage.

Conclusions

In summary when both HIIT and RT are performed iso-time and quasi iso-effort, HIIT provides a significantly greater energy expenditure; this might indicate that HIIT provides a more favourable stimulus for weight control. Both HIIT and RT had similar responses for testosterone, cortisol, growth hormone and glucose 15 min after exercise.

Having a LCHF diet did not impair exercise performance and probably influenced the expression of IL-6 post exercise favouring an anti-inflammatory effect. Hormonal elevations after exercise were slightly greater in magnitude for RT, however between group differences they were not detected. This might indicate the similar effect of both exercise modalities which was due to exercise effort rather than volume. However, the greater energy expenditure caused by HIIT was probably a result of the faster muscular contractions when performing this exercise and was reflected in a greater oxygen consumption. Consequently, a higher HR during exercise may be more beneficial for weight reduction and may be chosen if this was the main objective; otherwise these two modalities may be effective for improving metabolic health if performed systematically.

Supplementary material

Table 2-S1 Within groups differences

Within groups differences		
	HIIT	RT
Systolic blood pressure (mm Hg)		
PRE	121±11	120±8
15 min	118±11	122±10
p	0.614	0.369
Diastolic blood pressure (mm Hg)		
PRE	75±6	77±3
15 min	76±6	74±6
p	0.754	0.247
Glucose (mmol • L^{-1})		
PRE	5.4±0.7	5.2±0.6
15 min	5.9±1.4	5.4±0.5
p	0.663	0.626
Interleukin-6 (pg • mL^{-1})		
PRE	5.6±1.6	5.0±0.5
15 min	6.4±1.8	5.7±0.7
p	0.174	0.050
Cortisol (nmol • L^{-1})		
PRE	428.2±176.9	433.6±115.8
15 min	836.6±85.9	855.4±91.6
p	<0.001	<0.001
Testosterone (ng • mL^{-1})		
PRE	2.6±1.8	2.8±1.9
15 min	2.8±1.9	3.7±2.6
p	0.260	0.051
Growth hormone (ng • mL^{-1})		
PRE	0.97±1.13	0.95±1.13
15 min	3.94±1.03	4.05±1.05
p	0.008	0.007

HIIT= High-Intensity Interval Training RT= Resistance Training.
Within group difference calculated with ANOVA, pairwise comparisons used Bonferroni correction
Results expresed using mean ± SD and significance

- In addition to obtaining the 15 min sample, also were able to obtain a blood sample and blood pressure mesurement at 24 h after the last bout of exercise. These are presented in the box plots below.

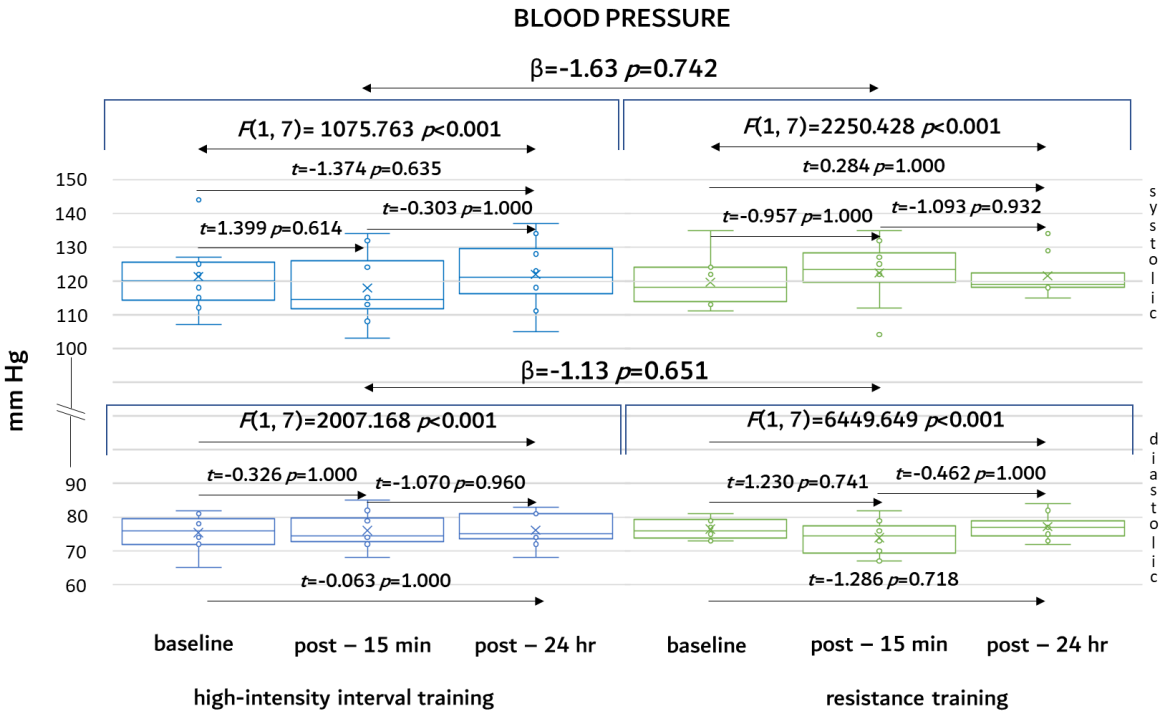

Figure 2-S1 Systolic and diastolic blood pressures.

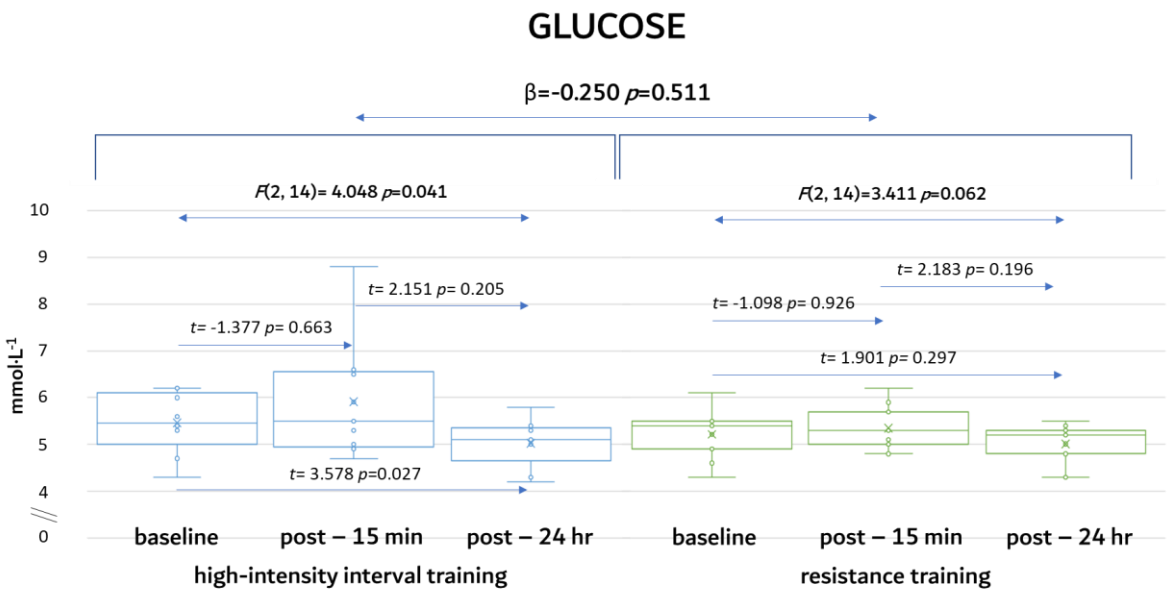

Figure 2-S2 Glucose.

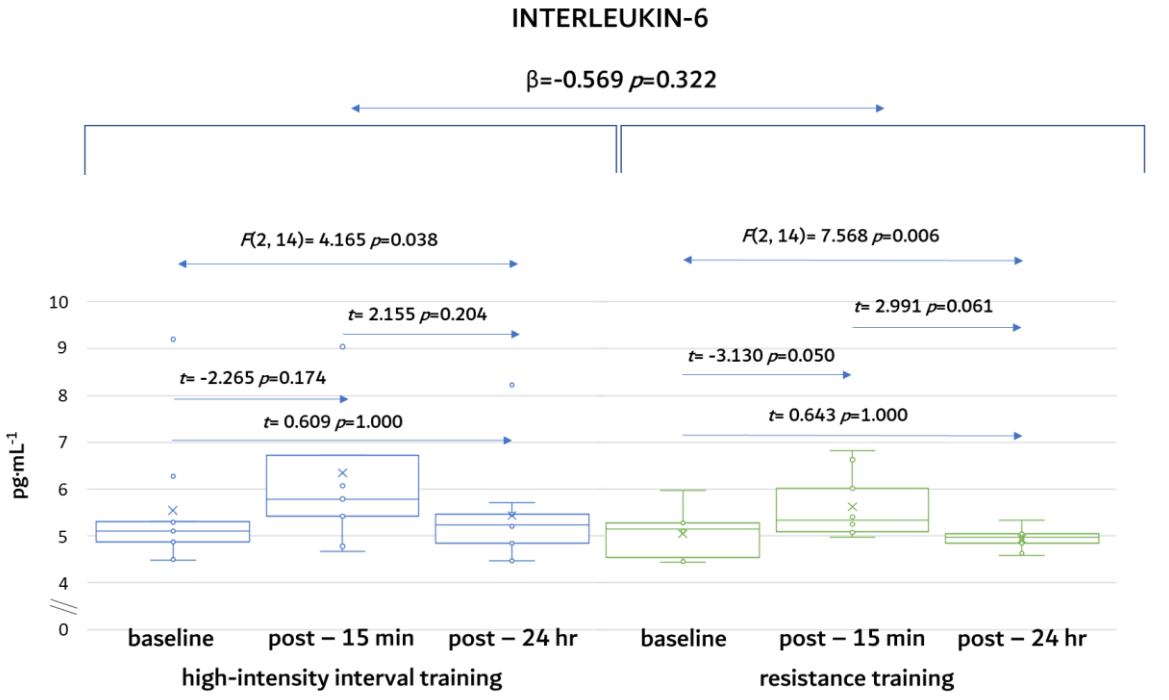

Figure 2-S3 Interleukin-6.

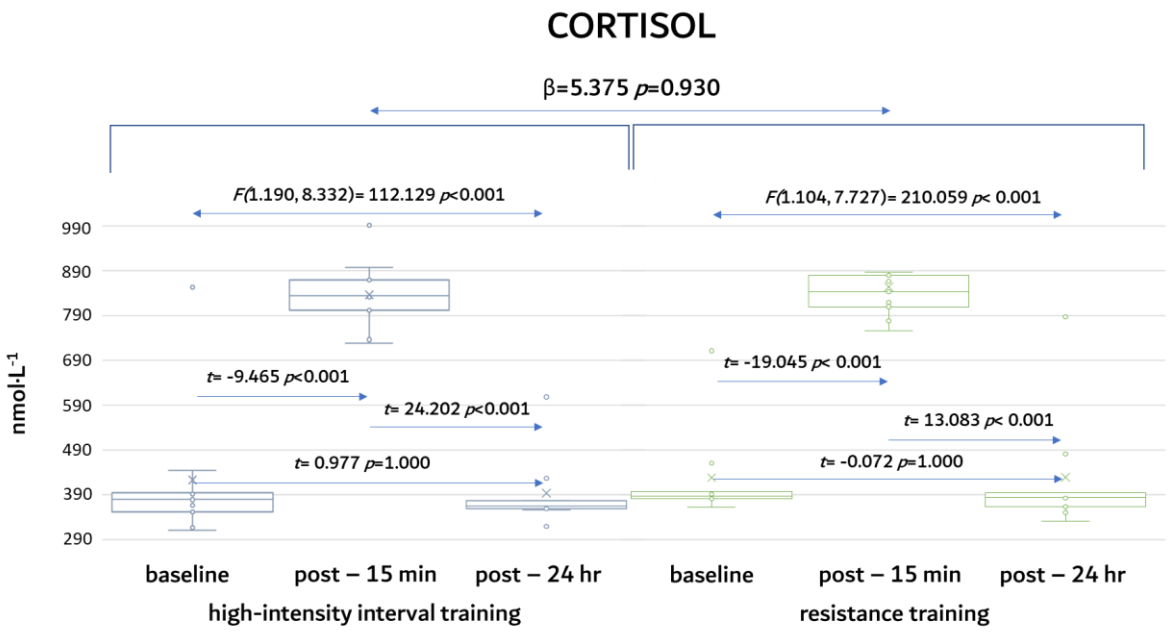

Figure 2-S4 Cortisol.

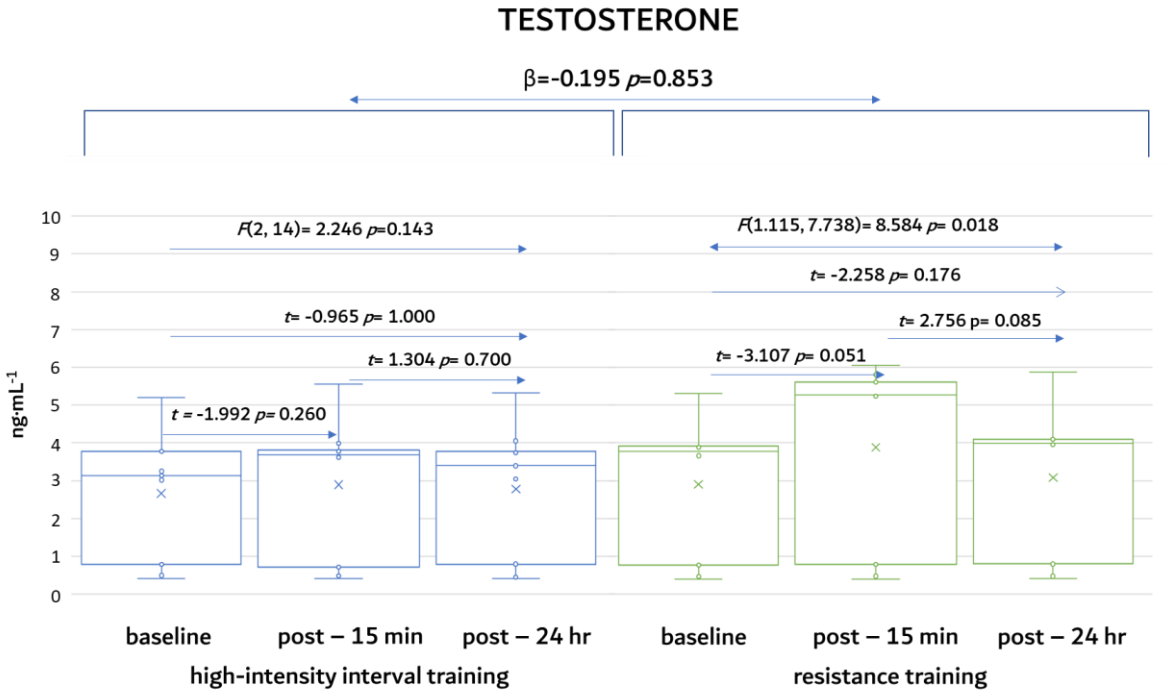

Figure 2-S5 Testosterone.

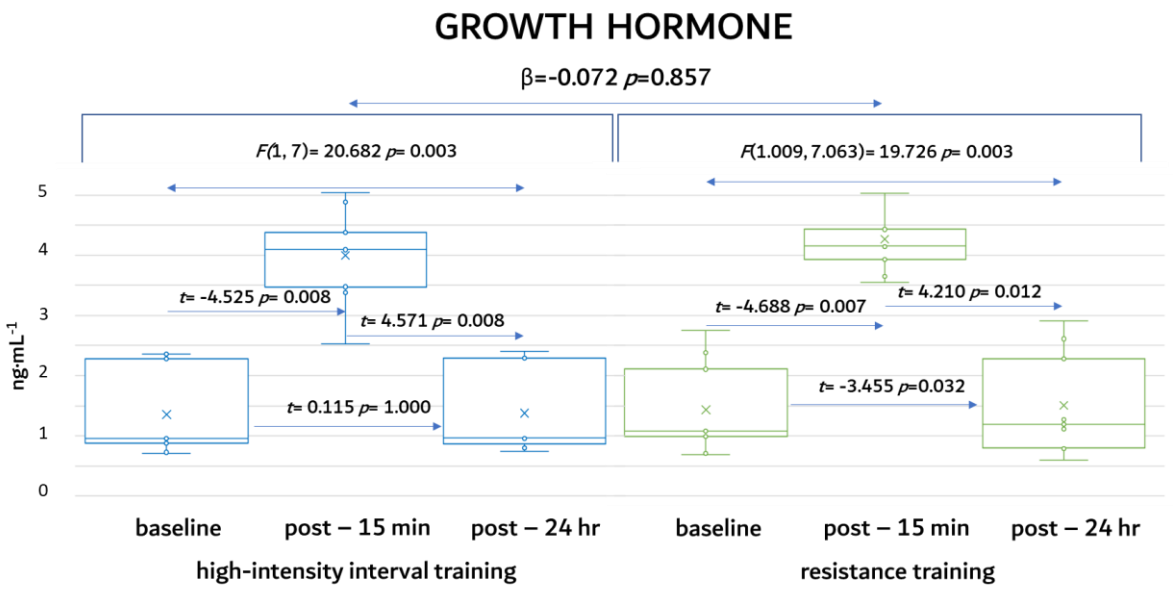

Figure 2-S6 Growth hormone.

Romijn correction for energy expenditure

For energy expenditure calculation and because urinary nitrogen was not determined, a simple correction was proposed by Romijn et al. (239), using 135mcg ·kg-1·min-1 of Ṅ that would be equivalent of an intake of ~85g of protein per day for a 70 kg individual:

Ox PRO •day^{-1} = (135 µg•kg^{-1}•min^{-1} x 1440 min•day^{-1} x 70kg / 1000000) / 0.16

Ṅ=~85 g OxPRO •day^{-1}

Based on that we used participants' protein intake and calculated the presumably excreted Ṅ which was estimated:

Ṅ = (PRO x 0.16)/1440 min•day^{-1})/kg) x 1000000 = estimated Ṅ (µg•kg^{-1}•min^{-1}) excretion

3 Effects of iso-time, quasi iso-effort high-intensity interval training, resistance training or both combined with low-carbohydrate high fat diet.

Prelude

After knowing what the events of a single session of either HIIT or RT are, and what their physiological effects are, it is possible to use that information for the interpretation of the effects of this 12-week intervention. This chapter presents in a detailed manner all investigations with each of its components (i.e. comprehensive assessment, nutritional approach, and exercise interventions). It is an original contribution to the literature, as to the best of our knowledge, presents for the first time a direct comparison between HIIT, RT or both when performed iso-time and quasi iso-effort with the addition of a LCHF diet for improving metabolic health. This investigation shows the possibility of combining high-intensity exercise with carbohydrate restriction, and provides the reader with valuable information that may be used for the design and implementation of a similar programme, and questions what are the aspects that require closer attention to minimise unwanted outcomes.

ABSTRACT:

Exercise and a healthy diet improve metabolic health. However, the ideal combination is unknown. We compared the effects of iso-time and quasi iso-effort high-intensity interval training (HIIT), resistance training (RT), or both (COMBO), all including a low carbohydrate high-fat diet (LCHF). Fifty-four sedentary and overweight individuals (18-60 y, M=24, F=30) were randomised to 1 of 3 experimental groups: LCHF+HIIT, LCHF+RT or LCHF+COMBO. Participants performed their 20-min exercise protocol 3/week/12 weeks while following the LCHF diet (≤100 g CHO, ~1.5g PRO/kg and unrestricted fat intake). Sessions involved 10x1 min of high-intensity effort (all ~17 RPE on a 6-20 scale) interspersed with 1 min recovery periods. Intensity: HIIT (≥90% heart rate reserve); RT (~70-80% of 1 repetition maximum, ~2-repetitions short of failure). Outcomes assessed included body composition, glycaemic control, blood lipids, hsCRP, uric acid, and performance measures. Adjusted between group differences were analysed with general or generalised linear models. Improvements in HbA1c were significantly greater for LCHF+HIIT than both LCHF+RT (β= 2.41, p=0.014) and LCHF+COMBO (β= 2.58; p=0.005). Body mass reduction was significantly greater for LCHF+HIIT relative to LCHF+COMBO (β= 1.88, p=0.049). Upper body strength was superior for LCHF+RT relative to LCHF+HIIT (β= 4.18; p=0.024). Resting metabolic rate (RMR) was greater for LCHF+COMBO (β= 896.02; p=0.004) and LCHF+RT (β= 690; p=0.024) both relative to LCHF+HIIT. Otherwise, there were no significant differences observed between groups. All interventions were similarly effective for improving cardiometabolic risk factors, potentially due to the carbohydrate restriction and the high effort exerted during HIIT and RT.

Keywords: Metabolic Syndrome, $\dot{V}O_2$peak, VAT, RMR, Weight loss, LCHF

Novelty bullets: • LCHF+COMBO or LCHF+RT provide an advantage vs LCHF+HIIT for metabolic health because RT spares LBM and increases RMR. • RT, HIIT or COMBO were equally effective for improving aerobic capacity. • RT, HIIT or COMBO + LCHF were equally effective for reducing VAT.

Introduction

Metabolic health is usually characterised by the cluster of metabolic risk factors (i.e. abdominal obesity, impaired glucose tolerance, hypertriglyceridemia, decreased HDL-C, and/or hypertension) known as the metabolic syndrome (MetS) (266). In this regard, it is generally acknowledged that metabolic health is highly influenced or even dependent on habitual nutrition and physical activity while genetic factors are also influential (266).

Within the nutritional approaches regarded as healthy, a low carbohydrate high fat diet (LCHF), as defined by Feinman et al. (24), typically comprises ≤ 100g of CHO per day (no more than 20-30% of total energy intake per day); a moderate protein (PRO) intake (15-25% of total energy), and comparatively high fat (50-60% of total energy) (23, 24). Such macronutrient distribution may reduce glycaemia and body weight in addition to improving lipids and inflammation markers (22, 24). LCHF has been referred to as the default diet for metabolic syndrome and diabetes (24), and usually favours eating food that is minimally processed (or 'whole food') while discouraging consumption of processed food.

Although any general physical activity may result in positive effects on metabolic health in previously sedentary individuals (16), high-intensity interval training (HIIT) and resistance training (RT) have recently attracted specific attention, owing to their potential potency and multifarious effects. HIIT is comprised of work bouts of 10 s to 4 min at >85% VO2max interspersed with low intensity active recovery period of various durations. Though half or most exercise in the HIIT condition is aerobic, periodic excursions involving anaerobic energy pathways stimulating the mitochondria to greater improvements in exercise capacity, mitochondrial biogenesis (17), enzymatic markers associated with glycolysis (18), aerobic metabolism and beta (β)-oxidation (18) than aerobic continuous training in a reduced time. There is agreement that this type of exercise is suitable and effective at improving health markers in people with prediabetes (19). RT can significantly improvement MetS risk factors such as obesity, high HbA1c levels, and systolic blood pressure, and therefore would also be efficacious in the management of type 2 diabetes and metabolic disorders (20).

It is generally considered that nutrition and exercise-based strategies to improve health are more effective when used in combination than either one in isolation (21). The traditional approach has been combining a low-calorie diet and aerobic or resistance training (21). However reducing calories may not necessarily improve metabolic health if carbohydrate content is not considered, arguably an influential component in factors such as glycaemic control (22, 23). Given the known benefits of HIIT, RT, and a combination of these modalities as independently effective options, it is

of interest to determine their relative efficacy, in particular when combined with a LCHF diet approach. Hence the purpose of this study was to describe the effect of a combination a LCHF and HIIT, RT or combined HIIT and RT (COMBO) in sedentary and overweight individuals at risk of metabolic disease on a range of metabolic health outcomes.

Materials and Methods

With the AUT Ethics Committee approval (approval number: 15/194), a 12-week randomised trial was conducted for which a total of 61 sedentary adults expressed their intention to participate. The inclusion criteria included: 18-60 years, self-assessed low active (≤150 min of physical activity per week), and overweight (BMI ≥25 kg/m2). The stated exclusion criteria were: pre-diagnosed with a medical condition limiting their ability to participate in the intervention; taking any medication with a direct effect on the outcome measures, including systolic blood pressure (BP) > 180 mmHg and/or diastolic BP > 110mmHg; type 1 diabetes; history of myocardial infarction, angioplasty, coronary artery bypass or cerebrovascular ischemia/stroke; symptomatic congestive heart failure; atrial flutter; unstable angina; unstable pulmonary disease; third degree heart block; recent history of alcoholism, drug abuse; pacemaker; unstable metabolic disease; and orthopaedic or rheumatologic problems that could impair the ability to exercise.

Potential participants had explained to them both the risks and the prospective benefits, and if they were willing to comply with all study requirements their written informed consent was obtained. Thereafter, participants were randomly assigned post baseline assessment to one of three groups using a computer assisted 1:1:1 allocation (267) (LCHF+HIIT, LCHF+RT or LCHF+COMBO) (see figure 1) and completed a range of assessments pre- and post-intervention.

Comprehensive assessment.

A comprehensive assessment at baseline and post-intervention, and is presented in the order it was conducted:

Resting metabolic rate (RMR)

RMR was assessed during the morning between 6:00-9:00 am following an overnight fast (~12 h) and no exercise for 12 h prior. Individuals were assessed while awake after lying supine for a minimum of 30 min in a thermo-neutral environment while connected by a face mask to a metabolic cart (ParvoMedics, East Sandy, UT). Every 15 s, oxygen consumption, carbon dioxide production and ventilation data were analysed to determine RMR during a steady state period of at least 4 min

or more (268), defined as ≤10% coefficient of variation (CV) in one or more of the following parameters: V̇O2, V̇CO2, RQ (≤5% CV), or min ventilation (268). Heart rate data was also collected using a standard Polar heart rate chest band (Polar Electro Oy, Kempele, Finland) and the data was then stored by the metabolic cart. Prior to each test, gas and ventilation calibration was carried out; all detachable components (hose, non-re-breathable valve and mask, filter, etc.) were clean and dry for each use following manufacturer recommendations. Blood pressure: Systolic and diastolic blood pressure (BP) were measured with an automated Blood Pressure Monitor (HEM-7321-E, Omron Corporation, Kyoto, Japan) after each participant had sat quietly for a period of 10 min. The average of three consecutive readings was used for analysis.

$\dot{V}O_2$peak test

After at least 4 h fast and no strenuous physical activity, participants arrived at the physiology lab. Using a cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands) while simultaneously measuring gas exchange with a metabolic cart (ParvoMedics TrueOne 2400, East Sandy, UT. USA), participants were tested for peak aerobic capacity using an incremental protocol, increasing 20 W ever y 3 min for the first three stages, then 20 W every 1 min until volitional exhaustion and not able to perform a cadence of at least 60 RPM. A test was considered maximal if RER ≥1.10 and participants were unable to continue cycling. When maximal exertion was reached, participants continued cycling (at 50 W) for an additional 10 min cool down. The Borg scale (269) of 6-20 was used during the last 30 s of each step. Maximum heart rate within the last 30_s of each stage and was automatically recorded by the metabolic cart.

Strength

Upper and lower body one repetition maximum strength (1RM) was assessed via the bench press and leg press exercises using the methods of Levinger et al. (270).

Physical Activity

The validated International Physical Activity Questionnaire long form (IPAQ-LF) was used to assess physical activity (PA) and quantified as METs·min^{-1}·day^{-1} (271).

Body composition

A whole-body dual-energy x-ray absorptiometry (DXA) scanner (GE-Lunar iDXA, GE Healthcare, Madison, WI. USA) with GE-Lunar enCORETM software (version 15) was used to determine total lean mass (kg), total bone mineral content (BMC) (g), total fat mass (kg) and estimated visceral fat mass (VAT) (g). Height (wall stadiometer to nearest 0.1 cm, baseline only), weight (to nearest 0.01 kg), waist circumference (WC) at the mid-point between the rib cage and the iliac crest (to the nearest 0.1 cm), and hip circumference were measured at the widest point of buttocks area (to the nearest 0.1 cm) and waist to hip ratio (WHR) was calculated.

Blood biomarkers

Blood samples were obtained from an antecubital vein and collected into PST II (REF 367375) and K2E (REF 367839) BD vacutainers. Overnight (12 h) fasting was confirmed by verbally asking participants before blood was collected by a certified phlebotomist between 06:00 and 09:00 am. Serum was isolated by centrifugation (1500 RPM at 4°C for 10 min) and frozen at -80°C until further analyses. Samples were subsequently thawed and analysed using specific assays on a Roche Modular E170 at the AUT Roche Diagnostic Laboratory. Blood biomarkers assessed included cardiometabolic biomarkers [C-Peptide ($nmol \cdot L^{-1}$), insulin ($pmol \cdot L^{-1}$), glucose ($mmol \cdot L^{-1}$), HbA1c ($mmol \cdot mol^{-1}$), total cholesterol ($mmol \cdot L^{-1}$), low-density lipoprotein cholesterol (LDL-C) ($mmol \cdot L^{-1}$), high-density lipoprotein cholesterol (HDL-C) ($mmol \cdot L^{-1}$), triglycerides (TG) ($mmol \cdot L^{-1}$), uric acid ($mg \cdot dL^{-1}$) and an inflammatory biomarker (high-sensitivity C reactive protein (hs-CRP) ($mg \cdot L^{-1}$)].The homeostasis model of assessment for insulin resistance (HOMA2) calculation was computed with the HOMA2 calculator (version 2.2.3 for Windows; available from https://www.dtu.ox.ac.uk/homacalculator). Values of >2 indicated insulin resistance (272).

Metabolic Syndrome estimation

The simple Metabolic Syndrome Score (siMS score) was used to determine the metabolic status that was developed to be used in clinical and research settings using a sample of individuals of similar characteristics of the present study (273).

$$\text{siMS score} = \frac{2 \times \text{waist}}{\text{height}} + \frac{\text{Glu}}{5.6} + \frac{\text{TG}}{1.7} + \frac{\text{systolic BP}}{130} - \frac{\text{HDLc}}{1.03 \text{ or } 1.28 \text{ (male or female)}}$$

Dietary assessment

Food and beverage intake at the baseline were quantified from a 3-day food diary that included two week days and one weekend day. Participants were instructed to measure their food and beverage intake using common household measurements (cups-250 g or ml, tablespoons 15 g, teaspoons 5 g). Data from food diaries were analysed using Foodworks Nutrient analysis software (Xyris Ltd, 2012). In addition, adherence was monitored pre- and post-intervention using a short food frequency questionnaire (FFQ) previously used elsewhere (42) with emphasis on foods containing carbohydrate. Participants were also requested to record their food intake during three days of the week as if they were completing a 3-day diary using a commercially available mobile apps (MyFitnessPal, EasyDietDiary, etc.) to help them complete their pre and post food diaries. Throughout the intervention the use of these apps was intended to maintain their awareness of following the CHO restriction. Participants were encouraged to ask questions about their diet during the exercise sessions each week to facilitate ongoing monitoring and adherence while reminded of the importance of tracking their nutritional intake.

Wellbeing

The Profile of Mood States (POMS) short version comprised of 37 mood-related adjectives developed by Shacham (274), and previously used in nutrition (275, 276) and exercise (277, 278) studies. It was used to calculate the total emotional disturbance, which is the overall indicator of global emotional well-being, obtained by adding the scores of all the sub-scales of negative emotional connotation (Anger-Hostility + Confusion-Bewilderment + Depression-Dejection + Fatigue-Inertia + Tension-Anxiety) and then subtracting the sum from the Vigour-Activity score.

Nutritional Intervention

All participants in all groups were instructed to limit their carbohydrate intake to a maximum of 100 g per day, and as a recommendation, to consume between 1-2 portions of PRO each meal, or approximately 30g PRO per meal (~1.5 g of PRO per kg of ideal body weight (IBW) in total for the day [IBW=height (cm)-100 or 110 (male and female)] (279), while no restrictions were placed on the amount of dietary energy or fat consumed, but to eat to satiety. In summary the dietary advice given was one that emphasised the consumption of minimally processed foods, including vegetables, unprocessed meats, eggs, nuts, oils and dairy products (such as butter, cream, Greek yogurt) and small amounts of fruits and starchy vegetables. All participants were provided with educational tools that consisted of a guide explaining the principles of carbohydrate restriction and how to balance the macronutrient composition. All participants had access to a website specifically created to provide additional information to help their understanding of the dietary protocol, and a nutritionist

with expertise in the LCHF approach was available to answer questions when required. These materials have been previously used in another LCHF study by this research group (42).

Exercise programme

Supervised exercise sessions were conducted three times a week, for a total of 30 min (see Figure 1). The main component of the sessions were 10 x 1 min exercise intervals interspersed with 1 min of passive or active recovery. The sessions were designed to be iso-time, and quasi iso-effort between groups, in that a target heart rate of ≥90% of heart rate reserve (HRR) was prescribed for HIIT sessions, while RPE was 17-18 for both HIIT and RT. Participants wore a heart rate monitor chest band (Polar Electro Oy Kempele, Finland) and recorded the maximum heart rate achieved during each work phase, along with their RPE (Borg 6-20). In addition to this, RT recorded the number of repetitions in reserve (RIR) (236), to provide ongoing feedback and inform the load prescription increments. During the intervention, all participants received verbal encouragement during exercise sessions from the attending researcher. Once a week, participants were weighed, waist and hip circumferences recorded and blood pressure was taken before exercise to allow them to track their ongoing progress. This moment was also used to confirm participants were tracking their food intake via mobile app and were also reminded of the importance of meeting their nutritional prescription.

LCHF + HIIT group

Both a cycle ergometer (95C Inspire cycle ergometer Life Fitness, Rosemont, IL) and treadmill (95T Engage treadmill, Life Fitness, Rosemont, IL) were used throughout the intervention. Participants completed 5 work sets at ≥90% of HRR on either the cycle or treadmill, then swapped to either the cycle or treadmill for the remaining 5 work sets. The number of work sets was incremented by one per session, such that by week 4 all participants performed all 10 work sets at the target intensity. ‘Recovery’ sets were performed at approximately 50%-60% HRR.

LCHF + RT group

Participants exercised in a circuit format, performing 6 compound exercises using large muscle groups. Initially resistance was set at 40-50% of 1RM until they acquired good form as assessed by the supervisor. At such time the resistance was increased, until participants reached the point where they reported RIR ≤ 5 (~70-80% of 1RM, ~2-repetitions short of failure), then weight was increased about 5% of 1RM and so on.

Combination group (LCHF + COMBO)

The combination group consisted of alternating two HIIT sessions interspersed with one RT session per week, then the following week with two RT sessions and one HIIT session. This alternating weekly pattern was repeated over the duration of the intervention. Figure 1 shows how exercise sessions were designed.

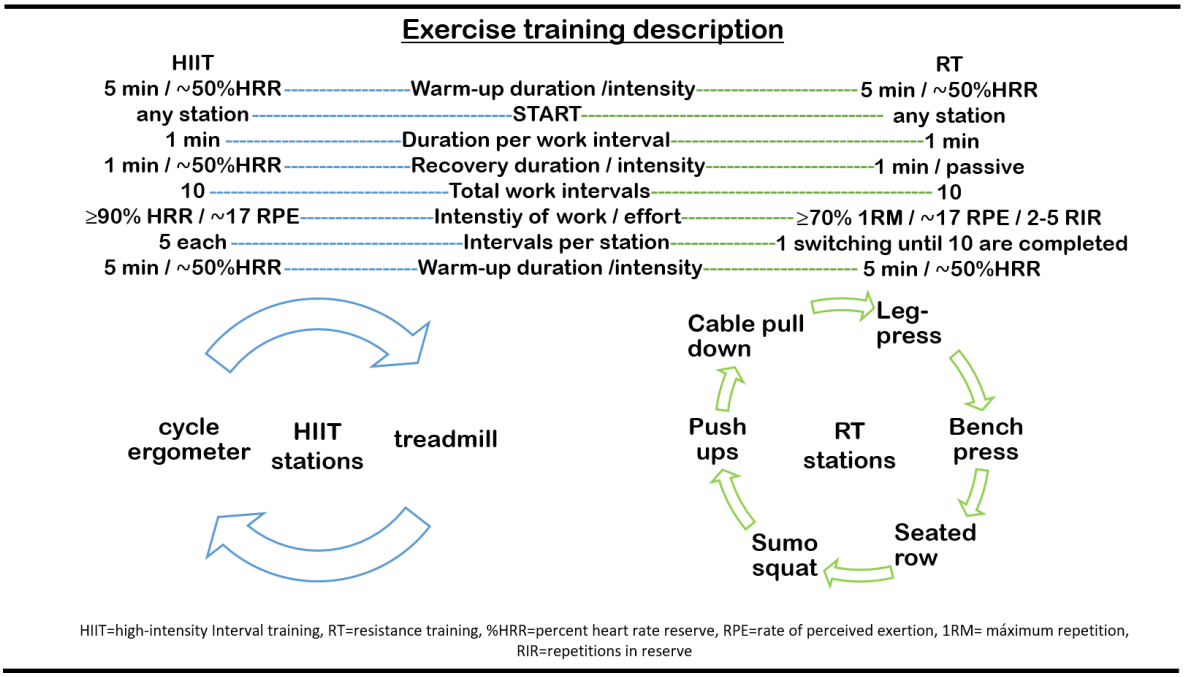

Figure 3-1 Exercise description.

Matching time and effort: Iso-time and Quasi Iso-effort

A commercially available mobile app metronome (WORKOUTS+, www.parabolicriver.com) with programmed voice audible prompts, indicated when to begin and end active and resting periods, and the tempo for both eccentric and concentric phases throughout the 20 min of exercise for every session. Throughout the entire 36 exercise sessions, tracking exercise progress and assuring intensity targets were being met, heart rate and RPE were recorded for HIIT training sessions and HR, RPE, RIR and weight loads, were recorded for all RT sessions. Participants wore a heart rate monitor watch and chest band (Polar Electro Oy, Kempele, Finland), and had a training record slip paper designed to manually record (for all training sessions) these parameters. Participants were

previously trained to record after each high-intensity interval/set RIR and/or RPE, and maximal heart rate that was reached. If target HR wasn't met and RPE was below 17 the speed was adjusted accordingly for HIIT. RIR is the subjective estimation of the potential repetitions that can possibly be performed after completing the prescribed number of repetitions. If RIR was ≥5 and RPE was lower than 17, the weight load was increased accordingly for RT. To obtain an estimation of how closely both HIIT and RT were quasi iso-effort, the session's average RPE and heart rate was obtained (MRPE). The average of all high-intensity work periods/intervals/sets, is considered the session's RPE expressed as MRPE (280). The MRPE was calculated for HIIT and RT sessions for the last month (last 6 sessions for HIIT and RT). Exercise accompaniment: Participants were monitored and provided with any assistance should they need it. Heart rate monitors, training session's paper slips to record heart rates, intensity level, the weight being lifted, RPE, RIR scores were obtained during the exercise performance.

Adherence to intervention

Arbitrarily, adherence to nutritional intervention was having a CHO intake of 100 g ± 10% measured with the food diary. Exercise session adherence was defined as minimum 90% of all exercise sessions attendance.

Control period

For assessing the stability of the measures, before the intervention started, we ran a control period of six weeks on some of the participants (n=15) from the total sample of the present study. It included all measures in the comprehensive assessment. We cannot call the present study a randomised control trial because this period was only half of the duration of the experimental phase. The reason for this was that the participant number was not large enough to compensate for the withdrawals that may have occurred with those participants that expressed their reluctance to be part of this study if they were assigned to the control group. This result was similar to Frarinha's study (281), with the difference that due to our limited resources we randomised participants to participate in this control phase and had a second randomisation for integrating the three experimental groups.

Statistical Analysis

All descriptive values are presented as means ± standard deviation (SD), or medians and interquartile range for not normally distributed data. All data was tested for normality using Shapiro-Wilk test and histograms, and Q-Q plots. Equivalence at the baseline was determined using one-way ANOVA or Kruskal-Wallis tests using Bonferroni correction and, homoscedasticity was

confirmed through Levine's test (pre- and post-testing). Within groups, differences were assessed using a paired samples t-Test or a Wilcoxon signed rank test; magnitude and direction of effect was detected using Hedges-g effect sizes, which corrects for small sample sizes, also reporting with its 95% confidence intervals. The coefficient of variation was computed for assessing the stability of the measures. To establish significant differences between groups and ultimately which combination was more effective for each outcome according to each variable, linear regression or generalised linear regression models (GLM) using HIIT as the reference group were conducted and evaluated to test whether there was a difference in the outcome variable between groups, controlling for baseline measures. For presenting results in text, adjusted between group differences are represented by β and the related p value. To compare if exercise was quasi iso-effort, the Wilcoxon signed rank was used.

Analyses were conducted using IBM-SPSS Statistics (version 24, IBM Corporation. Chicago, Illinois, USA), Stata (version 15, StataCorp LLC Texas, USA), and Excel (version 16, Microsoft Corporation Redmond, WA, USA).

RESULTS

Initial characteristics

Demographic and baseline characteristics by group are presented in Table 3-1. Baseline characteristics between groups were equivalent ($p>0.05$) for all outcome measures, except for fasting blood glucose ($p<0.05$), which was greater in the RT group; and did not change during the 6-week control phase (see S1[1] and S2[1]). Baseline and post-intervention outcomes for within groups' differences are depicted in Tables S3[1]- S8[1]. Between group outcomes are shown in Tables 3-2 and Figure 3- 2.

[1] Supplementary data are available with the article through the journal Web site at

Table 3-1 Demographic characteristics.

BASELINE CHARACTERISTICS BY GROUP (PARTICIPANTS THAT COMPLETED THE INTERVENTION)

		BASELINE			
FITNESS	CONTROL	HIIT	RT	COMBO	*p*
male / female	6/9	8/11	5/8	6/8	
age (y)	48 (46, 52)	53 (41, 55)	48 (46, 51)	45 (41, 49)	0.262
HEIGT (cm)	172±7	172±10	171±13	174±10	0.745
BMI (kg/m^2)	30 (29, 33)	29 (28, 31)	29 (28, 31)	30.4 (28, 34)	0.528
$\dot{V}O_2$peak (mL•kg^{-1}•min^{-1})	26.62±6.54	*23.54 (22.07, 31.37)*	27.63±5.28	28.03±4.57	0.622
BENCH PRESS (kg)	38 (32.5, 62.5)	*35 (30, 45)*	49.42±27.14	49±20	0.641
LEG PRESS (kg)	286±90	215±72	276±105	297±101	0.055
RMR (kJ•day^{-1})	6487±1315	*6360 (5630, 7226)*	6765±1991	7011±2277	0.959
PHYSICAL ACT (MET/min/day)	379±81	392±74	368±69	397±74	0.766
BODY COMPOSITION					
BODY MASS (kg)	91.5±15.2	88.2±16.3	89.93±21.87	91.6±20.4	0.948
FAT MASS (kg)	35.2±11.7	*32 (28.5, 36.7)*	*29.82 (28, 37.03)*	34.5±12.4	0.951
VAT (g)	1439±778	1389±769	1302±908	1135±688	0.699
LBM (kg)	53.3±9.8	51.7±11.0	53.36±14.5	54±11.7	0.946
BMC (g)	3075±450	*3115 (2427, 3436)*	2934±752	3051±583	0.958
WAIST (cm)	105±9.8	*105 (97.8, 106)*	*102.7 (96, 111)*	105.7±12.4	0.797
WAIST TO HIP RATIO	0.94±0.07	0.95±0.05	0.92±0.10	0.94±0.06	0.934
BIOMARKERS					
C-PEPTIDE (nmol•L^{-1})	*0.80 (0.65, 1.10)*	0.80±0.33	*0.81 (0.58, 0.99)*	*0.93 (0.32, 0.86)*	0.072
INSULIN (pmol•L^{-1})	*76.23 (41.34, 95.28)*	*81.1 (55.4, 100)*	*48.8 (39.9, 90.6)*	*69.2 (46.8, 100)*	0.673
HbA1c (mmol•mol^{-1})	36.86±3.33	*34.5 (31.1, 36.4)*	36.9±2.6	35.6±2.5	0.069
GLUCOSE (mmol•L^{-1})	*6 (5.8, 6.45)*	5.28±0.58	*6 (5.5, 6.65)*	5.9±0.7	0.003
CHOL (mmol•L^{-1})	5.53±1.19	*5 (4.5, 5.5)*	*5 (4, 6)*	*5 (4.25, 6)*	0.273
HDL-C (mmol•L^{-1})	*1.32 (1.18, 1.72)*	1.51±0.51	1.49±0.47	1.44±0.35	0.963
LDL-C (mmol•L^{-1})	3.93±1.28	*3.4 (3.09, 3.67)*	3.77±1	3.57±0.95	0.377
TG (mmol•L^{-1})	*1.33 (0.89, 1.49)*	*1.11 (0.78, 1.43)*	*1.14 (0.99, 1.35)*	*1.16 (0.89, 1.34)*	0.913
TG-HDL ratio	*0.40 (0.32, 0.47)*	*0.29 (0.18, 0.59)*	*0.33 (0.27, 0.49)*	*0.35 (0.26, 043)*	0.977
hsCRP (mg•L^{-1})	3.07±1.68	*2.2 (0.85, 3.2)*	*2.9 (1.6, 6)*	*2.35 (1.1, 3.5)*	0.305
URIC ACID (mg•dL^{-1})	0.38±0.10	0.32±0.09	0.39±0.14	0.34±0.08	0.163
METABOLIC HEALTH					
siMS score	2.74±0.79	2.52±0.85	2.75±0.77	2.62±0.61	0.889
INSULIN RESISTANCE					
HOMA2 IR	*1.70 (0.95, 2.1)*	*1.71 (1.16, 2.19)*	*1.08 (0.89, 1.99)*	*1.52 (1.09, 2.04)*	0.752
BLOOD PRESSURE					
SYSTOLIC BP (mm Hg)	117±16	126±16	118.77±13.48	119±12	0.427
DIASTOLIC BP (mm Hg)	75±8	80±10	76.62±6.95	76±5	0.196
DIET COMPOSITION					
ENERGY INTAKE (kJ)	*8630 (7814, 10341)*	8703±1517	*8017 (7661, 10333)*	8787±1704	0.744
CARBOHYDRATE %EI	54±2.7	*49.1 (46.4, 50.4)*	49.61±2.97	49.5±2.3	0.928
CARBOHYDRATE INTAKE (g)	293±44.1	275±57	290±46.68	287.4±57.7	0.771
PROTEIN %EI	16±1.9	16±1.17	15.7±2.64	16.1±1.5	0.941
PROTEIN INTAKE (g)	86.3±17.7	75.4 (71.3, 92.5)	*78 (64, 102.8)*	84.5±17.3	0.851
FAT %EI	29.3±2.4	*28.9 (27.8, 30.9)*	29.3±1.75	28.7±1.7	0.729
FAT intake g	70.1±10.9	*66.3 (58.5, 75.5)*	*63 (60, 76.8)*	66.8±12.9	0.744
WELLBEING					
TOTAL MOOD DISTURBANCE	16 (15, 18)	*15 (13.5, 15)*	*16 (14, 18)*	*16 (14, 17)*	0.014

Mean±SD or Median (IQR) (italic). Comparisons between groups, ANOVA or Kruskal-Wallis, significance ≤0.05
VAT= visceral adipose tissue, LBM= lean body mass, BMC= bone mineral content, CHOL= total cholesterol TG= triglycerides
hsCRP= high sensitive C reactive protein siMS score= Simple Metabolic Syndrome score
HOMA2-IR= Homeostasis Model Assessment 2 Insulin Resistance, %EI= percentage of total energy intake.

Adherence for both the exercise and nutritional programmes

Adherence for both the exercise and nutritional programmes (see Tables S3[1], S4[1]) were satisfactory. The CHO intake was within the desired limit of 100 g per day and the attendance was >90% of exercise of the total of 36. The Figure 3-2 CONSORT diagram presents the participant flow. All Tables show the results arranged by group, for practicality instead of LCHF+HIIT, LCHF+RT and LCHF-COMBO, groups are referred only as HIIT, RT and COMBO, in all tables and when presenting results between groups.

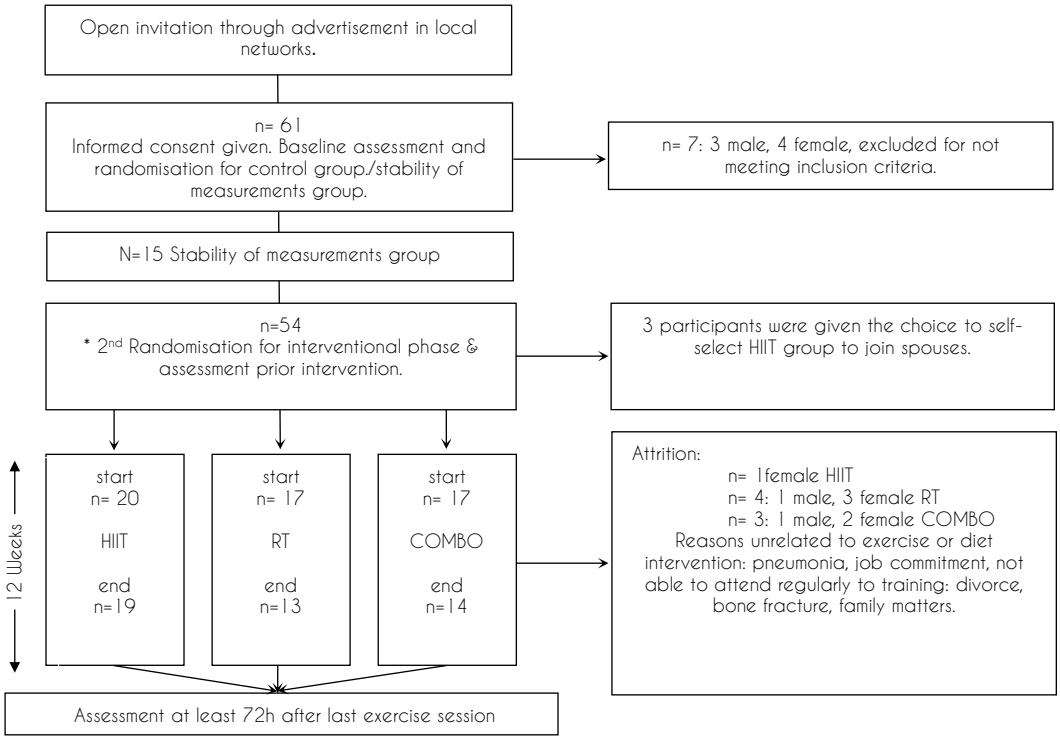

Figure 3-2 CONSORT diagram.

Comprehensive assessment results.

RMR

RMR was greater for LCHF+COMBO (β= 896.02; p=0.004) and LCHF+RT (β= 690; p=0.024) both relative to LCHF+HIIT (see Table S5[1] and Figure 3).

$\dot{V}O_2$peak test

Cardiorespiratory fitness improvements were significant within groups only, equivalent to 1.04 (+14%), 0.84 (+11%), and 1.29 (+16%) metabolic equivalent tasks (METs) gains for LCHF+HIIT, LCHF+RT, and LCHF+COMBO respectively, but not different between groups (HIIT vs RT: β= -0.64; p=0.440; HIIT vs COMBO: β= 0.95, 95% CI -0.68, 2.57; p=0.245). **Strength:** Bench press and leg press improved significantly for all exercise groups (see Table S5[1]), the LCHF+RT group had the most improvement for bench press relative to LCHF+HIIT (β= 4.18; p=0.024), with no significant between-group difference for the leg press (HIIT vs RT: *β*= 6.81; *p*=0.610; HIIT vs COMBO: *β*= 10.95; *p*=0.628. **Physical activity:** was maintained the same after 12 weeks of intervention (see Table S5[1]) (HIIT vs RT: *β*= 1.98; *p*=0.499; HIIT vs COMBO: *β*= 3.41; *p*=0.232).

Body composition

All intervention groups experienced significant improvements in body mass, fat mass, and visceral adipose tissue (see Table S7[1]), but only body mass was significantly different between groups; the LCHF+HIIT group had the greatest reduction in body mass relative to COMBO (*β*= 1.88, *p*=0.049) (see Table 2 and Figure 3). LBM was significantly reduced for the LCHF+HIIT group, (see Table S7[1]) but similar between groups (see Table 2). BMC was significantly reduced for LCHF+HIIT and LCHF+RT (See Table S7[1]) but similar between groups (HIIT vs RT: (β= -6.87; p=0.522; HIIT vs COMBO (*β*= 13.56; *p*=0.260) (Table 2).

Blood biomarkers

All measured metabolic parameters improved after 12 weeks of intervention. Most notably glycaemic control assessed by HbA1c was most improved for LCHF+HIIT relative to both LCHF+RT (*β*= 2.41; *p*=0.014) and LCHF+COMBO (*β*= 2.58; *p*=0.005). After 12 weeks, there were improvements across all groups for HDL-C, LDL-C, TG and TG/HDL-C ratio, with significant

[1] Supplementary data are available with the article through the journal Web site at

improvements only for LCHF+HIIT and LCHF+RT (see Table S6[1]) but there was no significant between group difference.

Metabolic health

The Simple Metabolic Syndrome score (siMS score) was significantly reduced for all groups (Table S8[1]); but there were no between group significant differences (HIIT vs RT: β= -0.02; p= 0.862. HIIT vs COMBO: β= 0.20; p= 0.130). Insulin resistance measured by HOMA2−IR, also significantly reduced for all interventions; but not different between groups (HIIT vs RT: β= 0.09; p= 0.560. HIIT vs COMBO: β= 0.00; p= 0.986). Although participants were normotensive at the start of the study, significant reductions were observed for systolic blood pressure (SBP) (all $p \leq 0.024$, see Table S8[1]), while only LCHF+HIIT and LCHF+COMBO were significantly different for diastolic blood pressure (DBP) (Table S8[1]). Nevertheless, between group differences showed no difference.

Dietary assessment

Between groups energy intake was similar ($p \geq 0.470$), but there was a significant reduction in the energy intake between pre- and post-assessment within all groups ($p < 0.001$) (see Table S4[1]) which was found for all participants. The energy intake reduction was a consequence of a significant reduction of ~183 g (~60%) in CHO intake between the baseline and post-12 weeks results ($p < 0.001$) that were similar for all groups (HIIT vs RT: β= 8.45; p= 0.608. HIIT vs COMBO: β= 2.45; p= 0.312). This can also be observed in the reduction of servings of CHO rich foods and the increase of foods with low carbohydrate content (see Table S3[1]). At baseline, participants reported they were consuming 10+ portions of bread per week, and they reduced it to 1-3 portions during the intervention, reflected in the post-intervention assessment. Conversely, they increased their intake of non-starchy vegetables and fruits in all groups (see Table S3[1]). Overall, the CHO content in the diet, as mentioned previously, was significantly reduced across all groups showing there was a good adherence to their dietary prescription. The protein intake was significantly ($p \leq 0.001$, Table S4[1]) increased (50-56%) (see Table S4[1]) and was similar between groups (HIIT vs RT: β= -2.48; p= 0.649. HIIT vs COMBO: β= 0.72; p= 0.826). Fat intake followed the same trend as protein registering significant increases (13-29%) between pre- and post-intervention ($p < 0.001$, see Table S4[1]) and was similar between groups (HIIT vs RT: β= -0.81; p= 0.801. HIIT vs COMBO: β= -0.34; p= 0.914). Exercise programme: successfully matched, the MRPE was for 17.2 HIIT vs 17.5 for RT.

[1] Supplementary data are available with the article through the journal Web site at

Wellbeing

In general, wellbeing that was measured by the POMS improved across all groups (see Table S9[1]), after 12 weeks of intervention as was shown by a similar reduction between groups in the total mood disturbance ($p \geq 0.187$) (see Table 3-2).

Table 3-2 Between groups' difference

	BETWEEN GROUPS' DIFFERENCE											
	HIIT - RT						HIIT - COMBO					
					β 95% CI						β 95% CI	
BODY COMPOSITION	β	SE	t	p	lower	upper	β	SE	t	p	lower	upper
***WEIGHT (kg)**	**1.36**	**0.98**	**1.40**	**0.163**	**-0.55**	**3.28**	**1.88**	**0.96**	**1.97**	**0.049**	**0.00**	**3.76**
FAT MASS (kg)	0.47	0.97	0.48	0.633	-1.49	2.42	1.11	0.95	1.17	0.249	-0.80	3.02
*VAT (g)	48.27	75.31	0.64	0.522	-99.34	195.88	30.02	74.33	0.40	0.686	-115.67	175.71
LBM (kg)	0.88	0.46	1.92	0.062	-0.05	1.80	0.72	0.45	1.61	0.116	-0.18	1.62
BMC (g)	-6.87	12.11	-0.57	0.573	-31.30	17.56	13.56	11.87	1.14	0.260	-10.39	37.52
WAIST (cm)	0.84	1.39	0.60	0.549	-1.97	3.65	2.24	1.36	1.64	0.108	-0.51	4.99
WHR	0.00	0.01	-0.24	0.814	-0.03	0.02	0.00	0.01	0.32	0.749	-0.02	0.03
BIOMARKERS												
C-PEPTIDE	0.01	0.06	0.26	0.800	-0.10	0.13	0.08	0.06	1.38	0.176	-0.04	0.19
*INSULIN	2.82	6.93	0.41	0.683	-10.75	16.40	-1.12	6.76	-0.17	0.868	-14.37	12.12
HbA1c (mmol•mol^{-1})	**2.41**	**0.94**	**2.57**	**0.014**	**0.51**	**4.30**	**2.58**	**0.87**	**2.95**	**0.005**	**0.81**	**4.34**
GLUCOSE (mmol•L^{-1})	0.15	0.14	1.06	0.293	-0.13	0.42	0.01	0.12	0.08	0.938	-0.24	0.26
CHOL (mmol•L^{-1})	0.03	0.24	0.11	0.912	-0.46	0.51	0.16	0.24	0.66	0.510	-0.32	0.64
*HDL-C (mmol•L^{-1})	0.00	0.09	0.03	0.975	-0.18	0.18	-0.07	0.09	-0.75	0.452	-0.24	0.11
LDL-C (mmol•L^{-1})	-0.02	0.21	-0.09	0.929	-0.44	0.41	0.14	0.21	0.68	0.500	-0.28	0.56
*TG (mmol•L^{-1})	-0.12	0.10	-1.17	0.240	-0.31	0.08	0.17	0.10	1.69	0.090	-0.03	0.36
*TG-HDL ratio	0.06	0.07	0.92	0.358	-0.07	0.20	-0.12	0.07	-1.72	0.086	-0.25	0.02
*hsCRP (mg•L^{-1})	-0.75	0.56	-1.33	0.183	-1.84	0.35	-1.03	0.54	-1.91	0.057	-2.08	0.03
*URIC ACID (mg•dL^{-1})	-0.02	0.01	-1.38	0.167	-0.04	0.01	-0.02	0.01	-1.56	0.118	-0.04	0.00
METABOLIC HEALTH												
siMS SCORE	-0.02	0.14	-0.17	0.862	-0.30	0.25	0.20	0.13	1.54	0.130	-0.06	0.47
INSULIN RESISTANCE												
*HOMA2 IR	0.09	0.15	0.58	0.560	-0.21	0.39	0.00	0.15	-0.02	0.986	-0.29	0.29
BLOOD PRESSURE												
SYSTOLIC BP (mm Hg)	0.82	2.29	0.36	0.722	-3.80	5.44	1.29	2.24	0.58	0.567	-3.22	5.80
*DIASTOLIC BP (mm Hg)	1.16	2.25	0.51	0.608	-3.25	5.56	2.25	2.23	1.01	0.312	-2.12	6.62
DIET COMPOSITION												
ENERGY INTAKE (kJ)	-61.64	130.89	-0.47	0.640	-325.78	202.50	-93.20	127.90	-0.73	0.470	-351.32	164.93
CARBOHYDRATE %EI	1.65	1.58	1.04	0.305	-1.55	4.84	0.32	1.55	0.21	0.838	-2.81	3.45
CARBOHYDRATE INTAKE (g)	8.45	5.05	1.67	0.102	-1.74	18.65	2.45	4.93	0.50	0.622	-7.50	12.41
PROTEIN %EI	-0.37	0.82	-0.46	0.649	-2.02	1.28	0.43	0.80	0.54	0.594	-1.18	2.04
*PROTEIN INTAKE (g)	-2.48	3.35	-0.74	0.460	-9.05	4.09	-0.72	3.28	-0.22	0.826	-7.15	5.70
FAT %EI	-0.31	1.26	-0.24	0.809	-2.84	2.23	-0.15	1.24	-0.12	0.907	-2.65	2.36
*FAT intake (g)	-0.81	3.23	-0.25	0.801	-7.14	5.51	-0.34	3.16	-0.11	0.914	-6.54	5.86
FITNESS												
$\dot{V}O_2$peak (ml•kg^{-1}•min^{-1})	-0.64	0.82	-0.78	0.440	-2.29	1.01	0.95	0.80	1.18	0.245	-0.68	2.57
BENCH PRESS (kg)	**4.10**	**1.81**	**2.26**	**0.024**	**0.55**	**7.64**	**-0.86**	**1.77**	**-0.48**	**0.628**	**-4.33**	**2.62**
LEG PRESS (kg)	6.81	13.24	0.51	0.610	-19.92	33.53	10.95	13.37	0.82	0.418	-16.04	37.93
ENERGY EXPENDITURE												
RMR (kJ•day^{-1})	**690**	**295**	**2.34**	**0.024**	**94.57**	**1285.64**	**896.02**	**289.63**	**3.09**	**0.004**	**311.52**	**1480.53**
PHYSICAL ACT (MET•min^{-1}•day^{-1})	1.98	2.91	0.68	0.499	-3.89	7.85	3.41	2.82	1.21	0.232	-2.27	9.10
WELLBEING												
TOTAL MOOD DISTURBANCE	1.261	0.955	1.320	0.187	-0.61	3.13	0.905	0.917	0.990	0.324	-0.89	2.70

Comparison between groups, Linear regression or (*) = Generalised Linear Regresion, HIIT group used as reference group,
VAT= visceral adipose tissue, LBM= lean body mass, BMC= bone mineral content, WHR= waist to hip ratio

CI= confidence intervals CHOL= total cholesterol TG= triglyceride hsCRP= high sensitive C reactive protein siMS score= Simple Metabolic Syndrome score
HOMA2-IR= Homeostasis ModelAssessment 2 Insulin Resistance. %EI= percentage of total energy intake, RMR= resting metabolic rate

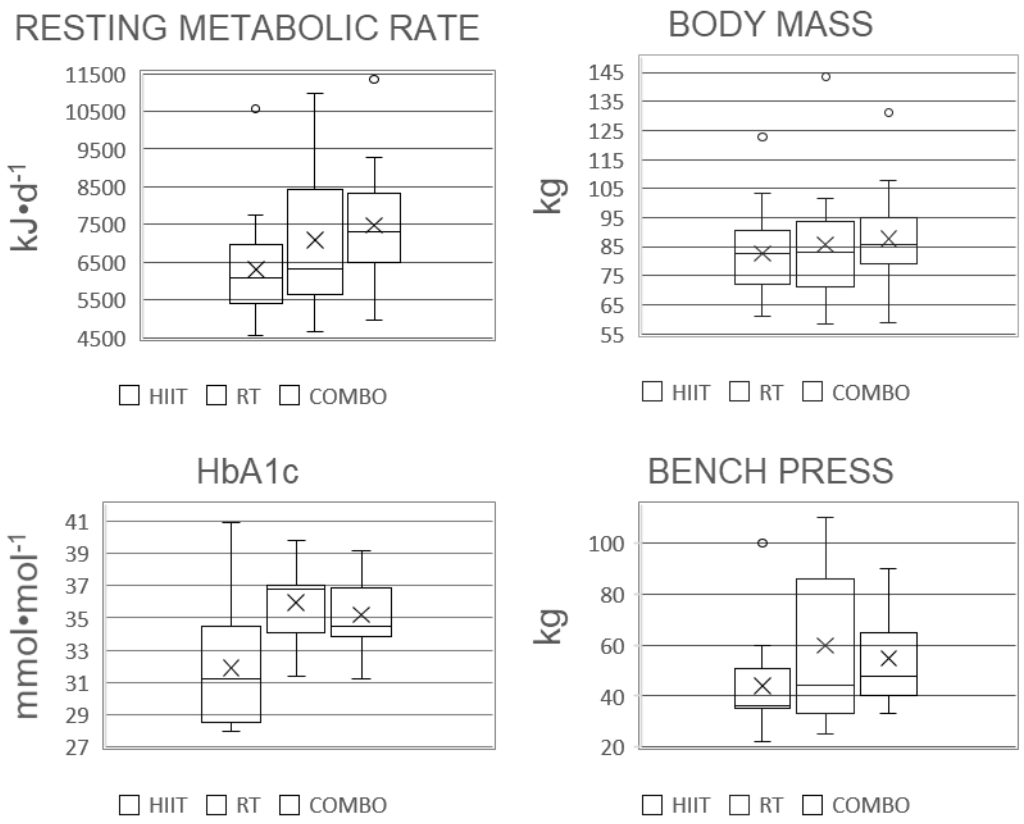

Figure 3-3 Boxplots between groups' difference

Discussion

The aim of this study was to compare the effectiveness of a novel combination of exercise and LCHF diet at improving cardio-metabolic risk factors associated with the development of metabolic disease. This is the first study, to our knowledge, that compared quasi iso-effort and iso-time LCHF+HIIT, LCHF+RT and LCHF+COMBO. The main finding was that all these combinations effectively improved almost all outcomes which translated in significant improvements in metabolic health especially reflected in the cardiorespiratory fitness, RMR, body composition and siMS score.

The cardiorespiratory fitness was significantly improved, with no differences between groups. It is interesting that the group using RT experienced an improvement of 2.94 $mL•kg^{-1}•min^{-1}$, that was similar to the gains of HIIT and COMBO. It has been identified that higher aerobic capacity is related to lower risk of developing metabolic disease, with a 10-20% reduction of cardiovascular mortality for each metabolic task (MET) that is increased (282). In this respect, Francois, Durrer, Pistawka, Halperin, Chang and Little (283) observed an improvement of 2.45 $mL•kg^{-1}•min^{-1}$ after 12

weeks of training involving HIIT twice a week and RT once a week, noting that this was an important improvement. While their HIIT protocol was very similar to ours, the RT and progression of exercise intensity were not. The resistance exercise consisted of as many repetitions as possible for each min of work intervals and only included lower body exercises. The RT load was based on an RPE~5 “hard” on the Borg CR-10 scale, or approximately 30-40% 1-RM. The progression started from 4 high-intensity intervals in week 1, to 10 in week 6. Intensity was given by the weight being lifted rather than the speed of movement, necessary to accommodate as many repetitions as possible per min of exercise. By contrast, although we prescribed a similar RPE (but different scale), we utilised a greater resistance load than that of Francois et al. and our tempo was 2 sec eccentric - 2 sec concentric, allowing a total of 15 reps per min. We prescribed the load to be no more than 2 repetitions short of failure, with a progression in set number. These differences could have been the reason why in our study, LCHF+RT group's aerobic capacity improvement was similar to the LCHF+HIIT and LCHF+COMBO. Also, the lower exercise volume performed during the first half of the trial of Francois et al. could have influenced this difference. In addition, the greater load used in our RT programme could explain the difference in gains by our group that performed COMBO compared to those of Francois, Durrer, Pistawka, Halperin, Chang and Little (283), because a greater load translates into greater intensity and the latter has been identified as the crucial factor to influence cardiorespiratory fitness improvement (284). Upper body strength was improved for all three groups; between the groups LCHF+RT (p=0.024) was significantly greater than the LCHF+HIIT but not the LCHF+COMBO. This was expected because HIIT only used lower body exercises (cycling and running) while RT directly exercised (bench press and push ups) the muscles used for the bench press test. Lower body strength also improved significantly for all groups (p<0.001), showing that all exercise combinations were effective in enhancing strength, in line with the work of Androulakis-Korakakis, Langdown, Lewis, Fisher, Gentil, Paoli and Steele (285) who reported that high-intensity training, regardless of modality (aerobic and RT), was able to improve lower body strength. Hence, strength gains can be achieved with HIIT using cycle ergometers and treadmills if a sufficiently high effort is applied.

It was found that reductions in body mass were greater in the LCHF+HIIT group; significantly more than the LCHF+COMBO but not the LCHF+RT. This result could be attributed to individual differences, and as a consequence of a transient exercise-induced energy expenditure that extends for up to 38 h (286) after the last bout of aerobic exercise (19). While transient and small, this could lead over time to an accumulated greater caloric deficit in this group. Indeed, Mazzetti, Douglass, Yocum and Harber (241) found that faster muscle contractions compared to slow contractions (2 s eccentric, 2 s concentric reps, same tempo used by RT exercise in our study) using a squat workout, resulted in 5.2±4.3% greater transient energy expenditure. Therefore, it could be reasonable to conjecture that the LCHF+HIIT group was exercising at a considerably faster rate of

muscular movement or contraction, which could have produced the highest energy expenditure resulting in a greater caloric deficit, that caused the greatest magnitude of change in body composition markers observed in this study. BMC was reduced after 12 weeks of combining the LCHF diet and HIIT and RT but not the COMBO, which may be a result of the small sample size, because the magnitude of change was very small for LCHF+HIIT and LCHF+RT, while it was non-significant for the LCHF+COMBO (Table S7), or could be as a result of the lean body mass reduction and the negative energy balance. Courteix, Valente-dos-Santos, Ferry, Lac, Lesourd, Chapier, Naughton, Marceau, Joao Coelho-e-Silva, Vinet, Walther, Obert and Dutheil (287) observed that after a year of dietary (CHO: ~50%, PRO: 15-20% 1.2 g•kg^{-1}•d^{-1}, E: -2090 kJ•d^{-1} ~500 kcal•d^{-1}) and exercise (15–20 h•wk^{-1}, high intensity) intervention, reductions in BMC were significantly and independently associated with reductions in LBM and a negative energy balance. Conversely, those individuals that maintained the exercise compliance closer to what was prescribed, showed a higher BMC despite energy restriction. Comparing that to the present study, their CHO intake was higher than the CHO intake in our study, while energy intake was similar to ours. CHO restriction combined with energy restriction could trigger BMC loss in the short term. Another difference is exercise volume that clearly was different from the exercise volume in our study, probably the reason why, despite high compliance, the volume may have influenced BMC loss. Indeed, Heikura, Burke, Hawley, Ross, Garvican-Lewis, Sharma, McKay, Leckey, Welvaert, McCall and Ackerman (288), recently demonstrated that CHO restriction under isocaloric conditions, impaired bone turnover makers after 3.5 weeks while performing prolonged high-intensity exercise. This impairment was partially reversed when acute CHO restoration took place (288). In line with this finding, Hammond, Sale, Fraser, Tang, Shepherd, Strauss, Close, Cocks, Louis, Pugh, Stewart, Sharples and Morton (289) observed that if CHO was supplemented before, during and after an acute training session, independent of energy availability, there were attenuated markers of bone resorption. Brinkworth, Wycherley, Noakes, Buckley and Clifton (290) compared an energy restricted LCHF (6686 ± 734 kJ•d^{-1}, 8 ± 3% [30.2±12.3 g•d^{-1}] CHO, 34±2% PRO, 57±4% fat [20± 2% saturated fat]) vs an iso-caloric HCLF diet (6474 ± 793 kJ•d$^{-1,}$ 44 ±11% [162.6 ± 44.3 g•d^{-1}] CHO, 24 ± 3% PRO, 30 ± 9% fat [7±4% saturated fat]) (6686 ± 734 kJ•d^{-1}, 8 ± 3% [30.2±12.3 g•d^{-1}] CHO, 34±2% PRO, 57±4% fat [20± 2% saturated fat]) vs an iso-caloric HCLF diet (6474 ± 793 kJ•d^{-1}, 44 ±11% [162.6 ± 44.3 g•d^{-1}] CHO, 24 ± 3% PRO, 30 ± 9% fat [7±4% saturated fat]) and after 12 months did not find any differences between groups nor significant loses in BMC nor bone mineral density (BMD). However, their participants did not perform high-intensity training and the authors highlighted that they did not assess clinically relevant sites; nor did we in the present study as this was not within scope.

The muscle-sparing effect of RT resulted in a significantly greater RMR in the LCHF+COMBO and LCHF+RT groups relative to the LCHF+HIIT group, with the most improved being the

LCHF+COMBO as previously stated. Indeed, after 12 weeks comparing RT vs aerobic training under the same very low-calorie diet (VLCD), Bryner, Ullrich, Sauers, Donley, Hornsby, Kolar and Yeater (291) noted similar results in that the AER+D group who lost more weight and had a lower RMR, whereas those in the RT+D group did not lose LBM and increased their RMR. In a recent study comparing aerobic training, RT, combined and a control group, Villareal, Aguirre, Gurney, Waters, Sinacore, Colombo, Armamento-Villareal and Qualls (193) reported that after six months those assigned to the RT and combined, decreased less than 2% and 3% of LBM respectively vs 5% losses in the aerobic training group. These two examples provide more evidence to suggest a LBM preservation effect of RT that supports the notion that RMR is highly dependent on LBM (292). It is important to notice that the greater body mass reduction in the LCHF+HIIT group in the present study may have been a consequence of the significant reduction in LBM which is not desirable. Backx, Tieland, Borgonjen-van den Berg, Claessen, van Loon and de Groot (293) compared a very well-controlled 25% reduced (in relation to habitual energy intake) weight loss normal PRO (NP) (~ 0.92 g•kg^{-1}) and high PRO (HP) (~1.7 g•kg^{-1}) diet only, in a population of older adults (~ 65 y), and found that an energy intake ~1894 kcal per day HP or NP diet their participants lost similar amounts of the LBM (1.8±2.2 and 2.1±1.4 kg) after 12 weeks. Despite the difference in age and the nature of their study, PRO and energy intakes were similar to our study, suggesting that the PRO intake of our cohort (~ 1.4 g•kg^{-1}) was insufficient to promote LBM retention, in line with the findings of a recent review (217).

Regarding body fat that accumulates in the abdominal area, it is characterised by higher blood pressure, lipid profile, hsCRP, LDL-C, and HOMA-IR and lower HDL-C levels (294, 295). After 12 weeks in the present intervention we observed improvements across all of these markers which might be an indication that the statistically significant improvements in VAT we also found. The reduction in VAT may have been originated by the high-intensity exerted (296), in addition to the contribution of the LCHF diet most likely due to carbohydrate restriction (198, 297) together with the obligated significantly lower energy intake, which took place between baseline and post-exercise (see Table S3). Recent evidence by Dupuit, Rance, Morel, Bouillon, Pereira, Bonnet, Maillard, Duclos and Boisseau (298) shows that HIIT and HIIT + RT can reduce visceral fat after 12 weeks of training in postmenopausal women using a HIIT protocol consisting of repeated cycles of sprinting/speeding for 8 s followed by slow pedalling (20–30 RPM) for 12 s until completing 20 min with a maximum of 60 sprints at 80-90% of peak HR and the RT program included two different training circuits with 10 exercises/each. In that study energy intake remained constant and RT did not provide an additional effect to VAT loss when added to HIIT; the authors concluded that HIIT produced this effect (298). That study may explain the similar findings we observed for LCHF+HIIT and LCHF+COMBO VAT loss in the present study. To explain the LCHF+RT group effect on VAT, that was also significantly reduced and similar to both LCHF+HIIT and LCHF+COMBO. Vargas,

Romance, Petro, Bonilla, Galancho, Espinar, Kreider and Benitez-Porres (299) compared the effects of RT + a normal diet vs RT + low CHO ketogenic diet (LCKD) vs a control group, observed that only RT+LCKD reduced VAT (299). Supporting those findings, a study by Miyashita, Koide, Ohtsuka, Ozaki, Itoh, Oyama, Uetake, Ariga and Shirai (198) comparing the effects of a LCHF (40% CHO, 25% PRO, 35% fat) vs high-carbohydrate low fat diet (65% CHO, 25% PRO, 10% fat) both providing 4184 kJ (1000 kcal) to reduce VAT observed that only the LCHF diet reduced VAT significantly. In agreement with those findings, Sasakabe, Haimoto, Umegaki and Wakai (297) investigating the associations of the reduction in carbohydrate intake and VAT, using a moderate LCHF (30-45% of total energy coming from CHO) among non-obese patients with T2DM who did not receive anti-diabetic drugs. After 3 months, they found that the reductions in VAT were significantly correlated with the reduction in CHO intake, independently of the energy intake. These findings (198, 297, 299) could explain why, in our study, the LCHF+RT was able to reduce VAT. In the present study, habitual physical activity measured by the IPAQ-LF, did not change over the 12-week intervention, indicating that changes in outcome measures were independent of habitual physical activity change. This is important to acknowledge as changes in habitual physical activity can influence energy expenditure and hence weight loss (300).

The siMS score is an accepted measure (301) to quantify the metabolic status of individuals at risk of metabolic disease by establishing the severity of its components (central obesity, hyperglycaemia, dyslipidaemia, insulin resistance, etc.). The siMS is a practical and simple method (273), that unlike the Metabolic Syndrome Z scores, the siMS score, is a continuous score based on each individual, not the sample. Hence, the siMS score offers the advantage for comparison within and between individuals across different studies. Additionally, it has a near perfect correlation that allows it to be compared to other metabolic scores (273). The siMS score improved significantly for all groups after 12 weeks as a result of the changes previously described; confirming that any of these modalities are effective in reducing the risk factors associated with metabolic syndrome. in the present study it is also important to highlight that energy intake was reduced as a result of CHO restriction, while PRO and fat were significantly increased.

The programme achieved over 90% attendance of exercise sessions; no difference between groups was observed. Attrition in our study was unrelated to the study intervention. It is important to mention that those participants that withdrew expressed they would have continued until the end of the intervention if their circumstances were different. In general, attrition rates for nutrition and exercise interventions are between 25-50% (160) due to time constraints, personal and work related issues; our study is slightly lower with an overall attrition of 15% probably due to the presence of support that was provided for the participants.

Exercise was successfully matched for time and effort; the latter was achieved and corroborated by obtaining the session RPE over the last 6 sessions of each exercise modality (MRPE for HIIT= 17.2 vs 17.5 for RT). The literature provides evidence of the utility and acceptability for prescribing and quantifying exercise intensity/effort using the 6-20 Borg scale (269, 302). On the other hand, it was interesting that despite perceived effort being similar between exercise modalities, the heart rate observed was higher for HIIT (equivalent to 90% HRmax as per prescription). This was possibly a consequence of the speed of movement during muscular contraction in RT not being fast enough to elicit the requisite cardiovascular response. Indeed Kaikkonen, Yrjama, Siljander, Byman and Laukkanen (244) used the speed of movement to adjust target heart rate for RT in their programme.

Strengths and disadvantages

The strengths or advantages of our study are: the robustness of the comprehensive assessments at all time points; all exercise sessions were supervised and continuously monitored throughout each session, also allowing for monitoring of the diet. The utilisation of DXA allowed us to quantify VAT which plays a crucial role to quantify metabolic health. The several limitations that can be observed in our study, included that the self-reported food diaries used common household measures to quantify food intake, therefore inaccuracies cannot be ruled out. However, participants were trained and given precise instructions as to how to measure and quantify food intake to minimise this limitation, and this is common in real world dietary interventions. We did not quantify adherence apart from monitoring dietary compliance verbally and by using commercially available mobile apps. However, as mentioned above, regular discussions about diet throughout the exercise sessions allowed for adherence to be monitored, albeit informally. The lack of a diet only precluded identifying the extent of the contribution of the LCHF to exercise modalities in improving metabolic health. Regarding the no control group, ethically it is difficult to justify instructing a cohort identifying as inactive and perceived overweight to continue with habitual inactivity.

Conclusions

In conclusion, combining a LCHF diet with iso-time, iso-effort HIIT, RT or COMBO all improve aerobic capacity, strength, metabolic biomarkers and reduced VAT in 12 weeks. HIIT might elicit a greater improvement in HbA1c; while RT confers the body a muscle-sparing effect and greater upper body strength, whereas combining HIIT and RT may contribute to improve RMR. These findings may be clinically significant as they indicate that these strategies are effective, eliciting a sufficiently high effort to improving metabolic health and only requiring a short exercise time commitment.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Supplementary material

Table 3-S1 Control period results

	6-WEEK CONTROL PERIOD								
FITNESS	PRE		POST				ES and 95% CI		
	mean/median SD/*IQR*	CV	mean/median SD/*IQR*	CV	t / *z*	*p*	*g*	lower	upper
VO_2peak (ml/kg/min)	26.58±6.35	0.24	26.62±6.54	0.25	-0.19	0.855	0.01	-0.63	0.72
BENCH PRESS (kg)	*36 (29.5, 61.5)*	0.53	*38 (32.5, 62.5)*	0.50	*2.77*	0.004	0.11	-0.53	0.83
LEG PRESS (kg)	287±100	0.35	286±90	0.31	0.13	0.897	-0.01	-0.65	0.70
RMR (kJ/day)	6339±1185	0.19	6487±1315	0.20	-0.68	0.509	0.11	-0.53	0.84
PHYSICAL ACT (MET/min/day)	376±83	0.22	379±81	0.21	-1.38	0.188	0.04	-0.60	0.75
BODY COMPOSITION									
BODY MASS (kg)	91.2±15.4	0.17	91.5±15.2	0.17	-0.71	0.489	0.02	-0.62	0.73
FAT MASS (kg)	34.5±11.4	0.33	35.2±11.7	0.33	-1.81	0.093	0.05	-0.59	0.77
VAT (g)	1474±843	0.57	1439±778	0.54	1.01	0.330	0.46	-0.04	-0.68
LBM (kg)	53.6±10	0.19	53.3±9.8	0.18	1.04	0.315	-0.04	-0.67	0.68
BMC (g)	2990±462	0.15	3075±450	0.15	-1.22	0.242	0.18	-0.46	0.91
WAIST (cm)	105.2±10.1	0.10	105±9.8	0.09	0.22	0.829	-0.01	-0.65	0.70
WAIST TO HIP RATIO	0.93±0.07	0.07	0.94±0.07	0.07	-0.52	0.609	0.04	-0.60	0.76
BIOMARKERS									
C-PEPTIDE (nmol/L)	*0.84 (0.31, 0.78)*	0.36	*0.80 (0.65, 1.10)*	0.37	*1.62*	0.121	0.17	-0.47	0.89
INSULIN (pmol/L)	*62.73 (36.27, 82.74)*	0.60	*76.23 (41.34, 95.28)*	0.55	*2.27*	0.022	0.20	-0.45	0.92
HbA1c (mmol/mol)	36.81±3.42	0.09	36.86±3.33	0.09	-0.18	0.857	0.01	-0.62	0.73
GLUCOSE (mmol/L)	*6 (5.65, 6.3)*	0.08	*6 (5.8, 6.45)*	0.11	*1.95*	0.058	0.28	-0.36	1.01
CHOL (mmol/L)	5.73±1.03	0.18	5.53±1.19	0.21	1.00	0.334	-0.17	-0.80	0.53
HDL-C (mmol/L)	*1.39 (1.2,1.93)*	0.44	*1.32 (1.18, 1.72)*	0.35	*2.22*	0.026	-0.22	-0.84	0.49
LDL-C (mmol/L)	3.99±1.05)	0.26	3.93±1.28	0.32	0.37	0.717	-0.04	-0.68	0.67
TG (mmol/L)	*1.06 (0.83, 1.59)*	0.63	*1.33 (0.89, 1.49)*	0.55	*0.28*	0.804	-0.06	-0.69	0.66
TG-HDL ratio	*0.33 (0.21, 0.47)*	0.95	*0.40 (0.32, 0.47)*	0.81	*0.11*	0.934	-0.02	-0.66	0.69
hsCRP (mg/L)	2.53±1.9	0.75	3.07±1.68	0.54	-2.12	0.052	0.30	-0.35	1.02
URIC ACID (mg/dL)	0.38±0.09	0.24	0.38±0.10	0.26	0.45	0.662	-0.03	-0.67	0.68
METABOLIC HEALTH									
siMS score	2.65±0.93	0.34	2.74±0.79	0.28	-1.09	0.296	0.10	-0.54	0.82
INSULIN RESISTANCE									
HOMA2 IR	*1.39 (0.84, 1.89)*	0.61	*1.70 (0.95, 2.1)*	0.57	*2.27*	0.022	0.20	-0.44	0.93
BLOOD PRESSURE									
SYSTOLIC BP (mm Hg)	121±13	0.11	117±16	0.14	1.74	0.104	-0.26	-0.88	0.45
DIASTOLIC BP (mm Hg)	75.5±7	0.10	75±8	0.11	0.70	0.497	-0.07	-0.71	0.64
DIET COMPOSITION									
ENERGY INTAKE (kJ)	*8523 (7864, 10444)*	0.16	*8630 (7814, 10341)*	0.15	*0.11*	0.934	0.01	-0.62	0.73
CARBOHYDRATE %EI	54.3±2.2	0.04	54±2.7	0.05	0.65	0.526	-0.11	-0.75	0.60
CARBOHYDRATE INTAKE (g)	292.9±49.4	0.17	293±44.1	0.15	-0.18	0.861	0.01	-0.63	0.73
PROTEIN %EI	15.9±2.1	0.13	16±1.9	0.12	-0.19	0.856	0.02	-0.61	0.74
PROTEIN INTAKE (g)	86.2±20.9	0.24	86.3±17.7	0.21	-0.06	0.950	0.00	-0.71	0.72
FAT %EI	29.4±2.9	0.10	29.3±2.4	0.08	0.19	0.850	-0.04	-0.68	0.67
FAT intake g	70±10.7	0.15	70.1±10.9	0.16	-0.08	0.938	0.01	-0.62	0.73
WELLBEING									
TOTAL MOOD DISTURBANCE	*18 (16, 19)*	0.15	16 (15, 18)	0.19	1.45	0.168	-0.314	-1.015	0.39

Differences assessed by t student or *Wilcoxon signed rank test, (italic)* , *CV= coeficient of variation* , Hedges g effect size, and 95% CI= confidence intervals CHOL= total cholesterol TG= triglyceride hsCRP= high sensitive C reactive protein

◊ Simple Metabolic Syndrome score ♦ Homeostasis Model Assessment 2 Insulin Resistance %EI= total energy intake

Table 3-S2 Main dietary Carbohydrate sources food frequency control period

CONTROL		
Main Dietary Carbohydrate Sources		
FOOD	PRE	POST
–BREAD– (bread slices, bread rolls, breakfast cereal.)	10–10+	9–10+
–PASTA–	1–8	2–9
–TUBERS– (potato, taro, kumara, parsnip, etc.)	6–10+	5–10+
–LEGUMES– (alfalfa, beans, lentils, chickpeas, peas, peanuts, etc.)	3–10+	4–10
–GRAINS– (rice, corn, cous cous, etc.)	6–10+	4–10+
–TAKEAWAYS– (McDonalds, Domino's, KFC, etc.)	3–10+	3–7
-SNACKS- (biscuits, chips, rice crackers, etc.)	8–10+	7–10
–BEVERAGES– (fruit juices, soft drinks, sport drinks, energy drinks, etc.)	10+	7–10
–SWEETS– (lollies, chocolate, confectionary, etc.)	9–10+	0–4
–BAKERY– (baked goods, home or factory made.)	5–10+	0–6
–FULL FAT DAIRY– (milk, butter, cheese, yoghurt, etc.)	1–10	2–10
–LOW FAT DAIRY– (milk, cheese, yogurt, etc.)	8–10+	9–10+
–FRUITS– (apple, banana, kiwi, etc.)	9–10+	6–10+
–VEGETABLES– (brocolli, cauliflower, spinach, tomato, etc.)	6–10+	10–10+

Results are ranges in absolute numbers from 1 time to more than ten (10+) for a seven-day period.

Table 3-S3 Diet composition results within group differences (12-week intervention)

WITHIN GROUP'S DIFFERENCE

DIET COMPOSITION		PRE	POST			ES and 95% CI		
		mean/*median* SD/*IQR*	mean/*median* SD/*IQR*	t / *z*	*p*	*g*	lower	upper
ENERGY INTAKE (kJ)	HIIT	8703±1517	6673±666	8.33	<0.001	-1.70	-2.26	-1.13
	RT	*8017 (7661, 10333)*	*6565 (6064, 7341)*	3.18	<0.001	-1.60	-2.29	-0.91
	COMBO	8787±1704	6611±651	6.74	<0.001	-1.64	-1.63	-1.64
CARBOHYDRATE %EI	HIIT	*49.1 (46.4, 50.4)*	*26 (21.1, 28.6)*	*3.82*	<0.001	-4.57	-4.99	-4.16
	RT	49.61±2.97	26.7±3.41	18.58	<0.001	-6.94	-7.22	-6.67
	COMBO	49.5±2.3	25.4±5.1	16.22	<0.001	-5.97	-5.81	-6.12
CARBOHYDRATE INTAKE (g)	HIIT	275±57	97.7±12.6	12.99	<0.001	-4.23	-4.66	-3.79
	RT	290±46.68	105.6±10.36	14.72	<0.001	-5.29	-5.74	-4.84
	COMBO	287.4±57.7	99.6±17.9	10.70	<0.001	-4.27	-4.17	-4.36
PROTEIN %EI	HIIT	16±1.17	30.1±2.4	-24.16	<0.001	6.61	5.75	7.47
	RT	15.7±2.64	29.53±2.30	-19.76	<0.001	5.43	4.43	6.42
	COMBO	16.1±1.5	30.4±2.4	-20.44	<0.001	7.04	6.74	7.34
PROTEIN INTAKE (g)	HIIT	*75.4 (71.3, 92.5)*	*116.3 (107.6, 134.4)*	3.82	<0.001	1.96	*1.25*	*2.67*
	RT	*78 (64, 102.8)*	*116.7 (102.8, 137.8)*	3.17	0.001	1.28	0.5	2.11
	COMBO	84.5±17.3	120±14.3	-18.59	<0.001	2.18	2.05	2.31
FAT %EI	HIIT	*28.9 (27.8, 30.9)*	*43.4 (40.8, 45.7)*	*3.78*	<0.001	3.49	2.73	4.25
	RT	29.3±1.75	43.4±2.97	-14.24	<0.001	5.60	4.60	6.60
	COMBO	28.7±1.7	43±4.5	-12.17	0.001	4.21	4.01	4.41
FAT intake (g)	HIIT	*66.3 (58.5, 75.5)*	*77.7 (68.3, 86.6)*	*2.94*	<0.001	0.65	-0.01	1.31
	RT	*63 (60, 76.8)*	*76.4 (67.8, 84.6)*	*2.55*	0.008	0.67	-0.13	1.47
	COMBO	66.8±12.9	76.3±13.4	-4.02	0.001	0.70	0.63	0.78

Means ± SD or *Median (IQR)*. Within group differences assessed by t student test or (*italic*)*Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals.

Table 3-S4 Main dietary carbohydrate sources food frequency questionnaire (12-week intervention)

Main Dietary Carbohydrate Sources					
Food		Baseline		Post intervention	
		ocassions over a 7-day period (ranges)			
–Bread–	all participants	10–10+		1–3	
(bread slices, bread rolls, breakfast cereal.)	HIIT	10+			1–3
	RT	10+			1–3
	COMBO	10–10+			1–3
–Pasta–	all participants		1–8	0–2	
	HIIT	1–8			0–2
	RT	3–8			0–1
	COMBO	2–6			0–1
–Tubers–					
(potato, taro, kumara, parsnip, etc.)	all participants		6–10+	0–2	
	HIIT	6–10+			0–2
	RT	8–10+			0–1
	COMBO	6–10+			0–1
–Legumes–					
(alfalfa, beans, lentils, chickpeas, peas, peanuts, etc.)	all participants		3–10+	0–2	
	HIIT	3–10+			0–2
	RT	3–10+			0–2
	COMBO	3–10+			0–1
–Grains–					
(rice, corn, cous cous, etc.)	all participants		6–10+	0–3	
	HIIT	6–10+			0–3
	RT	6–10+			0–2
	COMBO	6–10+			1–3
–Takeaways–					
(McDonalds, Domino's, KFC, etc.)	all participants		3–10+	0–1	
	HIIT	3–10+			0–1
	RT	5–10+			0–1
	COMBO	3–10+			0–1
-Snacks-					
(biscuits, chips, rice crackers, etc.)	all participants		8–10+	0–6	
	HIIT	9–10+			0–5
	RT	8–10+			0–6
	COMBO	10+			1–5
–Beverages–					
(fruit juices, soft drinks, sport drinks, energy drinks, etc.)	all participants		10+	0–2	
	HIIT	10+			0–4
	RT	8–10+			0–3
	COMBO	8–10+			0–3

HIIT high-intensity interval training, RT resistance training, COMBO combination training
Results are ranges in absolute numbers from 1 time to more than ten (10+) for a seven-day period.

Main Dietary Carbohydrate Sources

-Sweets-					
(lollies, chocolate, confectionary, etc.)	all participants	9–10+	0–4		
	HIIT	9–10+		0–4	
	RT	9–10+		0–3	
	COMBO	9–10+		0–3	
-Bakery-					
(baked goods, home or factory made.)	all participants	**5–10+**	**0–6**		
	HIIT	5–10+		0–5	
	RT	9–10+		0–6	
	COMBO	6–10+		0–4	
-Full fat dairy-					
(milk, butter, cheese, yoghurt, etc.)	all participants	1–10	7–10+		
	HIIT	1–10+		7–10+	
	RT	4–9		7–10+	
	COMBO	4–10+		**7–10+**	
-Low fat dairy-					
(milk, cheese, yogurt, etc.)	all participants	8–10+	0–3		
	HIIT	10–10+		0–3	
	RT	8–10+		0–2	
	COMBO	10+		0–2	
-Fruits-					
(apple, banana, kiwi, etc.)	all participants	9–10+	7–10+		
	HIIT	8–10+		7–10+	
	RT	8–10+		7–10+	
	COMBO	9–10		9–10	
-Vegetables-					
(brocolli, cauliflower, spinach, tomato, etc.)	all participants	6–10+	10–10+		
	HIIT	6–10+		10–10+	
	RT	7–10		10–10+	
	COMBO	7–10		10–10+	

HIIT high-intensity interval training, RT resistance training, COMBO combination training
Results are ranges in absolute numbers from 1 time to more than ten (10+) for a seven-day period.

Table 3-S5 Within group differences fitness variables (12-week intervention)

WITHIN GROUP'S DIFFERENCE

		PRE	POST			ES and 95% CI		
FITNESS		mean/*median SD/IQR*	mean/*median* SD/*IQR*	t / *z*	*p*	*g*	lower	upper
$\dot{V}O_2$peak (ml•kg^{-1}•min^{-1})	HIIT	*23.54 (22.07, 31.37)*	*27.72 (26.45, 33.03)*	*3.74*	<0.001	0.57	-0.09	1.23
	RT	27.63±5.28	30.58±5.52	-4.60	0.001	0.53	-0.27	1.32
	COMBO	28.03±4.57	32.55±5.67	-7.15	<0.001	0.85	0.77	0.93
BENCH PRESS (kg)	HIIT	*35 (30, 45)*	*36 (35, 51)*	*3.44*	<0.001	0.33	-0.31	0.98
	RT	49.42±27.14	59±31	-5.58	0.001	0.34	-0.44	1.13
	COMBO	49±20	55±19	-5.30	<0.001	0.27	0.20	0.33
LEG PRESS (kg)	HIIT	215±72	286±87	-12.52	<0.001	0.86	0.19	1.53
	RT	276±105	353±88	-7.36	<0.001	0.77	-0.04	1.57
	COMBO	297±101	377±115	-6.87	<0.001	0.72	0.64	0.80
ENERGY EXPENDITURE								
RESTING METABOLIC RATE -(kJ•day^{-1})	HIIT	*6360 (5630, 7226)*	*6084 (5414, 6968)*	*1.53*	0.134	-0.22	-0.84	0.41
	RT	6765±1991	7083±2026	-1.19	0.258	0.15	-0.62	0.93
	COMBO	7011±2277	7472±1686	-1.70	<0.001	0.22	0.16	0.28
PHYSICAL ACTIVITY (MET•min^{-1}•day^{-1})	HIIT	392±74	394±77	-0.91	0.374	0.02	-0.61	0.66
	RT	368±69	372±65	-1.75	0.106	0.06	-0.71	0.83
	COMBO	397±74	402±73	-3.59	<0.001	0.07	0.01	0.13

Means ± SD or *Median (IQR)*. Within group differences assessed by t student test or (*italic*)*Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals

Table 3-S6 Blood biomarkers within group differences (12-week intervention)

		WITHIN GROUP'S DIFFERENCE						
		PRE	POST			ES and 95% CI		
		mean/*median* SD/*IQR*	mean/*median* SD/*IQR*	t / *z*	*p*	*g*	lower	upper
BIOMARKERS								
C-PEPTIDE (nmol•L^{-1})	HIIT	0.80±0.33	0.65±0.24	3.43	0.003	-0.51	-1.12	0.11
	RT	*0.81 (0.58, 0.99)*	*0.63 (0.51, 0.80)*	2.55	0.008	-0.46	-1.21	0.28
	COMBO	*0.93 (0.32, 0.86)*	*0.81 (0.23, 0.70)*	*1.73*	0.045	-0.43	-0.46	-0.39
INSULIN (pmol•L^{-1})	HIIT	*81.1 (55.4, 100)*	*49.5 (42.1, 74.1)*	*3.18*	0.001	-0.75	-1.36	-0.15
	RT	*48.8 (39.9, 90.6)*	*39.3 (31.3, 48.9)*	*3.11*	<0.001	-0.44	-1.19	0.30
	COMBO	*69.2 (46.8, 100)*	*44.64 (33.24, 73.66)*	*2.10*	<0.001	-0.52	-0.56	-0.49
HbA1c (mmol•mol^{-1})	HIIT	*34.5 (31.1, 36.4)*	*31.2 (28.5, 34.45)*	*2.17*	0.029	-0.74	-1.35	-0.14
	RT	36.9±2.6	35.9±2.3	2.19	0.049	-0.37	-1.13	0.38
	COMBO	35.6±2.5	35.19±2.35	1.16	0.265	-0.15	-0.20	-0.10
GLUCOSE (mmol•L^{-1})	HIIT	5.28±0.58	5.19±0.57	1.10	0.287	-0.15	-0.78	0.48
	RT	*6 (5.5, 6.65)*	*5.6 (5.5, 6.5)*	*1.81*	0.077	-0.24	-1.00	0.51
	COMBO	5.9±0.7	5.64±0.68	2.06	0.060	-0.32	-0.37	-0.28
TOTAL CHOLESTEROL (mmol•L^{-1})	HIIT	*5 (4.5, 5.5)*	*5 (4.5, 5)*	*0.85*	0.492	-0.14	-0.77	0.49
	RT	*5 (4, 6)*	*5 (4, 6)*	*0.73*	0.375	-0.13	-0.89	0.64
	COMBO	*5 (4.25, 6)*	*5 (4.3, 6)*	*0.44*	0.845	0.06	0.00	0.11
HDL-C (mmol•L^{-1})	HIIT	1.51±0.51	1.62±0.54	-2.05	0.055	0.22	-0.42	0.87
	RT	1.49±0.47	1.62±0.44	-1.61	0.134	0.26	-0.52	1.05
	COMBO	1.44±0.35	1.50±0.39	-0.91	0.378	0.16	0.10	0.21
LDL-C (momol•L^{-1})	HIIT	*3.4 (3.09, 3.67)*	*3.17 (2.95, 3.67)*	*1.43*	0.169	-0.25	-0.88	0.38
	RT	3.77±1	3.48±1.14	1.92	0.079	-0.26	-1.02	0.49
	COMBO	3.57±0.95	3.46±0.97	0.91	0.377	-0.11	-0.16	-0.06
TRIGLYCERIDES (mmol•L^{-1})	HIIT	*1.11 (0.78, 1.43)*	*0.75 (0.68, 1.13)*	*2.94*	0.002	-0.51	-1.12	0.11
	RT	*1.14 (0.99, 1.35)*	*0.86 (0.65, 0.93)*	*2.97*	0.001	-0.76	-1.50	-0.03
	COMBO	*1.16 (0.89, 1.34)*	*0.99 (0.80, 1.26)*	*1.15*	0.138	-0.16	-0.21	-0.12
TG•HDL ratio	HIIT	*0.29 (0.18, 0.59)*	*0.24 (0.14, 0.41)*	*2.82*	0.003	-0.44	-1.06	0.18
	RT	*0.33 (0.27, 0.49)*	*0.21 (0.17, 0.31)*	*2.97*	0.001	-0.60	-1.34	0.14
	COMBO	*0.35 (0.26, 043)*	*0.29 (0.16, 0.40)*	*0.97*	0.934	-0.08	-0.13	-0.03
hsCRP (mg•L^{-1})	HIIT	*2.2 (0.85, 3.2)*	*1.5 (0.5, 2.3)*	*2.02*	0.044	-0.09	-0.72	0.54
	RT	*2.9 (1.6, 6)*	*2.4 (1, 3.2)*	*3.18*	<0.001	-0.51	-1.25	0.24
	COMBO	*2.35 (1.1, 3.5)*	*1.2 (0.73, 2.65)*	*3.30*	<0.001	-0.58	-0.62	-0.55
URIC ACID (mg•dL^{-1})	HIIT	0.32±0.09	0.31±0.07	1.52	0.147	-0.13	-0.76	0.50
	RT	0.39±0.14	0.35±0.12	2.95	0.012	-0.31	-1.06	0.44
	COMBO	0.34±0.08	0.30±0.07	3.35	<0.001	-0.44	-0.48	-0.40

Means ± SD or *Median (IQR)*. Within group differences assessed by t student test or (*italic*)*Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals.

Table 3-S7 Within group differences body composition (12-week intervention)

		WITHIN GROUP'S DIFFERENCE						
		PRE	POST			ES and 95% CI		
BODY COMPOSITION		mean/*median SD/IQR*	mean/*median* SD/*IQR*	t / *z*	*p*	*g*	lower	upper
BODY MASS (kg)	HIIT	88.2±16.3	82.6±15	11.11	<0.001	-0.35	-0.97	0.27
	RT	89.93±21.87	85.63±21	4.67	0.001	-0.19	-0.95	0.57
	COMBO	91.6±20.4	87.7±18	4.00	<0.001	-0.20	-0.24	-0.15
FAT MASS (kg)	HIIT	*32 (28.5, 36.7)*	*26.94 (23.29, 31.65)*	*3.82*	<0.001	-0.54	-1.15	0.08
	RT	*29.82 (28, 37.03)*	*26.81 (21.66, 32.16)*	*3.18*	<0.001	-0.33	-1.08	0.42
	COMBO	34.5±12.4	30.7±9.6	3.61	<0.001	-0.33	-0.37	-0.29
VAT (g)	HIIT	1389±769	1010±590	6.07	<0.001	-0.54	-1.15	0.07
	RT	1302±908	996±754	3.56	0.004	-0.36	-1.11	0.40
	COMBO	1135±688	856±470	3.27	<0.001	-0.46	-0.50	-0.42
LBM (kg)	HIIT	51.7±11.0	50.9±10.6	3.19	0.005	-0.07	-0.71	0.56
	RT	53.36±14.5	53.42±14.95	-0.19	0.853	0.00	-0.77	0.77
	COMBO	54±11.7	53.9±11.7	0.25	0.810	-0.01	-0.06	0.04
BMC (g)	HIIT	*3115 (2427, 3436)*	*3118 (2382, 3374)*	*2.31*	0.020	-0.04	-0.68	0.59
	RT	2934±752	2901±749	5.50	<0.001	-0.04	-0.81	0.72
	COMBO	3051±583	3036±3037	2.09	0.057	-0.02	-0.08	0.03
WAIST (cm)	HIIT	*105 (97.8, 106)*	*95 (93, 97.5)*	*3.82*	<0.001	-0.75	-1.35	-0.14
	RT	*102.7 (96, 111)*	*97.6 (89.5, 100.2)*	*3.18*	<0.001	-0.43	-1.18	0.31
	COMBO	105.7±12.4	100±11	4.24	<0.001	-0.47	-0.51	-0.43
WAIST TO HIP RATIO	HIIT	0.95±0.05	0.92±0.06	5.33	<0.001	-0.62	-1.23	0.00
	RT	0.92±0.10	0.88±0.11	5.71	<0.001	-0.39	-1.14	0.36
	COMBO	0.94±0.06	0.91±0.08	3.39	<0.001	-0.47	-0.51	-0.44

Means ± SD or *Median (IQR)*. Within group differences assessed by t student test or (*italic*)*Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals

Table 3-S8 Within group differences, metabolic health and blood pressure (12-week intervention)

		WITHIN GROUPS' DIFFERENCE						
		PRE	POST			ES and 95% CI		
		mean/*median SD/IQR*	mean/*median* SD/*IQR*	t / *z*	*p*	*g*	lower	upper
METABOLIC HEALTH								
siMS SCORE◊	**HIIT**	2.52±0.85	2.06±0.80	4.82	<0.001	-0.55	-1.16	0.07
	RT	2.75±0.77	2.23±0.59	4.34	0.001	-0.74	-1.47	-0.01
	COMBO	2.62±0.61	2.36±0.72	2.87	<0.001	-0.38	-0.42	-0.35
INSULIN RESISTANCE								
HOMA2- IR♦	**HIIT**	*1.71 (1.16, 2.19)*	*1.05 (0.91, 1.58)*	*3.14*	*0.001*	-0.75	-1.36	-0.15
	RT	*1.08 (0.89, 1.99)*	*0.88 (0.69, 1.13)*	*3.11*	*<0.001*	*-0.44*	*-1.19*	*0.31*
	COMBO	*1.52 (1.09, 2.04)*	*0.99 (0.72, 1.69)*	*2.10*	*<0.001*	-0.53	-0.57	-0.50
BLOOD PRESSURE								
SYSTOLIC BP (mm Hg)	**HIIT**	126±16	117±11	4.65	<0.001	-0.65	-1.26	-0.04
	RT	118.77±13.48	113.28±11.50	2.59	0.024	-0.42	-1.17	0.32
	COMBO	119±12	114±9	2.50	<0.001	-0.50	-0.53	-0.46
DIASTOLIC BP (mm Hg)	**HIIT**	80±10	76±10	2.31	0.033	-0.48	-1.09	0.14
	RT	76.62±6.95	74.69±5.77	1.58	0.140	-0.29	-1.05	0.46
	COMBO	76±5	75±5	0.41	<0.001	-0.11	-0.16	-0.06

◊ Simple Metabolic Syndrome score ♦ Homeostasis model assessment 2 insulin resistance.

Means ± SD or *Median (IQR)*. Within group differences assessed by t student test or (*italic*) *Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals.

Table 3-S9 Within group differences, POMS (12-week intervention)

		WITHIN GROUP'S DIFFERENCE						
PROFILE OF MOOD STATES		PRE	POST			ES and 95% CI		
		median IQR	*median IQR*	*z*	*p*	*g*	lower	upper
TOTAL MOOD DISTURBANCE	HIIT	*15 (13.5, 15)*	*4 (1, 4.5)*	3.82	<0.001	-3.21	-3.70	-2.72
	RT	*16 (14, 18)*	*5 (4, 6)*	3.18	0.001	-4.95	-5.43	-4.48
	COMBO	*16 (14, 17)*	*5 (3, 6)*	3.30	<0.001	-3.72	-3.65	-3.80

Median (IQR). Within group differences assessed by *Wilcoxon signed rank test*. Effect sizes are Hedges' (g) and associated 95% confidence intervals.

Sample size determination

- Based on data from Stensvold et al. (303) using C-Peptide as the primary outcome (as it is a robust indicator of MetS), a total sample size of 32 (11 per arm group) was determined using G-Power Software (Version 3.1.9.2 Franz Faul, Universität Kiel, Germany), ($\alpha = 0.05$, 1-b = 0.80): C-Peptide 16.9% decrease in representing 0.22 $nmol \cdot L^{-1}$, allowing for the correlation between repeated measures of 0.8 and a 20% dropout rate between baseline and follow-up. However, to account for more conservative estimates of dropout rate, and a possible smaller effect size in other key outcome measures, we targeted at least 15 participants per group in each of the three interventions.

Dietary accompaniment

- Participants received the Go to Guide for a low carbohydrate healthy fat diet (LCHF) (see Appendix H)
- This guide was created for another study (42), it contains complete and succinct information that was available for them to have as a reference and for trouble shooting. This guide included a description of what is the LCHF diet, what to expect and how to overcome common situations and problems when switching from a CHO based diet to a LCHF protocol. A complete list of the most common foods available in New Zealand, and the carbohydrate content next to each food in brackets; this list is ordered according to the major nutrient that is contained in the food (i.e. PRO, FAT and CHO), with a green label for those foods that are encouraged and with a red label for those not recommended. Suggestions for breakfast, lunch and dinner are also contained in this guide.

- Throughout the study participants were encouraged to continue having their meals according to their prescription, while recording their dietary intake using their mobile app, which was reviewed every other week during the exercise sessions. The objective was to detect if participants were adhering to their dietary prescription. These occasions were also used to remind them of the importance of being “in control” of their own success.

Food acquisition (shopping list)

- Participants were asked to prepare a shopping list according to the CHO content of the food. All participants received a booklet with a detailed food list classified according to nutrient content, indicating which choices contained more CHO, PRO or FAT.

Exercise accompaniment

- All through the intervention, exercise sessions were managed by the principal researcher, making sure all participants were safe and performing their exercise regimes as planned. Participants were monitored and provided with any assistance should they need it. Heart rate monitors, training session's paper slips to record heart rates, intensity level, the weight being lifted, RPE, RIR scores were obtained during the exercise performance.

Diet and Exercise facilitators and barriers

Post-12 weeks

- Adherence to a nutritional and exercise intervention is defined as the compliance with the nutritional or behavioural treatment that has been recommended. It has been found to be directly implicated with the success of intervention (304) preferences which play a fundamental role (likes and dislikes) (305). Logan et al. (306) created these questions based on Motl et al. (307). In addition to these questions, in part 2 participants were to indicate what they believed they liked and disliked the most given in questions 1 and 2. In part 3, participants were to rate the likelihood that they engage in the present nutrition and exercise programme during the following 6 months. They Used a Likert scale ranging from 1 (not likely at all) to 5 (most likely) adapted from Little et al. (167).

- To analyse the responses, they were all coded individually to identify major themes that were created according to the frequency and similitudes of the opinions, until no more themes could be generated (308, 309). For a theme to be generated it was required that at least two participants shared a similar response. The themes obtained were used to identify facilitators and barriers presented, and focused on intrapersonal (knowledge, attitudes, behaviour, self concept, skill, etc.) and interpersonal (social support, family, friends, etc.) issues using a social ecological approach (309, 310). It is a model that helps to understand behaviour and considers that it is influenced as a result of the interplay between different factors (intrapersonal, interpersonal, organisational, community and public policy) (309, 310).

Diet and exercise facilitators and barriers

- Participants completed a three-part questionnaire after the end of the intervention on the last day of training. If participants considered, the response was incomplete or had the impression that they could add or improve their responses, they were able to make amendments until the moment when all other assessments were finished. Responses (Part

1) are not presented by group unless the answer gave a direct inference to their specific exercise programme, because there were no differences in dietary intake (p>0.050) nor in attendance to training over 90% with no difference between groups. Likewise, both the nutrition and the exercise segments of the intervention are together, specifying clearly if the theme was nutritional or exercise related. All themes were either identified as facilitators or barriers of diet and exercise uptake. Themes were classified as intrapersonal when the theme referred to a behaviour, attitude, etc. without social influence and interpersonal when the theme was determined by social intervention. Table 3-S10 (Part 2) presents the main facilitators and barriers that were most likely to influence the adherence to the present intervention. Table 3-S11 present all the themes that were recognised and the question(s) from which they originated This table also presents those themes originated from the 6-month follow-up. Part 1 questions and sample answers are presented in Table 3-S12. Part 3 was asking the participants the likelihood in engaging in the present intervention over a 6 month period using a 1 to 5 Likert scale, there was no difference between groups being HIIT= 4.63±0.49; RT= 4.63±0.51; COMBO= 4.64±0.50. globally 4.63±0.49.

—What did you like about the LCHF/exercise program?

The first question provided information of those aspects that clearly were facilitators during this intervention and most likely key in promoting participants adherence to LCHF. Within the main themes, diet practicality was identified; participants pointed out (76%) that CHO restriction, the main characteristic of this dietary approach, was one of the main facilitators identified (See Table 3-S10). They alluded that because it was the only compulsory requisite, there was nothing else to worry about (76%), easy to manage once they got used to it (61%), no need to count CHO once they mastered portion sizes (54%). Another of the main themes was diet resources; participants reported that having the aid of the mobile app (56%) was a plus because it was easy to use (56%) and allowed them to be within the limit of carbohydrate intake throughout the study. Another facilitator was the website developed for the programme; it allowed participants to obtain information at any time because it was conveniently available 24/7 (45%). Another diet facilitator within the theme of diet practicality was that LCHF encourages to eat “real” minimally processed food, which was found as an advantage despite the work involved. “…cauliflower became my top food, so versatile and I can pack tons of it… top facilitator…”. The participants reason was that by choosing more vegetables and fruits instead of bread or pasta or any other processed food, reduced the “struggle” of counting the carbohydrate content from the labels and became a matter of selecting the right amount in household measures, which was a straightforward process (58%).

In regards to exercise, the main themes identified were exercise convenience, in this respect at the end of the 12-week intervention participants reported that this was a great opportunity and were happy about it. The main facilitator was short intense exercises (top facilitator) (45%) which gave participants the chance to experience a feeling of achievement, with gains in strength and body composition improving despite the short time commitment, which was even more satisfying. Revealing another main facilitator, was the sense of wellbeing and physical improvement. The latter was a generalised realisation for all the participants (100%) of the study regardless of whether their outcomes were large or small. Another facilitator that was reported by participants was the research gym laboratory (100%). The theme of support resources was also unveiled by the participants responses which identified the support of the researcher/trainer as a key facilitator as it provided them with the sense or feeling of being attended to which pointed out as a strong motivation. Participants enjoyed having supervision on site; this was perceived as an advantage and considered an additional motivator to show up for training (52%). Another main facilitator was group support (76%), participants reported having enjoyed the interaction with other participants during the programme, and this made it more attractive to come to training sessions.

—What aspects of the LCHF/exercise programme did you NOT like and why?

The main theme that was identified as a barrier was lack of social support beyond the other participants. Family members, especially those in their immediate family, not willing to share participants' new journey, was definitely a turn off (21%) and was identified as the 2nd most important barrier for those individuals that reported it. Another identified dislike was adaptation to the new diet, (28%) – the first few days of adaptation. At the beginning, switching to a new way of eating was complicated and difficult; however, it was no worse than getting used to any other new diet, regardless of its carbohydrate content. Also, it was difficult getting used to balancing their diet until the point participants did not feel hunger. A few participants reported having light headaches. Adding more fat to their diet for some participants was a challenge, therefore they needed to approach it by treating it like it was medically prescribed, until they got accustomed to it and it became effortless. There was always the feeling of going against the norm, regardless of which the participants felt they were improving their wellness.

The number one complaint was not being able to choose their exercise programme (39%); not being able to switch days for exercising; maintaining the same exercises apart from changing or modifying resistance was perceived as a turn off (11%). Exercising in the morning (and not having the choice to train at another time of the day) was also a general response of dislike. At the end of the programme participants wanted to continue coming and did not like that the programme was not

going to be extended after the 12 weeks; many of the participants wanted to continue coming to the exercise sessions (26%).

—How would you use this style of diet in the future, if at all?

To the third question, all of the participants reported that they would certainly adopt this way of eating but with some “slack” or room for an occasional treat, not in the same strict manner as they were conducting themselves during the course of the present study. Participants perceived it was necessary to be able to participate with the rest of their family members in celebrations without feeling guilt, for this reason they would introduce the LCHF diet to their immediate family members (in the same household), instead of going back to the same habits, which was the primary reason for entering the programme. However, a concern was raised in regard to supervision; participants expressed some doubts whether they were going to be able to achieve the same level of commitment. Because reinforcement was intensive but friendly, even if no direct communication was received, listening to other conversations between the facilitator and other participants was available. Also, having interacted with other individuals in the same situation was powerful. The positive and constant feedback they received was recognised as one of the most potent behavioural modification reinforcements in addition to the weekly weigh-in that also pushed them towards achieving their personal weight loss goal; some also felt they needed to deliver for themselves, for their group and for the programme.

A general response to this question expressed that participants would continue after the exercise programme was concluded and no longer were required to show up three times a week. It was more the number of participants wishing to add HIIT than the opposite; three individuals from HIIT wanted to incorporate RT into their exercise routine vs four from RT said that they would want to add some kind of HIIT into their training. Participants belief was that it was necessary to have both exercise modalities to improve strength or aerobic capacity.

Table 3-S10 Main facilitators and barriers

	Aspect	Themes	Main facilitators
⇧	Intrapersonal	Diet practicality	Only CHO restriction ■
⇧	Intrapersonal	Diet practicality	Not counting calories ■
⇧	Intrapersonal	Diet practicality	Diet easy to follow ■
⇧⌂	Intrapersonal	Programme resource	Researcher / Trainer ■
⇧	Intrapersonal	Diet resources	Diet App & website ■
⇧	Interpersonal	Group/Social support	Group / peer support ■
⇧	Interpersonal	Group/Social support	Family support ■▲
⇧⌂	Intrapersonal	Health, Wellbeing and satisfaction	Sense of wellbeing ■▲
⇧⌂	Intrapersonal	Physical wellbeing	Physical improvements ■▲
	Intrapersonal	Exercise convinience	Short intense exercise ■▲
	Aspect	**Themes**	**Main barriers**
⇧⌂	Interpersonal	Diet and the family	Family or partner following a different diet Family or partner not wishing to get involved ■
	Intrapersonal	Diet adaptation	Balancing energy intake to counteract hunger ■
⌂	Intrapersonal	Time commitment	Not enough time due to other commitments ▲
⇧⌂	Interpersonal	Programme support	Not having a support group ▲ Absence feedback or motivation ▲
⌂	Intrapersonal	Gym configuration	Gym too crowded, not suitable ▲
		LCHF related=⇧ Post 12-wk= ■	Exercise related=⌂ 6-month= ▲

Table 3-S11 Themes with questions of origin

Themes	Generated by
Achievement	■○Q1, ▲⇑Q1; ●○⇑⌂Q1
Health, wellbeing and satisfaction	■⌂Q1; ▲⌂Q2; ●○⇑⌂Q1;●○⇑⌂Q3
self-awareness	■⌂Q1, ▲⇑Q1; ▲⌂Q2; ●○⇑⌂Q3
physical improvements (strength and endurance)	▲⌂Q2; ●○⇑⌂Q3
Healthy weight	●○⇑⌂Q1
General health	●○⇑⌂Q1
information aids	▲⇑Q2
Researcher support	●○⇑⌂Q8
Group/Social support	▲○⇑⌂Q3; ●○⇑⌂Q8
Sessions-duration	▲⌂Q4
time commitment	■○Q1; ■⌂Q1; ▲⌂Q3;
Time constraints - sessions timing	■⌂Q1
Convenience	●○⇑⌂Q1
Group allocation	■⌂Q2; ●○⌂Q5
Programme and family integration	●○⇑⌂Q3; ●○⇑⌂Q7
Programme promotion	●○Q2
LCHF themes	
CHO restriction	▲⇑Q4
Diet adaptation	■⇑Q2
Diet adequation	▲⇑Q4
Diet and the family	■⇑Q3; ▲⇑Q1; ●○⇑Q5;
Diet awareness	▲⇑Q2
Diet composition	■⇑Q1
Diet differences	▲⇑Q3
Diet effects-weight control	■⇑Q1; ▲⇑Q2
Diet integration	■⇑Q2; ■⇑Q3
Diet practicality	■⇑Q1; ●⇑Q1; ●○⇑Q4
Diet support	▲⇑Q3; ●○⇑Q8
Diet structure	●○⇑Q6
Diet support-Cooking skills	▲⇑Q3; ●○⇑Q8
Exercise adequation	▲⌂Q1
Exercise combination	■⌂Q3; ▲⌂Q2; ▲⌂Q4
Exercise convenience - duration	■⌂Q3; ●⌂Q1; ●○⌂Q4
Exercise facilities	▲⌂Q2
Exercise frequency	▲⌂Q1
Exercise health and wellbeing effects	▲⌂Q2; ●○⌂Q4
Exercise modality	▲⌂Q4
Exercise purpose	■⌂Q3
Exercise situations	■⌂Q2
Exercise structure	●○⌂Q5; ●○⌂Q6; ●○⌂Q7
Gym configuration	▲⌂Q3

Programme related= ○
LCHF related= ⇑
Exercise related= ⌂
Part 1; Post-12 wk questionnaire= ■
Part 1; 6-month questionnaire= ▲
Part 4; 6-month questionnaire= ●
Question= Q

Table 3-S12 Questions with sample answers with themes post-12 weeks

	Part 1 post 12 weeks
Themes	1. What did you like about the LCHF/exercise programme?
Achievement	"After all that effort I can feel the difference... I love it!"
Exercise facilities	" I liked the gym it kept me motivated."
LCHF practicality	"I liked the diet it was easy to follow"
Time commitment	"… great exercise, fast, hard and in the morning"
Physical improvements	"I liked that suddenly lifting the groceries… was easier and easier…"
	2. What aspects of the LCHF/exercise programme did you NOT like and why?
Group allocation	"I didn't like the group I got because the combination group seem to be more fun... in the end, I loved it!"
Exercise and the family	"… being with my family was difficult at dinner time… they ate all the carbs… hate it!"
Exercise structure	"…always doing the same exercises started to be boring…at least I got stronger..."
Programme duration	"…I didn't like it got to an end… I wanted to continue…"
	3. How, if at all, would you use this style of LCHF/exercise in the future?
Diet adequation	"… yes I will continue but with some slack… every now and then you need more carbs."
Exercise adequation	"… I will combine it, not just HIIT… I was told, you also need RT."

Follow up at 6 months (description)

- After six months and at the end of the 12-week intervention, participants were invited to assist in contributing to the final comprehensive assessments to investigate what they had retained of their respective programmes, how many had continued after the cessation exercise and nutritional supervision, and the end of the exercise training.

- Participants were also given the opportunity to express their opinion regarding both the nutritional and exercise intervention separately using a four part instrument that substituted the one given at the end of the 12 week programme. This instrument was integrated to inform the perceived barriers and facilitators toward the participation in the present study. The first part consisted of 4 direct questions to obtain what were their major barriers and facilitators. These questions were based on previous research questionnaires (309, 311, 312). In part 2, participants were to indicate what they believed was their major facilitator (question 2) and their major barrier (question 3). In part 3, participants were to rate the likelihood that they would find themselves engaging in the present nutrition and exercise programme during the following 6 months, using a Likert scale ranging from 1 (not likely at all) to 5 (most likely) adapted from Little et al. (167). Part 4 was intended to assess the perception of participants in relation to their participation in similar exercise and nutrition

programmes barriers and facilitators (see appendix). These 8 questions were developed for assessing an exercise programme conducted in firefighters. It was intended to complement the inquiry of the perceived facilitators and barriers in the present study, and used in a focus group.

- The wording of the questions and face validity was tested in a sample of 16 individuals, who were asked if any item of the questions was ambiguous or difficult to understand, and if it was easy to understand the answers, besides checking if there were inconsistencies in the responses (313). Participants were notified in advance that this follow-up assessment was going to take place after six months of concluding this intervention. It was explained how and when they would be contacted, and the procedure of this assessment. The same analysis approach used for the post-12 week assessment was used (309, 310). In part 3, the results of the question, are presented as an average having an estimation of how likely participants would in the coming 6 months, engage in a programme using diet and exercise, adapted from Little et al. (167). Part 4 questions were initially intended to be asked during a focus group, but due to participants work commitments that was not possible. Questions were asked individually, and main ideas were transcribed verbatim using short sentences. The same approach as the analysis for post-12 week was used (309, 310).

Follow up – 6 months (results)

- After six months most of the participants were lost to the final assessment (follow-up) with only 13 of the 46 individuals that completed the programme being available. The response was similar between interventions (4, 4, and 5 for HIIT, RT and COMBO respectively). Because of the low numbers, no statistical analyses were performed. Tables below (3-S13 to 3-S18) present the raw data for all available results at 12 weeks and the follow-up results are expressed as percentage change. All participants reported that exercise commitment was easier than continuing with CHO restriction; food diaries reflected that all returning participants except for one (who had further reduced her CHO intake by 8%), increased their CHO intake to some degree (see Table 3-S14). Those participants that were more consistent with their nutrition and physical exercise habits reported more favourable outcomes to their metabolic health. Table 3-S18 shows fitness outcomes, most of the participants experienced a reduction in aerobic capacity as a consequence of discontinuing their structured exercise programmes.

Table 3-S13 Follow-up. Demographics.

FOLLOW UP RESULTS RAW DATA

GROUP	HIIT	HIIT	HIIT	HIIT	RT	RT	RT	RT	COMBO	COMBO	COMBO	COMBO	COMBO
GENDER	♂	♂	♀	♀	♀	♀	♀	♂	♀	♀	♂	♂	♂
AGE (y)	56	54	55	57	47	45	51	53	48	51	19	54	56
HEIGHT (cm)	179	188	169	173	166	160	165	181	172	169	175	178	188

Table 3-S14 Follow up. Diet Composition (Part 1).

FOLLOW UP RESULTS RAW DATA													
GROUP	HIIT	HIIT	HIIT	HIIT	RT	RT	RT	RT	COMBO	COMBO	COMBO	COMBO	COMBO
DIET COMPOSITION													
ENERGY INTAKE (kJ)	7205	7369	6554	6251	6565	6012	6198	7306	6605	6511	7022	7007	7091
% CHANGE vs POST-INTERVENTION	15%	22%	-	9%	-3%	22%	7%	19%	1%	15%	35%	34%	37%
CHO INTAKE (g)	98	79	103	100	98	106	110	96	104	114	90	119	67
% CHANGE vs POST-INTERVENTION	90%	202%	-	77%	6%	85%	25%	126%	-8%	62%	176%	132%	302%
CHO INTAKE % TOTAL ENERGY	23	18	26	27	25	30	30	22	26	29	21	28	16
% CHANGE vs POST-INTERVENTION	66%	148%	-	63%	10%	52%	17%	90%	-8%	40%	105%	73%	193%
PRO intake (g)	115	145	115	125	117	99	110	137	118	117	128	137	145
% CHANGE vs POST-INTERVENTION	11%	-7%	-	-14%	8%	4%	4%	-5%	3%	9%	5%	-6%	-4%
PRO INTAKE % TOTAL ENERGY	27	33	29	33	30	28	30	31	30	30	30	33	34
% CHANGE vs POST-INTERVENTION	-3%	-23%	-	-21%	11%	-15%	-3%	-20%	3%	-6%	-22%	-30%	-30%
FAT INTAKE (g)	87	89	78	67	80	68	69	85	76	69	85	69	89
% CHANGE vs POST-INTERVENTION	-14%	-26%	-	-18%	-15%	-13%	-8%	-14%	4%	-14%	-10%	-3%	-16%
FAT INTAKE % TOTAL ENERGY	45	46	45	41	46	42	42	44	44	40	46	37	47
% CHANGE vs POST-INTERVENTION	-25%	-39%	-	-25%	-12%	-29%	-14%	-28%	4%	-26%	-33%	-28%	-39%

Table 3-S15 Fitness and energy expenditure.

FOLLOW UP RESULTS RAW DATA													
GROUP	*HIIT*	*HIIT*	*HIIT*	*HIIT*	*RT*	*RT*	*RT*	*RT*	*COMBO*	*COMBO*	*COMBO*	*COMBO*	*COMBO*
FITNESS													
$\dot{V}O_2$peak (mL•kg^{-1}•min^{-1})	40.6	36.1	22.3	27.3	29.1	31.4	26.6	32.4	25.3	33.2	41.9	35.3	31.8
% CHANGE vs POST-INTERVENTION	-5%	-12%	-9%	-18%	-6%	-8%	-9%	-6%	-13%	0%	-17%	-18%	-11%
BENCH PRESS (kg)	60	60	34	35	62	33	42	90	35	52	64	65	80
% CHANGE vs POST-INTERVENTION	10%	22%	-6%	0%	-7%	21%	0%	18%	-	-52%	-6%	-8%	-19%
LEG PRESS (kg)	355	349	128	238	356	318	263	453	248	383	504	500	473
% CHANGE vs POST-INTERVENTION	1%	0%	-10%	-19%	-6%	-6%	-17%	-5%	-	-34%	4%	-1%	-4%
ENERGY EXPENDITURE													
RESTING METABOLIC RATE (kJ•d^{-1})	5745	7113	5414	6920	5862	5393	5167	7531	6720	6494	6552	8171	9288
% CHANGE vs POST-INTERVENTION	20%	-10%	13%	-7%	1%	-0.4%	-10%	0.5%	-11%	-19%	6%	-10%	-20%
PHYSICAL ACTIVITY (MET•min^{-1}•d^{-1})	380	486	400	349	369	384	303	470	323	402	514	386	498
% CHANGE vs POST-INTERVENTION	8%	7%	37%	40%	40%	2%	35%	10%	32%	33%	19%	10%	9%

Table 3-S16 Follow up. Body composition.

FOLLOW UP RESULTS RAW DATA													
BODY COMPOSITION													
BODY MASS (kg)	87.2	93.8	77.2	82.6	83.1	71	75.8	97.8	95	85.6	94.2	86.2	108
% CHANGE vs POST-INTERVENTION	5%	4%	1%	2%	-5%	5%	1%	2%	-7%	4%	3%	7%	2%
BMI ($kg \cdot m^2$)	27.2	26.4	27.1	27.5	29.7	27.8	27.5	29.7	32	29.9	30.8	26.9	30.3
% CHANGE vs POST-INTERVENTION	6%	7%	0%	2%	-4%	5%	2%	3%	-6%	5%	3%	8%	3%
% BODY FAT	27.1	31.8	45.1	41.7	34.2	38.6	39.3	28.4	48	38.4	36	25.3	31.7
% CHANGE vs POST-INTERVENTION	8%	7%	0%	2%	-	6%	6%	2%	-4%	17%	2%	15%	0%
WAIST (cm)	97	102	95.9	96.8	91	89.5	78.7	105	98.2	100	105	97.7	111
% CHANGE vs POST-INTERVENTION	5%	6%	0.1%	1%	-5%	12%	6%	6%	5%	6%	5%	10%	1%
HIP (cm)	105	106	109	109	110	103.9	108.7	105.3	120.5	108	114	101	112
% CHANGE vs POST-INTERVENTION	4%	2%	2%	1%	-2%	3%	3%	3%	-5%	4%	2%	7%	2%
WHR	0.93	0.96	0.88	0.89	0.82	0.86	0.72	1.00	0.81	0.93	0.92	0.97	0.99
% CHANGE vs POST-INTERVENTION	2%	4%	-2%	-1%	-3%	8%	3%	3%	10%	2%	3%	2%	0%
VAT (g)	970	1847	1017	1436	379	952	286	1998	690	942	823	960	1659
% CHANGE vs POST-INTERVENTION	16%	22%	0.1%	-3%	-	16%	35%	21%	-43%	7%	-1%	78%	33%
BODY FAT (kg)	22.6	28.8	33.9	33.1	27.5	26.4	28.8	26.8	44.4	31.7	32.8	20.9	33.1
% CHANGE vs POST-INTERVENTION	14%	11%	0%	4%	-	12%	7%	4%	-10%	6%	5%	24%	14%
LEAN BODY MASS (kg)	60.7	61.7	41.2	46.3	53.1	41.9	44.4	67.6	48.0	50.7	58.2	61.8	71.2
% CHANGE vs POST-INTERVENTION	3%	1%	0%	0%	-	2%	-3%	1%	-3%	3%	2%	2%	-4%
BMC (g)	3677	3274	2106	3116	2508	2741	2698	3421	2577	3183	3198	3442	3735
% CHANGE vs POST-INTERVENTION	2%	1%	0%	-2%	-	-1%	2%	0%	1%	-1%	2%	2%	2%

Table 3-S17 Biomarkers (Follow up at 6 mo.).

FOLLOW UP RESULTS RAW DATA

GROUP	HIIT	HIIT	HIIT	HIIT	RT	RT	RT	RT	COMBO	COMBO	COMBO	COMBO	COMBO
BIOMARKERS													
GLUCOSE (mmol•L-1)	5.4	4.7	5.3	5.7	5.5	6.6	5.4	7.5	6	5.9	5.2	6.8	5.6
% CHANGE vs POST-INTERVENTION	9%	45%	-4%	-5%	-13%	2%	9%	-4%	-2%	-15%	4%	0%	2%
INSULIN (pmol•L^{-1})	31.09	35.42	49.5	87.58	39.3	37.3	20.4	111	43.99	61.4	45.3	82.5	31.1
% CHANGE vs POST-INTERVENTION	98%	176%	27%	-36%	27%	-1%	95%	-7%	-23%	18%	25%	21%	1%
HbA1c (mmol•mol^{-1})	30.6	28.8	37	37.2	37	37.8	36.8	36.9	35.3	37.5	34.1	38.9	36.9
% CHANGE vs POST-INTERVENTION	25%	29%	0%	0%	3%	-7%	-1%	5%	4%	6%	-2%	6%	-1%
C-PEPTIDE (nmol•L^{-1})	0.56	0.56	0.59	0.97	0.51	0.62	0.47	1.19	0.71	0.83	0.53	0.97	0.79
% CHANGE vs POST-INTERVENTION	14%	138%	-6%	-23%	-1%	0%	44%	3%	-26%	-11%	2%	-15%	-44%
TOTAL CHOLESTEROL (mmol•L^{-1})	4	5	6	7	4	6	7	7	6	6	4	5	4
% CHANGE vs POST-INTERVENTION	0%	-20%	0%	-14%	0%	0%	-14%	-14%	0%	-17%	0%	0%	0%
HDL-C (mmol•L^{-1})	1.28	1.23	2.53	1.53	1.25	1.32	2.41	1.03	1.32	1.51	1.16	1.55	1.43
% CHANGE vs POST-INTERVENTION	35%	-20%	-12%	-4%	21%	2%	-15%	-18%	58%	-23%	-4%	-7%	-8%
LDL-C (mmol•L^{-1})	2.94	2.96	3.93	5.89	2.39	4.85	4.68	5.58	4.03	4.42	3.05	3.38	2.12
% CHANGE vs POST-INTERVENTION	-9%	-9%	3%	-20%	-3%	1%	-5%	-21%	11%	-5%	3%	21%	10%
TRIGLYCERIDES (mmol•L^{-1})	0.67	0.75	0.46	1.54	0.53	1	0.65	1.96	1.32	1.05	0.89	0.96	1.06
% CHANGE vs POST-INTERVENTION	-13%	160%	15%	-9%	-2%	-1%	66%	56%	-45%	35%	-20%	2%	16%
TG-HDL-C	0.23	0.27	0.08	0.44	0.19	0.33	0.12	0.83	0.44	0.30	0.33	0.27	0.32
% CHANGE vs POST-INTERVENTION	-34%	223%	26%	-4%	-19%	-3%	95%	91%	-66%	75%	-16%	11%	27%
CRP (mg•L^{-1})	0.4	1.5	2	2	2.6	1.3	1	3.2	3.1	1	4.2	2.2	0.1
% CHANGE vs POST-INTERVENTION	125%	40%	115%	35%	-42%	92%	-50%	-19%	-3%	50%	-36%	118%	128%
URIC ACID (mg•dL^{-1})	0.31	0.29	0.23	0.35	0.2	0.31	0.28	0.47	0.42	0.24	0.37	0.35	0.33
% CHANGE vs POST-INTERVENTION	32%	-17%	-13%	-11%	25%	3%	-25%	6%	-5%	-4%	8%	6%	30%

Table 3-S18 Metabolic health, insulin resistance and blood pressure.

FOLLOW UP RESULTS RAW DATA													
GROUP	HIIT	HIIT	HIIT	HIIT	RT	RT	RT	RT	COMBO	COMBO	COMBO	COMBO	COMBO
METABOLIC HEALTH													
siMS SCORE	1.99	2.01	0.76	2.97	2.22	2.66	1.33	3.51	2.79	2.59	2.38	2.20	2.38
% CHANGE vs POST-INTERVENTION	-11%	67%	112%	-2%	-16%	9%	54%	26%	-36%	18%	3%	20%	18%
INSULIN RESISTANCE													
HOMA2-IR	0.69	0.75	1.08	1.93	0.87	0.88	0.45	2.64	1.00	1.38	0.99	1.93	0.70
% CHANGE vs POST-INTERVENTION	102%	204%	25%	-36%	21%	0%	99%	-8%	-24%	12%	26%	20%	3%
BLOOD PRESSURE													
SYSTOLIC BLOOD PRESSURE (mm Hg)	104	111	116	146	105	104	118	113	108	118	113	109	128
% CHANGE vs POST-INTERVENTION	16%	-4%	12%	2%	4%	8%	3%	6%	-6%	6%	3%	24%	12%
DIASTOLIC BLOOD PRESSURE (mm Hg)	68	70	75	102	64	73	76	71	79	79	67	83	80
% CHANGE vs POST-INTERVENTION	24%	6%	7%	-5%	4%	5%	9%	9%	0%	10%	-2%	11%	12%

Follow up questionnaire

Part 1

—How, if at all, have you been incorporating the LCHF/exercise used during the study into your own diet?

After 6 months on their own, the LCHF undertaking was almost abandoned, only 15% of the 13 individuals that return for assessment maintain the CHO restriction to no more of 100 $g \cdot d^{-1}$. One response from a participant was: “Just been more aware of carbs and have tried to keep them to a minimum. But if I feel the craving, – I have a small treat, to avoid overindulging later”. In general the

majority of the responses to this question, informs the study that the present information was useful for creating a culture to avoid eating to excess of CHO (84%) which was the central concern of the programme. The 38% considers family integration is important.

The same question for exercise let us see that participants have been exercising more often since the completion of the programme (77%), however this in some cases, exercise practice as per the programme; has not been constant (84%). Participants from the combination group have stopped doing either RT or HIIT, depending on individual preferences. Some, on the contrary, have stopped completely and only have been exercising doing moderate intensity continuous training like hiking outdoors (15%).

—What have been facilitators to LCHF/exercise uptake?

To this question the responses varied from: The effects on body weight and overall fitness motivated them to continue (15%) and kept them interested. For others, the tools they were given were found to be quite useful and helped them (38%). The information they received, especially the recipes, were perceived as useful tools to follow the LCHF diet eating plan (15%). Another facilitator for the LCHF diet for the participants in the present study have been external information sources (15%).

Some of the participants have signed in to a gym right after finishing the programme or taken advantage of using their employer's gym membership and started to use it as much as possible (46%). Another facilitator has been the excellent results (physical improvement and sense of wellbeing) they had during the programme and for those who were more dedicated, apparently improved more throughout these six months prior to the last assessment (15%). A crucial motivator was the strength gains they have noticed in their usual everyday activities and the sense of wellbeing (23%).

—What have been barriers to LCHF/exercise uptake?

One of the main LCHF barriers perceived after 6 months of the intervention, was not having a support group doing the same programme to reinforce the LCHF diet, as happened during the intervention. Participants commented that peer pressure at work or comments coming from another family member with different ideas was easier to deal with while in the programme (23%), because coming to the exercise sessions was a constant reinforcement. Seeing another person going through the same experience and being successful was a positive feedback that was not there when the programme finished. Another person responded: “A barrier was my husband – not that he is against it – he just doesn’t participate”.

Among common responses stating there were barriers was “family”; it was hard to keep the LCHF diet going around family members that enjoyed having higher CHO meals and were not willing to let go of their “way” (46%). Another response against LCHF and related to time commitment, was the lack of cooking skills within participants (23%). Because processed foods and ready-to-eat meals are normally high CHO meals, participants that were not skilled in food preparation or because of a busy lifestyle (little time to cook) were put off the meals that were not ready-to-eat or required some preparation time (15%). Time was a main barrier for continuing with the exercise programme after the end of the end of the 12-week intervention (46%); another barrier has been the absence of a facilitator that is able to be there and support the participants and able to find/suggest any other exercise substitution, or simply be there for the participants that need assistance and external motivation (23%). Another common response was the impossibility of recreating entirely the circuit programme in a standard gym (23%), and also the absence of a suitable machine arrangement and machine availability (the machine being used by another gym user).

—How if at all, would you use this style of LCHF/exercise in the future?

It was almost unanimous the intention to follow this dietary pattern, however many of these participants (77%) added by saying that it was going to be a modified pattern that included the possibility to enjoy higher CHO content foods and this way include their family members (84%). Participants agreed that exercise was a key element and the main interest of the programme; all participants reported they were going to continue using the 20 min model of interval training. Some would continue using high intensity (23%), while others would only focus on keeping their exercise as a short circuit (23%). Maintaining a good level of physical activity exercising regularly was going

to be their focus (30%). While there was a group of individuals that were going to try to match the programme as much as possible as it was (23%), some also stated that the combined programme was the model they implemented and will continue to use as it may be a more complete full body workout.

Table 3-S19 Questions and sample answers with themes Part 1 6-month follow-up

	Part 1 6-month follow up
	1. How, if at all, have you been incorporating the LCHF/exercise used during the study into your diet/exercise?
Exercise and LCHF adequation	"… I did the training, as much as I could… the carbs, I just couldn't… ... I was more aware of what I was eating..."
Exercise and LCHF adequation	"…yes I adopted it as my way of living… every now and then I binge on carbs…"
Time commitment	"…I wanted but… was difficult to find the time to train…"
	2. What have been facilitators to LCHF/exercise uptake?
Health, wellbeing and satisfaction	"… the results are evident… I feel way better… am not stopping…"
Information aids	"… the guide and resources…"
Information aids	"… that book… What the fat?..."
Exercise combination	"… I find combining weights with interval training…quite fun…"
	3. What have been barriers to LCHF/exercise uptake?
Diet differences	"…my family and friends… it makes it harder… carb lovers…"
Time commitment	"… the time to cook, the time to exercise… very busy these days…"
Group/social support absence	"… the group was so important… social presure you know…"
Gym configuration	"…the gym itself not made for that… people don't let you... especially at peak hours… when I can go after work…"
	4. How, if at all, would you use this style of diet (LCHF)/ exercise in the future?
Time commitment	"… the 20-min session is great, helps me keep exercising…"
Diet adequation	"… the diet would be low in carbs but with the possibility to have more..."
Exercise combination	"… definitely exercise is a must… a combination between HIIT and RT… sessions 20-30 min…"
Diet adequation	"…my family is important to me I will focus on quality… every now and then carbs as low as during the programme…"

In Part 2 (presented in Table 3-S9) participants indicated which were their main facilitators and barriers from questions 2 and 3 according to their perception. Whereas Part 3 is presented in Table 3-S9, where participants indicated the likeliness of engaging in an intervention such as the present study for the following 6 months.

Table 3-S20 Likeliness to engage in a LCHF and exercise programme for 6 months

How likely would you find engaging in a LCHF and exercise program during the following 6 months?

GROUP	HIIT	HIIT	HIIT	HIIT	RT	RT	RT	RT	COMBO	COMBO	COMBO	COMBO	COMBO
Post-12 wk	5	4	4	5	4	5	5	4	4	5	5	4	5
LIKELINESS	4	4	4	4	5	4	4	4	5	4	4	4	4

Part 4

Table 3-S21 Questions with sample answers with themes Part 4 6-month follow up

Themes	Questions Part 4 and example answers
	1. What was your main reason for participating in this study?
Healthy weight	" to improve my health and lose some weight"
Health, wellbeing and satisfaction	"I was thinking of joining a gym, this was ideal to me"
Healthy weight	"…needed to improve my health… physical endurance…"
	2. What would help motivate individualsin your circumstances to participate in a LCHF and exercise programme?
Promotion of LCHF and exercise	"…offer state of the art facilities, fun and rewarding experience… personalised and engaging!.."
Promotion of LCHF and exercise	"…offer the opportunity to have personalised nutrition and exercise..."
Promotion of LCHF and exercise	"… let them know... short, intense workouts to get rid of stubon body fat… think it might work… ...like you did to get to us..."
	3. What changes did you notice in your fitness and body after doing the programme?
Physical wellbeing	"… I felt much stronger"
Physical wellbeing	"…I felt better, lighter and in better shape...
Physical wellbeing	"…thiner...like a version of a younger me!..."
Physical wellbeing	"…absolutly am wearing pants I haven't in a long time."
	4. What did you like about the programme?
Exercise convinience - duration	"… sessions were fast and experienced improvements … I liked that…"
LCHF practicality	"… diet was easy to follow… I liked it."
LCHF practicality	"…not counting calories… sweet as…"
Exercise convinience -duration	"…20 minutes and I was gone… that was awesone…"
	5. What did you not like about the programme?
Exercise structure	"…I did not like that I wasn't able to choose the group I wanted to be in… but not an issue…"
Exercise structure	"I did not like having the same exercises."
LCHF and the family	"I did not like that it was difficult to eat with my family, when they were eating carbs…"
	6. What changes would you make to the programme?
Exercise structure	"… maybe having a different routine… for a change..."
LCHF structure	"… what about having a *no* diet day…"
	7. What would make it more practical for people like you to do the programme?
Exercise sturcture	"…maybe being able to change exercise days…"
Programme and family integration	"…giving ideas of how to involve your family…"
Programme and family integration	"…being able to exercise at home to involve your family"
	8. What would help people like you to do the programme over the long-term?
Group/Social support	"…provide support, to help you…"
Group/Social support	"…having an exercise buddy…"
LCHF support	"…cooking lessons to innovate when you don´t know what to cook."
Group/Social support	"…a support group for extra motivation,.. perhaps."
Programme Innovation	"…what about providing the meals…"

Diet and exercise facilitators and barriers (questionnaire part 4)

1. What was your main reason for participating in this study?

The participants main reasons for joining the present intervention were around their need to improve their health and to reduce their body fat and to improve CVD risk. A main theme related to this question was healthy weight, and health and wellbeing, which uncovered facilitators such as sense of wellbeing and physical improvements, which seems to be the main reasons for joining the present study (100%).

2. What would help motivate individuals like you to participate in a programme like this?

In this question, the theme expressed was the LCHF diet and exercise promotion, where facilitators represented the experience of participants when they were invited to participate in the present study. It includes responses where participants suggest that a way to motivate people is to talk about their success and used theme as living examples (84%).

3. What changes did you notice in your physical abilities after doing the LCHF diet and exercise training?

The main facilitators were a sense of wellbeing and physical improvements. One response to the question was that there were a series of positive health manifestations after being exposed to the present intervention, which can be summarised by saying that the participation in the present study brought vitality and a generalised sense of wellbeing (100%).

4. What did you like about the LCHF diet and exercise programme?

This question's theme summarised the answers that participants gave previously in the post-12 weeks questionnaire in question 1. The themes found are: personal achievement, nutritional health, wellbeing and satisfaction, and diet practicality. The main facilitators a sense of wellbeing and physical improvements, etc. which are presented in Table 3-S9 (100%)

5. What did you not like about the LCHF diet and exercise programme?

Like question 5 this question was a reflection of question 2, being the main themes and barriers presented in Table 3-S9: time commitment, programme support and gym configuration, and barriers

identified were not enough time due to work and other commitments (84%), not having a group support or absence of feedback and motivation (84%).

6. What changes would you make to the programme (LCHF diet and exercise)?

Responses were summarised in the them of programme structure (LCHF structure and Exercise structure), among their suggestions were to use a variety of exercises (30%), a day out of the diet (15%) and family inclusion at home (46%).

7. What would make it more practical for individuals like you to follow a LCHF and exercise programme?

The main theme was programme and family integration and exercise structure, suggestions were to provide ideas for integrating the family at home (46%), add different routines, and possibility for changing exercise days (30%)

8. What would help individuals like you to perform LCHF diet and exercises over the long-term?

The main themes were around group and social support and programme innovation, and the main facilitator was group and peer support (84%). It was commented that if long-term commitment is the objective, the presence of support is vital.

Diet and exercise facilitators and barriers (Discussion)

After the 12 weeks of intervention it was found that the main facilitators for the present study may have been influenced by intrapersonal motivations which according to the social ecological model are influences of behaviour by knowledge, skills, and self-efficacy (314). This way the knowledge realisation of the efficacy of the programme represented by the programme characteristics powered the behaviour of the individual towards the obtention of their goals. While the skills that they are learning and confirming the their efficacy propelled the behaviour in direction of the adherence to the programme. It seems that a diet that restricts to 100 g was easy to follow, with nothing else to worry about, no counting calories (that were main facilitators), along with the reduced time commitment that was possible because of the nature of the exercise programme used for this intervention that used short, intense exercise. Research has evidence that LCHF diets that are not as restrictive as ketogenic diets and still provide the benefits of carbohydrate restriction (42).

Altogether (diet and exercise facilitators) potentiated the physical improvements that gave participants benefits that were translated into a sense of wellbeing (also main facilitators). On the side of the intrapersonal ground, the social ecological model postulates that the environment, in this case represented by the intrapersonal facilitators also motivated the participants to the acquisition of their goals, keeping them on track and directs, in this case, the participants' behaviour towards adherence to the programme This way the tools provided, proved to be useful and effective means (researcher, diet app and website) for support. The latter was reinforced by the positive peer pressure. Characteristics that together provide a positive feedback potentiating effect toward the adherence of the present study. Characteristics or aspects apparently were lost during the 6 months post intervention and may be an indication that it is necessary to provide this or similar facilitators to individuals at risk of metabolic disease to be successful. The indication of it, probably was that a great number of participants were lost after 6 months of being without the structure of support that was offered with the programme. An effect that has been observed in other interventions that noticed when support is withdrawn patients that were submitted to bariatric surgery after successful treatment, they start to regain weight after they are being discharged. Situation that is reversed once patients are reinstated psychological support (315).

Follow up, six months after the end of the intervention

While follow up analysis was indicated to the participants once the intervention had finished, overall numbers that participated in the 6 mo. follow up was too low for statistical analyses at this time point to be completed. In the literature there is evidence that follow up after 3 to 12-week post-intervention reported greater compliance after 6 months or even a year. It is possible to compare those participants that remained more active and compliant with the diet, are those that are showing greater results (316). However, those studies that reported a small dropout rate at follow-up had structured visits within that period. These regular meetings were used to weigh participants and use that time for solving any issues that arise (316, 317). In the present study, participants that did participate in the follow up mentioned in the final questionnaire that the absence of a facilitator was a factor that may have contributed to lower compliance in maintaining both the exercise and the diet.

However, it was possible to observe that a great number of participants returned to a higher consumption of carbohydrate and only two participants were following their diets more closely, both of these participants continued to lose weight and improve their body composition even further. A similar pattern was observed with exercise; those who remained more active obtained better outcomes, however it was not possible to observe a clear pattern in the results. By contrast, it was evident that most of the participants discontinued the training as such and replaced it with sporadic

sessions of high intensity with moderate intensity walking throughout the wk. Only two participants continued exercising closer to their prescription, that is three or more sessions of 20 min•wk^{-1}.

Of all the participants, those with the lowest CHO intake and were exercising closer the prescribed exercise were those who lost more weigh and, however this did not manifest in lower glycaemia. In summary, there was a trend between self-compliance with the programme and better body composition. Facilitators and barriers that were identified as key motivators, at post 12 week assessment were also found as potential motivators for participants at this time point. It was also found that barriers identified earlier may have been responsible for the reduction of the adherence to what the have learnt to be effective to improve metabolic health; possibly and indication that support may be necessary to reinforce intrapersonal facilitators an increase adherence after an intervention of LCHF and short intense exercise potentially proven to be effective.

4 Overall discussion

Importance of this research

This study was necessary because, in recent years the healthcare and scientific community have increased their interest for developing more potent strategies/treatments to stop the growth of non-communicable diseases to epidemic proportions. Especially those that have their origin in poor food habits and inactive lifestyles causing the deterioration of cardiometabolic health, which increases the incidence of CVD and T2DM. Hence, it has a negative impact on the economy worldwide, especially the economies of emerging countries that show a higher incidence of these diseases.

It has been observed that non-pharmacological treatments have produced the largest improvement in the reduction of the incidence and the progression of metabolic disease (12). Among non-pharmacologic strategies, exercise and nutrition are utilised mainly in the form of a low fat, reduced calorie diet and moderate intensity continuous aerobic and RT exercise (36). However, there are other and probably more potent approaches that have shown a great potential. The LCHF dietary

approach, and HIIT and RT, have been identified as potent tools that have produced positive results when they have been used as stand-alone treatments (36).

In the literature there is a paucity regarding the acute effects of a 10x1 min HIIT protocol (146, 189, 197) and full body circuit type RT when are combined with a CHO restricted diet. Nor has the direct comparison of the training effects of these exercise modalities been reported, either on their own or combined when exercise is performed iso-time and quasi iso-effort. Hence the main purpose of the present thesis was to determine which combination of a LCHF diet plus HIIT, RT or both, was more effective to improve the cardiometabolic risk when both exercise modalities were equated by time and effort. To answer this question, it was necessary to understand the acute effects and if there was a difference between HIIT and RT cardiometabolic responses after a single exercise session. Keeping in mind that the training effects are the cumulative effect provided by systematic repetition of an exercise session (presented in Chapter 2).

This study for the first time investigated these three different combinations of a LCHF diet (≤100 g CHO restriction) and high-intensity interval training (aerobic [HIIT]), resistance training [RT] and HIIT and RT, when both exercise modalities are equated by time and effort. The rationale behind this intervention was the utilisation of a diet and exercise regime that together could potentiate positive metabolic effects. The LCHF diet is a way of eating that favours the consumption of whole foods, while restricting CHO intake. It encourages the consumption of minimally processed, nutrient dense vegetables, healthy fats and high value protein sources, and could be a more suitable nutritional approach to stop the progression of MetS and T2DM (24). Limiting CHO to up to ≤ 100 g per day in the present study was considered sufficiently low to induce positive changes across all groups without being as restrictive as a very low-carbohydrate ketogenic diet. The latter, being more restrictive, may influence adherence and sustainability of this eating pattern. This was the case for all groups and is discussed in Chapter 3. HIIT allows the individual to reach higher intensities that are more effective in improving aerobic capacity and energy utilisation (167), RT using heavy weights is favourable as well for improving aerobic capacity when higher intensity is involved, but also and probably the most wanted effect is its capacity for the preservation of muscle mass and strength (37). RT is also effective for improving body composition and resting energy expenditure (318).

The main question of this thesis was to answer which form of exercise, when combined with carbohydrate restriction, is better to improve metabolic health? To respond to this question, it is important to comment first on the differences in the acute responses after one session of either HIIT or RT combined with a LCHF diet, because it can help to understand the training effects.

Differences of acute effects of HIIT vs RT

Energy expenditure (EE), aerobic capacity ($\dot{V}O_2$peak), and heart rate (HR)

In the present study, individuals following a LCHF diet performed iso-time and quasi iso-effort HIIT and RT exerted a significantly different energy expenditure. When individuals performed the HIIT exercise session, their energy expenditure was almost twice as much than RT exercise (when the RT used a 2 s concentric and 2 s eccentric tempo for each phase of the lift). This may demonstrate that the HIIT exercise combined with a LCHF diet may provide an advantage for improving weight loss. HIIT's greater energy expenditure probably was the result of the engagement of a larger muscle mass during the exercise session at all times. Exercise was performed with the legs causing a more constant oxygen uptake, while only 30% of RT work was performed with the lower extremities (leg press and sumo squats). The $\dot{V}O_2$peak was consequently greater for the HIIT group as demonstrated also by the GEE β= -8. 005 p <0.001 despite the same duration and effort. The latter was confirmed by a similar RPE demonstrated by the (GEE β= 0.425 p= 0,454) and also similar RER (GEE β= 0.003 p= 0,810). Another possibility that may explain the greater EE was the speed of muscular contraction. It seems that the type of contraction that involves HIIT may be similar to the explosive contractions during the leg press exercise described elsewhere by Mazzetti et al. (241). They observed that the leg press explosive contractions generated a greater energy expenditure than leg press exercises carried out, using 2 s x 2 s for concentric and eccentric phases respectively. This was the same tempo used in the present study for all RT exercises and was in line with the study conducted by Francois et al. (243) who compared upper and lower body sprint interval training (SIT) (5x30 s all-out sprints, interspersed with 4.5 min recovery). They found that both upper and lower body sprints with a resistance proportional to arms and legs' muscle mass, produced a similar metabolic response including HR. Allowing to say that when similar speed is achieved for upper and lower body exercises, the energy expenditure may be the same. These studies support the hypothesis that contraction speed was a determinant for producing a higher energy expenditure in the present study. Another study that supports this rationale was performed by Roberson et al. (242) who tested three circuit training full body RT protocols that used different speeds and loads; they observed that the rate of energy expenditure was significantly greater when exercise used high load and explosive concentric and controlled eccentric (2 s). All together this evidence may indicate that speed in the execution of upper and lower body exercise produces greater energy expenditure than lower speed even when the load is high.

Another parameter that allowed us to determine with confidence that HIIT exerts a greater energy expenditure is the heart rate, which is a parameter that depends on the oxygen demand of the working muscle, and is highly correlated with the energy expenditure (319). In the present study, HR was significantly greater for HIIT (GEE β= -19.306 p=0.0.017), showing a greater oxygen

demand demonstrated by the significantly greater $\dot{V}O_2$ peak (GEE β= -8.005 p<0.001) during working periods. This is likely achieved due to the greater muscle mass involved during the HIIT exercise periods compared to RT (GEE β= -3.229 p<0.001). In addition, lower HR and EE during RT may be due to the speed and the total number of contractions of each exercise, which was significantly lower than HIIT (15 rep•min^{-1} vs ~100 rpm). Proof of this rationale may be supported by the study carried out by Kaikkonen et al. (244) that showed that it is possible to control the HR during RT by controlling the speed of movement, and thus it is possible to regulate oxygen demand and therefore EE.

Acute blood pressure responses

In the present study blood pressure responses were similar between exercise modalities, with no changes at any time point being observed. This is not unusual, and is also documented by la Scala-Teixeira et al. (245), who compared the acute effects of manual RT and free weights RT in a group of normotensive and hypertensive individuals. Both protocols were matched by time and intensity and BP was measured pre-, during and after 15 min, 30 min, 45 min and 60 min post-training. In their study, normotensive individuals did not show any reduction in BP at any time point. Likewise, no changes were identified by Rossow et al. (320) who investigated the post-exercise hypotension (PEH) after high-intensity interval cycling vs continuous high-intensity cycling. These researchers observed no BP changes within the first 30 minutes after the exercise session, PEH occurred until 60 minutes after the exercise session for both high-intensity interval cycling and continuous cycling. Indeed, studies that have investigated the effects of a single bout of HIIT or RT have been observed to produce positive results starting at one hour and up to ten hours post-exercise in hypertensive individuals. In the present study there were no posterior measurements beyond the 15 min time point; as a consequence, it is impossible to rule out PEH. It has been observed that PEH may take up to 45 min after exercise to manifest (246, 320) and is a possible explanation of why PEH was not present 15 minutes after the session of HIIT or RT in the present study. It may be that when exercise is performed at a high-intensity, the stress generated by the mechanical stress of the muscle contractions induces an increase in the arterial stiffness, reducing the arterial compliance; in other words, its ability to expand (321-323). This in turn increases blood pressure, thus the speed the blood travels through the arteries to reach the working muscles. After exercise is finished, it takes around an hour to subside, allowing the blood pressure to return to normal or lower (PEH). Despite this, the objective of taking BP measurements to detect a possible increment in BP at 15 mins after exercise was to match the blood markers measurement. A limitation of the present study was the absence of more frequent BP measurements during and after exercise to obtain a better mapping and the detection of the possible changes in BP during this period. No adverse effects were detected, indicative of the safety of both modalities. When HIIT and RT have been used, studies have found 24 hour reductions in blood pressure in normo and in hypertensive individuals

(324, 325). Participants, in the HIIT study were normotensive and 50% were hypertensive, the exercise protocol was a 10-min warmup and 5 × 4 min intervals at 90% of HRpeak interspersed with 3 min of active recovery at 70% HRpeak (324) Whereas the RT study exercise protocol consisted of 3 sets of repetitions until moderate fatigue (slowing of movement) using 7 exercises (chest press, leg press, lat pull down, squat, arm curl, right leg curl, and left leg curl) with an intensity of 50% of 1RM with 90 s resting intervals between sets. Participants were 26 adults (12 hypertensive) between 30 and 60 y. Contrary in our study, all participants were normotensive, the exercise intervals lasted 1 min of exercise with one min of rest, another difference was the exercise selection for RT included two upper body exercises and one leg exercise for a total of 6 exercises, that were repeated until a total 10 exercises, 15 repetitions that accounted for 1 min of work with 1 min of rest between exercises. Probably in the present study, the volume of exercise accounted for not observing BP changes from the baseline, or probably because individuals were showing normal BP values since then. It is documented that exercise lowering BP properties is due to the PEH effect of acute exercise are more likely to occur when participants are hypertensive (320).

Acute glycaemic response

In relation to the baseline, HIIT and RT had similar responses in glucose, testosterone, cortisol, IL-6 and growth hormone after a single session of either HIIT or RT at any of the two time points (post-15 min and after 24 post exercise vs baseline). This was found regardless of the differences in muscle engagement (i.e. ballistic movements vs controlled 2 s concentric, 2 s eccentric), indicating a similar metabolic effect. In the case of glucose, it could be explained that the main reason for showing similar results between and within groups was that individuals at baseline were normoglycemic for both exercise modalities. The literature suggests that when normal glucose levels exist prior to exercise, there is unlikely to be a substantial glucose reduction. During HIIT, in normoglycemic individuals there is a slight increase in circulating glucose that persists for up to one hour after exercise ceases (326). In normal conditions during exercise there is a rise in glycaemia to allow sufficient energy for the working muscle. This may indicate the body's ability to cope with glucose variations due to exercise, as these were normalised and similar to baseline at the 15 min mark. The 24 h result was also not different from the baseline. This is consistent with studies looking at the 24 h fasting glucose response after a single session of RT (247) or HIIT (327) that observed no change in fasting glucose values over 24 hours. It could be that the exercise did not reach a sufficiently high intensity that is necessary to trigger a reduction in fasting glucose (328), despite the mean RPE results. In the present study it is indicated that participants perception of the intensity (as measured by RPE) was 16.9 for HIIT and 17.0 for RT corresponding to a very hard exertion for them; perhaps they were potentially accustomed to this intensity and therefore it was

not enough to cause a reduction. Conversely, the reverse might be true; they may have perceived a higher intensity than what physiologically was found.

Acute hormone and IL-6 responses

Evidence in the literature has established that the combination of duration, intensity and volume is required to generate changes in the hormonal anabolic responses (215). To address this matter the RT and HIIT programmes were designed to exert the highest possible hormonal responses. For RT, research showed that compound exercises have been found to be better for improving muscular strength and maximal oxygen consumption than exercises involving muscles in isolation (329), with 15 repetitions per set involving controlled movements and lifting weights close to failure (≥70 1RM): a pull and a push, interspersed with either a pull or a push lower body exercise, two to three sets per exercise (See Figure 1). In the case of HIIT, running or cycling was used and matched with the effort performed during RT. This way we intended to equate effort.

After one exercise session of both HIIT and RT, it was found there was a similar anabolic elevation of all hormones assessed. The duration of exercise plays a crucial role for the two hormones testosterone and IL-6 (222, 248, 252). However, in our study it seems that the combination of heavy loads and the order of upper and lower body exercises in RT was important for testosterone to reach a significant increase after only a 20 min exercise session. While the IL-6 increase was significant, it was quite conceivably influenced by a LCHF diet that possibly led to reduced glycogen depots (254, 330). Reduced glycogen levels combined with eccentric and concentric muscular contractions while lifting heavy loads have been reported (257) to augment the release of IL-6 in contrast with high glycogen concentration which inhibits IL-6 release (251, 257, 331).

In the present study, growth hormone was significantly increased for both exercise modalities. Previously, it has been reported that GH is also elevated when cortisol and lactate are significantly elevated (259), which shows that these increases are highly dependent on exercise that is meeting the threshold between volume and intensity (259). Budnar et al. (262) also reported that a short exercise duration session was also able to demonstrate significant increases in testosterone, GH, and cortisol, and their exercise programme involved 12 x 30 s bouts of kettlebell swings. It was also reported that the cortisol and GH concentrations registered their greatest concentration at immediately after and the 15 min mark post-exercise, whereas Budnar et al. reported that testosterone elicited its maximum level immediately after exercise. In the present study HIIT did not promote a significant increase in testosterone, probably because the overload generated was not as great as the RT overload. Supporting published data suggests that it is the load factor which plays a crucial role for the increase of testosterone, cortisol and GH (255). In the present study GH

was significantly increased for both conditions, with a slightly greater magnitude for RT. This again suggests the load was slightly greater for RT. In another study, Raymond, Renshaw and Duncan (263) provided evidence of the pivotal role of the stimulus of total load given by the total weight lifted which potentiates the increase in testosterone, cortisol and GH. They compared 12 swing cycles of 30 s using a load of 8 kg vs 16 kg kettlebell. It was the 16 kg load that provided the greatest increases in these hormones. Research also points out that using 15 repetitions per set and rest of 1 min between exercises in a circuit-like fashion seems to be effective to promote significant results for GH (260). In the present study, participants were lifting the maximum possible weight that they could use for performing at least 15 repetitions and no more than 2 repetitions in reserve per set, in a circuit-like fashion RT involving compound exercises. In line with the published data, this points to the belief that intensity (heavy load) played a key role for the elevations in testosterone, cortisol, and GH.

In summary, HIIT exerted a more pronounced energy expenditure than RT, however all other metabolic responses measured in the present study were similar. The magnitude of change resulted after RT for testosterone and GH was slightly larger. The same applies to the change of glycemia after HIIT. This might indicate that the body composition improvements when doing HIIT is the result of a greater energy utilisation coming from carbohydrates, (also improving glycaemia), while RT may promote the improvement of body composition as a result of the release of anabolic hormones that favour muscle synthesis, the energy utilisation from carbohydrate and fat by the working muscle mass which remains constant. Now that the acute effects of these combinations of carbohydrate restriction and exercise have been discussed, the following questions have been formulated.

Which combination of exercise and LCHF is more effective in reducing the risk of metabolic dysfunction and cardiometabolic risk factors?

It was hypothesised that combining a LCHF diet with either HIIT, RT or a combination of both was going to be beneficial for improving cardiometabolic risk factors. Indeed, previous work using a combination of aerobic exercise and RT conducted in type 2 diabetic individuals obtained better results than either of the two modalities alone (332). On the other hand, exchanging aerobic exercise with HIIT might be better and more achievable, since it produces a better or at least an equal response with a minimal time commitment (333). Supporting this statement and our hypothesis, a meta-analysis found that aerobic interval training and resistance training combined were more effective for improving $\dot{V}O_2$peak when compared to aerobic interval training of similar energy expenditure alone (334). Also it is documented that the concomitant use of LCHF and RT

had been found to preserve muscle mass (46). Therefore, combining both HIIT and RT, or a combination of both with LCHF was of specific interest.

We observed an improvement in almost every measured marker in the intervention trial, indicating that all of these combinations are effective to promote positive metabolic outcomes that may lead to improve the overall metabolic health in overweight individuals at risk of developing metabolic disease. However, there were significant differences between these interventions, and these were glycaemic control (HbA1c), body mass, RMR, and upper body strength (bench press).

Glycaemic control measured by HbA1c, and added sugars

Starting with the HbA1c, the HIIT group was the most improved; it may have been influenced by the training effect. The HIIT exercise session produced the greatest energy expenditure (see acute study) and CHO was the principal fuel being utilised, as measured by indirect calorimetry (see acute study). This difference in HbA1c also could have been influenced by a lower intake of added sugars. The HIIT group had the greatest reduction of absolute intake and the percentage of added sugars of total energy intake according to the post-training intervention dietary assessment. The lower added sugars intake may have reduced the glucose availability after the ingestion of foods having as a result lower glycaemia. Indeed, it is well documented that consuming a lower CHO food intake produces a lower postprandial glycaemic response (335). Therefore, having a greater energy expenditure per exercise session and eating less added sugar may have resulted in a lower HbA1c.

Body mass and RMR

The significant difference in body mass between HIIT and COMBO (p=0.049) could be explained by the training effect of HIIT that had a superior energy expenditure per exercise session. According to research, this transient exercise-induced energy expenditure can extend for up to 38 h (286) after the last bout of aerobic exercise (19). This over the course of the 12 week in addition to the spontaneous energy restriction of the LCHF diet may had an impact on HIIT body mass. Together these two factors with in addition to a the protein intake of ~1.4 g•kg^{-1}, that according to research may not be enough for muscle preservation(217) during energy restriction in combination of exercise training, in some degree may have caused by the reduction in LBM of the HIIT group (HIIT g= -0.07; p=0.005) vs the muscle sparing capacity of RT seen in both RT and COMBO (RT g= 0.00; p= 0.850; COMBO g= -0.01; p=0.810) possibly because of LBM preservation. It is also known that metabolism slows down when body weight is reduced (336), since energy expenditure has a high correlation with LBM; that could explain why RT and COMBO had a greater RMR than HIIT. Another example that provided more evidence to suggest the LBM sparing effect of RT (supporting

the notion that RMR is highly dependent on LBM (292)) are Bryner et al. (291) and Villareal et al. (193). The first one (291) is a study comparing RT vs AET, both follow a very low calorie diet for 12 wk. They obtained similar results in that the AET+D group manage to lose significant body weight but lost LBM and had a lower RMR, while those in the RT+D group did not lose LBM while still reduced body weight significantly and increased their RMR. The second study Villareal et al. (193) compared AET vs RT vs combined vs a control for six months. This group observed that AET lost 5% LBM and as a consequence had a greater decline in RMR vs minimal reductions in LBM (≤2 - 3%) and a smaller decrease in RMR for those who performed RT.

Upper body strength

It was expected that strength was going to be improved for all groups, since individuals that are previously sedentary benefit the most when exposed to an exercise programme. The RT group was significantly different from HIIT, but not the COMBO for upper body strength. However, participants of both the RT and COMBO groups had the benefit of exercising the upper body when performing RT. The participants of the COMBO group were influenced by HIIT performance and this could have interfered in the upper body strength development. This may explain that the RT-only group was the most improved in upper body strength. In the literature, a meta-analysis looking at the effect of concurrent aerobic training and RT vs RT alone, quantified the overall strength development using effect size (ES) which is an statistical estimate of the magnitude of a given effect (337, 338). As it is the larger the ES the larger magnitude of an effect (338). Therefore considering this metric, RT and concurrent training had twice as much the effect of endurance training: 1.76, for RT; for concurrent training, it was 1.44; and for endurance training, it was 0.78 (339). This meta-analysis may give a clear image of how strength development is influenced by concomitant RT and aerobic training, reflecting the results observed in the present study. However another more recent meta-analysis comparing the compatibility of concurrent HIIT and RT vs RT alone, did not observe this interference between these modalities of exercise when performed together for upper body strength (340). Which led me to think that similar results in upper body strength with HIIT was because the COMBO was less exposed to RT, and therefore less upper body training, since half of the total of 36 exercise sessions were used for HIIT and for that reason upper body strength was not much different from HIIT.

The clinical significance of this intervention

This study is clinically significant because it demonstrates it is possible to improve aerobic capacity (all $p \leq 0.001$) using high-intensity intermittent exercise that used different exercise modalities (HIIT and RT), a time commitment under the exercise recommendations of 150 min•wk^{-1} (341) with a protocol of 10 x 1 min interspersed with 1 min recovery periods. Interestingly RT an exercise

modality valued for its ability to improve strength and muscle accretion (37) improved significantly the aerobic capacity as well. This fact is beneficial and important because it allows more freedom to choose this exercise modality to achieve both objectives, without ignoring that both together provided a greater effect size effect (g= 0.57 HIIT; g= 0.53 RT; g= 0.85 COMBO); In addition to this the improvement in strength (all $p \leq 0.001$) is also of interest because all modalities improved this parameter. The fact that RT was the more effective to improve upper body strength is probably a result of having included exercises that are used for the upper body strength test and the fact that HIIT only used running and cycling. specifically upper body exercises and using any of these three combinations. These improvements are quite important because these two parameters are strongly advocated as an effective and potent treatment/tool for the reduction of cardiovascular disease risk, metabolic disease, and improvements in quality of life (342, 343). It is established that individuals that improve their aerobic fitness may trigger a better muscle oxidative capacity that ameliorates fat oxidation leading to better body composition and glucose utilisation (344-346). Individuals with increased muscular strength have better glycaemic control, lower blood pressure, and better oxidative capacity (227, 347). Increased muscular strength is related to an improved and independent protective effect on all-cause mortality in healthy middle-aged men, in men with hypertension, and individuals with heart failure (227, 347). In addition, Ortega et al. (348) investigated the association of muscular strength and CVD. In their study, a sample of over one million participants was followed for 18+ years and found that muscular strength was inversely related to CVD risk.

The present study also provides evidence that all the tested combinations of LCHF, HIIT, and/or RT close to failure can be used safely by people who are overweight, currently inactive (less than 150 minutes physical activity per week (349) and at risk of developing metabolic disease, provided that they are able to perform high intensity exercise. Despite these combinations were equally effective in reducing VAT and fat mass, the present study suggests that the LCHF diet and HIIT may be the least effective combination for improving body composition because it produced a significant but minimal in magnitude (g= -0.07) LBM loss; while at the same time the best for glycaemic control than any of the other two combinations. This is probably because the protein intake was not enough to spare muscle mass during energy deficit due to CHO restriction (217), in addition that of exercise. For glycaemic control, it may be explained because HIIT produces a greater energy expenditure per exercise session (see acute study), therefore it may have increased the need for glucose, that led to greater muscle glucose uptake compared to the RT exercise. This effect seems to be potentiated by the increased insulin sensitivity in the working muscle after exercise, as it was observed by Dela et al. (350) who demonstrated that a one-legged HIIT 10 x 10 was capable of improving the enzymatic action of the enzymes citrate and glycogen synthases, both important in energy metabolism, in both healthy (controls) and T2DM participants. They observed that HIIT

improved the insulin-stimulated glucose clearance by ~30% (which facilitates glucose uptake) with no difference between groups. When Dela et al compared the untrained limb vs the trained limb, they observed a significant difference between the two legs. This improvement was only localised in the trained leg (350). In the present study, then, that same effect, combined with the lower carbohydrate intake, may have been the reason why the HIIT group did better than the other two combinations. However, the RT and COMBO group's HbA1c reductions were significantly different within groups indicating that they are also effective for long term-glycaemic control. However, the differences for fasting glucose were not significant between pre- and post-evaluation within all groups, which may be an indication that these exercise modalities must be performed on a regular basis. After 72 h of the last exercise session, all the differences within groups were similar to the baseline results. This rationale is also reinforced by the fact that after one session the HIIT and RT combined with a LCHF diet also did not show any difference between the pre- and the 24 h fasting glucose assessment in the present study.

Improvements in cardiometabolic health biomarkers

This intervention successfully improved the metabolic health of overweight sedentary individuals, who showed an improvement in the siMS score for all groups, as a reflection of the similar, and in most of the cases significant reductions in the biomarkers. After 12 weeks, we also saw the reduction in C-peptide. C-peptide is an important biomarker that in recent years has been receiving more attention as its role is now considered to be more than just a surrogate of insulin secretion and pancreatic cell mass (351, 352). C-peptide is excreted in equimolar proportion to endogenous insulin but is secreted at a more constant rate over longer periods of time (353). It serves as an ideal means to identify the presence of T2DM in combination with fasting glucose and BMI (352). This biomarker holds a close link to cardiometabolic risk factors, a negative correlation between the level of serum C-peptide and HDL-C concentration and abnormal levels of TG has been identified in the non-diabetic population (354). According to Lee et al., (354) C-peptide is elevated when insulin resistance is present. They performed a multivariate analysis and confirmed that central obesity measured by waist circumference, elevated TG, and HbA1c are the independent predictors of elevated serum C-peptide level. Their findings support that the nature of elevated concentration of C-peptide is insulin resistance, and may be associated with the development of metabolic syndrome (351). For the above, we chose this marker to calculate the ideal sample size for the present intervention.

There is evidence that C-peptide levels can be lowered with HIIT. Ramos et al. (355), after 16 weeks of HIIT (4x4 @ 85–95% of HRpeak interspersed with 3 min active rest @ 50–70% of HRpeak) vs MICT (30 min @ 60–70% HRpeak) vs HIIT (1x4 @ 85–95% HRpeak and 3 min of

active recovery @ 50–70% HRpeak), also observed significant reductions in other metabolic markers such as insulin, SBP, and DBP. Additionally, non-significant reductions in body mass, %BF and fat free mass, waist circumference and WHR and an increase in HDL-C was achieved. In our study the improvement in C-peptide can be explained by the changes in the levels of insulin and TG, which both improved significantly. Likewise, there was a lowered fasting glucose, HbA1c, LDL-C, and a modest rise in HDL-C. This was despite the somewhat higher saturated fat intake which was elevated for all three groups (significantly higher within group only for the HIIT). When looking at the percentage intake of SFA as total energy, it was significantly increased for all three groups, as a consequence of CHO reduction. In our study, despite moderate improvements, the lipemia was similar for all groups. Total cholesterol was unchanged, HDL-C increased slightly without reaching statistical significance, LDL-C decreased within all interventions but was not significant. Whereas triglycerides and TG-HDL ratio were significantly reduced for all interventions ($p \leq 0.003$). Being a combination of the LCHF diet and RT, followed by LCHF-HIIT, those who obtained the greatest magnitude of change was ($g = -1.50$) and ($g = -1.34$) respectively.

We also observed using DEXA that VAT was diminished in all three groups which is in agreement with previous research. For example, Gillen et al. tested the effect of feeding or fasting while performing 18 sessions of HIIT (10x 60-s cycling efforts at ~90% maximal heart rate, 60-s recovery) over 6 wk. Eight women were enrolled in this trial and at the end of 6 weeks there were no differences between fed or fasting states, and even body mass was unchanged, however there were reductions in abdominal and leg fat as a percentage measured by DEXA (187). A recent published meta-analysis determined that HIIT is effective for reducing VAT, however due to the large variety of protocols it is not possible to establish the effect size. It seems that running vs cycling poses a better impact, however it cannot be established for sure (296). RT has also been found to be useful for the purpose of weight loss, however its main objective is to preserve or gain muscle mass. A meta-analysis exploring the combined effect of AET and RT concluded that AET is the one that is useful for fat loss and a good degree of visceral fat; the inclusion of RT is necessary but should not replace the time for AET (356). Indeed, RT alone seemed to fail when it came to reducing visceral fat, in a recent study by Keating et al., they concluded that RT was not effective in reducing VAT, and added that AET should be included in any exercise programme if VAT is the target (357). But Vargas et al. observed that when RT is combined with a very low carbohydrate high fat diet, VAT is reduced, and LBM is preserved. This evidence suggests that it is the CHO reduction that is responsible in reducing VAT while RT in synergy preserves muscle mass (299). The reduction of VAT with the concomitant reduction in waist circumference and of course the significant improvement in the insulin resistance measured by HOMA-IR provides evidence of this programme's effectiveness to reduce the cardiometabolic risk factors of MetS.

Another potentially important finding of this study was uric acid (UA) reduction, because hyperuricemia has been found to be directly proportional when correlated to impaired glucose tolerance. Also worth mentioning is that is has been found that UA may be directly related to fructose intake (358) the presence of a high volume of dietary fructose increases the expression of UA, LCHF reduces considerably fructose intake due to CHO restriction (124). Hyperuricemia has also been related to the proliferation of adipocyte fatty acid binding protein (aFABP) (359, 360), increasing the accumulation of TG and the higher expression of pro-inflammatory markers and markers of MetS (359, 360). Kawamoto et al. investigated the relationship between high serum uric acid and MetS, where they found a significant association between serum uric acid and MetS only in women, while in men, hyperuricemia was an independent risk factor for the incidence of carotid atherosclerosis (361). A recent review urges the implementation of large clinical trials to establish the value of lowering UA strategies to reduce hyperuricemia, because it seems it is not just an end product of purine metabolism but a central player in the development of metabolic and cardiovascular disease (362). In the meantime, strategies such as those discussed here may be worth exploring further.

In the last two decades, inflammation has become one of the silent enemies implicated in the development of metabolic disease. Inflammation is intimately linked to the pathogenesis of T2D (363) and chronic inflammation may lead to insulin resistance. Since insulin is crucial for the homeostatic regulation of glucose, lipid, and energy metabolism, an intervention that is capable of reducing inflammation may be ideal (364). Therefore, having identified that CRP (which is a reactant, or substance that increases if inflammation is present), has reduced post-intervention is another positive outcome of the present study. It has been observed that a combination of high-intensity aerobic exercise and RT, or each on its own, were able to reduce hsCRP, while combined aerobic exercise and RT had the largest reductions (365). In the present study, COMBO was also the group that experienced the largest magnitude of change [g= -0.09 HIIT; vs g= -0.51 RT; vs g= -58 for COMBO]. Another study (366) comparing high-intensity RT (75% 1RM) to moderate aerobic exercise for 10 weeks found that the group performing RT had significantly reduced hsCRP, despite the lower improvements in body mass and cardiovascular fitness. This supports the notion that high-intensity activity plays an important role when it comes to reducing inflammation.

Blood pressure is another risk factor involved in CVD and this was improved after the intervention. In the past, exercise interventions combining HIIT and RT, or implementing each modality on its own, have achieved similar results as ours, where only HIIT, like in our study, was the only exercise modality to improve SBP after 8 weeks of intervention (196). In another study, after a 16 weeks intervention, it was reported that HIIT produced reductions in both SBP and DBP (367). The authors identified that the high intensity level played an important role in improving cardiorespiratory fitness

which was implicated in blood pressure improvement (367). A more recent study comparing HIIT vs RT showed that HIIT and RT ameliorated blood pressure (368). These findings along with ours show that exercise is an effective strategy for improving blood pressure and suggest that high intensity activity provides a more robust effect for improving aerobic capacity which in turn improves blood pressure. Indeed, aerobic capacity is inversely related to the presence of hypertension (369).

After the present study was conducted, almost all the parameters were similar and a few significant differences between the three interventions were noted; we can say that a positive aspect of the present study is that it can provide the freedom of choosing from any of these modalities to fit the needs and preferences for those that may benefit from this approach. However, in the absence of diet-only and exercise-only groups, it is not possible to dissociate the LCHF diet effect.

Under these circumstances, we can say that the LCHF diet contributed to these improvements because of the difference in macronutrient composition, as it is evident between pre- and post-dietary assessments. The reduction in CHO especially is a strong and positive argument in favour of the LCHF diet. Indeed, high CHO intake has been implicated in the development of metabolic syndrome, a study by Kwon et al. (107) looking at the patterns of CHO and FAT intake (in a population of 6737 males and 8845 females), found that irrespective of FAT intake, MetS increased in males with higher CHO intake, whereas in females, the risk of MetS was more prevalent in those females with lowest FAT intake and greater CHO proportion. In our study we observed a reduction in the siMS score after 12 weeks of intervention, which may reduce the progression of MetS.

Another point in its favour that the LCHF diet poses for metabolic health, is that it encourages a greater intake of vegetables, and to a lesser extent fruit, that are nutrient dense while at the same time discouraging the consumption of processed foods. In the present study we observed a positive change and larger intake of these foods that allowed our participants to maintain a similar fibre intake between baseline and post-intervention ($p \geq 0.217$). The increase normally found in LCHF studies (370) mainly comes from non-starchy vegetables that are lower in CHO, rich in vitamins and minerals and in our study was preferred to other CHO sources. Because CHO intake is reduced, circulating glucose levels are lower and insulin levels tend to decrease; this in turn improves insulin resistance. All groups in our study had improvements in both fasting insulin and insulin resistance (HOMA2-IR) as previously mentioned. The added sugars intake, another component of the diet, could have been implicated in the reduction of these two parameters. As previously discussed (see lipids), the substitution of added sugars and refined starches with unsaturated fat and egg protein caused a reduction of 18% in triglycerides levels in other research (371). In Maki et al. study, CHO intake was even higher than ours, which indicates that even a small reduction in added sugars can

improve triglycerides levels. This is supported by a statement of the International Atherosclerosis Society position paper that states that diet composition independent of energy intake and body weight may have an influence on the metabolic profile (372).

This outcome should be used as an indication of the possibility of LCHF diet combined with any of these three exercise programmes as an effective strategy for improving fasting insulin levels and insulin resistance. This is a typical result for the LCHF diet, observed in previous studies comparing LCHF diet and other type of diets, especially HCLF diets (46, 107). When comparing our study with previous studies investigating dietary intakes (373, 374), we found similarities in eating patterns at baseline, which show a moderate PRO intake, greater CHO and a lower fat intake. Looking at metabolic improvements, it may be possible to indicate that after this intervention, these modifications were effective in improving metabolic parameters and diet composition, and took place with the initiation of the LCHF diet. Having a diet-only comparison group could have been desirable to isolate the diet effects and measure the extent of unwanted adverse effects, however the resources and the number of participants made that a non-viable alternative.

Unwanted adverse effects

For some individuals, where a minimal but statistically significant LBM loss occurred, we recommend a close supervision by a qualified nutrition and exercise expert to adjust protein and energy intake and avoid this from happening. Prior to the beginning of the study, all participants were instructed to round up their protein intake ~1.5 g•kg^{-1}, was intended to avoid any LBM loss and since the diet was ad libitum but it wasn't enough. We were not expecting to have any significant loss, based on research such as that by Sartors et al. who also used a calorie-restricted low carbohydrate diet with a protein intake of ~1.2 g•kg^{-1} and they did not observe any LBM loss (207) .

A posteriori, it seems that the spontaneous energy intake reduction that is mainly caused by a reduction in CHO (24), is what helped participants adhere to the diet, especially when the CHO restriction is not conducive to dietary ketosis (24). When it is combined with the greater energy expenditure of a HIIT exercise session three times a week for 12 weeks, it may have increased the energy deficit over the days of training study that was not covered by any additional food intake. This energy deficit may have recreated what Backx et al. (293) observed in individuals following a restricted weight loss diet with 1.7 g•kg^{-1} of PRO intake (which was about the average PRO intake in the present study ~1.4 g•kg^{-1}), was not enough to avoid LBM loss. They concluded that a normal protein intake may not be enough (even if it is twice as much as the RDI for a healthy adult) to maintain LBM despite individuals not following any specific exercise programme except for maintaining their habitual exercise/physical activity (293). In this respect, a recent review

researching the appropriate PRT intake for muscle accretion, provides evidence to explain that during negative energy balance the need for protein is greater than the normal protein intake and it recommends 2.3-3 g of PRT intake is required for muscle hypertrophy and preservation during times of energy restriction while performing exercise training (217).

A minimal yet significant BMC reduction for HIIT and RT (g= -0.04) but not COMBO (g= -0.02) and LBM reduction for HIIT (g= -0.07) and COMBO (g= -0.01) was also observed. The RT group was the only group that maintained LBM (g= 0.00), which shows that RT in our sample had a protective effect which is ideal in combination with the LCHF diet. These undesirable events may have something in common, muscle mass requires a positive energy balance. Energy intake was lower, and the energy deficit greater despite the higher protein in relation to baseline, it wasn't sufficient enough to prevent this happening; due to CHO restriction and exercise energy expenditure, this wasn't the case for HIIT and the COMBO but not significant for the latter. Apparently HIIT oxidises more energy than RT despite the iso-time and quasi iso-effort as we observed in the acute effects' study. That energy expenditure added to the energy deficit of CHO restriction may have caused a larger deficit that triggered LBM loss. According to a study conducted by Courteix (287), a negative energy balance and LBM loss are significantly and independently associated with BMC reduction. These events may have influenced these two inconveniences. However, the absence of a significant BMC loss in the COMBO group raises doubt. To make a more solid conjecture for the possible cause of that result warrants more research to identify what could have influenced the COMBO. Other studies that have used a greater carbohydrate restriction and similar energy intake have not reported BMC loss, which warrants more research (290, 375, 376). However, it may have been the additional energy expenditure as a result of exercise. Given that it provides sufficient energy and enough protein, the consumption of the LCHF diet for months/years has not been found to lead to adverse effects (89, 377, 378). Therefore, it may be recommended to have a close control of protein and energy intake while concomitant with HIIT. Quite recently Heikura et al. (288) shown that LCHF combined with exercise may negatively influence markers of bone turnover at least in short term. This may be triggered by energy deficit. There is evidence that a significant calorie deficit may trigger this (379, 380).

What is the additive effects difference of combining HIIT+RT to LCHF on cardiometabolic risk factors?

An advantage of adding both exercise modalities to the LCHF was the larger magnitude of change in aerobic capacity, that combined with the ability of RT to spare LBM, probably translated in a greater RMR for COMBO. Both COMBO and RT had greater energy expenditure (RMR).

Indeed, the literature gives many examples of how the addition of RT to aerobic training provides an advantage vs the use of any of the two in isolation; it seems they both act in synergy providing a more potent effect for improving metabolic health. A recent meta-analysis found that HIIT and RT are more effective in improving aerobic capacity than other exercise modalities (381). In the present study we observed a larger magnitude of change in aerobic capacity for the COMBO in line with this meta-analysis. While another found that concurrent HIIT and RT does not interfere with each other for the development of strength performed (340), we also observed that HIIT, RT and COMBO all increased participant's strength for the upper and lower body. The non-significant difference between pre- and post-assessment for upper body strength for HIIT may have been a matter of the lack of upper body exercises for that group during the present intervention.

What is the adherence and acceptability of this dietary and exercise combination?

The LCHF diet was well tolerated, with no adverse reports being filed during the intervention; in fact this in combination of all three exercise modalities improved wellbeing. This was indicated by an improvement of the total mood disturbance (TMD) for all combinations as measured by POMS. Despite the exercise training not being supramaximal, it involved the performance of high-intensity exercise that was not compromised by the low intake of carbohydrates throughout the intervention. Similar findings were observed by Cipryan et al. who reported that the intake of a VLCHF diet did not impair the performance of high-intensity interval training after 4 weeks of training (382).

Adherence Dietary intervention

It was noticed that participants were compliant with the programme and assumed a great commitment for keeping the nutritional target of, or less than, 100 g of CHO during the entire intervention. Research shows that this modest but effective carbohydrate restriction is more manageable and individuals are less troubled by having a larger reduction of CHO per day (383). Adherence was reflected in the food diaries and food frequency questionnaires. This was also demonstrated during the exercise training sessions where participants shared with their peers

anecdotes of what they were doing at home. These exchanges during the training sessions were a good indicator of an enhanced motivation. The profile of mood states (POMS) score improved after 12 weeks of intervention, with no difference between groups. Participants reported that the actions they engaged in during the programme regardless of group was tangible on their health. The key motivators were almost the same for the majority of participants. These were: 1) the realisation of self-improvement reflected in the sense of feeling healthier; 2) being able to wear clothing again that they were previously unable to fit but was kept because it was meaningful for them. Where only a few weeks into the programme it was referred to as an excellent gauge to recognise their effort was worth it; and 3) increased physical strength for coping with everyday life, lifting objects, and better mobility. This was not simply because of the thought that they were getting old but also because the physical effort required for doing those actions was the same as when they were younger. All of these were potent motivators which is in line with the study by Lanoye et al. (384). Most of our participants (>30 y) were more motivated, with those motivations concerned with healthy outcomes rather than appearance. Which was in line with our programme design, directed to improve metabolic health and was the motive behind the advertisement of the present study used losing excess body fat to feel healthier in the advertisement and implied that by doing so they would also look better; however we attracted a few individuals that can be described as emerging adults (18-25 y age group) that are normally inclined to favour appearance more than health motivations (384). These individuals were showing, an overlap between the motivation of being healthier and the motivation of losing weight for aesthetics only. In other words, most of our participants wanted to lose weight, because that was the path to achieve their main motive for being in the programme which was to be healthier. While the youngest was to look better by losing weight having as a side effect a better health which was also a motivator to maintain their participation during the 12-week trial.

We observe positive peer pressure, coming from constant contact and interaction with other participants doing the same programme and being successful, and looking, feeling, and acting empowered by the intervention. Indeed, when individuals are following healthy habits there are physical and cognitive benefits that allow them to realise they are improving their body composition, emotional well-being and self-concept, and reducing the risk of CVD, stress, and anxiety (385). In the literature there is evidence that positive peer pressure can serve to positively influence the actions of participants (386) making them stay engaged in the programme. In line with the results of Young et al. (387) that identified these behaviours have also been recognised by others to be effective for ◦maintaining individuals on target, when dieting or in an exercise programme. Recent research by Halali et al. (388) also supports the proposition that health, wellbeing, maintaining mobility and the ability to work were top motivators for successful weight management, while lack of time and stress were identified as the top barriers for successful weight loss and management.

Adherence to exercise programme

The combined adherence between all groups of the present study was over 90% attendance of exercise sessions, and there were no differences between groups. The attrition in our study was unrelated to the study intervention and it was lower for HIIT 1 (5%) vs RT=4 (24%) vs COMBO=3 (18%). Among the participants that quit the intervention, either at the middle or at the end by not showing up for their assessment appointment, the majority, if not all expressed that they would have continued until the end of the intervention if their circumstances were different. A participant from the COMBO went even further to show appreciation for the researchers, expressing that the reason for quitting was that he “already knew exactly what to do to continue on his own”, after that he apologised for his decision and left. In general, attrition rates for nutrition and exercise interventions are between 25-50% (160, 383) due to time constraints, personal and work related issues; our study is slightly lower with an overall attrition of 15%. Which have been influenced by constant supervision and encouragement during the study, which has been reported to increase adherence (389).

Iso-time and iso-effort as a measure of adherence to exercise prescription

A very important part of the programme was that both exercise modalities needed to be of the same exertion for the participants in each of the groups, to assure the goal of providing the same or as closely as possible, to make the comparisons for this study. The mode to equate all exercise groups’ modalities was by matching it iso-time and quasi iso-effort. Using a chronometer, exercise was successfully administered in 10 x 1 min interspersed with 10 x1 min of rest. Exercise effort was measured by RPE 6-20 Borg Scale. Exercise was successfully matched for effort and corroborated by obtaining the session RPE over the last 6 sessions of each exercise modality (MRPE for HIIT= 17.2 vs 17.5 for RT). The literature provides evidence of the utility and acceptability for prescribing and quantifying exercise intensity/effort using the 6-20 Borg scale (224, 238). On the other hand, despite effort and time being successfully paired and corroborated, it was perceived that effort was similar between exercise modalities. Interestingly, the HR was observed as higher for HIIT (equivalent to 90% HRmax as per prescription). The possibility here was that the HR as a consequence of the speed of movement during the muscular contraction in RT was not fast enough to elicit the requisite cardiovascular response. Indeed Kaikkonen et al. used the speed of movement to adjust the target heart rate for RT in their programme (244). The research confirmed this; Francois et al. compared upper body vs lower body SIT and found that the average heart rate for upper vs lower body was the same even though the resistance used was proportional to muscle

mass. In absolute units, the resistance used for the leg exercise was larger, yet the exercise heart rate was not different between the upper and lower body exercise (243).

Facilitators and barriers, adherence motivations

Using a social-ecological approach main facilitators and barriers were identified using a group of questions that were adapted from previous research and checked for face validity for using it with the participants of the present study. The social-ecological model sees that behaviour is modified by the environment at five levels, intrapersonal, interpersonal, organisational, community and public policy (390). The study centres its interest in the first two aspects to try to understand the origin of the motivation and how it may influence lead to modifying the behaviour during and after this intervention (309). The qualities of the LCHF diet, referring to the needless requirement of counting calories, the easiness to follow the diet, and the content of carbohydrate as the only requirement to worry about; are facilitators of the intrapersonal level. They added to the quality of the exercise "short and intense" that was effective also an intrapersonal facilitator, were adding together to the sense of wellbeing most likely because of the physical improvements participants also reported. In addition to the support resources (diet app, website, and researcher). These also intrapersonal level facilitators were reinforced with the positive reinforcement of peer and group support along with the family support; were strong motivations to adhere to the intervention. All these viewed through the optics of the social-ecological framework, that states behaviour is modified knowledge, beliefs and self-efficacy, at the intrapersonal level (314, 390). While attitudes and behaviours (interpersonal level) are also modifiers of conduct (309). Similar findings have been published by Mayer et al. (309) found that exercise adherence increased as a result of positive feedback and group support. Also, Tulloch et al. found that peer/group support from family, health improvements, the sense of well-being and fitness benefits were reported as facilitators from individuals adhere to exercise (391).

To this extent, the observed barriers the reluctance of family members to follow the same LCHF diet approach or not wishing to get involved in the process of participants (interpersonal barriers) were not potent enough to reduce adherence that was sufficiently motivated by facilitators reported by participants. Probably as a result of positive peer pressure that has been found a very potent motivator (392).

Follow up, six months after the end of the intervention.

After six months of the last assessment a follow-up took place. It was expected that a larger number of participants would turnout for this 6-month follow-up. Unfortunately, due to the low numbers no

statistical analysis was performed. This result was poor and as a consequence of the small numbers no solid conclusions could be made and only applies to these individuals. In the literature there is evidence that follow up after 3 to 12-week interventions reported greater compliance after 6 months or even a year. It is possible to compare those participants that remained more active and compliant with the diet, are those that are showing greater results (316). However, those studies that reported a small dropout rate at follow up, had structured visits within the follow-up period. These regular meetings were used to weigh participants and use that time for resolving doubts (316, 317). In the present study, participants mentioned in the final questionnaire that the absence of a facilitator was a factor that may have helped to maintain both the exercise and diet. The poor response of participants to return for the follow up assessment was the reason that no follow up procedure took place.

Nevertheless, from the results obtained, it was possible to observe that a great number of participants returned to a higher consumption of carbohydrates and only two participants were following their diets more closely than the rest. These two participants continued to lose weight and improve their body composition even further as they continued to rely on each other. It seems that an important element that made these participants compliant during the 12-week intervention was the constant contact during the exercise sessions with the other participants and the principal researcher to solve any doubts or queries as they arose.

Exercise-wise, a similar pattern was observed. Those who remained more active seemed to have better outcomes, however it was not possible to observe a clear pattern in the results. By contrast it was evident that most of the participants discontinued the training as such and replaced it with sporadic sessions of high intensity with moderate intensity walking throughout the week. Only two participants continued exercising closer to their prescription; that is three or more sessions of 20 min•wk^{-1}.

Of all participants, also those with the lowest CHO intake were those who lost more weight – however, this did not manifest in lower glycaemia. This is probably because of their inconsistency with their exercise regime. It seems that the structure of the sessions and the systematic repetitions 3 / wk / 12 weeks made the difference. In summary, there was an indication that those participants with self-compliance with the programme had better biomarkers and body composition.

In terms of the facilitators and barriers, after being 6 months on their own, participants reported that those facilitators related to the intrapersonal level absence became the main barriers to the self-adherence of the exercise and nutritional intervention after the end of the 12 week supervised

programme. Being the absence of a group support, nor having interaction between fellow participants probably played the main reason why they did not continue. There are several examples of published papers that point out that not having support is one of the main barriers reported (315, 391, 393, 394). While others have found that the presence of professional support is an important facilitator that besides enhances the success of an intervention (308) it is necessary to assure adherence post intervention participants require ongoing monitoring and encouragement (308).

Strengths and limitations

Strengths

One of the strengths was the robustness of the comprehensive assessments at all time points. Constant supervision and continuously being monitored throughout each session during the study, was also a strength and helped with diet adherence also. The acute exercise assessment (Chapter 2) allowed a better understanding of the influence of an individual session on the training effect. The statistical analysis was selected according to the behaviour of the data to assure the best reflection of the intervention; in other words, to match its behaviour to ensure its validity.

Limitations

Our study had limitations despite all efforts to minimise them. A) Sample size was small and having a larger sample size per group probably would have allowed differences to be seen between some parameters that had small variation between the participants. B) The second limitation was the number of experimental conditions. Having a diet and exercise only per condition, would have made it possible to isolate diet and exercise effects and let us calculate the extent of the effect per condition. C) We were not able to include all participants in the control phase of six weeks, nor complete 12 weeks for the control period. Ethically it is difficult to justify instructing a cohort identified as inactive and perceived overweight to continue with habitual inactivity. Second of all, the limited resources did not allow us to include all of the participants even for the six-week period. Participants needed to be randomised twice. Once to integrate the control period and the second time to obtain the experimental groups, that as we had to include them all in the experimental groups as well and having participants idle for that long we would probably lose them from the study if we had to wait three months for the control period to finish. Not having a control period of the same duration does not allow the experimental periods of the control phase to be compared. Qualitative analysis was carried out only by the main researcher, therefore strict methodology was

implemented to reduce subjective bias. Finally, not having the resources to be able to connect with participants post-intervention meant that most were lost to follow-up, thus we are unable to establish differences between groups 12 weeks post-intervention.

Practical applications

Firstly, this nutritional and exercise programme can be replicated and adapted to individual needs and used for multiple purposes related to any of the metabolic risk factors associated with the MetS that were improved after 12 weeks of intervention. RT may be used when losing muscle mass is a concern. Any of the three combinations could be adopted to improve aerobic capacity.

This programme can be used to improve and gain strength and aerobic fitness for individuals that wish to reduce their cardiometabolic risk and improve health.

Future Research

- First of all, the two findings that provide more questions than answers of causality must be fully investigated until it is known what the reason was, and most importantly, how to avoid the undesirable outcome of LBM and BMC loss.

- A study that closely monitors and tracks the food intake specifically of protein intake. Using weighted food diaries and professionally administered instead of self-administered questionnaires. Also assessing body composition half-way through or even three times to establish when the greatest impact on these measures occur.

- A study using a greater protein intake (~2.3–3.1 $g \cdot kg^{-1} \cdot d^{-1}$) which has been recently recommended for periods during weight loss to promote lean body mass retention (217).

Conclusions

Acute responses

- Both HIIT and RT were performed iso-time and quasi iso-effort, and HIIT provide a significantly greater energy expenditure; this might indicate that HIIT provides a more favourable stimulus for weight loss.

- The similar responses of HIIT and RT for testosterone, cortisol, growth hormone and glucose at all time points (15 min post and 24 h post) might indicate the similar effect of both exercise modalities was due to exercise load rather than volume. RT had a slightly higher magnitude of anabolic hormone response which may give some anabolic advantage and that was reflected in the muscle mass preservation of that group and the better result of COMBO vs HIIT (g= -0.01 vs g= -0.07 respectively).

- Having a LCHF diet does not impair exercise performance acutely and probably influenced the expression of IL-6 post-exercise, favouring an anti-inflammatory effect.

Chronic responses (12 weeks)

- HIIT combination may be a better modality for weight management and an excellent strategy for improving aerobic capacity.

- The addition of RT to LCHF has a muscle sparing effect while it improves strength and aerobic capacity.

- Evidence suggests that combining both exercise modalities in addition to the LCHF diet provides similar effects to any of the two exercise modalities alone, except for an additional muscle sparing effect; however, this difference was not statistically significant.

- More research is needed to be specifically directed on the aspect of potential BMC loss in some participants to identify the effects on bone health and clarify this very important health concern.

- Finally this thesis provides evidence that these interventions HIIT, RT or COMBO plus LCHF diet may be an important tool for the prevention of cardiometabolic risk factors and stop the progression to cardiometabolic disease suggesting further research to continue expanding the knowledge of applying carbohydrate restriction and high-intensity iso-time and high intensity quasi iso-effort exercise models.

References

1. Lindstrom J, Eriksson JG, Valle TT et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *J Am Soc Nephrol*. 2003;14(7 Suppl 2):S108-13.
2. Ried-Larsen M, MacDonald CS, Johansen MY, Hansen KB, Christensen R, Almdal TP, Pedersen BK, Karstoft K. Why prescribe exercise as therapy in type 2 diabetes? We have a pill for that! *Diabetes Metab Res Rev*. 2018;34(5):e2999.
3. VanWormer JJ, Boucher JL, Sidebottom AC, Sillah A, Knickelbine T. Lifestyle changes and prevention of metabolic syndrome in the Heart of New Ulm Project. *Preventive medicine reports*. 2017;6:242-5.
4. Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. *Translational research : the journal of laboratory and clinical medicine*. 2017;183:57-70.
5. Modell H, Cliff W, Michael J, McFarland J, Wenderoth MP, Wright A. A physiologist's view of homeostasis. *Adv Physiol Educ*. 2015;39(4):259-66.
6. O'Neill S, O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev*. 2015;16(1):1-12.
7. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. 2019.
8. Cho NH, Shaw JE, Karuranga S et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract*. 2018;138:271-81.
9. Gordon-Larsen P, Nelson MC, Popkin BM. Longitudinal physical activity and sedentary behavior trends: adolescence to adulthood. *Am J Prev Med*. 2004;27(4):277-83.
10. Song SH. Emerging Type 2 Diabetes in Young Adults. In: SI Ahmad editor. *Diabetes: An Old Disease, a New Insight*. New York, NY: Springer New York; 2013, pp. 51-61.
11. Buysschaert M, Medina JL, Bergman M, Shah A, Lonier J. Prediabetes and associated disorders. *Endocrine*. 2015;48(2):371-93.
12. Schwarz PE. Public health implications: translation into diabetes prevention initiatives--four-level public health concept. *Med Clin North Am*. 2011;95(2):397-407, ix.
13. Delahanty LM. The look AHEAD study: implications for clinical practice go beyond the headlines. *J Acad Nutr Diet*. 2014;114(4):537-42.
14. Van Name MA, Camp AW, Magenheimer EA et al. Effective Translation of an Intensive Lifestyle Intervention for Hispanic Women With Prediabetes in a Community Health Center Setting. *Diabetes Care*. 2016;39(4):525-31.
15. Diabetes Prevention Program Research G. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care*. 2002;25(12):2165-71.
16. Hayes C, Kriska A. Role of physical activity in diabetes management and prevention. *J Am Diet Assoc*. 2008;108(4 Suppl 1):S19-23.
17. Little JP, Jung ME, Wright AE, Wright W, Manders RJ. Effects of high-intensity interval exercise versus continuous moderate-intensity exercise on postprandial glycemic control assessed by continuous glucose monitoring in obese adults. *Appl Physiol Nutr Metab*. 2014;39(7):835-41.
18. Perry CG, Heigenhauser GJ, Bonen A, Spriet LL. High-intensity aerobic interval training increases fat and carbohydrate metabolic capacities in human skeletal muscle. *Appl Physiol Nutr Metab*. 2008;33(6):1112-23.
19. Rynders CA, Weltman A. High-intensity exercise training for the prevention of type 2 diabetes mellitus. *Phys Sportsmed*. 2014;42(1):7-14.
20. Strasser B, Siebert U, Schobersberger W. Resistance training in the treatment of the metabolic syndrome: a systematic review and meta-analysis of the effect of resistance training on metabolic clustering in patients with abnormal glucose metabolism. *Sports Med*. 2010;40(5):397-415.

21. Gaesser GA, Angadi SS, Sawyer BJ. Exercise and diet, independent of weight loss, improve cardiometabolic risk profile in overweight and obese individuals. *Phys Sportsmed*. 2011;39(2):87-97.
22. Al-Sarraj T, Saadi H, Calle MC, Volek JS, Fernandez ML. Carbohydrate restriction, as a first-line dietary intervention, effectively reduces biomarkers of metabolic syndrome in Emirati adults. *J Nutr*. 2009;139(9):1667-76.
23. Nielsen JV, Joensson E. Low-carbohydrate diet in type 2 diabetes. Stable improvement of bodyweight and glycemic control during 22 months follow-up. *Nutr Metab (Lond)*. 2006;3:22.
24. Feinman RD, Pogozelski WK, Astrup A et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. *Nutrition*. 2015;31(1):1-13.
25. Feinman RD, Volek JS. Carbohydrate restriction as the default treatment for type 2 diabetes and metabolic syndrome. *Scand Cardiovasc J*. 2008;42(4):256-63.
26. Baptista LC, Machado-Rodrigues AM, Martins RA. Back to basics with active lifestyles: exercise is more effective than metformin to reduce cardiovascular risk in older adults with type 2 diabetes. *Biol Sport.* . 2018;35 (4):363-72.
27. Mudaliar U, Zabetian A, Goodman M et al. Cardiometabolic Risk Factor Changes Observed in Diabetes Prevention Programs in US Settings: A Systematic Review and Meta-analysis. *PLoS medicine*. 2016;13(7):e1002095.
28. Viana AA, Fernandes B, Alvarez C, Guimaraes GV, Ciolac EG. Prescribing high-intensity interval exercise by RPE in individuals with type 2 diabetes: metabolic and hemodynamic responses. *Appl Physiol Nutr Metab*. 2019;44(4):348-56.
29. Jung ME, Bourne JE, Beauchamp MR, Robinson E, Little JP. High-intensity interval training as an efficacious alternative to moderate-intensity continuous training for adults with prediabetes. *J Diabetes Res*. 2015;2015:191595.
30. Tjonna AE, Lee SJ, Rognmo O et al. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. *Circulation*. 2008;118(4):346-54.
31. Gibala MJ, McGee SL. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exerc Sport Sci Rev*. 2008;36(2):58-63.
32. Gibala MJ, McGee SL, Garnham AP, Howlett KF, Snow RJ, Hargreaves M. Brief intense interval exercise activates AMPK and p38 MAPK signaling and increases the expression of PGC-1alpha in human skeletal muscle. *J Appl Physiol (1985)*. 2009;106(3):929-34.
33. Trombold JR, Christmas KM, Machin DR, Kim IY, Coyle EF. Acute high-intensity endurance exercise is more effective than moderate-intensity exercise for attenuation of postprandial triglyceride elevation. *J Appl Physiol (1985)*. 2013;114(6):792-800.
34. Earnest CP, Lupo M, Thibodaux J et al. Interval training in men at risk for insulin resistance. *Int J Sports Med*. 2013;34(4):355-63.
35. Earnest CP. Exercise interval training: an improved stimulus for improving the physiology of pre-diabetes. *Med Hypotheses*. 2008;71(5):752-61.
36. Diabetes Canada Clinical Practice Guidelines Expert Committee, Sigal RJ, Armstrong MJ, Bacon SL, Boulé NG, Dasgupta K, Kenny GP, Riddell MC. *Can J Diabetes*. 2018;42 Suppl 1:S54-S63.
37. Ishiguro H, Kodama S, Horikawa C et al. In Search of the Ideal Resistance Training Program to Improve Glycemic Control and its Indication for Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Sports Med*. 2016;46(1):67-77.
38. Hollings M, Mavros Y, Freeston J, Fiatarone Singh M. The effect of progressive resistance training on aerobic fitness and strength in adults with coronary heart disease: A systematic review and meta-analysis of randomised controlled trials. *Eur J Prev Cardiol*. 2017;24(12):1242-59.
39. Wewege MA, Thom JM, Rye KA, Parmenter BJ. Aerobic, resistance or combined training: A systematic review and meta-analysis of exercise to reduce cardiovascular risk in adults with metabolic syndrome. *Atherosclerosis*. 2018;274:162-71.
40. Feinman RD, Volek JS. Carbohydrate restriction as the default treatment for type 2 diabetes and metabolic syndrome. *Scand Cardiovasc J*. 2008;42(4):256-63.

41. Noakes TD, Windt J. Evidence that supports the prescription of low-carbohydrate high-fat diets: a narrative review. *Br J Sports Med*. 2016;51(2):133-9.
42. Zinn C, McPhee J, Harris N, Williden M, Prendergast K, Schofield G. A 12-week low-carbohydrate, high-fat diet improves metabolic health outcomes over a control diet in a randomised controlled trial with overweight defence force personnel. *Appl Physiol Nutr Metab*. 2017;42(11):1158-64.
43. Francois ME, Gillen JB, Little JP. Carbohydrate-Restriction with High-Intensity Interval Training: An Optimal Combination for Treating Metabolic Diseases? *Front Nutr*. 2017;4:49.
44. Volek JS, Quann EE, Forsythe CE. Low-Carbohydrate Diets Promote a More Favorable Body Composition Than Low-Fat Diets. *Strength Cond J*. 2010;32(1):42-7.
45. American Diabetes A. 5. Lifestyle Management: Standards of Medical Care in Diabetes-2019. *Diabetes Care*. 2019;42(Suppl 1):S46-S60.
46. Jabekk PT, Moe IA, Meen HD, Tomten SE, Hostmark AT. Resistance training in overweight women on a ketogenic diet conserved lean body mass while reducing body fat. *Nutr Metab (Lond)*. 2010;7:17.
47. Tjønna AE, Lee SJ, Rognmo Ø, Stølen TO, Circulation B-A. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome. *Circulation*. 2008.
48. Alvarez C, Ramirez-Campillo R, Henriquez-Olguin C, Castro-Sepulveda M, Carrasco V, Martinez C. [Eight weeks of combined high intensity intermittent exercise normalized altered metabolic parameters in women]. *Rev Med Chil*. 2014;142(4):458-66.
49. Alvarez C, Ramirez R, Flores M, Zuniga C, Celis-Morales CA. [Effect of sprint interval training and resistance exercise on metabolic markers in overweight women]. *Rev Med Chil*. 2012;140(10):1289-96.
50. Alvarez C, Ramirez-Campillo R, Ramirez-Velez R, Izquierdo M. Effects of 6-Weeks High-Intensity Interval Training in Schoolchildren with Insulin Resistance: Influence of Biological Maturation on Metabolic, Body Composition, Cardiovascular and Performance Non-responses. *Front Physiol*. 2017;8:444.
51. American Diabetes A. 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2019. *Diabetes Care*. 2019;42(Suppl 1):S29-S33.
52. Dehghan M, Mente A, Zhang X et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2017;390(10107):2050-62.
53. Gower BA, Goss AM. A lower-carbohydrate, higher-fat diet reduces abdominal and intermuscular fat and increases insulin sensitivity in adults at risk of type 2 diabetes. *J Nutr*. 2015;145(1):177S-83S.
54. Ferrannini E, Gastaldelli A, Iozzo P. Pathophysiology of prediabetes. *Med Clin North Am*. 2011;95(2):327-39, vii-viii.
55. de Luca C, Olefsky JM. Inflammation and insulin resistance. *FEBS letters*. 2008;582(1):97-105.
56. Hopps E, Noto D, Caimi G, Averna MR. A novel component of the metabolic syndrome: the oxidative stress. *Nutrition, metabolism, and cardiovascular diseases : NMCD*. 2010;20(1):72-7.
57. Astrup A, Finer N. Redefining type 2 diabetes: 'diabesity' or 'obesity dependent diabetes mellitus'? *Obes Rev*. 2000;1(2):57-9.
58. Stein CJ, Colditz GA. The epidemic of obesity. *J Clin Endocrinol Metab*. 2004;89(6):2522-5.
59. American Diabetes A. 3. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. 2018;41(Suppl 1):S28-S37.
60. American Diabetes A. 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. 2018;41(Suppl 1):S38-S50.
61. Mora-Rodriguez R, Ortega JF, Morales-Palomo F, Ramirez-Jimenez M. Weight loss but not gains in cardiorespiratory fitness after exercise-training predicts improved health risk factors in metabolic syndrome. *Nutr Metab Cardiovasc Dis*. 2018;28(12):1267-74.
62. Lee S, Kuk JL, Katzmarzyk PT, Blair SN, Church TS, Ross R. Cardiorespiratory fitness attenuates metabolic risk independent of abdominal subcutaneous and visceral fat in men. *Diabetes Care*. 2005;28(4):895-901.

63. Kennedy AB, Lavie CJ, Blair SN. Fitness or Fatness: Which Is More Important? *JAMA*. 2018;319(3):231-2.
64. Vidigal Fde C, Ribeiro AQ, Babio N, Salas-Salvado J, Bressan J. Prevalence of metabolic syndrome and pre-metabolic syndrome in health professionals: LATINMETS Brazil study. *Diabetol Metab Syndr*. 2015;7:6.
65. Gonzalez-Zapata LI, Deossa GC, Monsalve-Alvarez J, Diaz-Garcia J, Babio N, Salas-Salvado J. Metabolic syndrome in healthcare personnel of the university of Antioquia-Colombia; LATINMETS study. *Nutr Hosp*. 2013;28(2):522-31.
66. Kim TJ, Shin HY, Chang Y et al. Metabolically healthy obesity and the risk for subclinical atherosclerosis. *Atherosclerosis*. 2017;262:191-7.
67. Livingston EH, Zylke JW. Progress in obesity research: reasons for optimism. *JAMA*. 2012;308(11):1162-4.
68. Mozaffarian D, Rosenberg I, Uauy R. History of modern nutrition science-implications for current research, dietary guidelines, and food policy. *BMJ*. 2018;361:k2392.
69. MMWR. Trends in intake of energy and macronutrients--United States, 1971-2000. *MMWR Morb Mortal Wkly Rep*. 2004;53(4):80-2.
70. Ritten A, LaManna J. Unmet needs in obesity management: From guidelines to clinic. *J Am Assoc Nurse Pract*. 2017;29(S1):S30-S42.
71. Collaboration NCDRF. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet*. 2016;387(10026):1377-96.
72. Eriksson KF, Lindgärde F. Prevention of Type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise The 6-year Malmö feasibility study. *Diabetologia*. 1991;34(12):891-8.
73. Pan XR, Li GW, Hu YH et al. Effects of Diet and Exercise in Preventing NIDDM in People With Impaired Glucose Tolerance: The Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20(4):537-44.
74. Lindstrom J, Louheranta A, Mannelin M et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care*. 2003;26(12):3230-6.
75. Aguilar M, Bhuket T, Torres S, Liu B, Wong RJ. Prevalence of the metabolic syndrome in the United States, 2003-2012. *JAMA*. 2015;313(19):1973-4.
76. International Diabetes Federation. IDF DIABETES ATLAS. 2017.
77. Ludwig DS, Hu FB, Tappy L, Brand-Miller J. Dietary carbohydrates: role of quality and quantity in chronic disease. *BMJ*. 2018;361:k2340.
78. Nguyen PK, Lin S, Heidenreich P. A systematic comparison of sugar content in low-fat vs regular versions of food. *Nutr Diabetes*. 2016;6:e193.
79. Moreno-Valdespino CA, Luna-Vital D, Camacho-Ruiz RM, Mojica L. Bioactive proteins and phytochemicals from legumes: Mechanisms of action preventing obesity and type-2 diabetes. *Food Res Int*. 2020;130:108905.
80. Chang SK, Alasalvar C, Shahidi F. Superfruits: Phytochemicals, antioxidant efficacies, and health effects - A comprehensive review. *Crit Rev Food Sci Nutr*. 2019;59(10):1580-604.
81. Edwards CM, Cusi K. Prediabetes: A Worldwide Epidemic. *Endocrinol Metab Clin North Am*. 2016;45(4):751-64.
82. Barazzoni R, Deutz NEP, Biolo G et al. Carbohydrates and insulin resistance in clinical nutrition: Recommendations from the ESPEN expert group. *Clin Nutr*. 2017;36(2):355-63.
83. Snorgaard O, Poulsen GM, Andersen HK, Astrup A. Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. *BMJ Open Diabetes Res Care*. 2017;5(1):e000354.
84. Song S, Song WO, Song Y. Dietary carbohydrate and fat intakes are differentially associated with lipid abnormalities in Korean adults. *Journal of clinical lipidology*. 2017;11(2):338-47 e3.
85. Mozaffarian D, Ludwig DS. The 2015 US Dietary Guidelines: Lifting the Ban on Total Dietary Fat. *JAMA*. 2015;313(24):2421-2.

86. Schnyder S, Svensson K, Cardel B, Handschin C. Muscle PGC-1alpha is required for long-term systemic and local adaptations to a ketogenic diet in mice. *Am J Physiol Endocrinol Metab*. 2017;312(5):E437-E46.
87. Hu T, Mills KT, Yao L et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 2012;176 Suppl 7:S44-54.
88. Mansoor N, Vinknes KJ, Veierod MB, Retterstol K. Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials. *Br J Nutr*. 2016;115(3):466-79.
89. Bueno NB, de Melo IS, de Oliveira SL, da Rocha Ataide T. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. *Br J Nutr*. 2013;110(7):1178-87.
90. Pichler G, Amigo N, Tellez-Plaza M et al. LDL particle size and composition and incident cardiovascular disease in a South-European population: The Hortega-Liposcale Follow-up Study. *International journal of cardiology*. 2018;264:172-8.
91. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr*. 2010;91(3):535-46.
92. Cheng P, Wang J, Shao W, Liu M, Zhang H. Can dietary saturated fat be beneficial in prevention of stroke risk? A meta-analysis. *Neurol Sci*. 2016;37(7):1089-98.
93. McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol*. 1984;119(5):667-76.
94. Yamagishi K, Iso H, Kokubo Y et al. Dietary intake of saturated fatty acids and incident stroke and coronary heart disease in Japanese communities: the JPHC Study. *Eur Heart J*. 2013;34(16):1225-32.
95. Yaemsiri S, Sen S, Tinker L, Rosamond W, Wassertheil-Smoller S, He K. Trans fat, aspirin, and ischemic stroke in postmenopausal women. *Ann Neurol*. 2012;72(5):704-15.
96. Wallstrom P, Sonestedt E, Hlebowicz J et al. Dietary fiber and saturated fat intake associations with cardiovascular disease differ by sex in the Malmo Diet and Cancer Cohort: a prospective study. *PLoS One*. 2012;7(2):e31637.
97. Larsson SC, Virtamo J, Wolk A. Dietary fats and dietary cholesterol and risk of stroke in women. *Atherosclerosis*. 2012;221(1):282-6.
98. Atkinson C, Whitley E, Ness A, Baker I. Associations between types of dietary fat and fish intake and risk of stroke in the Caerphilly Prospective Study (CaPS). *Public Health*. 2011;125(6):345-8.
99. Yamagishi K, Iso H, Yatsuya H et al. Dietary intake of saturated fatty acids and mortality from cardiovascular disease in Japanese: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC) Study. *Am J Clin Nutr*. 2010;92(4):759-65.
100. Maekawa S, Kawahara T, Nomura R et al. Retrospective study on the efficacy of a low-carbohydrate diet for impaired glucose tolerance. *Diabetes Metab Syndr Obes*. 2014;7:195-201.
101. Tay J, Luscombe-Marsh ND, Thompson CH et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: a randomized trial. *Am J Clin Nutr*. 2015;102(4):780-90.
102. Krieger JW, Sitren HS, Daniels MJ, Langkamp-Henken B. Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression. *Am J Clin Nutr*. 2006;83(2):260-74.
103. Soenen S, Martens EA, Hochstenbach-Waelen A, Lemmens SG, Westerterp-Plantenga MS. Normal protein intake is required for body weight loss and weight maintenance, and elevated protein intake for additional preservation of resting energy expenditure and fat free mass. *J Nutr*. 2013;143(5):591-6.
104. Tobias DK, Chen M, Manson JE, Ludwig DS, Willett W, Hu FB. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2015;3(12):968-79.

105. Estruch R, Ros E, Salas-Salvado J et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med*. 2018;378(25):e34.
106. Ha K, Joung H, Song Y. Low-carbohydrate diet and the risk of metabolic syndrome in Korean adults. *Nutr Metab Cardiovasc Dis.* 2018 Nov;28(11):1122-1132
107. Kwon YJ, Lee HS, Lee JW. Association of carbohydrate and fat intake with metabolic syndrome. *Clin Nutr*. 2018;37(2):746-51.
108. Wood RJ, Volek JS, Davis SR, Dell'Ova C, Fernandez ML. Effects of a carbohydrate-restricted diet on emerging plasma markers for cardiovascular disease. *Nutr Metab (Lond)*. 2006;3:19.
109. van Wyk HJ, Davis RE, Davies JS. A critical review of low-carbohydrate diets in people with Type 2 diabetes. *Diabet Med*. 2016;33(2):148-57.
110. Volek JS, Fernandez ML, Feinman RD, Phinney SD. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res*. 2008;47(5):307-18.
111. Volek JS, Feinman RD. Carbohydrate restriction improves the features of Metabolic Syndrome. Metabolic Syndrome may be defined by the response to carbohydrate restriction. *Nutr Metab (Lond)*. 2005;2:31.
112. Diabetes Prevention Program Research G, Knowler WC, Fowler SE et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet*. 2009;374(9702):1677-86.
113. Sartorius K, Sartorius B, Madiba TE, Stefan C. Does high-carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis. *BMJ Open*. 2018;8(2):e018449.
114. Korsmo-Haugen HK, Brurberg KG, Mann J, Aas AM. Carbohydrate quantity in the dietary management of type 2 diabetes: A systematic review and meta-analysis. *Diabetes Obes Metab*. 2018.
115. Verma P, Srivastava RK, Jain D. Association of Lifestyle Risk Factors with Metabolic Syndrome Components: A Cross-sectional Study in Eastern India. *Int J Prev Med*. 2018;9:6.
116. Kang H, Greenson JK, Omo JT et al. Metabolic syndrome is associated with greater histologic severity, higher carbohydrate, and lower fat diet in patients with NAFLD. *Am J Gastroenterol*. 2006;101(10):2247-53.
117. Jung SH, Jung CH, Reaven GM, Kim SH. Adapting to insulin resistance in obesity: role of insulin secretion and clearance. *Diabetologia*. 2018;61(3):681-7.
118. AlEssa HB, Cohen R, Malik VS et al. Carbohydrate quality and quantity and risk of coronary heart disease among US women and men. *Am J Clin Nutr*. 2018;107(2):257-67.
119. Sluijs I, van der Schouw YT, van der AD et al. Carbohydrate quantity and quality and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) study. *Am J Clin Nutr*. 2010;92(4):905-11.
120. AlEssa HB, Bhupathiraju SN, Malik VS et al. Carbohydrate quality and quantity and risk of type 2 diabetes in US women. *Am J Clin Nutr*. 2015;102(6):1543-53.
121. Gannon MC, Nuttall FQ. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. *Diabetes*. 2004;53(9):2375-82.
122. Velazquez-Lopez L, Gonzalez-Figueroa E, Medina-Bravo P et al. Low calorie and carbohydrate diet: to improve the cardiovascular risk indicators in overweight or obese adults with prediabetes. *Endocrine*. 2013;43(3):593-602.
123. Schwingshackl L, Hoffmann G. Comparison of effects of long-term low-fat vs high-fat diets on blood lipid levels in overweight or obese patients: a systematic review and meta-analysis. *J Acad Nutr Diet*. 2013;113(12):1640-61.
124. Liebman M. When and why carbohydrate restriction can be a viable option. *Nutrition*. 2014;30(7-8):748-54.

125. Noakes M, Foster PR, Keogh JB, James AP, Mamo JC, Clifton PM. Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. *Nutr Metab (Lond)*. 2006;3:7.
126. Garg A, Grundy SM, Unger RH. Comparison of effects of high and low carbohydrate diets on plasma lipoproteins and insulin sensitivity in patients with mild NIDDM. *Diabetes*. 1992;41(10):1278-85.
127. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab*. 2003;88(4):1617-23.
128. Foster GD, Wyatt HR, Hill JO et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med*. 2003;348(21):2082-90.
129. Samaha FF, Iqbal N, Seshadri P et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *N Engl J Med*. 2003;348(21):2074-81.
130. Volek JS, Sharman MJ, Gomez AL, Scheett TP, Kraemer WJ. An isoenergetic very low carbohydrate diet improves serum HDL cholesterol and triacylglycerol concentrations, the total cholesterol to HDL cholesterol ratio and postprandial pipemic responses compared with a low fat diet in normal weight, normolipidemic women. *J Nutr.* 2003;133(9):2756-61.
131. Meckling KA, O'Sullivan C, Saari D. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. *J Clin Endocrinol Metab*. 2004;89(6):2717-23.
132. Sharman MJ, Gomez AL, Kraemer WJ, Volek JS. Very low-carbohydrate and low-fat diets affect fasting lipids and postprandial lipemia differently in overweight men. *J Nutr.* 2004;134(4):880-5.
133. Stern L, Iqbal N, Seshadri P et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med*. 2004;140(10):778-85.
134. Volek J, Sharman M, Gomez A et al. Comparison of energy-restricted very low-carbohydrate and low-fat diets on weight loss and body composition in overweight men and women. *Nutr Metab (Lond)*. 2004;1(1):13.
135. Volek JS, Sharman MJ, Gomez AL et al. Comparison of a very low-carbohydrate and low-fat diet on fasting lipids, LDL subclasses, insulin resistance, and postprandial lipemic responses in overweight women. *J Am Coll Nutr*. 2004;23(2):177-84.
136. Yancy WS, Jr., Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med*. 2004;140(10):769-77.
137. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA*. 2005;293(1):43-53.
138. McAuley KA, Hopkins CM, Smith KJ et al. Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia*. 2005;48(1):8-16.
139. Nielsen JV, Jonsson E, Nilsson AK. Lasting improvement of hyperglycaemia and bodyweight: low-carbohydrate diet in type 2 diabetes--a brief report. *Ups J Med Sci*. 2005;110(1):69-73.
140. Yancy WS, Jr., Foy M, Chalecki AM, Vernon MC, Westman EC. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutr Metab (Lond)*. 2005;2:34.
141. Truby H, Baic S, deLooy A et al. Randomised controlled trial of four commercial weight loss programmes in the UK: initial findings from the BBC "diet trials". *BMJ*. 2006;332(7553):1309-14.
142. Gardner CD, Kiazand A, Alhassan S et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA*. 2007;297(9):969-77.
143. Lecheminant JD, Gibson CA, Sullivan DK et al. Comparison of a low carbohydrate and low fat diet for weight maintenance in overweight or obese adults enrolled in a clinical weight management program. *Nutr J*. 2007;6:36.

144. Perez-Guisado J, Munoz-Serrano A, Alonso-Moraga A. Spanish Ketogenic Mediterranean Diet: a healthy cardiovascular diet for weight loss. *Nutr J*. 2008;7:30.
145. Shai I, Schwarzfuchs D, Henkin Y et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med*. 2008;359(3):229-41.
146. Brinkworth GD, Noakes M, Buckley JD, Keogh JB, Clifton PM. Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *Am J Clin Nutr*. 2009;90(1):23-32.
147. Davis NJ, Tomuta N, Schechter C et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. *Diabetes Care*. 2009;32(7):1147-52.
148. Volek JS, Phinney SD, Forsythe CE et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009;44(4):297-309.
149. Foster GD, Wyatt HR, Hill JO et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med*. 2010;153(3):147-57.
150. Iqbal N, Vetter ML, Moore RH et al. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese, diabetic participants. *Obesity*. 2010;18(9):1733-8.
151. Yancy WS, Jr., Westman EC, McDuffie JR et al. A randomized trial of a low-carbohydrate diet vs orlistat plus a low-fat diet for weight loss. *Arch Intern Med*. 2010;170(2):136-45.
152. Paoli A, Cenci L, Grimaldi KA. Effect of ketogenic Mediterranean diet with phytoextracts and low carbohydrates/high-protein meals on weight, cardiovascular risk factors, body composition and diet compliance in Italian council employees. *Nutr J*. 2011;10:112.
153. Gu Y, Yu H, Li Y et al. Beneficial Effects of an 8-Week, Very Low Carbohydrate Diet Intervention on Obese Subjects. *Evid Based Complement Alternat Med*. 2013;2013:760804.
154. Liu X, Zhang G, Ye X et al. Effects of a low-carbohydrate diet on weight loss and cardiometabolic profile in Chinese women: a randomised controlled feeding trial. *Br J Nutr*. 2013;110(8):1444-53.
155. Bazzano LA, Hu T, Reynolds K et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med*. 2014;161(5):309-18.
156. Saslow LR, Mason AE, Kim S et al. An Online Intervention Comparing a Very Low-Carbohydrate Ketogenic Diet and Lifestyle Recommendations Versus a Plate Method Diet in Overweight Individuals With Type 2 Diabetes: A Randomized Controlled Trial. *J Med Internet Res*. 2017;19(2):e36.
157. Gardner CD, Trepanowski JF, Del Gobbo LC et al. Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion: The DIETFITS Randomized Clinical Trial. *JAMA*. 2018;319(7):667-79.
158. Aguiar EJ, Morgan PJ, Collins CE, Plotnikoff RC, Young MD, Callister R. The PULSE (Prevention Using LifeStyle Education) trial protocol: a randomised controlled trial of a Type 2 Diabetes Prevention programme for men. *Contemp Clin Trials*. 2014;39(1):132-44.
159. Hordern MD, Dunstan DW, Prins JB, Baker MK, Singh MA, Coombes JS. Exercise prescription for patients with type 2 diabetes and pre-diabetes: a position statement from Exercise and Sport Science Australia. *J Sci Med Sport*. 2012;15(1):25-31.
160. Linke SE, Gallo LC, Norman GJ. Attrition and adherence rates of sustained vs. intermittent exercise interventions. *Ann Behav Med*. 2011;42(2):197-209.
161. Netz Y, Zeev A, Arnon M, Tenenbaum G. Reasons attributed to omitting exercising: A population-based study. *Int J Sport Exerc Psychol.* 2008;6(1):9-23.
162. Carroll JK, Winters PC, Sanders MR, Decker F, Ngo T, Sciamanna CN. Clinician-targeted intervention and patient-reported counseling on physical activity. *Prev Chronic Dis*. 2014;11:E89.
163. Abramson S, Stein J, Schaufele M, Frates E, Rogan S. Personal exercise habits and counseling practices of primary care physicians: a national survey. *Clin J Sport Med*. 2000;10(1):40-8.
164. Balducci S, Sacchetti M, Haxhi J et al. Physical exercise as therapy for type 2 diabetes mellitus. *Diabetes Metab Res Rev*. 2014;30 Suppl 1:13-23.
165. Buresh R, Berg K. Exercise for the management of type 2 diabetes mellitus: factors to consider with current guidelines. *J Sports Med Phys Fitness*. 2018;58(4):510-24.

166. Colberg SR, Sigal RJ, Fernhall B et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. *Diabetes Care*. 2010;33(12):2692-6.
167. Little JP, Gillen JB, Percival ME et al. Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. *J Appl Physiol (1985)*. 2011;111(6):1554-60.
168. Mancilla R, Torres P, Alvarez C, Schifferli I, Sapunar J, Diaz E. [High intensity interval training improves glycemic control and aerobic capacity in glucose intolerant patients]. *Rev Med Chil*. 2014;142(1):34-9.
169. Hameed UA, Manzar D, Raza S, Shareef MY, Hussain ME. Resistance Training Leads to Clinically Meaningful Improvements in Control of Glycemia and Muscular Strength in Untrained Middle-aged Patients with type 2 Diabetes Mellitus. *N Am J Med Sci*. 2012;4(8):336-43.
170. Thompson PD, Crouse SF, Goodpaster B, Kelley D, Moyna N, Pescatello L. The acute versus the chronic response to exercise. *Med Sci Sports Exerc*. 2001;33(6 Suppl):S438-45; discussion S52-3.
171. Parker L, Shaw CS, Banting L et al. Acute Low-Volume High-Intensity Interval Exercise and Continuous Moderate-Intensity Exercise Elicit a Similar Improvement in 24-h Glycemic Control in Overweight and Obese Adults. *Front Physiol*. 2017;7:661.
172. Wadley AJ, Chen YW, Lip GY, Fisher JP, Aldred S. Low volume-high intensity interval exercise elicits antioxidant and anti-inflammatory effects in humans. *J Sports Sci*. 2016;34(1):1-9.
173. Aguiar SS, Sousa CV, Simoes HG et al. Acute metabolic responses following different resistance exercise protocols. *Appl Physiol Nutr Metab*. 2018;43(8):838-43.
174. Francois ME, Baldi JC, Manning PJ et al. 'Exercise snacks' before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance. *Diabetologia*. 2014;57(7):1437-45.
175. Gillen JB, Little JP, Punthakee Z, Tarnopolsky MA, Riddell MC, Gibala MJ. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. *Diabetes Obes Metab*. 2012;14(6):575-7.
176. Rozenek R, Salassi JW, 3rd, Pinto NM, Fleming JD. Acute Cardiopulmonary and Metabolic Responses to High-Intensity Interval Training Protocols Using 60 s of Work and 60 s Recovery. *J Strength Cond Res*. 2016;30(11):3014-23.
177. Schaun GZ, Alberton CL, Ribeiro DO, Pinto SS. Acute effects of high-intensity interval training and moderate-intensity continuous training sessions on cardiorespiratory parameters in healthy young men. *Eur J Appl Physiol*. 2017;117(7):1437-44.
178. Paoli A, Moro T, Marcolin G et al. High-Intensity Interval Resistance Training (HIRT) influences resting energy expenditure and respiratory ratio in non-dieting individuals. *J Transl Med*. 2012;10:237.
179. Steele J, Butler A, Comerford Z et al. Similar acute physiological responses from effort and duration matched leg press and recumbent cycling tasks. *PeerJ*. 2018;6:e4403.
180. Morais PK, Campbell CS, Sales MM et al. Acute resistance exercise is more effective than aerobic exercise for 24h blood pressure control in type 2 diabetics. *Diabetes Metab*. 2011;37(2):112-7.
181. Hansen E, Landstad BJ, Gundersen KT, Torjesen PA, Svebak S. Insulin sensitivity after maximal and endurance resistance training. *J Strength Cond Res*. 2012;26(2):327-34.
182. Grontved A, Rimm EB, Willett WC, Andersen LB, Hu FB. A prospective study of weight training and risk of type 2 diabetes mellitus in men. *Arch Intern Med*. 2012;172(17):1306-12.
183. Almenning I, Rieber-Mohn A, Lundgren KM, Shetelig Lovvik T, Garnaes KK, Moholdt T. Effects of High Intensity Interval Training and Strength Training on Metabolic, Cardiovascular and Hormonal Outcomes in Women with Polycystic Ovary Syndrome: A Pilot Study. *PLoS One*. 2015;10(9):e0138793.
184. De Sousa SMD, Norman RJP. Metabolic syndrome, diet and exercise. *Best Pract Res Clin Obstet Gynaecol*. 2016;37:140-51.
185. Hawley JA, Houmard JA. Introduction -Preventing Insulin Resistance through Exercise: A Cellular Approach. *Med Sci Sports Exerc*. 2004;36(7):1187-90.

186. Hood MS, Little JP, Tarnopolsky MA, Myslik F, Gibala MJ. Low-volume interval training improves muscle oxidative capacity in sedentary adults. *Med Sci Sports Exerc*. 2011;43(10):1849-56.
187. Gillen JB, Percival ME, Ludzki A, Tarnopolsky MA, Gibala MJ. Interval training in the fed or fasted state improves body composition and muscle oxidative capacity in overweight women. *Obesity*. 2013;21(11):2249-55.
188. Liu JX, Zhu L, Li PJ, Li N, Xu YB. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. *Aging Clin Exp Res*. 2018.
189. Tremblay A, Simoneau JA, Bouchard C. Impact of exercise intensity on body fatness and skeletal muscle metabolism. *Metab Clin Exp*. 1994;43(7):814-8.
190. Costa EC, Hay JL, Kehler DS et al. Effects of High-Intensity Interval Training Versus Moderate-Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension: A Systematic Review and Meta-Analysis of Randomized Trials. *Sports Med*. 2018;48(9):2127-42.
191. Martland R, Mondelli V, Gaughran F, Stubbs B. Can high-intensity interval training improve physical and mental health outcomes? A meta-review of 33 systematic reviews across the lifespan. *J Sports Sci*. 2020;38(4):430-69.
192. Hunter GR, Singh H, Carter SJ, Bryan DR, Fisher G. Sarcopenia and Its Implications for Metabolic Health. *J Obes*. 2019;2019:8031705.
193. Villareal DT, Aguirre L, Gurney AB et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. *N Engl J Med*. 2017;376(20):1943-55.
194. Johannsen NM, Swift DL, Lavie CJ, Earnest CP, Blair SN, Church TS. Combined Aerobic and Resistance Training Effects on Glucose Homeostasis, Fitness, and Other Major Health Indices: A Review of Current Guidelines. *Sports Med*. 2016;46(12):1809-18.
195. Gillen JB, Gibala MJ. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? *Appl Physiol Nutr Metab*. 2014;39(3):409-12.
196. Alvarez C, Ramirez R, Flores M, Zuñiga C, Celis-Morales C. Effect of sprint interval training and resistance exercise on metabolic markers in overweight women [Efectos del ejercicio físico de alta intensidad y sobrecarga en parámetros de salud metabólica en mujeres sedentarias, pre-diabéticas con sobrepeso u obesidad]. *Rev Med Chil* 2012; 140 1289-96.
197. Rowan CP, Riddell MC, Gledhill N, Jamnik VK. Aerobic Exercise Training Modalities and Prediabetes Risk Reduction. *Med Sci Sports Exerc*. 2017;49(3):403-12.
198. Miyashita Y, Koide N, Ohtsuka M et al. Beneficial effect of low carbohydrate in low calorie diets on visceral fat reduction in type 2 diabetic patients with obesity. *Diabetes Res Clin Pract*. 2004;65(3):235-41.
199. Nielsen JV, Joensson EA. Low-carbohydrate diet in type 2 diabetes: stable improvement of bodyweight and glycemic control during 44 months follow-up. *Nutr Metab (Lond)*. 2008;5:14.
200. Lim SS, Noakes M, Keogh JB, Clifton PM. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. *Nutr Metab Cardiovasc Dis*. 2010;20(8):599-607.
201. Naude CE, Schoonees A, Senekal M, Young T, Garner P, Volmink J. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. *PLoS One*. 2014;9(7):e100652.
202. Westman EC, Feinman RD, Mavropoulos JC et al. Low-carbohydrate nutrition and metabolism. *The Am J Clin Nutr*. 2007;86(2):276-84.
203. Dahlgren K, Gibas KJ. Ketogenic diet, high intensity interval training (HIIT) and memory training in the treatment of mild cognitive impairment: A case study. *Diabetes Metab Syndr*. 2018;12(5):819-22.
204. Ramirez-Velez R, Castro-Astudillo K, Correa-Bautista JE et al. The Effect of 12 Weeks of Different Exercise Training Modalities or Nutritional Guidance on Cardiometabolic Risk Factors, Vascular Parameters, and Physical Fitness in Overweight Adults: Cardiometabolic High-Intensity Interval Training-Resistance Training Randomized Controlled Study. *J Strength Cond Res*. 2020.

205. Lesser IA, Guenette JA, Hoogbruin A et al. Association between exercise-induced change in body composition and change in cardiometabolic risk factors in postmenopausal South Asian women. *Appl Physiol Nutr Metab*. 2016;41(9):931-7.
206. Meex RC, Schrauwen-Hinderling VB, Moonen-Kornips E et al. Restoration of muscle mitochondrial function and metabolic flexibility in type 2 diabetes by exercise training is paralleled by increased myocellular fat storage and improved insulin sensitivity. *Diabetes*. 2010;59(3):572-9.
207. Sartor F, de Morree HM, Matschke V et al. High-intensity exercise and carbohydrate-reduced energy-restricted diet in obese individuals. *Eur J Appl Physiol*. 2010;110(5):893-903.
208. Pan B, Ge L, Xun YQ et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *Int J Behav Nutr Phys Act*. 2018;15(1):72.
209. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective Exercise Modality to Reduce Insulin Resistance in Women With Type 2 Diabetes. *Diabetes Care*. 2003;26(11):2977-82.
210. Wormgoor SG, Dalleck LC, Zinn C, Harris NK. Acute blood glucose, cardiovascular and exaggerated responses to high-intensity interval training and moderate-intensity continuous training in men with type 2 diabetes mellitus. *J Sports Med Phys Fitness*. 2017.
211. Schneider SH, Khachadurian AK, Amorosa LF, Clemow L, Ruderman NB. Ten-year experience with an exercise-based outpatient life-style modification program in the treatment of diabetes mellitus. *Diabetes Care*. 1992;15(11):1800-10.
212. Bartlett JD, Hawley JA, Morton JP. Carbohydrate availability and exercise training adaptation: too much of a good thing? *Eur J Sport Sci*. 2015;15(1):3-12.
213. Saleem A, Hood DA. Acute exercise induces tumour suppressor protein p53 translocation to the mitochondria and promotes a p53-Tfam-mitochondrial DNA complex in skeletal muscle. *J. Physiol*. 2013;591(14):3625-36.
214. Howarth KR, Phillips SM, MacDonald MJ, Richards D, Moreau NA, Gibala MJ. Effect of glycogen availability on human skeletal muscle protein turnover during exercise and recovery. *J Appl Physiol (1985)*. 2010;109(2):431-8.
215. Manninen AH. Very-low-carbohydrate diets and preservation of muscle mass. *Nutr Metab (Lond)*. 2006;3:9.
216. Carbone JW, McClung JP, Pasiakos SM. Skeletal muscle responses to negative energy balance: effects of dietary protein. *Adv Nutr*. 2012;3(2):119-26.
217. Stokes T, Hector AJ, Morton RW, McGlory C, Phillips SM. Recent Perspectives Regarding the Role of Dietary Protein for the Promotion of Muscle Hypertrophy with Resistance Exercise Training. *Nutrients*. 2018;10(2).
218. Dyson PA, Beatty S, Matthews DR. A low-carbohydrate diet is more effective in reducing body weight than healthy eating in both diabetic and non-diabetic subjects. *Diabet Med*. 2007;24(12):1430-5.
219. Batrakoulis A, Jamurtas AZ, Georgakouli K et al. High intensity, circuit-type integrated neuromuscular training alters energy balance and reduces body mass and fat in obese women: A 10-month training-detraining randomized controlled trial. *PLoS One*. 2018;13(8):e0202390.
220. Thum JS, Parsons G, Whittle T, Astorino TA. High-Intensity Interval Training Elicits Higher Enjoyment than Moderate Intensity Continuous Exercise. *PLoS One*. 2017;12(1):e0166299.
221. Phillips SM, Winett RA. Uncomplicated resistance training and health-related outcomes: evidence for a public health mandate. *Curr Sports Med Rep*. 2010;9(4):208-13.
222. Leite RD, Prestes J, Rosa C et al. Acute effect of resistance training volume on hormonal responses in trained men. *J Sports Med Phys Fitness*. 2011;51(2):322-8.
223. Francois ME, Little JP. Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes. *Diabetes Spectr*. 2015;28(1):39-44.
224. McGregor G, Nichols S, Hamborg T et al. High-intensity interval training versus moderate-intensity steady-state training in UK cardiac rehabilitation programmes (HIIT or MISS UK): study protocol for a multicentre randomised controlled trial and economic evaluation. *BMJ Open*. 2016;6(11):e012843.
225. Pugh JK, Faulkner SH, Jackson AP, King JA, Nimmo MA. Acute molecular responses to concurrent resistance and high-intensity interval exercise in untrained skeletal muscle. *Physiol Rep*. 2015;3(4).

226. Grace F, Herbert P, Elliott AD, Richards J, Beaumont A, Sculthorpe NF. High intensity interval training (HIIT) improves resting blood pressure, metabolic (MET) capacity and heart rate reserve without compromising cardiac function in sedentary aging men. *Exp Gerontol*. 2018;109:75-81.
227. Jurca R, Lamonte MJ, Barlow CE, Kampert JB, Church TS, Blair SN. Association of muscular strength with incidence of metabolic syndrome in men. *Med Sci Sports Exerc*. 2005;37(11):1849-55.
228. Senechal M, McGavock JM, Church TS et al. Cut points of muscle strength associated with metabolic syndrome in men. *Med Sci Sports Exerc*. 2014;46(8):1475-81.
229. Barboza González P, Chirosa Ríos LJ, Ulloa Díaz D et al. Effect of muscle strength at different intensities on resting energy expenditure. *J Hum Sport Exerc.* 2017;12(3):668-79.
230. Miller T, Mull S, Aragon AA, Krieger J, Schoenfeld BJ. Resistance Training Combined With Diet Decreases Body Fat While Preserving Lean Mass Independent of Resting Metabolic Rate: A Randomized Trial. *Int J Sport Nutr Exerc Metab*. 2018;28(1):46-54.
231. Cabral-Santos C, Gerosa-Neto J, Inoue DS et al. Physiological Acute Response to High-Intensity Intermittent and Moderate-Intensity Continuous 5 km Running Performance: Implications for Training Prescription. *J Hum Kinet*. 2017;56:127-37.
232. Pugh JK, Faulkner SH, Turner MC, Nimmo MA. Satellite cell response to concurrent resistance exercise and high-intensity interval training in sedentary, overweight/obese, middle-aged individuals. *Eur J Appl Physiol*. 2018;118(2):225-38.
233. Haskell WL, Lee IM, Pate RR et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1423-34.
234. Salazar MR, Espeche WG, Aizpurua M et al. Should the first blood pressure reading be discarded? *J Hum Hypertens*. 2015;29(6):373-8.
235. Rey E, Lago-Penas C, Casais L, Lago-Ballesteros J. The effect of immediate post-training active and passive recovery interventions on anaerobic performance and lower limb flexibility in professional soccer players. *J Hum Kinet*. 2012;31:121-9.
236. Zourdos MC, Klemp A, Dolan C et al. Novel Resistance Training-Specific Rating of Perceived Exertion Scale Measuring Repetitions in Reserve. *J Strength Cond Res*. 2016;30(1):267-75.
237. Scott CB. Combustion, respiration and intermittent exercise: a theoretical perspective on oxygen uptake and energy expenditure. *Biology (Basel)*. 2014;3(2):255-63.
238. Ferrannini E. The theoretical bases of indirect calorimetry: a review. *Metab Clin Exp*. 1988;37(3):287-301.
239. Romijn JA, Coyle EF, Sidossis LS et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *Am J Physiol*. 1993;265(3 Pt 1):E380-91.
240. Lyons S, Richardson M, Bishop P, Smith J, Heath H, Giesen J. Excess post-exercise oxygen consumption in untrained men following exercise of equal energy expenditure: comparisons of upper and lower body exercise. *Diabetes Obes Metab*. 2007;9(6):889-94.
241. Mazzetti S, Douglass M, Yocum A, Harber M. Effect of explosive versus slow contractions and exercise intensity on energy expenditure. *Med Sci Sports Exerc*. 2007;39(8):1291-301.
242. Roberson KB, Jacobs KA, White MJ, Signorile JF. Loads and movement speed affect energy expenditure during circuit resistance exercise. *Appl Physiol Nutr Metab*. 2017;42(6):637-46.
243. Francois ME, Graham MJ, Parr EB, Metabolism R-NJ. Similar metabolic response to lower-versus upper-body interval exercise or endurance exercise. *Metab Clin Exp*. 2017.
244. Kaikkonen H, Yrjama M, Siljander E, Byman P, Laukkanen R. The effect of heart rate controlled low resistance circuit weight training and endurance training on maximal aerobic power in sedentary adults. *Scand J Med Sci Sports*. 2000;10(4):211-5.
245. la Scala Teixeira CV, Ferreira SE, Azevedo PH et al. Effects of manual resistance training and free weight resistance training on postexercise blood pressure in hypertensive men: a pilot study. *J Sports Med Phys Fitness*. 2017;57(10):1367-74.
246. Zeigler ZS, Swan PD. Acute effects of whole-body vibration with resistance exercise on postexercise blood pressure and oxygen consumption in prehypertensive adults. *J Exerc Sci Fit*. 2016;14(1):14-23.

247. Koopman R, Manders RJ, Zorenc AH et al. A single session of resistance exercise enhances insulin sensitivity for at least 24 h in healthy men. *Eur J Appl Physiol*. 2005;94(1-2):180-7.
248. Fischer CP. Interleukin-6 in acute exercise and training: what is the biological relevance? *Exerc Immunol Rev*. 2006;12:6-33.
249. Pedersen BK. Anti-inflammatory effects of exercise: role in diabetes and cardiovascular disease. *Eur J Clin Invest*. 2017;47(8):600-11.
250. Eaton M, Granata C, Barry J, Safdar A, Bishop D, Little JP. Impact of a single bout of high-intensity interval exercise and short-term interval training on interleukin-6, FNDC5, and METRNL mRNA expression in human skeletal muscle. *J Sport Health Sci*. 2018;7(2):191-6.
251. Agarwal M, Singh S, Narayan J, Pandey S, Tiwari S, Sharma P. Cardiovascular Response and Serum Interleukin-6 Level in Concentric Vs. Eccentric Exercise. *J Clin Diagn Res*. 2017;11(4):CC04-CC8.
252. Cullen T, Thomas AW, Webb R, Hughes MG. Interleukin-6 and associated cytokine responses to an acute bout of high-intensity interval exercise: the effect of exercise intensity and volume. *Appl Physiol Nutr Metab*. 2016;41(8):803-8.
253. Phinney SD, Bistrian BR, Evans WJ, Gervino E, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: Preservation of submaximal exercise capability with reduced carbohydrate oxidation. *Metab Clin Exp*. 1983;32(8):769-76.
254. Harber MP, Schenk S, Barkan AL, Horowitz JF. Alterations in carbohydrate metabolism in response to short-term dietary carbohydrate restriction. *Am J Physiol Endocrinol Metab*. 2005;289(2):E306-12.
255. Keller C, Steensberg A, Pilegaard H et al. Transcriptional activation of the IL-6 gene in human contracting skeletal muscle: influence of muscle glycogen content. *FASEB J*. 2001;15(14):2748-50.
256. Steensberg A, Fischer CP, Keller C, Moller K, Pedersen BK. IL-6 enhances plasma IL-1ra, IL-10, and cortisol in humans. *Am J Physiol Endocrinol Metab*. 2003;285(2):E433-7.
257. Keller C, Steensberg A, Hansen AK, Fischer CP, Plomgaard P, Pedersen BK. Effect of exercise, training, and glycogen availability on IL-6 receptor expression in human skeletal muscle. *J Appl Physiol (1985)*. 2005;99(6):2075-9.
258. Chang CK, Borer K, Lin PJ. Low-Carbohydrate-High-Fat Diet: Can it Help Exercise Performance? *J Hum Kinet*. 2017;56(1):81-92.
259. Kraemer WJ, Ratamess NA. Hormonal responses and adaptations to resistance exercise and training. *Sports Med*. 2005;35(4):339-61.
260. Zafeiridis A, Smilios I, Considine RV, Tokmakidis SP. Serum leptin responses after acute resistance exercise protocols. *J Appl Physiol (1985)*. 2003;94(2):591-7.
261. Benini R, Prado Nunes PR, Orsatti CL, Barcelos LC, Orsatti FL. Effects of acute total body resistance exercise on hormonal and cytokines changes in men and women. *J Sports Med Phys Fitness*. 2015;55(4):337-44.
262. Budnar RG, Jr., Duplanty AA, Hill DW, McFarlin BK, Vingren JL. The acute hormonal response to the kettlebell swing exercise. *J Strength Cond Res*. 2014;28(10):2793-800.
263. Raymond LM, Renshaw D, Duncan MJ. Acute Hormonal Response to Kettlebell Swing Exercise Differs Depending on Load, Even When Total Work Is Normalized. *J Strength Cond Res*. 2018.
264. Velasco-Orjuela GP, Dominguez-Sanchez MA, Hernandez E et al. Acute effects of high-intensity interval, resistance or combined exercise protocols on testosterone - cortisol responses in inactive overweight individuals. *Physiol Behav*. 2018;194:401-9.
265. de Pereda D, Romero-Vivo S, Ricarte B, Rossetti P, Ampudia-Blasco FJ, Bondia J. Real-time estimation of plasma insulin concentration from continuous glucose monitor measurements. *Comput Methods Biomech Biomed Engin*. 2016;19(9):934-42.
266. Grundy SM. Metabolic syndrome update. *Trends Cardiovasc Med*. 2016;26(4):364-73.
267. Suresh K. An overview of randomization techniques: An unbiased assessment of outcome in clinical research. *J Hum Reprod Sci*. 2011;4(1):8-11.

268. Fullmer S, Benson-Davies S, Earthman CP et al. Evidence analysis library review of best practices for performing indirect calorimetry in healthy and non-critically ill individuals. *J Acad Nutr Diet*. 2015;115(9):1417-46 e2.
269. Loe H, Rognmo O, Saltin B, Wisloff U. Aerobic capacity reference data in 3816 healthy men and women 20-90 years. *PLoS One*. 2013;8(5):e64319.
270. Levinger I, Goodman C, Hare DL, Jerums G, Toia D, Selig S. The reliability of the 1RM strength test for untrained middle-aged individuals. *J Sci Med Sport*. 2009;12(2):310-6.
271. Maddison R, Ni Mhurchu C, Jiang Y et al. International Physical Activity Questionnaire (IPAQ) and New Zealand Physical Activity Questionnaire (NZPAQ): a doubly labelled water validation. *Int J Behav Nutr Phys Act*. 2007;4:62.
272. Grant AM, Taungapeau FK, McAuley KA et al. Body mass index status is effective in identifying metabolic syndrome components and insulin resistance in Pacific Island teenagers living in New Zealand. *Metab Clin Exp*. 2008;57(4):511-6.
273. Soldatovic I, Vukovic R, Culafic D, Gajic M, Dimitrijevic-Sreckovic V. siMS Score: Simple Method for Quantifying Metabolic Syndrome. *PLoS One*. 2016;11(1):e0146143.
274. Shacham S. A shortened version of the Profile of Mood States. *J Pers Assess*. 1983;47(3):305-6.
275. Breymeyer KL, Lampe JW, McGregor BA, Neuhouser ML. Subjective mood and energy levels of healthy weight and overweight/obese healthy adults on high-and low-glycemic load experimental diets. *Appetite*. 2016;107:253-9.
276. Brinkworth GD, Buckley JD, Noakes M, Clifton PM, Wilson CJ. Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Arch Intern Med*. 2009;169(20):1873-80.
277. Evangelista A.L., Evangelista R.A.G.T., Machado A.F. et al. Effects of High-Intensity Calisthenic Training on Mood and Affective Responses. *JEPonline*. 2017;20(6):15-23.
278. Vitale JA, La Torre A, Baldassarre R, Piacentini MF, Bonato M. Ratings of Perceived Exertion and Self-reported Mood State in Response to High Intensity Interval Training. A Crossover Study on the Effect of Chronotype. *Front Psychol*. 2017;8:1232.
279. Pai MP, Paloucek FP. The origin of the "ideal" body weight equations. *Ann Pharmacother*. 2000;34(9):1066-9.
280. Sweet TW, Foster C, McGuigan MR, Brice G. Quantitation of resistance training using the session rating of perceived exertion method. *J Strength Cond Res*. 2004;18(4):796-802.
281. Farinha JB, Ramis TR, Vieira AF et al. Glycemic, inflammatory and oxidative stress responses to different high-intensity training protocols in type 1 diabetes: A randomized clinical trial. *J Diabetes Complications*. 2018;32(12):1124-32.
282. Kodama S, Saito K, Tanaka S et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009;301(19):2024-35.
283. Francois ME, Durrer C, Pistawka KJ, Halperin FA, Chang C, Little JP. Combined Interval Training and Post-exercise Nutrition in Type 2 Diabetes: A Randomized Control Trial. *Front Physiol*. 2017;8:528.
284. Gorostegi-Anduaga I, Corres P, MartinezAguirre-Betolaza A et al. Effects of different aerobic exercise programmes with nutritional intervention in sedentary adults with overweight/obesity and hypertension: EXERDIET-HTA study. *Eur J Prev Cardiol*. 2018;25(4):343-53.
285. Androulakis-Korakakis P, Langdown L, Lewis A et al. Effects of Exercise Modality During Additional "High-Intensity Interval Training" on Aerobic Fitness and Strength in Powerlifting and Strongman Athletes. *J Strength Cond Res*. 2018;32(2):450-7.
286. Schuenke MD, Mikat RP, McBride JM. Effect of an acute period of resistance exercise on excess post-exercise oxygen consumption: implications for body mass management. *Eur J Appl Physiol*. 2002;86(5):411-7.
287. Courteix D, Valente-dos-Santos J, Ferry B et al. Multilevel Approach of a 1-Year Program of Dietary and Exercise Interventions on Bone Mineral Content and Density in Metabolic Syndrome--the RESOLVE Randomized Controlled Trial. *PLoS One*. 2015;10(9):e0136491.

288. Heikura IA, Burke LM, Hawley JA et al. A Short-Term Ketogenic Diet Impairs Markers of Bone Health in Response to Exercise. *Front Endocrinol (Lausanne)*. 2019;10:880.
289. Hammond KM, Sale C, Fraser W et al. Post-exercise carbohydrate and energy availability induce independent effects on skeletal muscle cell signalling and bone turnover: implications for training adaptation. *The Journal of physiology*. 2019;597(18):4779-96.
290. Brinkworth GD, Wycherley TP, Noakes M, Buckley JD, Clifton PM. Long-term effects of a very-low-carbohydrate weight-loss diet and an isocaloric low-fat diet on bone health in obese adults. *Nutrition*. 2016;32(9):1033-6.
291. Bryner RW, Ullrich IH, Sauers J et al. Effects of Resistancevs.Aerobic Training Combined With an 800 Calorie Liquid Diet on Lean Body Mass and Resting Metabolic Rate. *Journal of the American College of Nutrition*. 1999;18(2):115-21.
292. Zurlo F, Larson K, Bogardus C, Ravussin E. Skeletal muscle metabolism is a major determinant of resting energy expenditure. *J Clin Invest*. 1990;86(5):1423-7.
293. Backx EM, Tieland M, Borgonjen-van den Berg KJ, Claessen PR, van Loon LJ, de Groot LC. Protein intake and lean body mass preservation during energy intake restriction in overweight older adults. *Int J Obes (Lond)*. 2016;40(2):299-304.
294. Baek SH, Kim M, Kim M et al. Metabolites distinguishing visceral fat obesity and atherogenic traits in individuals with overweight. *Obesity*. 2017;25(2):323-31.
295. Kang M, Lee A, Yoo HJ et al. Association between increased visceral fat area and alterations in plasma fatty acid profile in overweight subjects: a cross-sectional study. *Lipids in health and disease*. 2017;16(1):248.
296. Maillard F, Pereira B, Boisseau N. Effect of High-Intensity Interval Training on Total, Abdominal and Visceral Fat Mass: A Meta-Analysis. *Sports Med*. 2018;48(2):269-88.
297. Sasakabe T, Haimoto H, Umegaki H, Wakai K. Association of decrease in carbohydrate intake with reduction in abdominal fat during 3-month moderate low-carbohydrate diet among non-obese Japanese patients with type 2 diabetes. *Metab Clin Exp*. 2015;64(5):618-25.
298. Dupuit M, Rance M, Morel C et al. Moderate-Intensity Continuous Training or High-Intensity Interval Training with or without Resistance Training for Altering Body Composition in Postmenopausal Women. *Med Sci Sports Exerc*. 2020;52(3):736-45.
299. Vargas S, Romance R, Petro JL et al. Efficacy of ketogenic diet on body composition during resistance training in trained men: a randomized controlled trial. *J Int Soc Sports Nutr*. 2018;15(1):31.
300. Livingstone MBE, Strain JJ, Prentice AM et al. Potential contribution of leisure activity to the energy expenditure patterns of sedentary populations. *The British journal of nutrition*. 2007;65(02):145.
301. van Loon SLM, Deneer R, Nienhuijs SW et al. Metabolic Health Index (MHI): Assessment of Comorbidity in Bariatric Patients Based on Biomarkers. *Obes Surg*. 2020;30(2):714-24.
302. Sweet TW, Foster C, McGuigan MR, Brice G. Quantitation of resistance training using the session rating of perceived exertion method. *J Strength Cond Res*. 2004;18(4):796–802.
303. Stensvold D, Tjonna AE, Skaug EA et al. Strength training versus aerobic interval training to modify risk factors of metabolic syndrome. *J Appl Physiol (1985)*. 2010;108(4):804-10.
304. Alhassan S, Kim S, Bersamin A, King AC, Gardner CD. Dietary adherence and weight loss success among overweight women: results from the A TO Z weight loss study. *Int J Obes (Lond)*. 2008;32(6):985-91.
305. Sherman AM, Bowen DJ, Vitolins M et al. Dietary adherence: characteristics and interventions. *Control Clin Trials*. 2000;21(5 Suppl):206S-11S.
306. Logan GR, Harris N, Duncan S, Plank LD, Merien F, Schofield G. Low-Active Male Adolescents: A Dose Response to High-Intensity Interval Training. *Med Sci Sports Exerc*. 2016;48(3):481-90.
307. Motl RW, Dishman RK, Saunders R, Dowda M, Felton G, Pate RR. Measuring enjoyment of physical activity in adolescent girls. *American journal of preventive medicine*. 2001;21(2):110-7.
308. McPhail SM, Schippers M, Marshall AL, Waite M, Kuipers P. Perceived barriers and facilitators to increasing physical activity among people with musculoskeletal disorders: a qualitative investigation to inform intervention development. *Clin Interv Aging*. 2014;9:2113-22.

309. Mayer JM, Nuzzo JL, Dagenais S. Use of participant focus groups to identify barriers and facilitators to worksite exercise therapy adherence in randomized controlled trials involving firefighters. *Patient Prefer Adherence*. 2013;7:207-15.
310. Bethancourt HJ, Rosenberg DE, Beatty T, Arterburn DE. Barriers to and facilitators of physical activity program use among older adults. *Clin Med Res*. 2014;12(1-2):10-20.
311. Smith LT, Johnson DB, Beaudoin S, Monsen ER, LoGerfo JP. Qualitative assessment of participant utilization and satisfaction with the Seattle Senior Farmers' Market Nutrition Pilot Program. *Prev Chronic Dis*. 2004;1(1):A06.
312. Groth SW, David T. New mothers' views of weight and exercise. *MCN Am J Matern Child Nurs*. 2008;33(6):364-70.
313. Mulero-Portela AL, Santaella CL, Gomez CC. Development of a questionnaire to assess the determinants of exercise among breast cancer survivors in Puerto Rico. *Physiother Theory Pract*. 2013;29(5):379-92.
314. Golden SD, Earp JA. Social ecological approaches to individuals and their contexts: twenty years of health education & behavior health promotion interventions. *Health education & behavior : the official publication of the Society for Public Health Education*. 2012;39(3):364-72.
315. Bradley LE, Forman EM, Kerrigan SG, Butryn ML, Herbert JD, Sarwer DB. A Pilot Study of an Acceptance-Based Behavioral Intervention for Weight Regain After Bariatric Surgery. *Obes Surg*. 2016;26(10):2433-41.
316. Henderson RM, Miller ME, Fielding RA et al. Maintenance of Physical Function 1 Year After Exercise Intervention in At-Risk Older Adults: Follow-up From the LIFE Study. *The journals of gerontology. Series A, Biological sciences and medical sciences*. 2018;73(5):688-94.
317. Andersen RE, Wadden TA, Bartlett SJ, Zemel B, Verde TJ, Franckowiak SC. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. *JAMA*. 1999;281(4):335-40.
318. Hunter GR, Byrne NM, Sirikul B et al. Resistance training conserves fat-free mass and resting energy expenditure following weight loss. *Obesity*. 2008;16(5):1045-51.
319. Keytel LR, Goedecke JH, Noakes TD et al. Prediction of energy expenditure from heart rate monitoring during submaximal exercise. *J Sports Sci*. 2005;23(3):289-97.
320. Rossow L, Yan H, Fahs CA et al. Postexercise hypotension in an endurance-trained population of men and women following high-intensity interval and steady-state cycling. *American journal of hypertension*. 2010;23(4):358-67.
321. DeVan AE, Anton MM, Cook JN, Neidre DB, Cortez-Cooper MY, Tanaka H. Acute effects of resistance exercise on arterial compliance. *J Appl Physiol (1985)*. 2005;98(6):2287-91.
322. Carter SJ, Goldsby TU, Fisher G et al. Systolic blood pressure response after high-intensity interval exercise is independently related to decreased small arterial elasticity in normotensive African American women. *Appl Physiol Nutr Metab*. 2016;41(5):484-90.
323. Mutter AF, Cooke AB, Saleh O, Gomez YH, Daskalopoulou SS. A systematic review on the effect of acute aerobic exercise on arterial stiffness reveals a differential response in the upper and lower arterial segments. *Hypertension research : official journal of the Japanese Society of Hypertension*. 2017;40(2):146-72.
324. Morales-Palomo F, Ramirez-Jimenez M, Ortega JF, Pallares JG, Mora-Rodriguez R. Acute Hypotension after High-Intensity Interval Exercise in Metabolic Syndrome Patients. *Int J Sports Med.* 2017;38(7):560-7.
325. Queiroz AC, Sousa JC, Cavalli AA et al. Post-resistance exercise hemodynamic and autonomic responses: Comparison between normotensive and hypertensive men. *Scand J Med Sci Sports*. 2015;25(4):486-94.
326. Adams OP. The impact of brief high-intensity exercise on blood glucose levels. *Diabetes, metabolic syndrome and obesity : targets and therapy*. 2013;6:113-22.
327. Lithgow HM, Leggate M. The Effect of a Single Bout of High Intensity Intermittent Exercise on Glucose Tolerance in Non-diabetic Older Adults. *Int J Exerc Sci*. 2018;11(3):95-105.

328. Metcalfe RS, Tardif N, Thompson D, Vollaard NB. Changes in aerobic capacity and glycaemic control in response to reduced-exertion high-intensity interval training (REHIT) are not different between sedentary men and women. *Appl Physiol Nutr Metab*. 2016;41(11):1117-23.
329. Paoli A, Gentil P, Moro T, Marcolin G, Bianco A. Resistance Training with Single vs. Multi-joint Exercises at Equal Total Load Volume: Effects on Body Composition, Cardiorespiratory Fitness, and Muscle Strength. *Front Physiol*. 2017;8:1105.
330. Phinney SD, Bistrian BR, Wolfe RR, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: Physical and biochemical adaptation. *Metab Clin Exp*. 1983;32(8):757-68.
331. Brown WM, Davison GW, McClean CM, Murphy MH. A Systematic Review of the Acute Effects of Exercise on Immune and Inflammatory Indices in Untrained Adults. *Sports Med Open*. 2015;1(1):35.
332. Sigal RJ, Kenny GP, Boule NG et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med*. 2007;147(6):357-69.
333. Jelleyman C, Yates T, O'Donovan G et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2015;16(11):942-61.
334. Smart NA, Dieberg G, Giallauria F. Intermittent versus continuous exercise training in chronic heart failure: a meta-analysis. *Int J Cardiol*. 2013;166(2):352-8.
335. Johnson RK, Appel LJ, Brands M et al. Dietary Sugars Intake and Cardiovascular Health. *Circulation*. 2009;120(11):1011-20.
336. Stiegler P, Cunliffe A. The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Med*. 2006;36(3):239-62.
337. Kelley K, Preacher KJ. On effect size. *Psychol Methods*. 2012;17(2):137-52.
338. Fritz CO, Morris PE, Richler JJ. Effect size estimates: current use, calculations, and interpretation. *J Exp Psychol Gen*. 2012;141(1):2-18.
339. Wilson JM, Marin PJ, Rhea MR, Wilson SM, Loenneke JP, Anderson JC. Concurrent training: a meta-analysis examining interference of aerobic and resistance exercises. *J Strength Cond Res*. 2012;26(8):2293-307.
340. Sabag A, Najafi A, Michael S, Esgin T, Halaki M, Hackett D. The compatibility of concurrent high intensity interval training and resistance training for muscular strength and hypertrophy: a systematic review and meta-analysis. *J Sports Sci*. 2018;36(21):2472-83.
341. Piercy KL, Troiano RP, Ballard RM et al. The Physical Activity Guidelines for Americans. *JAMA*. 2018;320(19):2020-8.
342. Crump C, Sundquist K, Sundquist J, Winkleby MA. Exercise Is Medicine: Primary Care Counseling on Aerobic Fitness and Muscle Strengthening. *J Am Board Fam Med*. 2019;32(1):103-7.
343. Tarp J, Stole AP, Blond K, Grontved A. Cardiorespiratory fitness, muscular strength and risk of type 2 diabetes: a systematic review and meta-analysis. *Diabetologia*. 2019;62(7):1129-42.
344. Roberts CK, Little JP, Thyfault JP. Modification of insulin sensitivity and glycemic control by activity and exercise. *Med Sci Sports Exerc*. 2013;45(10):1868-77.
345. Frank P, Andersson E, Ponten M, Ekblom B, Ekblom M, Sahlin K. Strength training improves muscle aerobic capacity and glucose tolerance in elderly. *Scand J Med Sci Sports*. 2016;26(7):764-73.
346. Al-Mallah MH, Sakr S, Al-Qunaibet A. Cardiorespiratory Fitness and Cardiovascular Disease Prevention: an Update. *Curr Atheroscler Rep*. 2018;20(1):1.
347. Volaklis KA, Halle M, Meisinger C. Muscular strength as a strong predictor of mortality: A narrative review. *Eur J Intern Med*. 2015;26(5):303-10.
348. Ortega FB, Silventoinen K, Tynelius P, Rasmussen F. Muscular strength in male adolescents and premature death: cohort study of one million participants. *BMJ*. 2012;345:e7279.
349. Al Tunaiji H, Davis JC, Mansournia MA, Khan KM. Population attributable fraction of leading non-communicable cardiovascular diseases due to leisure-time physical inactivity: a systematic review. *BMJ Open Sport Exerc Med*. 2019;5(1):e000512.

350. Dela F, Ingersen A, Andersen NB et al. Effects of one-legged high-intensity interval training on insulin-mediated skeletal muscle glucose homeostasis in patients with type 2 diabetes. *Acta Physiol (Oxf)*. 2019;226(2):e13245.
351. Lee WJ, Chong K, Ser KH et al. C-peptide predicts the remission of type 2 diabetes after bariatric surgery. *Obes Surg*. 2012;22(2):293-8.
352. Wu HX, Tang J, Li L et al. Body mass index and C-peptide are important for the promptly differential diagnosis of maturity-onset diabetes from familial type 2 diabetes in outpatient clinic. *Endocr J*. 2019;66(4):309-17.
353. Leighton E, Sainsbury CA, Jones GC. A Practical Review of C-Peptide Testing in Diabetes. *Diabetes Ther*. 2017;8(3):475-87.
354. Wahab N, Chen R, Curb JD, Willcox BJ, Rodriguez BL. The Association of Fasting Glucose, Insulin, and C-Peptide, with 19-Year Incidence of Coronary Heart Disease in Older Japanese-American Men; the Honolulu Heart Program. *Geriatrics (Basel)*. 2018;3(2).
355. Ramos JS, Dalleck LC, Borrani F et al. The effect of different volumes of high-intensity interval training on proinsulin in participants with the metabolic syndrome: a randomised trial. *Diabetologia*. 2016;59(11):2308-20.
356. Ismail I, Keating SE, Baker MK, Johnson NA. A systematic review and meta-analysis of the effect of aerobic vs. resistance exercise training on visceral fat. *Obes Rev*. 2012;13(1):68-91.
357. Keating SE, Hackett DA, Parker HM et al. Effect of resistance training on liver fat and visceral adiposity in adults with obesity: A randomized controlled trial. *Hepatol Res*. 2017;47(7):622-31.
358. Caliceti C, Calabria D, Roda A, Cicero AFG. Fructose Intake, Serum Uric Acid, and Cardiometabolic Disorders: A Critical Review. *Nutrients*. 2017;9(4).
359. Bluher S, Kapplinger J, Herget S et al. Cardiometabolic risk markers, adipocyte fatty acid binding protein (aFABP) and the impact of high-intensity interval training (HIIT) in obese adolescents. *Metab Clin Exp*. 2017;68:77-87.
360. Hao Y, Ma X, Luo Y et al. Associations of serum adipocyte fatty acid binding protein with body composition and fat distribution in nondiabetic Chinese women. *J Clin Endocrinol Metab*. 2015;100(5):2055-62.
361. Kawamoto R, Tomita H, Oka Y, Ohtsuka N. Relationship between serum uric acid concentration, metabolic syndrome and carotid atherosclerosis. *Intern Med*. 2006;45(9):605-14.
362. Kanbay M, Jensen T, Solak Y et al. Uric acid in metabolic syndrome: From an innocent bystander to a central player. *Eur J Case Rep Intern*. 2016;29:3-8.
363. Zand H, Morshedzadeh N, Naghashian F. Signaling pathways linking inflammation to insulin resistance. *Diabetes Metab Syndr*. 2017;11 Suppl 1:S307-S9.
364. Moriya J. Critical roles of inflammation in atherosclerosis. *J Cardiol*. 2019;73(1):22-7.
365. Balducci S, Zanuso S, Nicolucci A et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovasc Dis*. 2010;20(8):608-17.
366. Donges CE, Duffield R, Drinkwater EJ. Effects of resistance or aerobic exercise training on interleukin-6, C-reactive protein, and body composition. *Med Sci Sports Exerc*. 2010;42(2):304-13.
367. Ciolac EG, Bocchi EA, Bortolotto LA, Carvalho VO, Greve JM, Guimaraes GV. Effects of high-intensity aerobic interval training vs. moderate exercise on hemodynamic, metabolic and neuro-humoral abnormalities of young normotensive women at high familial risk for hypertension. *Hypertens Res*. 2010;33(8):836-43.
368. Alvarez C, Ramirez-Campillo R, Ramirez-Velez R, Izquierdo M. Effects and prevalence of nonresponders after 12 weeks of high-intensity interval or resistance training in women with insulin resistance: a randomized trial. *J Appl Physiol (1985)*. 2017;122(4):985-96.
369. Juraschek SP, Blaha MJ, Whelton SP et al. Physical fitness and hypertension in a population at risk for cardiovascular disease: the Henry Ford ExercIse Testing (FIT) Project. *J Am Heart Assoc*. 2014;3(6):e001268.

370. Clarke C, Best T. Low-carbohydrate, high-fat dieters: Characteristic food choice motivations, health perceptions and behaviours. *Food Qual Prefer.* 2017;62(December):162-71.
371. Maki KC, Palacios OM, Lindner E, Nieman KM, Bell M, Sorce J. Replacement of Refined Starches and Added Sugars with Egg Protein and Unsaturated Fats Increases Insulin Sensitivity and Lowers Triglycerides in Overweight or Obese Adults with Elevated Triglycerides. *J Nutr*. 2017;147(7):1267-74.
372. Expert Dyslipidemia Panel of the International Atherosclerosis Society Panel m. An International Atherosclerosis Society Position Paper: global recommendations for the management of dyslipidemia--full report. *Journal of clinical lipidology*. 2014;8(1):29-60.
373. Metcalf PA, Scragg RRK, Schaaf D. Dietary intakes of European, Māori, Pacific and Asian adults living in Auckland: the Diabetes, Heart and Health Study. *Aust N Z J Public Health*. 2008.
374. Sluyter JD, Schaaf D, Metcalf PA, Scragg RK. Dietary intakes of Pacific, Maori, Asian and European adolescents: the Auckland High School Heart Survey. *Aust N Z J Public Health*. 2010;34(1):32-7.
375. Churuangsuk C, Kherouf M, Combet E, Lean M. Low-carbohydrate diets for overweight and obesity: a systematic review of the systematic reviews. *Obes Rev*. 2018;19(12):1700-18.
376. Carter JD, Vasey FB, Valeriano J. The effect of a low-carbohydrate diet on bone turnover. *Osteoporos Int*. 2006;17(9):1398-403.
377. Chang CK, Borer K, Lin PJ. Low-Carbohydrate-High-Fat Diet: Can it Help Exercise Performance? *J Hum Kinet*. 2017;56:81-92.
378. Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obes Rev*. 2009;10(1):36-50.
379. Zanker CL, Swaine IL. Relation between bone turnover, oestradiol, and energy balance in women distance runners. *Br J Sports Med*. 1998;32(2):167-71.
380. Ihle R, Loucks AB. Dose-response relationships between energy availability and bone turnover in young exercising women. *J Bone Miner Res*. 2004;19(8):1231-40.
381. Menezes-Júnior F, J de, de J-ÍC, Israel VL, Leite N. Is the combination of interval and resistance training more effective on physical fitness? A systematic review and Meta-analysis. *Rev. Bras. Cineantropom. Desempenho Hum*. 2017;19(5):618-29.
382. Cipryan L, Plews DJ, Ferretti A, Maffetone PB, Laursen PB. Effects of a 4-Week Very Low-Carbohydrate Diet on High-Intensity Interval Training Responses. *J Sports Sci Med.* 2018;17(2):259-68.
383. Harvey CJdC, Schofield GM, Zinn C, Thornley SJ, Crofts C, Merien FLR. Low-carbohydrate diets differing in carbohydrate restriction improve cardiometabolic and anthropometric markers in healthy adults: A randomised clinical trial. *PeerJ*. 2019;7:e6273.
384. Lanoye A, Grenga A, Leahey TM, LaRose JG. Motivation for weight loss and association with outcomes in a lifestyle intervention: comparing emerging adults to middle aged adults. *Obes Sci Pract*. 2019;5(1):15-20.
385. Chacon-Cuberos R, Zurita-Ortega F, Martinez-Martinez A, Olmedo-Moreno EM, Castro-Sanchez M. Adherence to the Mediterranean Diet Is Related to Healthy Habits, Learning Processes, and Academic Achievement in Adolescents: A Cross-Sectional Study. *Nutrients*. 2018;10(11).
386. Rodriguez F, Harrington RA. The Role of Peer Support in Attaining Ideal Cardiovascular Health: Peer Pressure and Prevention. *Journal of the American College of Cardiology*. 2016;67(5):486-7.
387. Young DR, Gittelsohn J, Charleston J, Felix-Aaron K, Appel LJ. Motivations for exercise and weight loss among African-American women: focus group results and their contribution towards program development. *Ethn Health*. 2001;6(3-4):227-45.
388. Halali F, Lapvetelainen A, Karhunen L, Saarela AM, Lappalainen R, Kantanen T. Motivators, barriers and strategies of weight management: A cross-sectional study among Finnish adults. *Eat Behav*. 2018;31:80-7.

389. Dolan SE, Frontera W, Librizzi J et al. Effects of a supervised home-based aerobic and progressive resistance training regimen in women infected with human immunodeficiency virus: a randomized trial. *Arch Intern Med*. 2006;166(11):1225-31.
390. Newes-Adeyi G, Helitzer DL, Caulfield LE, Bronner Y. Theory and practice: applying the ecological model to formative research for a WIC training program in New York State. *Health Educ Res*. 2000;15(3):283-91.
391. Tulloch H, Sweet SN, Fortier M, Capstick G, Kenny GP, Sigal RJ. Exercise facilitators and barriers from adoption to maintenance in the diabetes aerobic and resistance exercise trial. *Can J Diabetes*. 2013;37(6):367-74.
392. Staley JA, Weiner B, Linnan L. Firefighter fitness, coronary heart disease, and sudden cardiac death risk. *Am J Health Behav*. 2011;35(5):603-17.
393. Casey D, De Civita M, Dasgupta K. Understanding physical activity facilitators and barriers during and following a supervised exercise programme in Type 2 diabetes: a qualitative study. *Diabet Med*. 2010;27(1):79-84.
394. Russell HA, Rufus C, Fogarty CT, Fiscella K, Carroll J. 'You need a support. When you don't have that . . . chocolate looks real good'. Barriers to and facilitators of behavioural changes among participants of a Healthy Living Program. *Fam Pract*. 2013;30(4):452-8.

Appendices

Appendix A AUTEC Letter of Approval

AUT UNIVERSITY | AUTEC SECRETARIAT

30 June 2015

Nigel Harris
Faculty of Health and Environmental Sciences

Dear Nigel

Re Ethics Application: **15/194 Novel combination of exercise and carbohydrate restriction for metabolic health.**

Thank you for providing evidence as requested, which satisfies the points raised by the Auckland University of Technology Ethics Committee (AUTEC).

Your ethics application has been approved for three years until 29 June 2018.

We have noted that the lay title 'Twelve weeks for metabolic health' will be used on recruitment material.

As part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 29 June 2018;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 29 June 2018 or on completion of the project.

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this.

To enable us to provide you with efficient service, please use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Abelardo Gil-Sotomayor agil@aut.ac.nz

Auckland University of Technology Ethics Committee
WA505F Level 5 WA Building City Campus
Private Bag 92006 Auckland 1142 Ph: +64-9-921-9999 ext 8316 email ethics@aut.ac.nz

Appendix B AUTEC Letter of Amendment

AUTEC Secretariat

Auckland University of Technology
D-89, WA505F Level 5 WA Building City Campus
T: +64 9 921 9999 ext. 8316
E: ethics@aut.ac.nz
www.aut.ac.nz/researchethics

24 July 2015

Nigel Harris
Faculty of Health and Environmental Sciences
Dear Nigel

Re: Ethics Application: **15/194 Novel combination of exercise and carbohydrate restriction for metabolic health.**

Thank you for your request for approval of an amendment to your ethics application.

I have approved the minor amendment to your ethics application allowing changes to the inclusion criteria.

I remind you that as part of the ethics approval process, you are required to submit the following to the Auckland University of Technology Ethics Committee (AUTEC):

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 29 June 2018;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 29 June 2018 or on completion of the project.

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this. If your research is undertaken within a jurisdiction outside New Zealand, you will need to make the arrangements necessary to meet the legal and ethical requirements that apply there.

To enable us to provide you with efficient service, please use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Abelardo Gil-Sotomayor agil@aut.ac.nz

Appendix C Informed Consent Form

Consent Form

Project title: ***Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health***

Project Supervisor: ***Dr Nigel Harris***

Researcher: ***Abelardo Gil-Sotomayor***

O I have read and understood the information provided about this research project in the Information Sheet dated 25 June 2015.

O I have had an opportunity to ask questions and to have them answered.

O I understand that I may withdraw myself or any information that I have provided for this project at any time prior to completion of data collection, without being disadvantaged in any way.

O I am not suffering or have history any disease, condition or characteristic that it is stated in the exclusion criteria of the information sheet that I have read and if anything of this arises during the time that the study takes place I agree to immediately inform the primary researcher or the supervisor of this study.

O I agree to provide blood samples and undertake all assessments that are stated in the information sheet that I read and fully understand their purposes.

O *I agree to provide my GP's contact information and in order to assure my wellbeing, I authorise the researcher to contact my GP in the event of any abnormal result is found during any time of this study, especially after blood samples have been analysed. This personalised abnormal findings' report will contain my name and the abnormal finding(s) and the date when it was found.*

O I agree to take part in this research.

O I wish to receive a copy of the report from the research (please tick one): YesO NoO

O I wish to have blood samples returned to me: YesO NoO

Participant's signature: .....

Participant's name: .....

Participant's Contact Details (if appropriate):

Phone/mobile : _____

Address : _____

Participant GP's name and contact details :

Name : _____

Phone : _____

Address: _____

Date: _____/_____/_____ .

Approved by the Auckland University of Technology Ethics Committee on 1 July 2015 AUTEC Reference number 15/194.

Note: The Participant should retain a copy of this form.

Appendix D Advertisement

HUMAN POTENTIAL CENTRE
AN AUT UNIVERSITY RESEARCH CENTRE

AUT UNIVERSITY

Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health Study

Advertisement

If you are a male, between 18-55 years old, sedentary (less than 150 minutes of structured exercise per week), overweight and you are willing to change your diet, and exercise three times per week totally supervised and at no cost to you or know someone that might match this description, this could be for YOU!

This is an invitation to participate in an exercise and nutrition programme that is going to be used to investigate how a combination of high intensity interval training, resistance training and a low carbohydrate high fat diet that are now widely recommended in gyms all over New Zealand and the world.

Research has shown that structured exercise and improved nutrition, as these tools are capable of addressing all of the metabolic imbalances associated with type 2 diabetes mellitus and other early stages of metabolic disease either alone or in combination.

For more information, please click here or contact Abelardo Gil-Sotomayor at agil@aut.ac.nz or Dr Nigel Harris at nharris@aut.ac.nz

Appendix E Information Sheet

Participant Information Sheet

Date Information Sheet Produced:

20 July 2015

Project Title

Twelve Weeks for Metabolic Health.

An Invitation

Hello my name is Abelardo Gil-Sotomayor, a PhD Candidate at AUT University, and a Coastguard volunteer in Browns Bay. I have 10 years of experience in providing nutrition and exercise consultation. Before coming to New Zealand I was a Certified Dietitian and Chief of the Nutrition and Exercise Division at Cardiovascular Institute of Puebla in Puebla, Mexico; a medical institution that is devoted to improving and preserving cardiovascular health.

I came to New Zealand because of the similarities with my country, in terms of good people, cultural diversity, and a high prevalence of type 2 diabetes, or its precursor known as metabolic syndrome. The latter has been my primary professional interest, because it can be PREVENTED!

For this reason and to obtain a PhD in Health, I wish to invite you to participate in this research that I believe will contribute to combatting type 2 diabetes in New Zealand, my new country, and around the world.

Therefore your participation would be greatly appreciated and I believe of value to you.

Please be aware that if you freely decide to participate you are also free to withdraw at any time if this is your desire, so don't feel obligated to finish; nevertheless what I'd like is for you to finish the study happy, satisfied and healthier than what you are just now.

Therefore it is important that you know that this study has come a long way, it has been very well thought and planned without mentioning it has undergone an extremely high and thorough scrutiny to put in place what I am offering for you today.

I consider that your wellbeing is the most important thing to look after, so I can assure you that the minimal risks involved are greatly outweighed by the benefits this research may bring to you and to science.

So now the decision is yours, but before you decide please read further to answer questions that you may already have regarding this invitation.

Sincerely,

Abelardo Gil-Sotomayor MSc, MA, BSc

What is the purpose of this research?

To improve the metabolic health of participants

To obtain a PhD in Health (Abelardo Gil-Sotomayor)

To inform which of three novel combinations of exercise and nutrition is more effective in improving metabolic health of individuals at risk of metabolic disease (e.g. type 2 diabetes, cardiovascular disease, etc.).

To produce various scientific publications in peer reviewed journals, and conference presentations.

How was I identified and why am I being invited to participate in this research?

You have received this information because you responded to an advertisement of any of the following: AUT related print or online media; Coastguard North Shore, or; Waitemata District Health Board.

In any study there are inclusion criteria, in other words YOU will be eligible if you are:

- A Male or Female aged between 18-55 years.
- Sedentary (less than 150 min/week of self-estimated physical activity/exercise).
- Regardless of your sex you have a body mass index of equal or more than 25, but less than 36 kg/m^2, this is obtained dividing your weight in kg by your squared height in meters and the result is a positive number known as body mass index or BMI.
- If you are a female, a waist circumference of equal or more than, 82.5cm, whereas if you are a male, waist circumference of equal or more than 96.5cm near the belly button.
- Not more than 150 minutes of structured exercise and
- A waist-to-hip ratio of more than 0.95 if you are a male, and of more than 0.85 if you are a female. This is calculated dividing your waist circumference in cm by your hip circumference in cm. The latter is measured at the widest point of your buttocks.

Research suggests that these parameters are predictive of impaired glucose tolerance (IGT), which is used clinically to diagnose a pre-diabetic condition (Earnest et al. 2013).

Because I want you to be safe the following exclusion criteria apply:

- If you are under medication or have a condition that has a direct effect on the outcome measures or your ability to perform intense exercise or you don't have the time.
- If you have systolic blood pressure (BP) > 180 mmHg and/or diastolic BP > 110mmHg
- If you are a using insulin or a type 1 diabetic
- History of myocardial infarction, angioplasty, coronary artery bypass or cerebrovascular ischemia/stroke; symptomatic congestive heart failure; atrial flutter; unstable angina; unstable pulmonary disease; second or third degree heart block
- If you are taking medications known to affect heart rate (such as beta blockers), or use of other medication that may interfere with study outcome measures
- If you have history of alcoholism, drug abuse or other emotional cognitive or psychiatric problems
- If you wear a pacemaker

- If you have any other condition or disease that could impair the ability to exercise.
- If you are following already a low carbohydrate diet (less than 150 g of carbohydrate per day).

What will happen in this research?

It is an exercise and nutrition programme (study), and is going to be administered as a randomised control study where you are going to be randomly assigned to one of four groups.

Then all participants will undertake a comprehensive assessment. Data obtained will be used to customise the exercise and nutrition programmes if you are assigned by chance, to one of the three exercise and diet groups. If you are in the control group you only have to continue doing what you normally are doing right now.

The comprehensive assessment will consist of three visits that will be scheduled within two weeks to minimise the time you have to spend in any one visit and avoid having you just waiting:

- Fasting blood analysis, for your comfort an experienced phlebotomist will be taking the blood samples. (5-10 minutes).
- Maximal aerobic capacity test, in order to assess your cardiorespiratory capacity. This will take place in the same lab that elite athletes like Olympic gold medallists Eric Murray and Hamish Bond have been tested! (10-15 minutes)
- Strength assessment which consists in performing two simple exercises to know how strong you are. (10-15 minutes)
- Body composition assessment using dual energy absorptiometry (DEXA) performed at Auckland Hospital know exactly how much muscle you have and fat mass and your bone density! (20 -25 minutes).
- Dietary assessment, to let you know exactly the distribution of your nutrient intake, for this I will teach you how to accurately measure what you eat, using cups, spoons and teaspoons. Then you will only have to write it down and fill an online questionnaire (food frequency questionnaire and a food diary for two week days and one weekend day). That simple!
- Resting energy expenditure rate, to know how much energy do you spend at rest and your carbohydrate and fat utilisation rates using indirect calorimetry. A non-invasive technique that requires you to breathe through a mask that collects your expired air and forces it into a chamber where the air is mixed and dried from moisture and two sensors measure the expired gases, oxygen and carbon dioxide then the a computer does the rest; while you are calmed and relaxed in a comfortable lying position (20- 30 minutes).
- Non-exercise related thermogenesis which is to measure your physical activity patterns, this study is performed by wearing an accelerometer for 7 days on your waist. It is simple and easy and you have nothing to worry about. At the end you will return the device and I will do the rest, that is to calculate your physical activity patterns while not exercising and how much energy do you spend on your daily activities.

The four possible groups are:

- High intensity interval training (HIIT) + low carbohydrate high fat diet (LCHF) group (A)
- Resistance training (RT) + LCHF group (B)
- HIIT + RT + LCHF group (C)
- Control group (D)

Why these combinations?

Recently, attention has been turned to high intensity intermittent exercise (HIIT) as a very potent and versatile exercise modality as it has been shown to improve blood sugar control, promote weight loss and improve lipid profile (e.g. cholesterol, triglycerides). Of highlight is its ability to produce these metabolic enhancements in as little as 10 to 20 minutes reducing considerably the time committed to exercise and tackling the most common perceived barrier to exercise by people which is "lack of time".

Resistance training (RT) has also proved a potent component in diabetes prevention and treatment.

Every well-structured preventive or treatment intervention should also provide nutritional guidance to people suffering or at risk of developing T2DM. Carbohydrate content of the diet is crucial to contribute to adequate glucose control; in this respect the low carbohydrate nutritional approach has proven to be effective in controlling glycaemia and body weight.

At present there have been no studies that have combined the three most effective means to ameliorate the metabolic condition of pre-diabetic or individuals with metabolic syndrome, nor compared these exercise modalities (HIIT vs RT vs both) equated by time while following a lower carbohydrate nutritional intake.

What involves being in groups A-C?

You will be given a customised exercise and nutrition plan that you will have to follow as closely as possible, you will receive personal assistance to implement your new diet with as much ease as possible. Be patient, changes are difficult but will pay off!

You will have to attend and meet 85% of all sessions, which will be held three days a week to perform your personalised exercise programme at the best that suits your schedule, please consider that you and I have other responsibilities but will try to match your requirements as much as possible all will last for about 30 minutes.

By week four you will be tested on the acute effects of your assigned exercise programme to help me/us find out how similar or dissimilar these exercise modalities are.

On the other hand if you are assigned to the control group:

If you are assigned to the control group you play a very important role in this investigation just like any other participant.

Your role is to certify that the changes in the intervention groups have not happened as a result of chance. Therefore you will receive the same care for the duration of the study as anybody else.

You will be evaluated in the same fashion.

Your task is to maintain what you normally do, and make sure to maintain the same behaviours, eat what you normally do not more but not less, for example if you are used to have a pizza on Fridays, then do so. Likewise your physical activity patterns, keep them the same, for example if you walk your dog every other day, you will have to walk your dog every other day.

This maybe tough but, with this you are helping us exactly the same way like anybody else participating in this study, and perhaps more because without you we will not be sure that what happened was due to chance or the intervention.

In return what you'll have is:

a) The chance to choose which exercise programme you would like to begin after these 12 weeks, you will have three choices:

-High intensity interval training (HIIT) only

-Resistance training (RT) only

-HIIT + RT

b) The chance to decide whether or not you would like to change your diet and give it a try to the LCHF we recommend it but it is your choice.

c) You will receive personalised nutrition and exercise programmes and the right to come to train with us while we tune your programme and get you started. Please remember all this will be free of charge to you, the only thing that we like you to do is to make an appointment every time you would like to come for checking gym availability, as we are very busy at AUT improving New Zealanders health.

What are the discomforts and risks?

Blood draws involve a degree of discomfort but it will be minimised as an experienced phlebotomist will be doing this task.

High intensity exercise may provide some discomfort as it is "intense", this will be minimised as the nature of the exercise programme is "progressive" it will allow you as a participant to adapt gradually imposing an attenuated effect of exertion as you will be getting fitter. Which actually will provide you with a sense of achievement which is extensively reported in exercise research.

In addition you are going to be thoroughly supervised and constantly reminded you can stop or express your discomfort to take corrective actions.

How will these discomforts and risks be alleviated?

For blood draws it will be minimised as an experienced phlebotomist will be doing this task.

Intensity discomfort will be minimised as the nature of the exercise programme is "progressive" it will allow you as a participant to adapt gradually imposing an attenuated effect of exertion as you will be getting fitter. Which actually will provide you with a sense of achievement which is extensively reported in exercise research.

To avoid embarrassment when training, all training sessions will be private.

In addition you are going to be thoroughly supervised and constantly reminded that you can stop or express your discomfort to take corrective actions.

What are the benefits?

You as a participant will be offered a closely supervised and monitored nutrition and exercise programmes that has been proven quite effective in reducing the likelihood of developing a cardio-metabolic disease that elsewhere it would cost an excess of $2,500 NZD.

For the lead researcher (that is me) is going to give me access to obtain my PhD in Health, and very valuable experience of how to administer and conduct a randomised controlled trial and other skills that are involved when you are the primary researcher.

To the wider community, this research will help to establish if HIIT and RT provide an equal or dissimilar effect to ameliorate cardio-metabolic risk factors when combined with a LCHF or if the combination of both and a LCHF is a better alternative. In addition if outcomes are as expected it may provide valuable information to reduce the number of type 2 diabetics worldwide.

What compensation is available for injury or negligence?

In the unlikely event of a physical injury as a result of your participation in this study, rehabilitation and compensation for injury by accident may be available from the Accident Compensation Corporation, providing the incident details satisfy the requirements of the law and the Corporation's regulations.

How will my privacy be protected?

Address any issues of confidentiality that have not already been identified in the sections on discomforts and risks. Remember that anonymity means that the researcher does not know who the participant is; in all other cases the issue is one of confidentiality.

As a participant you can be sure that your name or any reference to you will not be made, once you become a participant you will receive a code so all documents that may be generated will contain this code if the data pertains to you or any other participant. Therefore it won't be possible to identify you.

Despite this strict control any individual that may interact with you as a participant or your data will sign a confidentiality agreement.

What are the costs of participating in this research?

What you have to invest in this study is time.

All the assessments will take place over the course of two weeks, that you will have to attend for three occasions for up to 60 minutes the first two and up to 120 minutes the third time. These will happen in three occasions separated by 12 weeks and 6 months respectively. Groups A-D

Exercise sessions will last up to 30 minutes three times per week for 12 weeks. (In case you are in one of groups A-C.

What opportunity do I have to consider this invitation?

One week from the moment you receive an informative pack and be clearly explained the study and the contents of this information sheet.

How do I agree to participate in this research?

The day you attend to a pre-screening session is when you will sign the Consent form.

Will I receive feedback on the results of this research?

Yes you will.

What do I do if I have concerns about this research?

Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor, *Dr Nigel Harris, nharris@aut.ac.nz , +64 9 921 9999 ext. 7301.*

Concerns regarding the conduct of the research should be notified to the Executive Secretary of AUTEC, Kate O'Connor, *ethics@aut.ac.nz*, 921 9999 ext 6038.

Whom do I contact for further information about this research?

Researcher Contact Details:

Abelardo Gil-Sotomayor agil@aut.ac.nz,

Project Supervisor Contact Details:

Dr Nigel Harris, nharris@aut.ac.nz, +64 9 921 9999 x 7301.

Approved by the Auckland University of Technology Ethics Committee on *30th June 2015*, AUTEC Reference number *15/194*.

Appendix F Food Diary

HUMAN POTENTIAL CENTRE
AN AUT UNIVERSITY RESEARCH CENTRE

AUT UNIVERSITY

Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health Study
Food diary

Please answer questions honestly and to the best of your ability.
Date____ [*dd*] / ____ [*mm*] / _____ [*yyyy*]

Please write your name _____

_____

WEEK DAY ONE

Breakfast:
Morning Tea:
Lunch:
Afternoon tea:
Dinner:
Supper:
Snacks you consumed throughout the day:
Fluids you consumed throughout the day:

WEEK DAY TWO

Breakfast:
Morning Tea:
Lunch:
Afternoon tea:
Dinner:
Supper:
Snacks you consumed throughout the day:
Fluids you consumed throughout the day:

WEEKEND DAY ONE

Breakfast:
Morning Tea:
Lunch:
Afternoon tea:
Dinner:
Supper:
Snacks you consumed throughout the day:
Fluids you consumed throughout the day:

Once you finish and have reviewed your information click on the send button

Thank you for your time.
Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health Study.

Appendix G Wellbeing and FFQ

HUMAN POTENTIAL CENTRE
AN AUT UNIVERSITY RESEARCH CENTRE

AUT UNIVERSITY

Novel Combination of Exercise and Carbohydrate Restriction for Metabolic Health Study

Your participation in this study is completely voluntary. Your survey responses will be strictly confidential and data from this research will be reported only in the aggregate. Your information will be coded and will remain anonymous. If you have questions at any time about the survey or the procedures, you may contact Abelardo Gil-Sotomayor by email at the email on agil@aut.ac.nz. Thank you very much for your time and support. Please start with the survey now by clicking on the acceptance box below.

Profile of Mood States

This section is about your mood state. Below is a list of words that describe feelings people have. Please read each one carefully. Then click on ONE answer that best describes HOW YOU HAVE BEEN FEELING DURING THE LAST 24 HOURS. (Multiple Choice/ Select one option)

Q1) Tense
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q2) Angry
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q3) Worn out
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q4) Unhappy
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q5) Lively
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q6) Confused
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q7) Peeved
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q8) Sad
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q9) Active
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q10) On edge
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q11) Grouchy
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q12) Blue
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q13) Energetic
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q14) Hopeless
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q15) Uneasy
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q16) Restless
1. Not at all
2. A little
3. Moderately
4. Quite a bit

5. Extremely

Q17) Unable to concentrate
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q18) Fatigued
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q19) Annoyed
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q20) Discouraged
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q21) Resentful
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q 22) Nervous
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q23) Miserable
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q24) Cheerful
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q25) Bitter
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q33) Exhausted
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q26) Anxious
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q27) Helpless
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q28) Weary
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q29) Bewildered
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q30) Furious
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q31) Full of pep
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q32) Worthless
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q33) Forgetful
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q34) Vigourous
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q35) Uncertain about things
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Q36) Bushed
1. Not at all
2. A little
3. Moderately
4. Quite a bit
5. Extremely

Adherence

The following questions are to help assess the types of foods you might have consumed this week. This will help you to rate your adherence to the dietary protocol for the last seven days.

Q37) In the last 7 days on how many occasions did you consume bread/toast OR bread rolls?
1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. On more than 10 occasions

Q38) On the last 7 days, on how many occasions did you consume pasta or noodles? This includes all pasta dishes, lasagna, and noodles such as 2 minute noodles, Vietnamese noodles etc.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. On more than 10 occasions

Q39) On how many occasions over the past 7 days did you consume starchy or root vegetables such as potatoes, kumara, pumpkin, or beetroot?

1. 1
2. 2
3. 3
4. 4
5. 5
6. 6
7. 7
8. 8
9. 9
10. 10
11. More than 10 occasions

Q41) On how many occasions over the past 7 days did you consume legumes such as chickpeas, lentils, beans or peas (fresh or frozen)?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10 occasions

Q42) On how many occasions over the past 7 days did you consume rice? This includes brown or white rice and sushi.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10 occasions

Q42) On how many occasions over the last 7 days did you eat fast food or takeaways from places like McDonalds or Burger King? Think about breakfast, lunch, dinner and snacks.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

Q43) On how many occasions over the last 7 days have you consumed crackers and snacks such as rice crackers, potato chips and corn chips?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

Q42) On how many occasions over the past 7 days did you consume rice? This includes brown or white rice and sushi.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10 occasions

Q42) On how many occasions over the last 7 days did you eat fast food or takeaways from places like McDonalds or Burger King? Think about breakfast, lunch, dinner and snacks.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

Q43) On how many occasions over the last 7 days have you consumed crackers and snacks such as rice crackers, potato chips and corn chips?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

Q44) On how many occasions over the last 7 days did you drink fruit juices, soft drinks, sports drinks or energy drinks? Do not include diet varieties.

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

Q45) On how many occasions over the past 7 days did you consume lollies, sweets, chocolate or confectionary?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10 occasions

Q46) On how many occasions over the past 7 days did you consume baked goods such as manufactured or homemade biscuits or cakes?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10 occasions

On how many occasions over the past 7 days did you consume full fat milk, cheese or plain yoghurt (e.g. blue top milk, cheddar cheese, Greek yoghurt)?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

On how many occasions over the past 7 days did you consume low fat milk, cheese or yoghurt (e.g. green top, Edam cheese, lite yoghurt)?

1. 0
2. 1
3. 2
4. 3
5. 4
6. 5
7. 6
8. 7
9. 8
10. 9
11. 10
12. More than 10

The next question is about how easily you were able to stick to your dietary regime over the last 7 days.

Q47) Please indicate on the scale below how well you adhered to your dietary regime in the last 7 days. For example if you feel that you ate only foods from the 'Recommended' food list then you would slide the scale to 100. If you feel that 50% of the food you ate was from the 'Recommended' food list, you would slide the scale to 50%. Please answer this question honestly and accurately.

	0%						100%
	❑	❑	❑	❑	❑	❑	❑

Satiety, hunger, fullness

The next question is about your feelings of satiety or hunger/fullness.

Q48) Please indicate on the scale below your general feeling of satiety or hunger/fullness over the last 7 days: Here is a little more about what the numbers mean:

1: Very hungry; starving; desperate.
2: Moderately hungry; ready to eat.
3: Mildly hungry; beginning hunger.
4: Neutral. You feel no sensations of hunger or fullness.
5: Mildly full. You feel satisfied.
6: Very full.
7: Much too full.

	1	2	3	4	5	6	7
	❑	❑	❑	❑	❑	❑	❑

WEIGHT

Please enter your current weight in kilograms and grams.

Please weigh yourself at the same time each week, on the same scales and wearing approximately the same level of clothing.

Thank you for completing this questionnaire. You will receive your next questionnaire at the same time next week.

Appendix H Exercise Control Slip HIIT

Control Slip HIIT		
RPE	Description	Intensity Level
6	--No exertion--	
7	Easy	
8		
9	Very Light	
10		50%MHR
11	Light	
12		60%MHR
13	Somewhat Hard	
14		70%MHR
15	Hard (Heavy)	
16		80%MHR
17	Very Hard	
18		90%MHR
19	Very, Very Hard	
20	---Max effort---	

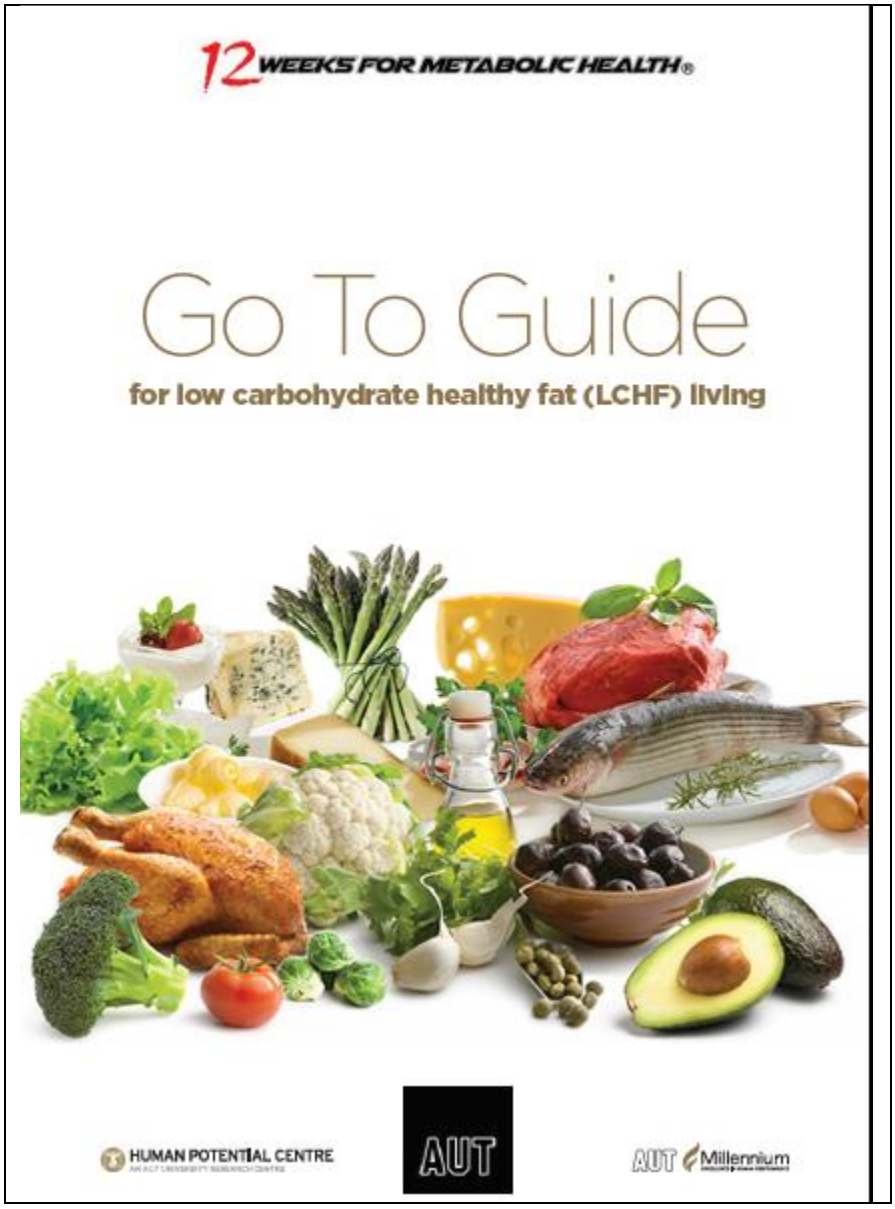
interval	Machine	Incline	Level/ speed	rPE	Heart Rate
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

Appendix I Exercise Control Slip RT

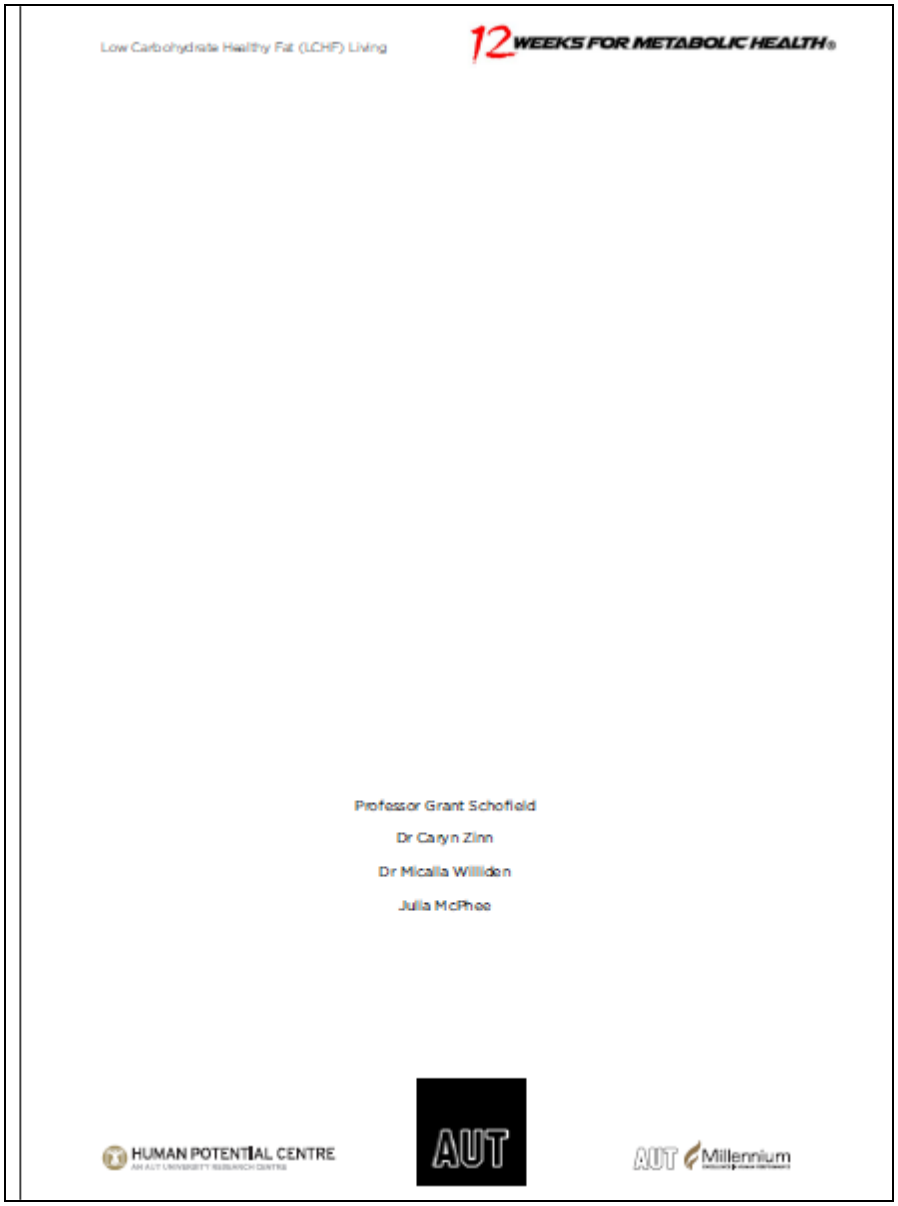
Control Slip RT		
RPE	Description	Intensity Level
6	--No exertion--	
7	Easy	
8		
9	Very Light	
10		50%MHR
11	Light	
12		60%MHR
13	Somewhat Hard	
14		70%MHR
15	Hard (Heavy)	
16		80%MHR
17	Very Hard	
18		90%MHR
19	Very, Very Hard	
20	---Max effort---	

set	exercise	rpe	Reps in reserve	weight	Heart Rate
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

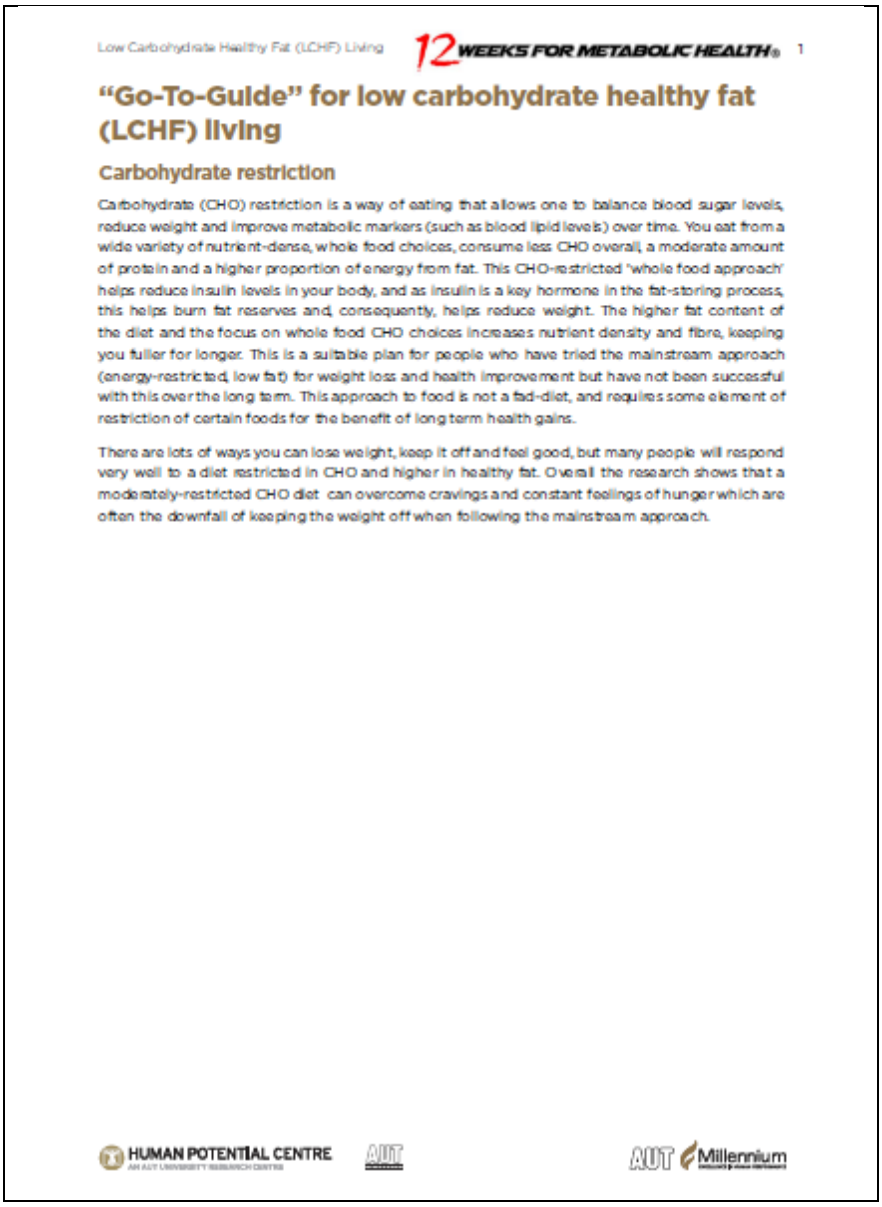
Appendix J Go to guide for low carbohydrate healthy fat living



Appendix H Go to guide for low carbohydrate healthy fat living



Appendix H Go to guide for low carbohydrate healthy fat living



"Go-To-Guide" for low carbohydrate healthy fat (LCHF) living

Carbohydrate restriction

Carbohydrate (CHO) restriction is a way of eating that allows one to balance blood sugar levels, reduce weight and improve metabolic markers (such as blood lipid levels) over time. You eat from a wide variety of nutrient-dense, whole food choices, consume less CHO overall, a moderate amount of protein and a higher proportion of energy from fat. This CHO-restricted 'whole food approach' helps reduce insulin levels in your body, and as insulin is a key hormone in the fat-storing process, this helps burn fat reserves and, consequently, helps reduce weight. The higher fat content of the diet and the focus on whole food CHO choices increases nutrient density and fibre, keeping you fuller for longer. This is a suitable plan for people who have tried the mainstream approach (energy-restricted, low fat) for weight loss and health improvement but have not been successful with this over the long term. This approach to food is not a fad-diet, and requires some element of restriction of certain foods for the benefit of long term health gains.

There are lots of ways you can lose weight, keep it off and feel good, but many people will respond very well to a diet restricted in CHO and higher in healthy fat. Overall the research shows that a moderately-restricted CHO diet can overcome cravings and constant feelings of hunger which are often the downfall of keeping the weight off when following the mainstream approach.

HUMAN POTENTIAL CENTRE AUT AUT Millennium

Appendix H Go to guide for low carbohydrate healthy fat living

Moderate CHO restriction (<100g per day)

- Eat three main meals per day (snacks if needed).
- Include a serve of protein at each meal (see below for serving sizes).
- Eat non-starchy vegetables in abundance at each meal.
- The remaining daily energy (calories) is derived from fat (see below for serving sizes).
- Because CHO restriction is moderate, apply some caution with eating fat *ad libitum* (as much as you want) as overall energy intake is still important to ensure weight loss.
- Use nutrition-tracking software on your computer or an application on your smart phone to track CHO intake. Some examples include: My Fitness Pal, CRON-o-meter, Easy Diet Diary (iPhone only) or Fat Secret. Most of these are free to download.

General guidelines for CHO restriction

- Where possible, choose minimally processed food as the basis of your daily food choices. It makes it easier to adapt to a lower CHO diet and provides important vitamins and minerals.
- Eat when hungry. While three meals a day can be beneficial for metabolic response to eating, let your appetite guide you and include snacks where necessary. However, if you are hungry within two hours of a meal, it's likely the previous meal was either too small or did not include optimal amounts of fat or protein.
- Spread protein out over your meals and snacks. A good rule of thumb is to consume the amount that fits on to the palm of your hand at each meal.
- Weigh, measure or use a portion guide initially so you become familiar with portion sizes of food choices. You don't have to do this forever. It's just a matter of relearning appropriate portion sizes.
- There is no need to trim fat from meat or skin from poultry, but if you want to that is fine. Just add olive oil/butter to vegetables to replace fat. In fact, when you are first getting started, if in doubt add more fat. You have years of following a "fat phobic" dogma to unlearn.
- Some people can overdo the amount of fat that they eat. It is important to add enough fat to be satisfied at each meal, but this isn't license to overdo it.
- Use good quality Extra Virgin olive oil, butter, ghee and coconut oil mainly for cooking, and flavoured oils such as avocado/nut/olive oils at other times (i.e., on salads/vegetables). If following a moderate CHO-restricted plan, aim for 1 tablespoon (tbsp) of oil or a knob of butter on salad or vegetables. See below for more details regarding the use of fats.
- Don't deep fry your food but make sure it doesn't burn by cooking with enough fat, at the correct temperature and for the correct cooking time.

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- A diet moderately restricted in CHO means that you will be eating no more than 100g of CHO per day- it is fine to eat less than the amount stated, but do not go above this limit. The majority of your CHO should come from non-starchy vegetables which are nutrient-dense, with a smaller amount from fruit and dairy products and starchy vegetables. Remember, once you are burning fat as your primary fuel, you will feel good and won't need those CHOs for energy.
- Learn to distinguish between hunger and habit, and adjust the quantity of food as your appetite decreases. When hungry, eat until you are satiated (feel satisfied). Eat mindfully and slowly, chewing food properly and swallowing before taking your next bite. If you are unsure if you are satisfied or not, have a glass of water, wait 10 minutes, and then decide whether you need more food. While there are no restrictions on this plan, the food choices should guide your hunger. Do not eat for the sake of eating.
- If you're not hungry at a meal time, eat a small low CHO snack.
- Don't starve yourself.
- Don't assume ANY food is low in CHO. Read the labels of pre-prepared foods and check the CHO counts.
- When dining out, beware of hidden CHO in gravies, sauces and salad dressings. If you are in doubt, ask the waiter. Avoid deep fried or crumbed/battered food.
- As you adapt to a different way of eating, your tastes will change. While you can use acceptable sweeteners where necessary, you will begin
- to appreciate the natural sweetness in food and
- potentially not require them. Do note that many sweeteners have a small CHO count to them.
- Drink a good amount of fluid per day (mainly water).
- When embarking on a CHO-restricted plan, people can initially experience fatigue, light-headedness, muscle cramps, constipation and/or headaches. Many of these initial adjustments to the diet can be alleviated through an increase in sodium intake. This is because when CHO is reduced, the body's ability to maintain a correct electrolyte balance can be compromised. It is recommended that initially, you add salt to your meals where possible or cook with stock. Some people benefit from having a drink of hot stock – 1 teaspoon of stock per cup, and 2 cups per day during the early stages of your dietary change. If you are on blood pressure or insulin-related medication, you will need to get advice from your medical professional about adjusting your medications.
- Be organised with shopping and preparing food.
- Travel: Take appropriate snack food along to airports and for airplane trips. Make sure you find a supermarket or suitable grocery shop when you arrive at your destination. If travelling by car, pack suitable food/snacks for the trip and shop on-route or at your destination.

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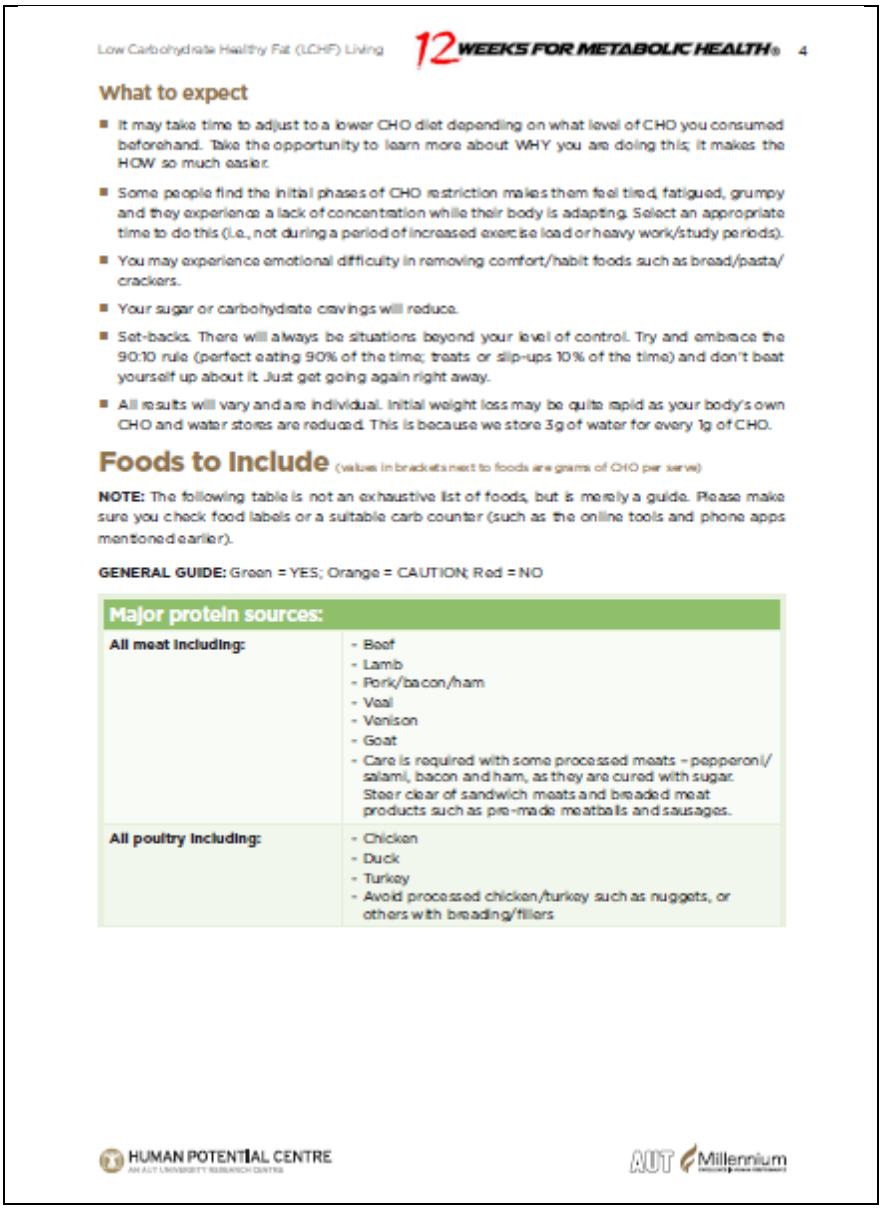

What to expect

- It may take time to adjust to a lower CHO diet depending on what level of CHO you consumed beforehand. Take the opportunity to learn more about WHY you are doing this; it makes the HOW so much easier.
- Some people find the initial phases of CHO restriction makes them feel tired, fatigued, grumpy and they experience a lack of concentration while their body is adapting. Select an appropriate time to do this (i.e., not during a period of increased exercise load or heavy work/study periods).
- You may experience emotional difficulty in removing comfort/habit foods such as bread/pasta/crackers.
- Your sugar or carbohydrate cravings will reduce.
- Set-backs. There will always be situations beyond your level of control. Try and embrace the 90:10 rule (perfect eating 90% of the time; treats or slip-ups 10% of the time) and don't beat yourself up about it. Just get going again right away.
- All results will vary and are individual. Initial weight loss may be quite rapid as your body's own CHO and water stores are reduced. This is because we store 3g of water for every 1g of CHO.

Foods to Include (values in brackets next to foods are grams of CHO per serve)

NOTE: The following table is not an exhaustive list of foods, but is merely a guide. Please make sure you check food labels or a suitable carb counter (such as the online tools and phone apps mentioned earlier).

GENERAL GUIDE: Green = YES; Orange = CAUTION; Red = NO

Major protein sources:	
All meat including:	- Beef - Lamb - Pork/bacon/ham - Veal - Venison - Goat - Care is required with some processed meats – pepperoni/salami, bacon and ham, as they are cured with sugar. Steer clear of sandwich meats and breaded meat products such as pre-made meatballs and sausages.
All poultry including:	- Chicken - Duck - Turkey - Avoid processed chicken/turkey such as nuggets, or others with breading/fillers

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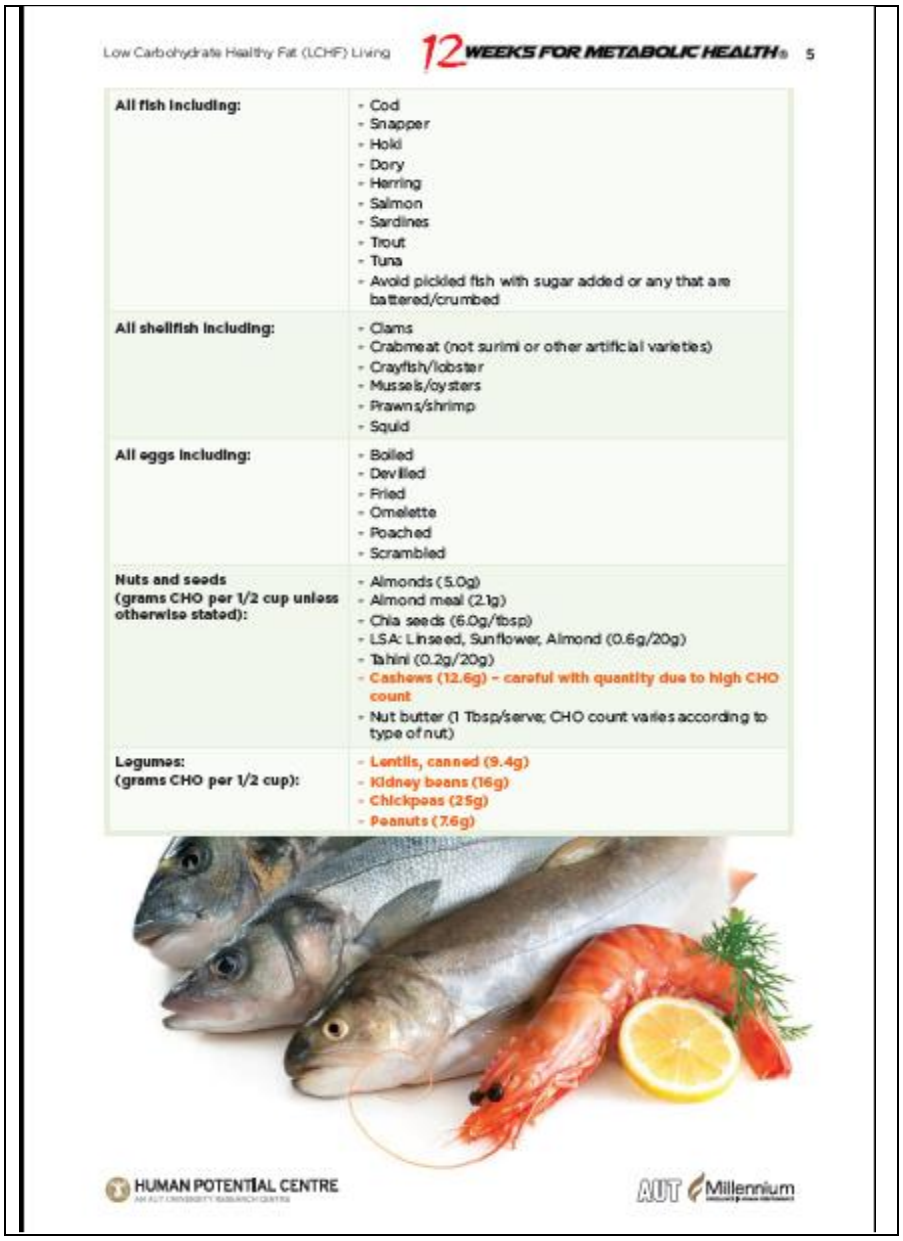

All fish including:	- Cod - Snapper - Hoki - Dory - Herring - Salmon - Sardines - Trout - Tuna - Avoid pickled fish with sugar added or any that are battered/crumbed
All shellfish including:	- Clams - Crabmeat (not surimi or other artificial varieties) - Crayfish/lobster - Mussels/oysters - Prawns/shrimp - Squid
All eggs including:	- Boiled - Devilled - Fried - Omelette - Poached - Scrambled
Nuts and seeds (grams CHO per 1/2 cup unless otherwise stated):	- Almonds (5.0g) - Almond meal (2.1g) - Chia seeds (6.0g/tbsp) - LSA: Linseed, Sunflower, Almond (0.6g/20g) - Tahini (0.2g/20g) - **Cashews (12.6g) – careful with quantity due to high CHO count** - Nut butter (1 Tbsp/serve; CHO count varies according to type of nut)
Legumes: (grams CHO per 1/2 cup):	- **Lentils, canned (9.4g)** - **Kidney beans (16g)** - **Chickpeas (25g)** - **Peanuts (7.6g)**

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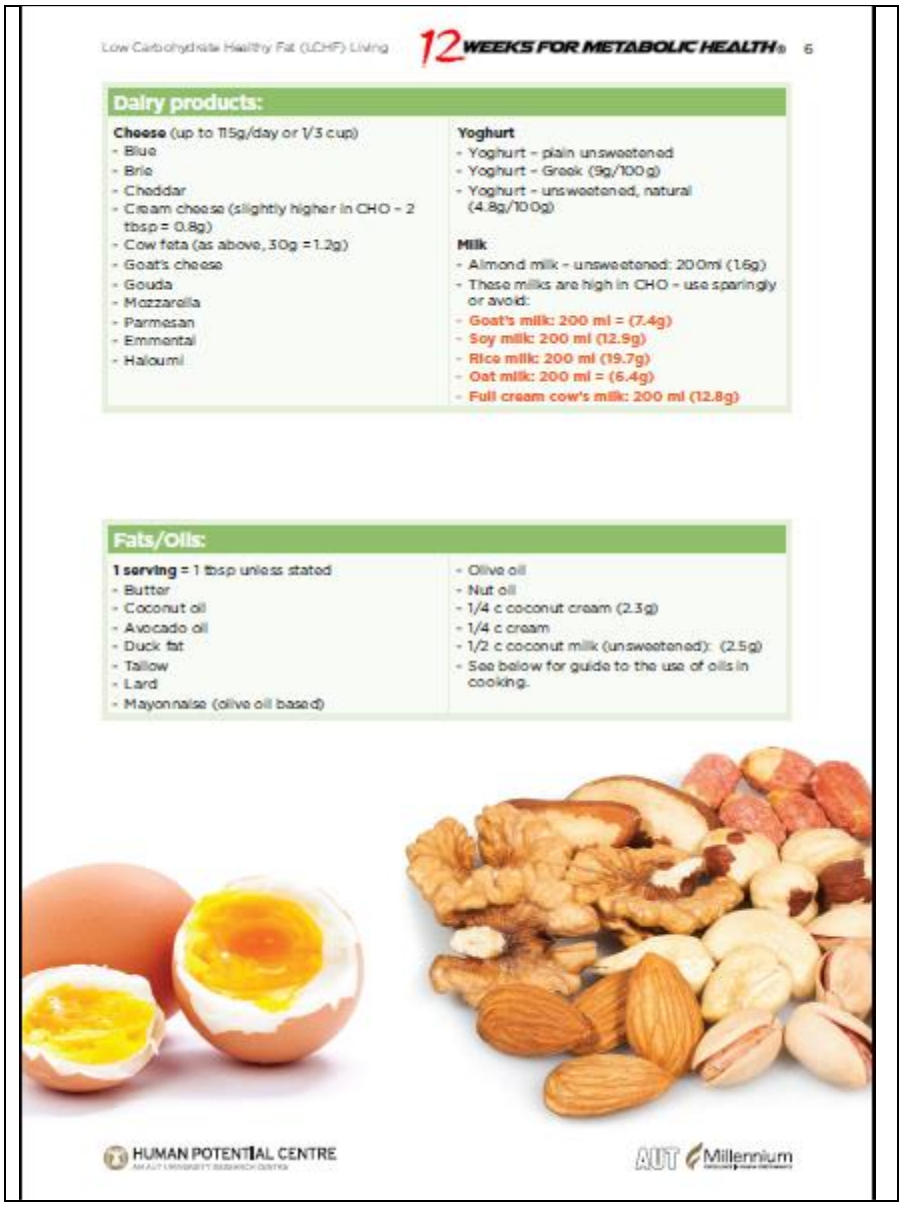

Dairy products:

Cheese (up to 115g/day or 1/3 cup)
- Blue
- Brie
- Cheddar
- Cream cheese (slightly higher in CHO – 2 tbsp = 0.8g)
- Cow feta (as above, 30g = 1.2g)
- Goat's cheese
- Gouda
- Mozzarella
- Parmesan
- Emmental
- Haloumi

Yoghurt
- Yoghurt – plain unsweetened
- Yoghurt – Greek (9g/100g)
- Yoghurt – unsweetened, natural (4.8g/100g)

Milk
- Almond milk – unsweetened: 200ml (1.6g)
- These milks are high in CHO – use sparingly or avoid:
- **Goat's milk: 200 ml = (7.4g)**
- **Soy milk: 200 ml (12.9g)**
- **Rice milk: 200 ml (19.7g)**
- **Oat milk: 200 ml = (6.4g)**
- **Full cream cow's milk: 200 ml (12.8g)**

Fats/Oils:

1 serving = 1 tbsp unless stated
- Butter
- Coconut oil
- Avocado oil
- Duck fat
- Tallow
- Lard
- Mayonnaise (olive oil based)
- Olive oil
- Nut oil
- 1/4 c coconut cream (2.3g)
- 1/4 c cream
- 1/2 c coconut milk (unsweetened): (2.5g)
- See below for guide to the use of oils in cooking.

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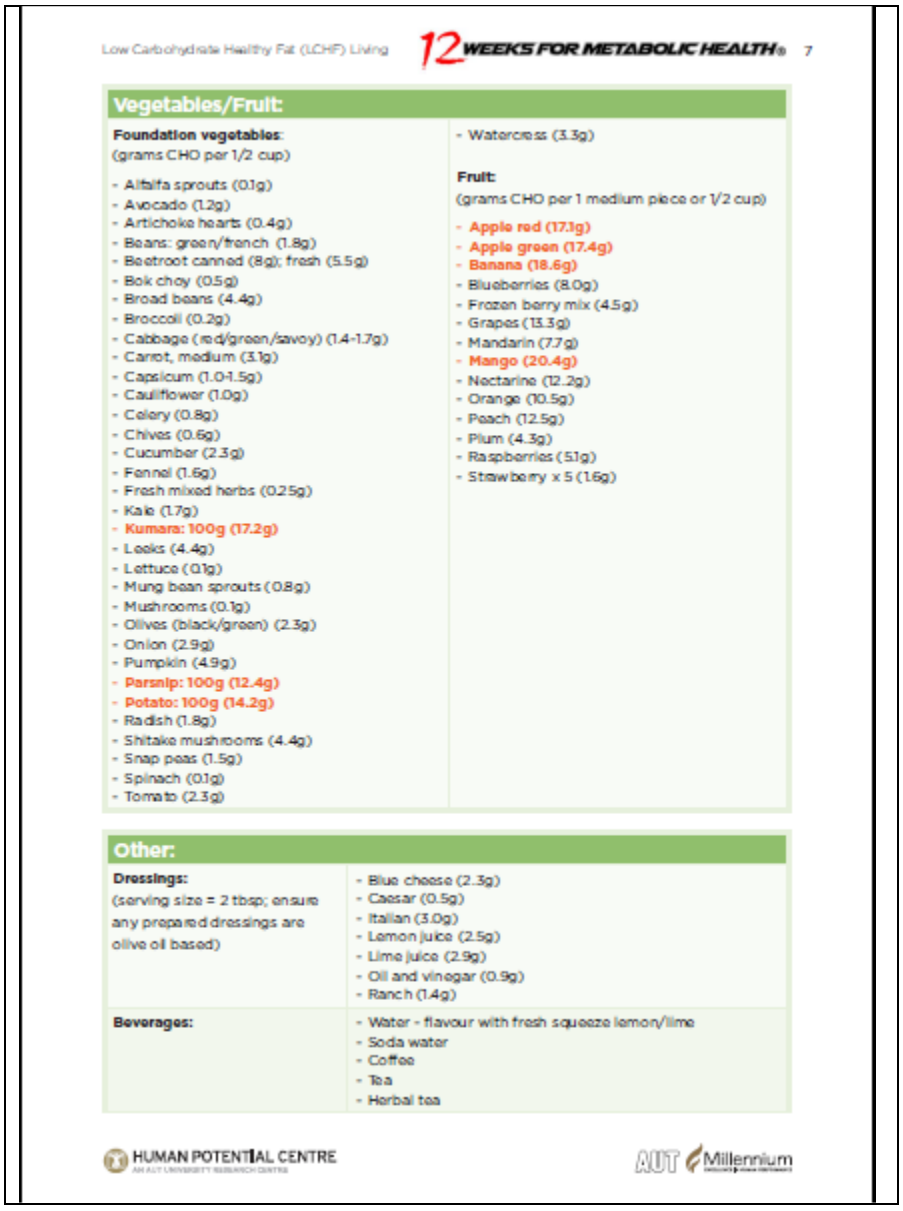

Vegetables/Fruit:

Foundation vegetables:
(grams CHO per 1/2 cup)

- Alfalfa sprouts (0.1g)
- Avocado (1.2g)
- Artichoke hearts (0.4g)
- Beans: green/french (1.8g)
- Beetroot canned (8g); fresh (5.5g)
- Bok choy (0.5g)
- Broad beans (4.4g)
- Broccoli (0.2g)
- Cabbage (red/green/savoy) (1.4-1.7g)
- Carrot, medium (3.1g)
- Capsicum (1.0-1.5g)
- Cauliflower (1.0g)
- Celery (0.8g)
- Chives (0.6g)
- Cucumber (2.3g)
- Fennel (1.6g)
- Fresh mixed herbs (0.25g)
- Kale (1.7g)
- **Kumara: 100g (17.2g)**
- Leeks (4.4g)
- Lettuce (0.1g)
- Mung bean sprouts (0.8g)
- Mushrooms (0.1g)
- Olives (black/green) (2.3g)
- Onion (2.9g)
- Pumpkin (4.9g)
- **Parsnip: 100g (12.4g)**
- **Potato: 100g (14.2g)**
- Radish (1.8g)
- Shitake mushrooms (4.4g)
- Snap peas (1.5g)
- Spinach (0.1g)
- Tomato (2.3g)
- Watercress (3.3g)

Fruit:
(grams CHO per 1 medium piece or 1/2 cup)

- **Apple red (17.1g)**
- **Apple green (17.4g)**
- **Banana (18.6g)**
- Blueberries (8.0g)
- Frozen berry mix (4.5g)
- Grapes (13.3g)
- Mandarin (7.7g)
- **Mango (20.4g)**
- Nectarine (12.2g)
- Orange (10.5g)
- Peach (12.5g)
- Plum (4.3g)
- Raspberries (5.1g)
- Strawberry x 5 (1.6g)

Other:

Dressings: (serving size = 2 tbsp; ensure any prepared dressings are olive oil based)	- Blue cheese (2.3g) - Caesar (0.5g) - Italian (3.0g) - Lemon juice (2.5g) - Lime juice (2.9g) - Oil and vinegar (0.9g) - Ranch (1.4g)
Beverages:	- Water - flavour with fresh squeeze lemon/lime - Soda water - Coffee - Tea - Herbal tea

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Non-caloric sweeteners: One sachet = 1g CHO limit to THREE per day	- Stevia-based products (check label) - Xylitol
Condiments:	- Black bean sauce: 1 tsp (3.0g) - Chipotle: 2 peppers (2.0g) - Cocoa powder 1 tbsp (1.2g) - Gherkin: 1/2 pickled: (1.0g) - Jalapeno: 45g (1.4g) - Ginger 1 tbsp grated (0.8g) - Miso paste: 1 tbsp (2.6g) - Mustard (Dijon): 1 tsp (0.5g) - Mustard plain: 1 tsp (0g) - Mustard wholegrain: 1 tsp (0.3g) - Pesto: 1 tbsp (0.6g) - Enchilada sauce: 4 tbsp (0.6g) - Garlic: 1 large clove (0.9g) - Salsa: (no sugar added): 1 tbsp (1.0g) - Soy sauce: 1 tbsp (0.9g) - Taco sauce: 1 tbsp (1.0g) - Tahini: 2 tbsp (1.0g) - Fish sauce: 1 tsp (0.2g) - Balsamic vinegar: 1 tbsp (2.3g) - Red wine/white wine vinegar: 1 tbsp (1.5g)
Confectionary/other:	- Dark chocolate (85% or greater): (2 large squares, 20g = 7.5g) - Sugar-free chewing gum: limit of 3 pieces per day (3.0g)
Alcohol:	- White wine, dry: 1 glass: (1.4g) - Red wine: 1 glass: (0g) - Spirit (Gin, Vodka, Whisky, Rum...): (0g)

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Foods to avoid

- Juice (fresh or concentrate)
- Fruit drinks (i.e. cordial)
- Caloric fizzy drinks (including energy drinks)
- Diet soft drink (while these are calorie-free, minimising intake of diet soft drink will help you enjoy the natural sweetness of other food choices) and will help change your palate and subsequent desire for sweet things.
- Flavoured milk
- Deep-fried food
- Shortening or any 'light' product
- All flour-based products (i.e., breads - white and wholegrain, all cereals, all pasta)
- Products that are 'gluten-free'
- Other grains including rice, quinoa, couscous and amaranth
- Foods with added hydrogenated/partially hydrogenated oils
- Foods with added sugar: dextrose, brown syrup, evaporated cane syrup, glucose, honey, corn syrup, maltodextrin
- General junk food: biscuits, cakes, ice cream, frozen yoghurt/sorbet, chips, crackers, muesli bars, most fast food

When in doubt, DON'T EAT IT!

Preparation for CHO-restriction

Before you begin: GET RID OF ALL FOODS YOU SHOULDN'T HAVE!!! If they are in your house it is too tempting. Clean out your fridge, pantry etc. If you don't want to waste food, give it away. This is important because in our experience willpower is an over-rated quality of all humans. It is really hard to not eat a bag of chips which are sitting in your pantry. It is much easier not to eat a bag of chips NOT in your pantry. Just remove temptation!

Restock your cupboards with ready-to-go easy foods to prepare a low CHO meal:

- **Fridge:** eggs, cheese, cream, full fat yoghurt, butter or ghee, rotisserie chicken (not flavoured or with stuffing), sliced roast beef, hard salami (check nutrition information for sugar content), other cooked, cold sliced meats, salad and vegetable ingredients.
- **Freezer:** hamburger patties (real meat, check nutritional information for sugar content), lamb chops, mince, prawns, chicken breasts (individually wrapped for quick defrosting), chicken portions, frozen fish fillets (not crumbed or battered), marinara mix, prawns/shrimps, frozen berries, frozen vegetables.
- **Cupboard/pantry:** canned tuna, salmon, sardines, crabmeat, coconut cream, coconut oil, nuts, seeds, oil, spices, herbs, almond flour, Stevia/Xylitol.

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Turning lists into meals

Your objective is to build meals around a wide array of protein sources, natural fats and non-starchy vegetables.

- If you love salads, eat LOTS of them. A large salad made with two cups of salad leaves with additional vegetables from the list equates to around 15g of carbohydrate.
- If you prefer cooked vegetables, 2-3 cups of cooked vegetables from the non-starchy vegetable list is approximately 15g of carbohydrate. When cooking vegetables, steam, sauté, roast or stir-fry; don't boil them as this destroys some of their vitamins and minerals.
- Meats, poultry, fish and shellfish may be grilled, roasted, stir-fried or poached; not deep fried.
- Three meals a day is often enough to satisfy hunger (due to the higher fat content), but snacks may be needed. Everyone is different. Snacks should contain fat and protein – any vegetables (and down the line, fruit or berries) should be combined with fat/protein to minimise impact on blood sugar levels.
- While dessert options are provided below, desserts should be considered a treat and consumed in moderation.

The use of fat in cooking: which are the best to use?

The stability of the fat source at different temperatures help determine the best use of them in the diet.

Fats which contain a higher amount of saturated fats (coconut, butter, ghee, duck fat, tallow and lard) are more heat stable and are less likely to break down during cooking; these are a good option for panfrying. Both monounsaturated and polyunsaturated fats are not as heat-stable and will break down more easily during the cooking process. They will become oxidised, increasing their overall inflammatory effect in the body. As nut oils and olive oil are more delicate at higher temperatures, they are best used as a dressing or at the end of cooking to retain their nutritive value. As a guide, choose a cooking fat that has a smoking point just above 170-240° Celcius. Oils that have been extracted via a mechanical process (and not a chemical process) are also better options to use during cooking.

Keep in mind that deep-frying foods is not a good option; you should use enough cooking fat to be able to cook your food and no more.

Best for hot use	Best for cold use
Lard, duck fat, tallow	Olive oil
Ghee	Macadamia oil
Macadamia oil	Avocado oil
Avocado oil	Sesame oil
Refined and unrefined coconut oil	Hazelnut oil
Sesame oil	Almond/walnut oil
Extra virgin olive oil	Flaxseed oil
Almond/walnut oil	Butter
Butter	Unrefined coconut oil

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Breakfasts/first meals

These contain approximately 6-8g of CHO.

Basics:

- Bacon and eggs, cooked in olive oil, coconut oil or butter, served with vegetables (mushroom/avocado/spinach).
- Vegetable omelette, made with 2 or 3 eggs, added grated cheese and plenty of vegetables.
- A cup of mixed berries (fresh or frozen, thawed), with natural Greek yoghurt - add a sprinkle of nuts or LSA (linseed, sunflower, almond) or a tbsp of nut butter.
- Smoothie: Blend 1/2-1 cup frozen berries, 1/2 cup unsweetened soy/almond milk and 1/2 cup unsweetened coconut milk.
- In addition, have coffee with cream (keep within daily limits in total).

For the foodies:

- Fish cakes/hash browns: replace potato with cauliflower or swede. Serve with bacon, eggs and vegetables.
- Grilled stuffed mushrooms: Grill two Portabello mushrooms for a minute or so both sides (spray with olive oil).
- Top with minced beef and some grated cheese. Return to grill until golden.
- Mini frittata: stir-fry sliced spring onion and ~50g bean sprouts in a little olive oil or butter in an oven proof fry pan until soft. Add 2-3 beaten eggs and cook. Finish off under grill. Serve with soy sauce or some no-sugar added salsa. Add grated zucchini, spinach or leftover vegetables if desired.

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Snacks

These snacks contain no more than 5g CHO per serve.

Basics:

- 30g cheese
- 1/3 cup nuts (eg. almonds)
- 1-2 eggs
- Vegetables (i.e. carrot or cucumber sticks)
- 5-10 green/black olives
- 50g beef jerky/biltong (cured without sugar; check packet)

For the foodies:

- Celery stuffed with cream cheese.
- Cucumber 'boats' filled with tuna mixed with an olive-oil based mayonnaise .
- Half an avocado seasoned with salt and pepper.
- A lettuce leaf wrapped around grated cheddar cheese.
- A lettuce leaf wrapped around small amount shredded chicken, avocado and pesto.
- Chopped, sliced ham from bone (or other meat).
- Unsweetened Greek or natural yoghurt with a sprinkle of nuts/seeds.
- Wrap slices of cheese and ham around a couple of cucumber sticks and eat with a mayonnaise and mustard dip.
- Fill smoked salmon with cream cheese and wrap in a lettuce leaf or two

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Dessert

Remember desserts should be considered a treat and consumed in moderation.
These contain no more than 5g CHO per serve.

- Chocolate pudding: 2 tbsp double cream, 1 tbsp unsweetened cocoa and 1/2 tsp stevia or xylitol. Blend together until it has consistency of soft ice cream.
- Mocha pudding: as above and add 1 tsp instant coffee.
- Handful of berries with 1/3 c whipped coconut cream.
- Chocolate coconut pudding: as above but add 1 tbsp dried unsweetened coconut or 1 tsp coconut extract.
- Rhubarb: Cut 1 stalk into pieces and cook over low heat in a pot with a little bit of water until soft. Add 1/2 tsp stevia/xylitol and serve warm or cold with 2 Tbsp whipped cream. Serves 2.

Eating out

Eating out is a major barrier for people when changing their diet but doesn't need to be. Most eating places now have low or no-CHO options, and this is on the increase as this way of eating becomes more mainstream. Rather than avoid socialising with friends and family, go out and simply make the best choices and get comfortable with asking the waiter/waitress about the details of ingredients in meals. While there are many gluten-free options available, remember not to replace one CHO source with another. This can happen as gluten-free choices are typically as high in CHO as their gluten-containing counterparts.

- **Café meals**: Egg (omelettes, eggs benedict) and mince-based breakfast options (without toast). Add salmon, bacon or vegetable sides (e.g., spinach, mushrooms). Big breakfasts often have commercial sausages/hash browns which are high in CHO and low in quality – these are best avoided if in doubt. Green salad with olive oil based dressing is always a good option to include with a protein source. Avoid pre-made salads, unless you are sure of the ingredients. Choose coffee with a small amount of cream or milk, or non-milk based options (espresso, long macchiato), or tea (not chai tea).

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- **Restaurants**: scrutinise ingredients and choose foods wisely.
- Avoid fast food restaurants as appropriate choices are limited and the quality of ingredients is typically poor.
  - KFC: grilled chicken only and order side salads.
  - Burger places: Bun-less options only.
  - Subway/Burger King/McDonalds breakfast menu: scrambled eggs, no bun/bread/roll.
  - Subway/Pita Pit: avoid sugar-based sauces/meatballs/teriyaki (sauce will contain sugar). Select salad with meats, cheese and avocado. No seafood or tuna (as has mayonnaise containing sugar) and select oil-based vinaigrette dressings. Avoid bread products.
  - Lots of dressings and sauces have sugar added to make them taste good. Ask for ingredients or avoid.
  - Avoid deep fried, battered foods.
  - Avoid gravy.
  - Don't be afraid to ask for what you want. You are the one paying for it.
  - Don't believe everything you read: the nutritional information isn't always correct.
  - 'Healthy' doesn't mean healthy for you.
  - Exercise portion control.
  - Salad options are usually good; however, avoid croutons, obvious CHO additions (pasta/rice/couscous/orzo...) and check the dressing (see above).
- **Italian**: prosciutto, parmigiano reggiano, antipasto, caponata, most salads, meat, fish, poultry. AVOID pasta, risotto, pizza, deep fried calamari, garlic bread. Ask for a bowl of olives for starters. To end, order coffee with cream (unsweetened) instead of milk.
- **Middle Eastern**: baba ghanoush, grilled skewered meat.
- **Mexican**: salsa (no sugar), guacamole, grilled chicken wings, grilled chicken or fish, prawns in garlic sauce, chicken or mince based sauce.
- **Indian**: tandoori, meat and fish curries, grilled prawns, meat, chicken, korma, saag and paneer.
  - Avoid rice, naan bread, poppadoms, samosas. Order a side of mixed veggies instead.
- **Chinese**: egg drop soup (no cornflour), hot and sour soup, sizzling prawn platter, steamed beef, stir-fried chicken and garlic, peking duck.
- **Japanese**: miso, sashimi, grilled fish or squid, steamed and grilled vegetables, pickled vegetables.
- **Thai**: Be mindful with Thai food as it often contains palm sugar or sweet chilli sauce. Choose fish, seafood, pork, beef and/or vegetable dishes, main dish, curries and salads without these additions. Check the ingredients with the waiter or chef, and opt for no potatoes, rice or noodles.
- **Korean**: grilled or stewed fish and shellfish, marinated grilled pork, beef and chicken (no rice/noodles), kalbi beef, any BBQ dish (no sugary sauce), kimchi, pickles.

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Recipes

Thai Meat Loaf

SERVES: 4 | CARB COUNT: 2.8 g per serve | ENERGY: 209 Cal per serve.

Method:

Mix all ingredients in a bowl. Bake in a loaf tin lined with baking paper for around 1 hour, check by inserting a knife. If no juices come out, or the juices are clear, then your loaf is cooked. It should be brown on top and firm to touch.

Serve with coleslaw. For extra tasty coleslaw, add a small amount of finely sliced apple and fennel bulb to your usual coleslaw mixture. Use an olive oil-based aioli as a dressing (not the sachet included in the bag).

Leftovers are a good option for lunch the next day. Like many of these recipes, the flavours are as good (if not better) the following day.

Ingredients:

- 500g chicken mince (beef or lamb are also an option)
- 2 carrots grated
- 1 zucchini grated
- 1 small red onion finely chopped
- 1 tbsp each of crushed garlic and ginger
- 1 tbsp Thai red curry paste
- 1 tsp chilli paste
- 4 tbsp chopped fresh coriander
- Salt and pepper to taste

NOTES:

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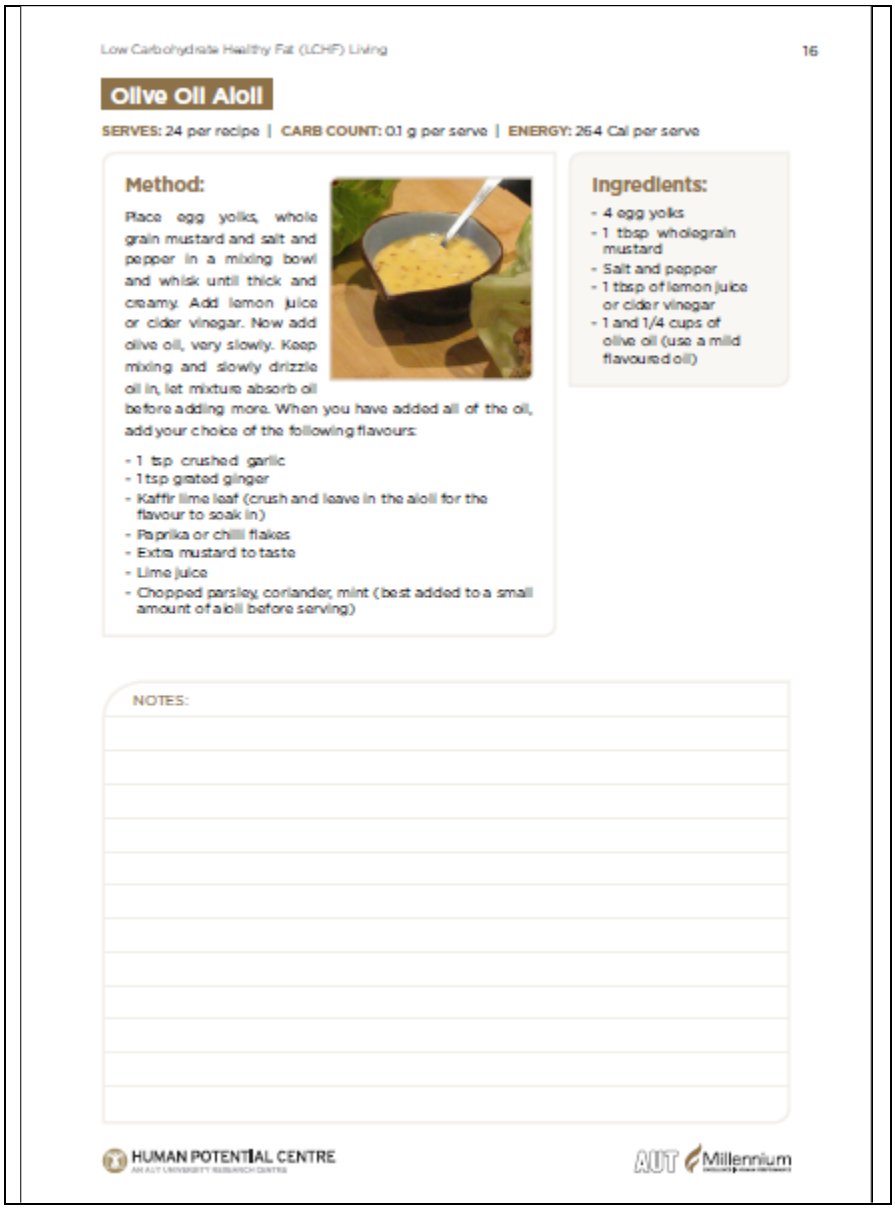

Olive Oil Aioli

SERVES: 24 per recipe | **CARB COUNT:** 0.1 g per serve | **ENERGY:** 264 Cal per serve

Method:

Place egg yolks, whole grain mustard and salt and pepper in a mixing bowl and whisk until thick and creamy. Add lemon juice or cider vinegar. Now add olive oil, very slowly. Keep mixing and slowly drizzle oil in, let mixture absorb oil before adding more. When you have added all of the oil, add your choice of the following flavours:

- 1 tsp crushed garlic
- 1 tsp grated ginger
- Kaffir lime leaf (crush and leave in the aioli for the flavour to soak in)
- Paprika or chilli flakes
- Extra mustard to taste
- Lime juice
- Chopped parsley, coriander, mint (best added to a small amount of aioli before serving)

Ingredients:

- 4 egg yolks
- 1 tbsp wholegrain mustard
- Salt and pepper
- 1 tbsp of lemon juice or cider vinegar
- 1 and 1/4 cups of olive oil (use a mild flavoured oil)

NOTES:

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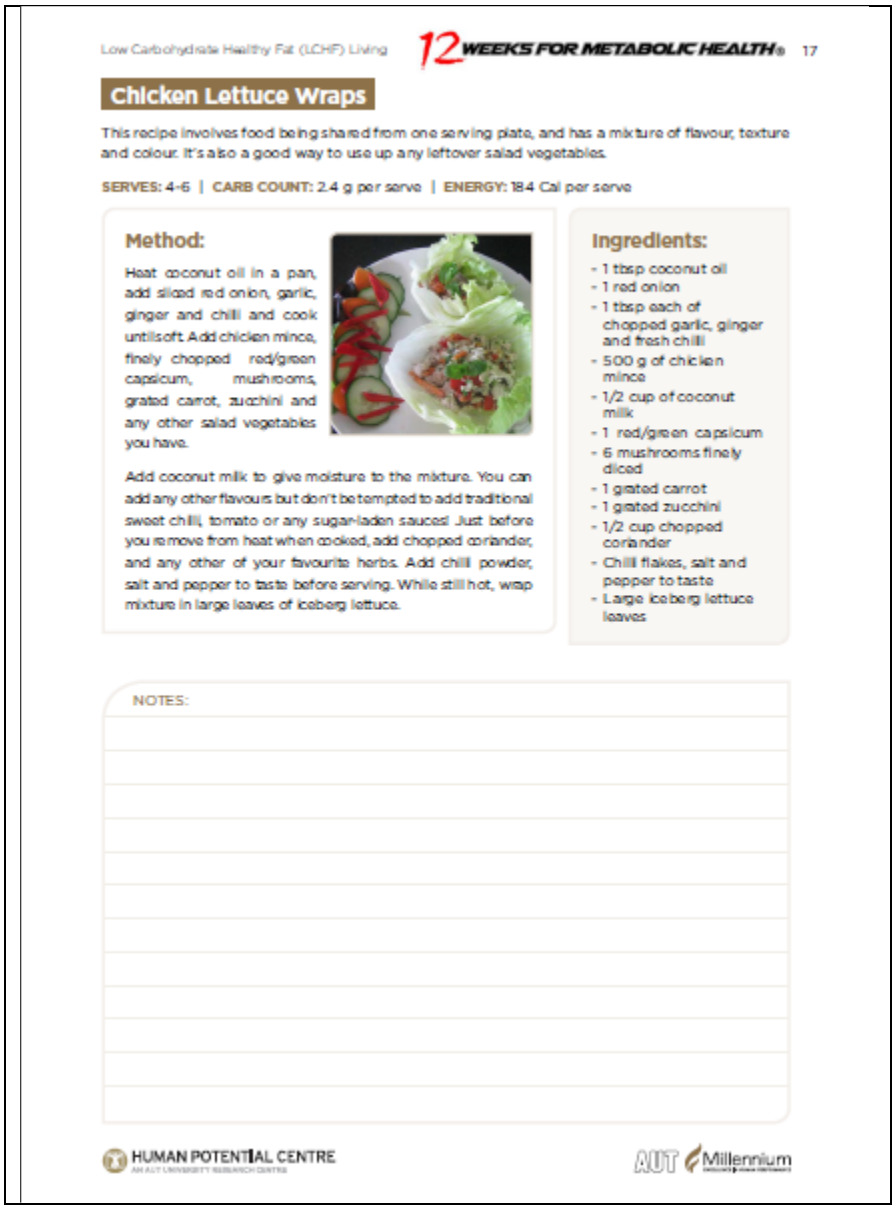

Chicken Lettuce Wraps

This recipe involves food being shared from one serving plate, and has a mixture of flavour, texture and colour. It's also a good way to use up any leftover salad vegetables.

SERVES: 4-6 | **CARB COUNT:** 2.4 g per serve | **ENERGY:** 184 Cal per serve

Method:

Heat coconut oil in a pan, add sliced red onion, garlic, ginger and chilli and cook until soft. Add chicken mince, finely chopped red/green capsicum, mushrooms, grated carrot, zucchini and any other salad vegetables you have.

Add coconut milk to give moisture to the mixture. You can add any other flavours but don't be tempted to add traditional sweet chilli, tomato or any sugar-laden sauces! Just before you remove from heat when cooked, add chopped coriander, and any other of your favourite herbs. Add chilli powder, salt and pepper to taste before serving. While still hot, wrap mixture in large leaves of iceberg lettuce.

Ingredients:

- 1 tbsp coconut oil
- 1 red onion
- 1 tbsp each of chopped garlic, ginger and fresh chilli
- 500 g of chicken mince
- 1/2 cup of coconut milk
- 1 red/green capsicum
- 6 mushrooms finely diced
- 1 grated carrot
- 1 grated zucchini
- 1/2 cup chopped coriander
- Chilli flakes, salt and pepper to taste
- Large iceberg lettuce leaves

NOTES:

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Creamy Chicken Casserole

This rich satisfying casserole gets more flavoursome overnight and leftovers make a great option for lunch the next day.

SERVES: 4 | CARB COUNT: 2.8 g per serve | ENERGY: 551 Cal per serve

Method:

Sauté chicken thighs in coconut oil with crushed garlic, chilli and ginger. When chicken has browned slightly, add cream, chicken stock, chilli powder and a sprinkle of chilli flakes. Cut capsicum, zucchini and onion into large chunks and add to the chicken cream mixture with whole button mushrooms and limes.

Pour into an oven dish, cover with tinfoil and bake at around 160oC for 60-90 minutes. The sauce should thicken and turn a rich red colour. Add chopped fresh parsley and spinach leaves before serving. Serve this dish on its own or with a side of cauliflower mash or cauliflower rice (see recipes below).

Ingredients:

- 6 chicken thighs (boneless or bone in)
- 1 tbsp each crushed garlic, chilli and ginger
- 1 cup of chicken stock
- 1/2 tsp chilli powder
- 1 cup of cream
- Chilli flakes
- 1 capsicum
- 1 onion
- 2 whole limes (cut into quarters)
- 6 whole button mushrooms
- Chopped fresh parsley
- Fresh spinach leaves

NOTES:

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Cauliflower Rice

This recipe is a great low CHO alternative to rice. For other flavours add turmeric, cumin or chilli. It makes for a great addition to salad-based lunches or as a side with your favorite curry.

SERVES: 4 (1 serve = 1 cup) | **CARB COUNT:** 31 g per serve | **ENERGY:** 59 Cal per serve

Method:

Chop cauliflower into chunks. Place half in the blender bowl and blend until cauliflower resembles rice. Transfer to a bowl and repeat with other half. Sauté onion in coconut oil and add season with salt, pepper and herbs if using.. Cook until cauliflower is just tender. Serve as an alternative to rice with a stir-fry or casserole.

Ingredients:

- 1 whole cauliflower
- 1 finely diced onion (optional)
- 1 tbsp coconut oil
- Coriander or parsley finely chopped (optional)
- Salt and pepper

NOTES:

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Cauliflower Mash

Cauliflower mash is a great alternative to mashed potato if you are trying to cut down on your starchy vegetables.

SERVES: 4 (1 serve = 1 cup) | **CARB COUNT:** 4.8 g per serve (when using milk)
ENERGY: 92 Cal per serve

Method:

Chop cauliflower into chunks, steam until tender. Drain and mix in a blender with butter and either milk, coconut milk, or cream, until smooth and creamy or the consistency of mashed potato. Add more milk if necessary. Season with salt and pepper.

Optional:

- Chopped parsley
- Parmesan or your favourite cheese
- Cauliflower mash can be used as an alternative topping to traditional Shepherd's pie, as a base to a creamy casserole, or to thicken a seafood chowder.

Ingredients:

- 1 head of cauliflower
- 2 tbsp butter
- 1/2 cup of milk, coconut milk, or cream
- Salt and pepper

NOTES:

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Margherita Cauliflower Pizza

And now for something completely different: Margarita Pizza with a wheat-free cauliflower base. Use leftover cauliflower mash to make this pizza base.

SERVES: 1 medium sized pizza base. CARB COUNT: 4.2 g per serve | ENERGY: 147 Cal per serve

Method:

Whisk cauliflower mash with eggs and grated cheese. Line a pizza pan with greaseproof paper, and spread cauliflower mixture. Bake at 180oC for around half an hour or until golden brown on top.

Remove from the oven and cool. Top with tomato paste, sliced tomato, basil leaves and grated cheese. Return to the oven and bake until cheese has melted and is golden brown on top. Alternatively top with your favourite pizza topping. Keep in mind that the base is not as firm as a traditional pizza base so a light, simple pizza topping is best.

Ingredients:

- 1 cup of leftover cauliflower mash
- 2 eggs
- 1 cup grated cheese
- 2 large tomatos sliced
- 1/2 cup tomato paste
- Basil leaves
- Grated cheese

NOTES:

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Zucchini Pesto Muffins

These muffins are great served hot or cold with butter and are a good snack for lunch boxes. They freeze well.

MAKES: 6 muffins | **CARB COUNT:** 2.4 g per serve | **ENERGY:** 156 Cal per serve

Method:

Mix the eggs, cream cheese and pesto together until well combined. Add the vegetables. Then sift in the dry ingredients. Spoon into large muffin cups/muffin tray and bake at 180oC for approximately

40 minutes or until firm to touch and golden brown on top.

This can also be made as a loaf (use a skewer to check if cooked through, it may require an additional 5-10 minutes cooking time).

This recipe has been adapted from Megan Roberts' recipe on the Primal Journey website.

Ingredients:

- 6 eggs
- 90g cream cheese, softened
- 1 tbsp pesto
- 1 large tomato, deseeded and chopped
- 1 spring onion, chopped
- 2 zucchinis (150 g each), grated and moisture squeezed out
- 20g coconut flour
- 20g almond meal
- 1 tsp baking powder
- Salt and pepper to taste

NOTES:

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Low Carb Lemon Cake

This cake has a strong lemony flavour and keeps well in the fridge for several days.

SERVES: 24 (small slices) | **CARB COUNT:** 0.8 g per serve | **ENERGY:** 123 Cal per serve

Method:

Beat eggs and sweetener until thick. In a food processor blend whole lemon, lime and juice until pulped. Fold together the pulped citrus, butter, egg mix, almond flour, baking powder and yoghurt. Pour into a greased ring tin and bake at

170oC for 35-40 minutes or until a skewer comes out clean. Cool in the tin and turn out when cold.

Icing Method:

Beat all ingredients together and ice cake when cold.

Ingredients:

- 1 whole lemon (and juice of another lemon)
- 1 whole lime (or an extra lemon)
- 6 eggs
- 3 tbsp Stevia or Xylitol (add an extra tbsp for a sweeter cake)
- 150g melted butter
- 1/2 cup natural yoghurt
- 1 cup almond meal/ flour
- 2 tsp baking powder

Icing:

- 100g cream cheese
- Lemon juice - to taste
- 1 tsp stevia/xylitol - to taste
- 1/2 cup thickened cream

NOTES:

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Banana Nut Butter Cake

This cake is great served hot or cold with butter or cream cheese.

SERVES: 24 (small slices) | **CARB COUNT:** 3.3g per serve* | **ENERGY:** 137 Cal per serve

**When made with peanut butter.*

Method:

Beat eggs and add mashed bananas and nut butter. Add in the remaining dry ingredients and mix well. Bake in a 30cm cake tin at 170oC for 25-30 minutes or until firm to touch.

Ingredients:

- 6 eggs
- 2 bananas mashed
- 1 cup peanut or cashew nut butter
- 1 cup almond meal
- 2 tsp baking powder
- 4 tsp ginger powder
- 1/4 cup chopped walnuts

NOTES: