

University of Porto

Faculty of Sport

Research Center in Physical Activity, Health and Leisure

**Combined exercise in individuals with type 2 diabetes:
mainly aerobic or resistance training?
The DICE intervention**

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Supervisor

Professor Doutor José Carlos Ribeiro

Co-Supervisor

Professora Doutora Joana Carvalho

César Filipe Chaves de Oliveira

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PALAVRAS-CHAVES: DIABETES TIPO 2; EXERCÍCIO COMBINADO; ATIVIDADE FÍSICA; NUTRIÇÃO; A1C.

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To my family

You are important!

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Table of contents

List of figures	XI
List of tables	XIII
List of attachments	XV
Resumo	XVII
Abstract	XIX
List of abbreviations	XXI
General introduction	23
Chapter 1	27
Theoretical background.....	29
Chapter 2	53
Experimental work.....	55
Paper I.....	57
Paper II.....	71
Paper III.....	93
Chapter 3	121
Overall discussion.....	123
Chapter 4	129
Conclusions.....	131
Perspectives for future research.....	132
References	133
Attachments	149

List of figures

Chapter 1

Figure 1. Worldwide diabetes prevalence and distribution..... 35

Chapter 2

Paper I

Figure 1. Search flow and results 60

Paper II

Figure 1. Percent of participants below, within or above
recommendations of selected nutrients and fiber intakes 81

Paper III

Figure 1. Participant’s flow chart 99

List of tables

Chapter 1

Table 1. Etiologic classification of diabetes mellitus.....	31
Table 2. Criteria for the diagnosis of diabetes	34
Table 3. Classification of physical activity intensity, based on physical activity lasting up to 60 min	47
Table 4. A comparison of the dietary guidelines for patients with type 2 diabetes, from the American Diabetes Association (ADA) and the International Diabetes Federation (IDF).....	48

Chapter 2

Experimental work

Table 5. Summary of the characteristics of the papers integrated in the dissertation	55
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Paper I

Table 1. General characteristics of combined exercise	61
Table 2. Combined exercise interventions and related glycated hemoglobin A (A1c) changes	62
Table 3. Combined exercise characteristics	64

Paper II

Table 1. Participant's main characteristics	79
Table 2. Participant's dietary intake characteristics	80
Table 3. Participant's daily physical activity characteristics	82

Paper III

Table 1. Baseline characteristics	105
Table 2. Hematologic data before and after intervention	106
Table 3. Body composition changes	107
Table 4. Physical fitness changes	108

List of attachments

Recruitment informative sheet.....	XXIII
Participant's informative sheet.....	XXIV
Informed consent.....	XXV
Letter to general physicians.....	XXVI
General questionnaire.....	XXVII
Food frequency questionnaire.....	XLI
Multipurpose evaluation sheet.....	XLVI
Workout sheet (front).....	XLVII
Workout sheet (back).....	XLVIII
Participant's insurance.....	XLIX
"How to properly exercise" leaflets.....	LII

Resumo

Introdução: A diabetes mellitus tipo 2 é uma das principais causas de mortalidade e morbidade mundiais. Apesar do avanço dos conhecimentos médicos e tecnológicos, a prevalência desta condição não cessa de aumentar, afetando já mais de 371 milhões de indivíduos. Sendo uma condição com etiologia essencialmente associada aos estilos de vida, diversas instituições de referência mundial têm emitido diretrizes para a adoção de determinados comportamentos alimentares e relativos à atividade física, onde se inclui a realização de exercícios aeróbios e de força. Todavia, os dados relativos às características nutricionais e de atividade física diária em populações portuguesas com diabetes do tipo 2 são escassos, e as características fundamentais que os programas de exercício combinado devem incluir ainda não são conhecidas. **Objetivos:** Os objetivos principais desta tese foram: analisar os efeitos do treino combinado e identificar as suas características mais relevantes para o controlo glicémico; analisar as características nutricionais e relativas à atividade física habitual, de uma amostra da população portuguesa, comparando esses dados com as recomendações internacionais; e comparar a eficácia de dois tipos de treino combinado no controlo glicémico, em indivíduos com diabetes do tipo 2. **Métodos:** para o primeiro objetivo foi realizada uma revisão sistemática da literatura referente ao treino combinado em indivíduos com diabetes do tipo 2 (n=2093); posteriormente, uma amostra de indivíduos com diabetes do tipo 2 foi selecionada (n=101), sendo recolhidos os dados hematológicos (A1c, glicose e insulina em jejum, perfil lipídico, PCR, HOMA-is e HOMA-bcf), sobre a composição corporal (DXA e antropometria), atividade física diária (Actigraph; GT3X) e hábitos alimentares (diário alimentar de três dias), sendo os últimos comparados com as recomendações do Colégio Americano de Medicina Desportiva, da Associação Americana de Diabetes e da Federação Internacional da Diabetes; finalmente, a partir desta amostra foram aleatoriamente selecionados 35 indivíduos para integrar um grupo de exercício combinado com ênfase na componente aeróbia, (45 minutos aeróbio, 15 minutos força), outro grupo com ênfase na componente de força (15 minutos aeróbio, 45 minutos força), ou um grupo de controlo. A intervenção durou 20 semanas, sendo 3 os treinos semanais, em dias não consecutivos. A intensidade do treino aeróbio foi definida com um mínimo de 55% da frequência cardíaca máxima e a intensidade do treino de força foi de 70% de 1 repetição máxima. **Resultados:** Os nossos dados confirmaram a relevância do treino combinado para um melhor controlo glicémico, em relação a formas isoladas de exercitação; a maior parte dos indivíduos com diabetes do tipo 2 não seguia as recomendações relativas aos hábitos nutricionais e de atividade física diária; o treino combinado com ênfase na componente aeróbia foi o mais eficaz na redução dos valores glicémicos. **Conclusões:** Idealmente, os programas de treino devem conjugar os exercícios aeróbios com os de força. A adesão às recomendações internacionais relativas à nutrição e atividade física deve ser incrementada, já que os baixos níveis de cumprimento encontrados na nossa amostra podem comprometer uma maior eficácia das intervenções para a prevenção e o controlo da diabetes tipo 2. Finalmente, os programas de exercício combinado devem privilegiar o treino aeróbio para um melhor controlo da glicemia nestas populações.

PALAVRAS-CHAVE: DIABETES TIPO 2; EXERCÍCIO COMBINADO; ATIVIDADE FÍSICA; NUTRIÇÃO; A1C.

Abstract

Introduction: Type 2 diabetes mellitus is one of the leading causes of mortality and morbidity across the globe. Despite the outstanding medical, technological and care breakthroughs of the past decades, the prevalence of this condition increases relentlessly, affecting already more than 371 million persons. As this condition is largely associated with specific lifestyles, several of the leading diabetes institutions have issued their recommendations for dietary intake and daily physical activity, including the performance of both aerobic and resistance activities. Nevertheless, data on the dietary and daily physical activity characteristics of Portuguese individuals with type 2 diabetes is scarce, and the main features of combined exercise interventions are still unknown. **Goals:** the goals of our work were: to analyze the effects of combined exercise interventions and identify their most relevant features; to analyze the dietary intake and daily physical activity characteristics of a Portuguese sample and compare them to international recommendations; and to compare the efficacy of two different combined interventions on the glycemic control of individuals with type 2 diabetes. **Methods:** for our first goal, a systematic review of the literature on combined exercise interventions was conducted (n=2093); then, a sample of individuals with type 2 diabetes was selected (n=101) and data on their hematological markers (A1c, fasting glucose and insulin, lipid profile, CRP, HOMA-is e HOMA-bcf), body composition (DXA e anthropometry), daily physical activity (Actigraph; GT3X) and dietary intake (3-day food diary), was collected and compared to recommendations from the American College of Sports Medicine, American Diabetes Association and International Diabetes Federation; finally, from this sample, 35 individuals were randomly allocated to a combined exercise group with emphasis on the aerobic component (45 minutes aerobic, 15 minutes resistance), to a combined exercise group with emphasis on the resistance component (15 minutes aerobic, 45 minutes resistance), or a control group. Intervention took place 3 days/week, in non-consecutive days, for 20 weeks. Aerobic intensity was set at a minimum of 55% of predicted maximal heart rate and resistance exercise intensity was set at 70% of 1 repetition maximum. **Results:** Our data confirmed the more pronounced effects of combined exercise for improved glycemic control, when compared to isolated forms of exercise; most of the participants in our study did not complied with recommendations for dietary intake and daily physical activity; combined exercise that emphasized the aerobic component was the most effective at reducing blood glucose levels. **Conclusions:** Ideally, exercise programmes should include both aerobic and resistance activities. Efforts to raise compliance with international recommendations for dietary intake and daily physical activity should be implemented, as the low levels found in our sample may compromise the outcomes of interventions for type 2 diabetes prevention and management. Finally, combined exercise interventions should emphasize the aerobic component for optimal glycemic control on these populations.

KEY WORDS: TYPE 2 DIABETES; COMBINED EXERCISE; PHYSICAL ACTIVITY; NUTRITION; A1C.

List of abbreviations

A+	45 min of aerobic exercise + 15 min of resistance exercise
A1c	Glycated hemoglobin A1c
ACSM	American College of Sports Medicine
ADA	American Diabetes Association
Aer	Aerobic Exercise Group
Aft.	After Intervention
Alt	Aerobic and resistance training performed on alternate sessions
Bef.	Before intervention
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
BW	Body Weight
BWP	Brisk Walking Programme
Com	Combined exercise
CrP	C-reactive Protein
DBP	Diastolic Blood Pressure
DEI	Dietary Energy Intake
DICE	Diabetes Combined Exercise
Dif	Absolute Difference
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
DPS	Diabetes Prevention Study
DXA	Dual Energy X-ray Absorptiometry
E+A	Exercise + Acarbose Group
EB	Elastic Bands
EDIPS	European Diabetes Prevention Study
EPOC	Excess Post-exercise Oxygen Consumption
FFM	Fat Free Mass
FPG	Fasting Plasma Glucose
Freq.	Frequency
Glut-4	glucose transporters type 4
HDL-cholesterol	High Density Lipoprotein – Cholesterol
HOMA-bcf	homeostasis model assessment – beta cell function
HOMA-is	homeostasis model assessment – insulin sensitivity
HRmax	Maximal Heart Rate
HRpeak	Heart Rate Peak

HRr	Heart Rate Reserve
HV	High Volume
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IRS-1	insulin receptor substrate-1
LDL cholesterol	Low Density Lipoprotein – cholesterol
Len.	Length
LV	Low Volume
ma	More exercises available
METS	Metabolic Equivalents
MFP	Medical fitness programme
MNT	Medical Nutrition Therapy
Mo	Month
mTOR	mammalian target of rapamycin/serine
na	non available
NGSP	National Glycohemoglobin Standardization Program
no. exe.	Number of exercises
OGTT	Oral Glucose Tolerance Test
pHRmax	Predicted Maximal Heart Rate
PI 3-kinase	phosphatidylinositol-3-kinase
R+	15 min of aerobic exercise + 45 min of resistance exercise
Reps	Repetitions
Res	Resistance Exercise Group
RM	Repetition Maximum
RMR	Resting Metabolic Rate
RPE	Rate of Perceived Exertion
SBP	Systolic Blood Pressure
Sig.	Significance
T2DM	Type 2 Diabetes Mellitus
USA	United States of America
VO ₂ max	Maximal Oxygen Consumption
VO ₂ R	Oxygen Consumption Reserve

General introduction

Diabetes Mellitus is a leading cause of morbidity and mortality in developed countries. Even when optimal treatment conditions are available, life expectancy can be reduced by as much as 15 years (Davies et al., 2004). In the last decades we have witnessed many medical and technological breakthroughs as well as treatment innovations, but despite that, the global number of adults with this condition already exceeds 8% of the total population and might be raising at a faster pace than previously expected (Whiting et al., 2011). It is a globally spread condition but some countries are especially affected, showing a diabetes prevalence that surprisingly exceeds 25% of its inhabitants, according to data from the International Diabetes Federation (IDF) (IDF, 2011).

Since the countries that are especially affected are the developed and developing ones, environmental and lifestyle characteristics have long been considered as critical factors for the progression of diabetes, and particularly type 2 diabetes. By pursuing a magical treatment that would prevent diabetes incidence, research has focused on a variety of pharmacological, dietary and physical activity interventions, which led to very promising and encouraging results. At a lower cost and with fewer adverse side effects, lifestyle modifications seem to be at least as effective as drug therapies, cutting by half the risk of diabetes development in individuals with impaired glucose tolerance (Knowler et al., 2002). In plain terms, this means that by adopting a “healthy” lifestyle, people can stay healthier for longer periods of time and delay or even prevent the onset of diabetes. However, some high-risk individuals eventually end up developing diabetes. In these, the standard treatment is engaged and many patients are generally able to control their glycemic levels to some extent. When diabetes is already present, some interventions can significantly reduce A1c hemoglobin levels (A1c, an indicator of the average glucose concentration over the past few weeks) (Sacks, 2011). Most surprisingly, a few studies show that whether by following a specific diet, combining exercise and diet or by caloric restriction, many individuals can achieve and maintain normal glucose

levels without the aid of drug therapies (Lim et al., 2011; Lindeberg et al., 2007; Roberts et al., 2006; Taylor, 2013; Williams et al., 1998). This diabetes reversal challenges previously established concepts about diabetes and glycemic control, but most of all, it encourages researchers to pursue the optimal treatment for this debilitating disease.

Several studies have shown that an exercise only intervention is able to reduce blood glucose levels (Colberg et al., 2010) but the effects of exercise are much more comprehensive than their specific glycemic action. This influence is highlighted by two studies that revealed that exercise capacity can predict the mortality risk of diabetic patients independently of body mass index (BMI) (Church et al., 2004), and that although unfit and sedentary diabetic individuals exhibit an increased cardiovascular disease risk, the dose–response relationship for physical activity/fitness is such that when they undertake high levels of activity (or have high fitness), their level of risk becomes similar to that of their normal weight or non-diabetic peers (Gill & Malkova, 2006). Aerobic and resistance exercises have been recommended for those with diabetes and although both forms can reduce blood glucose levels, their action mechanisms are thought to be different. While aerobic exercise seems to reduce glycemic levels through acute and repetitive bouts of exercise (Colberg & Grieco, 2009), resistance training seems to exert its glycemic lowering effects by increases in muscle mass and glucose uptake (Roden, 2012). Recently, researchers started analyzing the effects of combined exercise on glycemic control. The earliest study found that there were no differences among a combined intervention and the control group (Tessier et al., 2000). In both cases, A1c was raised after intervention, but to a lesser extent in the intervention group. Later, in 2004, other larger trial, with a similar intervention found that only the combined exercise group was able to reduce A1c levels, by a significant 1,2% (Balducci et al., 2004). Finally, another study compared the effects of combined exercise to isolated aerobic exercise, isolated resistance exercise, and a control group (Sigal et al., 2007). Although all exercise groups managed to reduce blood glucose levels, the highest reduction was found in the combined exercise

intervention. However, these results must be taken with care, as caloric expenditure was higher in the latter.

Presently it is thought that combined interventions seem to generate a better glycemic control than isolated forms of exercise, indicating that the effects of aerobic and resistance training may be synergistic. Guidelines from renowned institutions endorse individuals with type 2 diabetes to undertake an active lifestyle and to implement an exercise program that includes both aerobic and resistance exercises (Colberg et al., 2010). However, the optimal relationship between the aerobic component and the resistance component remains unaddressed and therefore, unknown. The possibility of additional benefits by favoring a certain type of exercise should not be neglected, as it could distinctly alter body composition and hematological markers. The results from this study are expected to be easily applicable and should provide additional information on the optimal exercise prescription for individuals with diabetes.

Finally, it is recognized that diabetes management comprises more than the exercise training part. An adequate diet and an active lifestyle are also determinants of the overall health of these populations. Nevertheless, little is known about these features in Portuguese individuals with diabetes. During the course of the experimental part of this thesis, we also aim to provide information on these important issues.

To reach these general topics, specific goals were drawn which led to the following original papers:

1. to review the effects of combined interventions on glycemic control and the training characteristics of combined interventions

Paper I – Oliveira C, Simões M, Carvalho J, Ribeiro J. Combined exercise for people with type 2 diabetes mellitus: A systematic review. Diabetes research and clinical practice. 2012: 10.1016/j.diabres.2012.08.004

2. to assess nutritional intakes and daily physical activity of a Portuguese sample comprised of individuals with type 2 diabetes and their compliance with guidelines.

Paper II – Oliveira, C; Abreu, S; Carvalho, J; Ribeiro, JC. Nutrition and physical activity characteristics of Portuguese older individuals with type 2 diabetes: compliance with recommendations. [submitted – under review]

3. to compared the glycemic effects of two combined exercise interventions, one with emphasis on the aerobic component, other with emphasis on the resistance component.

Paper III - Oliveira, C; Carvalho, J; Abreu, S; Chen, KY; Ribeiro, JC. Combined Exercise in individuals with type 2 diabetes: emphasis on the aerobic component. A Randomized, Controlled Trial. [submitted – under review]

Thus, the present dissertation is organized into four chapters. Chapter 1 provides a broad theoretical background to diabetes. Chapter 2 describes the experimental work, including the papers published or submitted to peer-reviewed scientific journals. An overall discussion is presented in Chapter 3, and in Chapter 4, the main conclusions of the present thesis and perspectives for future research are exposed.

Chapter 1

Theoretical background

Diabetes Mellitus

Definition of diabetes

The term *diabetes* refers to one of the symptoms usually associated to this condition, which is polyuria (excessive or abnormally large production or passage of urine). As a second century AD Greek physician, Aretus the Cappadocian, noted that some individuals “passed water like a siphon”, he termed the condition *diabetes*, which is derived from the Greek for “a passer through, a siphon” (Zisser et al., 2010). Latter in the 17th century, Thomas Willis added the term *mellitus*, from the latin “sweet as honey”, because the urine of individuals with diabetes had a sweetened flavor (Eknoyan, 2010). It was only almost a century later that Matthew Dobson (1775) experimentally showed that the sweetness in urine was due to the presence of glucose. In the same year, a distinction between diabetes with glucose in urine (*vera*, or *mellitus*) and diabetes without glycosuria (*insipidus*) was made. However, the two forms of diabetes are physiologically distinct and most people would only associate diabetes to its *mellitus* form. This thesis only addresses diabetes mellitus but the terms *diabetes* and *diabetes mellitus* are assumed as interchangeable, from this point onward.

According to the American Diabetes Association (ADA), diabetes can be defined as a group of metabolic diseases and is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (ADA, 2013a). Among other functions, insulin is a hormone that reduces blood glucose levels by increasing cellular glucose uptake. Under normal conditions, it is continuously produced by β -cells in the pancreas and the rate of excretion is increased in response to an elevation in glycemia or aminoacidemia (ADA, 2013b).

Chronically elevated levels of plasma glucose can cause damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. In particular, the long-term complications of this

condition include retinopathy with potential loss of vision, nephropathy leading to renal failure, peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints. Autonomic neuropathy can also lead to gastrointestinal, genitourinary, cardiovascular symptoms and sexual dysfunction. Frequently, individuals with diabetes exhibit an altered lipid profile and/or hypertension along with increased plasma glucose values.

Diabetes progression might occur silently and many people are not aware that they may be living with such disease. When present, the most common symptoms of hyperglycemia include polyuria, polydipsia (excessive thirst), weight-loss or weight-gain and blurred vision. Not rarely, it is the onset of these symptoms that drive individuals to attend their physician, who eventually confirms the disease through a series of blood tests.

Classification of diabetes

An early diagnosis of diabetes is relevant to attenuate disease progression and improve patient's quality of life and life expectancy. There are 2 main categories of diabetes (ADA, 2013a): individuals with type 1 diabetes cannot produce insulin, because their β -cells have been destroyed by a cellular-mediated autoimmune condition. Type 1 diabetes was formerly known as insulin-dependent diabetes, or juvenile diabetes, but as these can occur for other reasons than auto-immune destruction, those terminologies have been abandoned. Type 1 diabetes accounts from 5 to 10% of all diabetic cases. Genetic predispositions and environmental factors are thought to underlie the auto-immune response, but the mechanisms are still poorly understood.

The most prevalent form of diabetes, type 2 diabetes, represents the large majority of the diabetes cases (ADA, 2013a). In this condition, the cells in the body display a compromised insulin response, resulting in a reduced plasma glucose uptake. As high glucose values endure, a compensatory hyperinsulinemia can coexist with hyperglycemia. Over time, the overexpression of insulin can fatigue the β -cells, leading to an insufficient insulin secretion. As such, some of the individuals with type 2 diabetes might eventually need external insulin therapy.

A 3rd type of diabetes can be considered. In this case, etiology can be adequately defined. Primary causes range from genetic defects, to infections or drug-induced diabetes, among others.

Finally, a 4th form of diabetes (gestational diabetes) can be considered, when it onsets or is first recognized during pregnancy and can be defined as any degree of glucose intolerance during this period. It usually resolves with delivery, but it can persist in some women. Approximately 7% of all pregnancies are complicated by gestational diabetes, resulting in more than 200,000 cases annually.

Table 1 describes the etiologic classification of diabetes (ADA, 2013a).

Table 1 - Etiologic classification of diabetes mellitus.

I. Type 1 diabetes β -cell destruction, usually leading to absolute insulin deficiency)
A. Immune mediated
B. Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III. Other specific types
A. Genetic defects of β -cell function
1. MODY 3 (Chromosome 12, HNF-1a)
2. MODY 1 (Chromosome 20, HNF-4a)
3. MODY 2 (Chromosome 7, glucokinase)
4. Other very rare forms of MODY (e.g., MODY 4: Chromosome 13, insulin promoter factor-1; MODY 6: Chromosome 2, NeuroD1; MODY 7: Chromosome 9, carboxyl ester lipase)
5. Transient neonatal diabetes (most commonly ZAC/HYAMI imprinting defect on 6q24)
6. Permanent neonatal diabetes (most commonly KCNJ11 gene encoding Kir6.2 subunit of β -cell KATP channel)
7. Mitochondrial DNA
8. Others
B. Genetic defects in insulin action
1. Type A insulin resistance

2. Leprechaunism
3. Rabson-Mendenhall syndrome
4. Lipoatrophic diabetes
5. Others
C. Diseases of the exocrine pancreas
1. Pancreatitis
2. Trauma/pancreatectomy
3. Neoplasia
4. Cystic fibrosis
5. Hemochromatosis
6. Fibrocalculous pancreatopathy
7. Others
D. Endocrinopathies
1. Acromegaly
2. Cushing's syndrome
3. Glucagonoma
4. Pheochromocytoma
5. Hyperthyroidism
6. Somatostatinoma
7. Aldosteronoma
8. Others
E. Drug or chemical induced
1. Vacor
2. Pentamidine
3. Nicotinic acid
4. Glucocorticoids
5. Thyroid hormone
6. Diazoxide
7. β -Adrenergic agonists
8. Thiazides
9. Dilantin
10. γ -Interferon
11. Others
F. Infections

1. Congenital rubella
2. Cytomegalovirus
3. Others
G. Uncommon forms of immune-mediated diabetes
1. "Stiff-man" syndrome
2. Anti-insulin receptor antibodies
3. Others
H. Other genetic syndromes sometimes associated with diabetes
1. Down syndrome
2. Klinefelter syndrome
3. Turner syndrome
4. Wolfram syndrome
5. Friedreich ataxia
6. Huntington chorea
7. Laurence-Moon-Biedl syndrome
8. Myotonic dystrophy
9. Porphyria
10. Prader-Willi syndrome
11. Others
IV. Gestational diabetes mellitus
Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

Diagnostic criteria for Diabetes Mellitus

Diabetes can be confirmed through simple blood test analyses that access blood glucose values directly or indirectly (ADA, 2013a). Traditional methods analyze fasting or non-fasting glycemic scores and the glycemic response to an ingested glucose load. More recently, physicians use an indirect indicator of the average glucose concentrations over a more extended period of time, by analyzing the non-enzymatic attachment of glucose to the N-terminal valine of the β -chain of hemoglobin. As erythrocytes life span is around 120 days, A1c represents the average glucose concentration over the preceding 8–12 weeks (Sacks, 2011). This chronic marker for glycemia has several advantages to

fasting blood glucose analysis, including greater convenience since fasting is not required, and less day-to-day perturbations during periods of stress, illness or sudden changes in physical activity or dietary patterns. However, the greater cost of A1c testing and the limited availability of in certain regions of the developing world may limit an adequate widespread of this method of analysis.

As with most diagnostic tests, a positive result should be followed by a repetition of the test to rule out laboratory error, unless the results serve only to confirm classical symptoms of hyperglycemia of a given subject.

The specific cut-points for diagnostic criteria can be found in table 2 (ADA, 2013a).

Table 2 - Criteria for the diagnosis of diabetes.

A1C $\geq$ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
or
FPG $\geq$ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.*
or
2-h plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
or
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l).

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.

Some individuals who do not have diabetes may display higher than normal glucose values. These individuals are defined as having impaired fasting glucose (IFG) when increased fasting plasma glucose levels are present, yet not high enough as the cut-points to diabetes, or impaired glucose tolerance (IGT) when individuals exhibit a compromised response to the oral glucose

tolerance test (OGTT). People with IFG and/or IGT have been referred to as having pre-diabetes, and are at a higher risk of developing diabetes in the future. As such, an early detection of pre-diabetes should drive physicians and patients to engage in specific measures to reduce the risk of developing diabetes and maintaining life expectancy and quality-of-life.

Diabetes in the world

Diabetes can be found in every country in the world and despite the growing awareness and development of prevention and management programs, the number of individuals affected is increasing at a faster pace than previously expected (Danaei et al., 2011). The most common form of this disease, type 2 diabetes, is now a common and serious global health problem, which, for most countries, has developed together with rapid cultural and social changes, ageing populations, increasing urbanization, dietary changes, reduced physical activity, and other unhealthy behaviors. According to the latest global data for the prevalence of diabetes, it is estimated that 371 million people or 8.3% of the total population is living with this condition (IDF, 2011) (Fig.1).

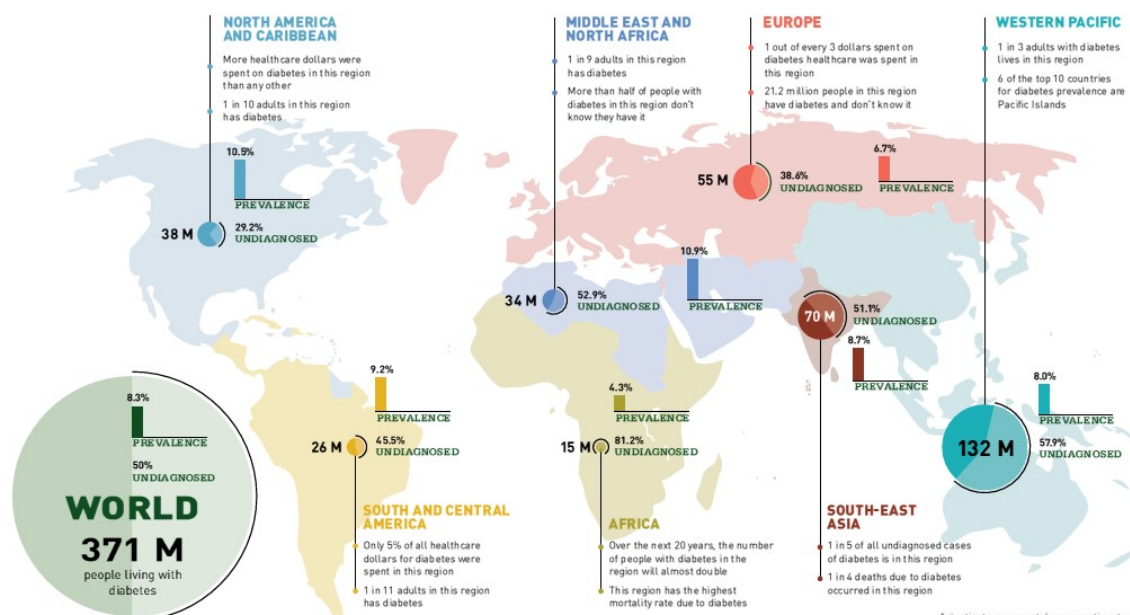


Fig. 1 – Worldwide diabetes prevalence and distribution (reprinted with permission of International Diabetes Federation).

In absolute terms, the countries with the highest number of people with diabetes are China (92.3 million), India (63.0 million) and the United States of America (USA) (24.1 million). Together, the top 10 countries represent more than 75% of all cases of diabetes in the world, and with the exception of the USA and Japan, all are middle-income countries and rapidly developing. However, when it comes to prevalence, we find that the top 10 countries are generally small in size and/or population. In the Federate States of Micronesia, more than 1/3 of the population has diabetes. The next four and the 10th countries are all from Oceania and are joined by four middle-east countries, and all exceed 20% of diabetes prevalence. It is believed that ethnicity and changing lifestyles are largely to blame for the high percentages of diabetes in such regions of the world.

Worryingly, 50% of the people with diabetes do not know they have the disease. As diabetes can go many years without showing symptoms, or symptoms may be neglected or misdiagnosed as other conditions, when the condition is finally identified, many organs may already reveal signs of advanced damage. Africa is the leading continent in terms of undiagnosed diabetes, with 81% of the total diabetes cases. Even in Europe, the estimate of 38% of undiagnosed cases is still very far from ideal and reveals a relative lack of awareness of the disease, both in the public and in the health community (IDF, 2011).

Increasing age is associated with higher diabetes prevalence. For example, at age 35, prevalence is less than 5%, but can surpass 20% at age 70. This phenomenon is especially observed in high-income countries. Nevertheless, half of the people who die from diabetes are under the age of 60.

Diabetes is also a burden in relation to health care costs. For example, in 2012, 471 billion US dollars were spent due to such disease. However, there is a great discrepancy between the amounts of investment in high-income countries compared to all the others. While the previous spent 387 million dollars, upper middle-income and lower middle-income countries spent 53 and 29 million dollars, respectively. As expected, low-income countries spent the least amount of money (1,2 millions).

Diabetes in Portugal

In Portugal, 12,7% of the population (approximately 1 million of individuals) between 20 and 79 years has diabetes, according to the *Relatório Anual do Observatório Nacional da Diabetes* (Gardete et al., 2013). Of these, it is estimated that 44% of the cases are not yet diagnosed. Similarly to global patterns, age is a risk factor for this condition. Between 20 to 39 years of age, only 2,6% of men and 1,5% of women are affected. However, between 40 and 59 years of age, prevalence raises dramatically, affecting 17,5% of men and 8,2% of women. As expected, the higher prevalence is among those with 60-79 years, where 30,3% of the men and 24,4% of the women are living with diabetes. These data also indicate that men have higher rates of diabetes prevalence than women (15,2% vs 10,4%), phenomenon that has consistently been observed worldwide (Danaei et al., 2009; Smith, 2007; Yang et al., 2010). Although the action mechanisms are not fully understood, it is believed that men develop diabetes at a lower BMI than women (Logue et al., 2011). This can be partially explained by a lower insulin sensitivity at a given BMI (Logue et al., 2011), the fact that middle-aged men generally have higher fasting glucose levels, higher triacylglycerol and lower high density lipoprotein cholesterol (HDL-cholesterol) levels than women of a similar age (even after adjusting for BMI) (The Emerging Risk Factors Collaboration, 2009, 2010) and the fact that men have greater visceral and hepatic fat compared with women (Logue et al., 2011). Furthermore, there is a relationship between BMI and diabetes prevalence. For example, it is estimated that 20% of the individuals with a BMI higher than 30 kg/m² (obese category) have diabetes, compared to only 5,7% of individuals with a BMI lower than 25 kg/m² (normal weight category). In fact, almost 90% of all individuals with diabetes are overweight (BMI of 25-29,9 kg/m²) or obese. More worrying is the data concerning individuals who do not have diabetes, but already exhibit IFG and/or IGT. These, together with those with diabetes represent almost 40% of the total Portuguese population.

Cases of type 1 diabetes among children and adolescents have remained relatively constant since 2008 to 2012 (0,14% of the total population). However,

gestational diabetes prevalence has increased over the past few years and now reaches almost 5% of the expecting mothers.

In Portugal, diabetes seems to shorten life expectancy by 7 years, and is responsible for 4,4% of all deaths. However, this percentage did not increase significantly over the past 10 years and seems to have plateaued (Gardete et al., 2013).

It is estimated that the direct costs of diabetes in Portugal range from 1.2 to 1.45 million of euros, which represents 0.8% of the Portuguese gross domestic product and 8% of the total health care costs. Most of this investment is due to hospitalizations and cost of diabetes medications (Gardete et al., 2013).

Etiology of Diabetes

The etiology of diabetes is not fully understood. However, it is widely recognized that the causes seem to be of multifactorial nature and that both genetic and environmental factors play a contributing role (ADA, 2013b).

Type 1 diabetes may not be a genetically predestined condition, but an increased susceptibility can be inherited. Several genetic markers have been found to significantly increase the risk of developing type 1 diabetes (Trevisan et al., 1998). In particular, specific combinations of proteins produced by human leukocyte antigens seem to be of great importance for genetic inducement of type 1 diabetes (Noble & Valdes, 2011). Autoimmune destruction of β -cells is one of the most well recognized causes for this type of condition. As T-cells attack and destroy β -cells, the pancreas ability to produce insulin gradually decreases. Finally, several environmental factors, including foods, viruses, and toxins, also play a role in the development of type 1 diabetes.

The causes for type 2 diabetes, of special interest for this thesis, can also be attributable to genetic factors (Grant et al., 2009; Lindgren & McCarthy, 2008), but seem to be much more related to lifestyle behaviors. As shown in numerous studies, physical inactivity and obesity are strongly associated with the development of type 2 diabetes (Chan et al., 1994 ; Gillies et al., 2007; Knowler et al., 2002; Pan et al., 1997). The Da Qing study in China included an

exercise-only treatment arm and reported that even modest changes in exercise (20 min of mild or moderate, 10 min of strenuous, or 5 min of very strenuous exercise one to two times a day) reduced diabetes risk by 46% (compared with 42% for diet plus exercise and 31% for diet alone) (Pan et al., 1997). Other two studies, the Finnish Diabetes Prevention Study (DPS) (Eriksson et al., 1999) and the U.S. Diabetes Prevention Program (DPP) (Knowler et al., 2002) included intensive, lifestyle modifications with both diet and increased physical activity. Lifestyle modification in both studies reduced incident diabetes by 58% and, in the DPP, had a greater effect than metformin (31%). The European Diabetes Prevention Study (EDIPS) extended the DPS to different European populations, using the same study design, and reached similar results (Penn et al., 2009). Weight loss was the dominant predictor of a lower incidence, but increased physical activity reduced the risk of type 2 diabetes even when weight loss goals were not achieved. These preventive effects of physical activity seem to occur across ethnic groups and in both sexes. In general terms, lifestyles interventions have shown to be at least as effective as the pharmacological ones in the prevention of type 2 diabetes (Gillies et al., 2007). Finally, other phenomena like oxidative stress (Henriksen et al., 2011) and endocrine disruptors (Alonso-Magdalena et al., 2011) are also known to increase the risk of developing diabetes.

Diabetes: a lifelong disease or a reversible condition?

Considered as a lifelong disease for many years, there is now sufficient evidence to state that type 2 diabetes can be reversed (individuals are able to maintain blood glucose levels under a normal range, without the use of glucose-lowering medications). In fact, the earliest evidence of that came from a study conducted more than 20 years ago, when a surgical treatment for obesity led to normalization of glycemia. More interestingly, 90% of the subjects remained free of diabetes at least 10 years after procedure (Pories et al., 1992). Medical surgical procedures targeted for weight loss have proven to be effective in diabetes reversal (Dixon et al., 2008) but the effects seem to be more related to the weight loss in itself than the procedures used (Ferrannini & Mingrone,

2009). Furthermore, the onset of glucose normalization only days after procedure, caused by an acute reduction of caloric intake, was found to be strongly associated with a marked reduction in liver fat (Colles et al., 2006). Since then, other researchers have been shown that whether by caloric restriction (Lim et al., 2011; Petersen et al., 2005; Petersen et al., 2012; Williams et al., 1998), by following a specific diet (Lindeberg et al., 2007) or combining exercise and diet (Roberts et al., 2006), diabetes can be reversed. Insulin resistance in muscle is the earliest detectable abnormality of type 2 diabetes (Petersen et al., 2012) and may be caused by an insulin signaling defect (Cusi et al., 2000), glucose transporter defect (Herman & Kahn, 2006), or others, like lipotoxicity (Roden et al., 1996). Careful separation of the contributions of muscle and liver has shown that the early improvements in control of fasting plasma glucose levels by caloric restriction are associated only with improvements in liver insulin sensitivity (Lim et al., 2011; Petersen et al., 2005). Nevertheless, exercise improves muscle but also liver insulin sensitivity (van der Heijden et al., 2009) even without weight loss (Duncan et al., 2003) and reduces liver fat content and its mediators, also independently of weight loss (Hallsworth et al., 2011). Taken together, the effects of exercise may play a role in diabetes reversal.

Glucose dynamics and uptake

Blood glucose levels are regulated by several hormones (Triplitt, 2012). Of particular interest to diabetes, insulin is a powerful hormone that, among other functions, lowers blood glucose levels by increasing muscle and liver glucose uptake and glycogenesis (Saltiel & Kahn, 2001). Insulin is especially expressed after ingestion of carbohydrate or protein rich meals. It then binds to an enzyme that is present in the surface of cell membranes, α (alpha) subunit, which acts as the insulin receptor. This stimulates tyrosine kinase activity in the β -subunit that is attached to the α -subunit, which in turn causes phosphorylation of the subsequent enzymes, mitogen-activated protein kinase and phosphatidylinositol-3-kinase (PI 3-kinase) (Cortright & Dohm, 1997). These are responsible for expressing the mitogenic (cell growth and gene expression) and

metabolic actions of insulin (synthesis of lipids, proteins and glycogen), respectively. Most importantly, the PI 3-kinase pathway stimulates vesicles that contain special glucose transporters type 4 (glut-4). This stimulation causes glut-4 to translocate to cell membrane and actively uptake blood glucose. Insulin expression itself is controlled by circulating glucose blood levels. Through a complex mechanism, glucose uptake by glut-2 transporters in the β -cells of the pancreas stimulates insulin release from the same cells. Under normal conditions, the higher the blood glucose levels, the greater the amount of insulin will be excreted. Exercise is also capable of stimulating glut-4 translocation. In this case, this process occurs in a non-insulin dependent manner and it is believed that the translocation of glut-4 by exercise occurs at glut-4 pool that is sensitive to exercise but not insulin (Coderre et al., 1995; Douen et al., 1990).

On the other hand, glucagon is a hormone released by the α -cells of the pancreas and acts to increase blood glucose levels by stimulating the liver to convert stored glycogen into glucose, and releasing it into the blood stream, in a process called glycogenolysis. Furthermore, glucagon promotes gluconeogenesis and decreases glycogenesis and glycolysis in a concerted fashion via multiple mechanisms (Jiang & Zhang, 2003). An increase in insulin is known to suppress glucagon secretion, and a decrease in insulin combined with low glucose levels, stimulates the secretion of glucagon. Meanwhile, in diabetic individuals, it has been reported that the absolute levels of glucagon or the ratios of glucagon to insulin are often elevated. This chronic hyperglucagonemia is correlated with and is at least partially responsible for increased hepatic glucose output and hyperglycemia in subjects with type 2 diabetes (Consoli, 1992).

In addition, blood glucose levels can raise in response to the expression of other hormones, such as catecholamines (Rassam et al., 2002), cortisol, growth hormone and triiodothyronine (Triplitt, 2012).

Physical activity and exercise

The relevance of physical activity and exercise in the prevention and management of type 2 diabetes is complex and exhibits both acute and chronic effects. Whether through a direct or an indirect action, exercise is able to improve quality-of-life and life expectancy of individuals with type 2 diabetes.

Contracting muscles cause increased glucose uptake into active muscles. This blood glucose reduction is counteracted by hepatic glucose production (glycogenolysis and/or gluconeogenesis) and thus, blood glucose levels remain relatively constant at initial stages of moderate intensity physical activity or exercise (Suh et al., 2007). However, in individuals with type 2 diabetes, hepatic glucose production may not suffice to match blood glucose uptake during moderate exercise intensity, resulting in a decline of blood glucose levels (Minuk et al., 1981). As exercise intensity increases, there is a shift from a predominant reliance on free fatty acids at rest to a blend of fat, glucose, and muscle glycogen, with a small contribution from amino acids at higher energy requirements (Boon et al., 2007). With higher exercise intensities or duration, blood glucose and especially muscle glycogen become the major energy sources for muscle contraction. As muscle glycogen stocks become depleted with prolonged exercise, muscles increase circulating blood glucose uptake, along with free fatty acids released from adipose tissue (Watt et al., 2002). Although this seem to be a highly regulated mechanism, hyperglycemia can occur in response to high intensity exercise, due to increases in plasma catecholamine levels and subsequent increase in glucose production (Marliss & Vranic, 2002). These effects can persist for up to 1–2 h, likely because plasma catecholamine levels and glucose production do not return to normal immediately after exercise cessation.

Acute effects of exercise

Aerobic exercise seems to increases glucose uptake *during* but also in the immediate hours *after* a single bout of exercise, by increased insulin action. Intensity and duration of exercise impact the extent of this effect, which may last for more than 24 hours (Boulé et al., 2005). Resistance training also seems to

reduce 24-hour blood glucose levels, with greater reductions seen with higher exercise intensities and durations (Black et al., 2010). Recently, it has been shown that a reduction of blood glucose levels can also occur during light to moderate resistance exercises performed in a circuit method (Moreira et al., 2012). However, with increased resistance exercise intensity (traditional sets method), blood glucose levels during exercise may not differ from levels found in non-exercising individuals (Bacchi et al., 2012). Data on the effects of combined exercise (aerobic and resistance exercises performed on the same session) in acute blood glucose levels, during exercise, is scarce. One study that addressed this issue in individuals with type 1 diabetes found that glycemic levels dropped during aerobic exercise and raised during subsequent resistance exercise. When the exercise order is inversed, glycemic levels remained constant during the resistance training and dropped after succeeding aerobic training. During recovery time, blood glucose levels tended to be higher when aerobic exercise was performed first (Yardley et al., 2012). Therefore, performing aerobic training after resistance training is advised in order to improve glycemic stability throughout exercise and to reduce the duration and severity of post-exercise hypoglycemia for individuals with type 1 diabetes. Glycemic changes during exercise in persons with type 2 diabetes are not completely known but we expect them to be similar to modifications found in their type 1 counterparts. Another study analyzed the effects of combined exercise on brachial-ankle pulse wave velocity and flow-mediated dilation in healthy subjects and found that although vascular function is not improved by aerobic exercise before resistance training, performing aerobic exercise thereafter can prevent the deteriorating of vascular function (Okamoto et al., 2007). Finally, the acute effects of other exercise modalities, like Tai-chi and yoga, have been scarcely investigated for their potential to improve glycemic control, and with mixed results. More studies with larger samples sizes and/or standardization of training sessions are needed to clarify this issue.

Chronic effects of exercise

The chronic effects of exercise are sometimes hard to distinguish from the accumulated acute effects of exercise. For some time, it was believed that the long term effects of aerobic training resulted from the successive acute effects of each bout of exercise (Colberg & Grieco, 2009). In this sense, if one should stop exercising, the glucose lowering effects would vanish in hours to a couple of days. Physiologically, one bout of aerobic exercise is able to activate several cellular pathways, mainly AMP-activated protein kinase, calcium signaling and p38 mitogen-activated protein kinase, stimulating glucose uptake by muscular cells (Benziane et al., 2008; Hussey et al., 2012). However, long-term training can enhance the responsiveness of skeletal muscles to insulin with increased expression and/or activity of proteins involved in glucose metabolism and insulin signaling. One study showed that after 8 weeks of exercise training, total glycogen synthase activity was increased in subjects with and without diabetes and the training-induced improvement in glucose disposal observed was due primarily by increased insulin-stimulated glucose storage (Christ-Roberts et al., 2004). Training also increased glut-4 protein by increased Akt expression but there were no enhancements in the ability of insulin to stimulate insulin receptor substrate-1 (IRS-1) associated PI 3-kinase activity (Christ-Roberts et al., 2004). Nevertheless, the duration of these effects after exercise cessation have seldom been analyzed. A relative chronic effect of aerobic exercise does occur, as it has been shown in a study that compared the effects of three different exercise protocols (low volume-moderate intensity, low volume-high intensity, high volume-high intensity) (Bajpeyi et al., 2009). In this case, the authors found that although without a marked absolute difference among all training protocols, the longer duration exercise regimens (low volume-moderate intensity and high volume-high intensity, 200 min/week each) were able to maintain increased insulin sensitivity after 15 days of exercise cessation. Relatively to the chronic effects of resistance training, data is scarce, since most post-exercise evaluations are performed within a 24-48h period after the last bout of exercise and as such, changes may be a simple reflection of an acute effect of the last exercise session. Nevertheless, solid evidence support the usefulness of

resistance training for glycemic control in individuals with type 2 diabetes (Dunstan et al., 2002; Ibañez et al., 2005; Snowling & Hopkins, 2006). A study that evaluated A1c changes at 2 and 14 months of resistance exercise and found that the largest part of A1c reductions were already occurring at 2 months and that the next 12 months did not reduce A1c levels further (Cohen et al., 2008). If occurring, the chronic long-term effects of resistance exercise may be related to the increases in glut-4 and skeletal muscle mass via activation of the mammalian target of rapamycin/serine (mTOR) kinase 6 pathway, which increases protein synthesis (Roden, 2012). Finally, discerning the chronic effects of combined exercise from the glycemic lowering effects due to the last bout of exercise is not easy. Nevertheless, some researches have compared the effects of combined exercise versus control subjects and isolated forms of exercise (aerobic only or resistance only). The earliest study randomized 20 subjects to a control group and 19 to a combined exercise intervention (3 times/week, for 16 weeks) which involved fast walking at moderate intensity for 20 minutes as the aerobic component and several exercises performed for 20 minutes at light to moderate intensity for the resistance component (Tessier et al., 2000). After intervention, there were no differences among a combined intervention and the control group. In both cases, A1c was raised after intervention, although to a lesser extent in the intervention group. Some years later, a larger trial assigned 58 individuals to the control group and 62 to a combined exercise group (3 times/week, for 1 year) (Balducci et al., 2004). This time, aerobic exercise was performed for 30 minutes in several different ergometers, while resistance exercise also was performed for 30 minutes. As a result, only the combined exercise group was able to reduce A1c levels, by a significant 1,2%. A third study compared the effects of combined exercise (n=64) to isolated aerobic exercise (n=60), isolated resistance exercise (n=64) and a control group (Sigal et al., 2007). All exercise groups managed to reduce A1c levels, but the highest reduction was found in the combined exercise intervention. However, in this study, caloric expenditure was higher in the combined exercise intervention as it involved completing the aerobic exercise

performed by the participants in the isolated aerobic group plus the resistance exercise performed by the participants in the isolated resistance group.

Meanwhile, the beneficial effects of exercise include more than the glycemic improvements. People with diabetes who have higher levels of fitness or physical activity exhibit a lower cardiovascular and all-cause mortality risk (Batty et al., 2002; Seyoum et al., 2006), independently of body mass (Church et al., 2004; McAuley et al., 2007). Multiple other beneficial outcomes contribute to quality of life and life expectancy increases in individuals with type 2 diabetes, such as an increased antioxidant activity (Castaneda-Sceppa et al., 2004), a reduction on inflammatory markers (Calle & Fernandez, 2010), and improvements in lipid profile (Kelley & Kelley, 2007), blood pressure (Pi-Sunyer et al., 2007), aerobic power and muscular strength (Zanuso et al., 2010), endothelial function (Hambrecht et al., 2000) and psychological aspects (Williamson et al., 2009).

Exercise intensity

When considering *intensity* in exercise prescription, one must fully understand the meaning of related terms such as “moderate” or “high-intensity”. In order to standardize exercise intensity, the American College of Sports Medicine (ACSM) issued a position stand entitled “The Recommended Quantity and Quality of Exercise for Developing and Maintaining Fitness in Healthy Adults” (Pollock et al., 1998). Intensity can be described in relative (percentages of oxygen consumption reserve, heart rate reserve and maximal heart rate, rate of perceived exertion or maximal voluntary contraction) or absolute terms (based on metabolic equivalents – METS and related to the age of the subject). For example, a subject that exercises at 55-69% of his/hers maximal heart rate is considered to be at a “moderate intensity” exercise. A full list of intensity categories can be found in table 3.

Table 3 - Classification of physical activity intensity, based on physical activity lasting up to 60 min (adapted from Pollock et al., 1998).

Intensity	Endurance-type activity							Resistance-type exercise
	Relative Intensity			Absolute intensity (METs) in healthy adults (age in years)				Relative Intensity*
	VO ₂ R (%) heart rate reserve (%)	Maximal heart rate (%)	RPE†	Young (28–39 yr)	Middle-aged (40–64 yr)	Old (65–79 yr)	Very old (80– yr)	Maximal voluntary contraction (%)
Very light	<20	<35	<10	<2.4	<2.0	<1.6	≤1.0	<30
Light	20–39	35–54	10–11	2.4–4.7	2.0–3.9	1.6–3.1	1.1–1.9	30–49
Moderate	40–59	55–69	12–13	4.8–7.1	4.0–5.9	3.2–4.7	2.0–2.9	50–69
Hard	60–84	70–89	14–16	7.2–10.1	6.0–8.4	4.8–6.7	3.0–4.25	70–84
Very hard	≥85	≥90	17–19	≥10.2	≥8.5	≥6.8	≥4.25	≥85
Maximal‡	100	100	20	12.0	10.0	8.0	5.0	100

*Based on 8–12 repetitions for persons under age 50–60 years and 10–15 repetitions for persons aged 50–60 years and older.

†Borg rating of Perceived Exertion 6–20 scale (Borg, 1982).

‡Maximal values are mean values achieved during maximal exercise by healthy adults. Absolute intensity (METs) values are approximate mean values for men. Mean values for women are approximately 1–2 METs lower than those for men; VO₂R = oxygen uptake reserve.

Nutrition

The optimal nutrient composition for diabetes management has been widely debated. For more than 3000 years, specialists have issued their recommendations, which have been inconsistent and often antagonistic (Davis et al., 2009). Today, current nutritional recommendations for diabetic are not markedly distinct from those for healthy populations. Nutritional recommendations from the ADA for the management of diabetes include monitoring total carbohydrate, whether by carbohydrate counting, choices or experienced-based estimations, using glycemic index and glycemic load for modest but additional benefits on glycemic control, limiting fat intake to less than 7% of dietary energy intake (DEI) and minimizing *trans* fat intake (ADA, 2012). The IDF has also issued dietary guidelines for individuals with type 2 diabetes (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2008), which are slightly different from ADA's in relation to macronutrient, fiber and sodium intakes (a brief comparison between ADA and IDF's recommendations can be found in table 4).

Table 4 – A comparison of the dietary guidelines for patients with type 2 diabetes, from the American Diabetes Association (ADA) and the International Diabetes Federation (IDF).

	ADA	IDF
Carbohydrate	Not specified	45-60%
Protein	15-20% not specified	10-20%
Fat	Not specified	20-35%
Saturated Fat	< 7 % of DEI	< 7% of DEI
Cholesterol (mg/day)	< 200	< 200
Fiber	≈ 14 gr/1000 kcal	25-50 gr/day
Sodium (mg/day)	< 2000	< 2300
Alcohol	< 15 gr women; < 30 gr men	

DEI= Dietary Energy Intake.

Clinical trials/outcomes studies have shown that a medical nutrition therapy (MNT) is able to reduce A1c levels by at least 0.25% and up to 2.9% (ADA, 2011). Furthermore, as stated previously, nutritional changes and in particular, caloric intake reductions have shown that type 2 diabetes can be reversed (Colles et al., 2006; Dixon et al., 2008; Ferrannini & Mingrone, 2009; Lim et al., 2011; Lindeberg et al., 2007; Petersen et al., 2005; Petersen et al., 2012; Pories et al., 1992; Williams et al., 1998). Nevertheless, dietary compliance is generally poor across European countries, either among individuals with type 1 (Toeller et al., 1996) or type 2 diabetes (Rivellese et al., 2008; Thanopoulou et al., 2004). In fact, the translation from the scientific basis of established recommendations into the daily routine of patients with type 2 diabetes has been challenging. As an example, a recent review analyzed the adherence outcomes of 38 dietary interventions and found that most of those outcomes were no different from the results in the control groups (Desroches et al., 2013).

Nutrition is widely accepted as a critical factor for the management of type 2 diabetes and therefore, the nutritional status of a given population should be known. However, despite the recognized relationship between diet and glycemic control and the availability of dietary guidelines, endorsed by reputed institutions (ADA, 2011; Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2008), little is known about what the patients with diabetes are actually eating, particularly in Portugal. As we pretend to provide a comprehensive view of lifestyle factors and their relationship with diabetes, in our work we will also cover the nutritional status of a Portuguese sample.

Our research

In this thesis, the relevance of both physical activity and exercise for diabetes prevention and management has been highlighted. Surprisingly, and despite all its well-known general benefits, including its reduced prevalence of undesired side effects and reduced maintenance costs, exercise remains, by far, the most underused strategy in diabetes management (Colberg, 2008). As usual, time constraints of patients (to exercise) and general practitioners (to recommend exercise) are thought to be some of the major barriers to exercise adherence and prescription, respectively. Nevertheless, many general practitioners may also not be familiarized with the exercise guidelines in type 2 diabetes or simply not agree with them (Colberg, 2008). This results in a gap in the knowledge regarding how to optimize adequate exercise intervention in order to achieve maximal enhancements with lowest risks, such that exercise can be used in a primary care recommendation (Beckman, 2004). As such, providing adequate information on the most successful exercise characteristics, methods and variables seems to be a critical step to enhance exercise prescriptions for the management of type 2 diabetes.

Currently, it is believed that a combination of aerobic and resistance training promotes the highest benefits on glycemic control. A joint statement between the ACSM and the ADA states that individuals with type 2 diabetes should engage in both aerobic and resistance activities (Colberg et al., 2010). As such, people with type 2 diabetes should undertake at least 150 min/week of

moderate to vigorous aerobic exercise spread out during at least 3 days during the week, with no more than 2 consecutive days between bouts of aerobic activity. In addition to aerobic training, persons with type 2 diabetes should undertake moderate to vigorous resistance training at least 2–3 days/week. However, information regarding the exercise methodology and a detailed analysis of the exercise features of successful combined interventions is lacking. Variables such as the order of the exercises, whether aerobic and resistance should be performed on the same day and many others issues have not been not addressed so far. Therefore, one of the purposes of this work is to review all interventions that used a combination of aerobic and resistance exercise on patients with type 2 diabetes, and to analyze their specific exercise characteristics and related effects on glycemic control. To our knowledge, this is the first study to directly address these two topics. Furthermore, while it is presently accepted that a combined exercise intervention is preferred to isolated forms of exercise, the optimal relationship between the aerobic component and the resistance component remains unaddressed and therefore, unknown. This is of particular interest, as additional benefits in glycemic control, and other health related variables, might be attained by favoring a certain type of exercise. In other words, the main goal of this study addresses the question: *should combined exercise emphasize one of its components?*

Finally, diabetes management should be regarded as a multidisciplinary endeavor. An adequate diet and an active lifestyle are also key features in glycemic control. Although it is known that diet compliance to recommendations is generally low and physical activity levels in individuals with diabetes is also lower than recommended (Morrato et al., 2007; Rivellese et al., 2008; Sluik et al., 2012), the data available for Portuguese individuals with diabetes is not abundant. During the course of the experimental part of this thesis, we also aim to provide information on these important topics.

In summary, with this work we expect to provide a small contribution towards a better understanding of the optimal exercise features in type 2

diabetes management. Furthermore, the results of this thesis will provide a broader illustration of the dietary and daily physical activity characteristics of Portuguese individuals with diabetes, in order to provide recommendations for future research concerning the improvement of quality of life and life expectancy in this population, throughout well-designed exercise interventions.

Experimental work

The basic characteristics of each paper, which are integrated in this dissertation, are shown in Table 5. More detailed information is included on the corresponding paper.

Table 5 - Summary of the characteristics of the papers integrated in the dissertation.

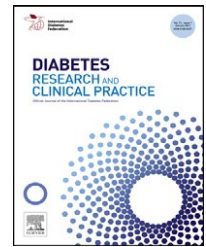
	Sample size	Main variables analyzed
Paper I <i>Combined exercise for people with type 2 diabetes mellitus: a systematic review</i>	2093	A1c, length, frequency, duration, intensity, mode, number of exercises, sets, repetitions.
Paper II <i>Nutrition and physical activity characteristics of Portuguese older individuals with type 2 diabetes: compliance with recommendations</i>	101	Counts/min, protein, carbohydrates, fat, saturated fat, cholesterol, fiber, sodium
Paper III <i>Combined Exercise in individuals with type 2 diabetes: emphasis on the aerobic component. A Randomized, Controlled Trial</i>	35	A1c, glucose, insulin, insulin sensitivity, beta cell function, blood lipids, c-reactive protein, weight, BMI, %fat, FFM, BMC, BMD, z-score, strength, aerobic power

A1c= glycated hemoglobin A1c; BMI= body mass index; FFM= fat free mass; BMC= bone mineral content; BMD= bone mineral density.

Paper I

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Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres
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Diabetes
Federation**


Review

Combined exercise for people with type 2 diabetes mellitus: A systematic review

César Oliveira ^{a,*}, Mário Simões ^a, Joana Carvalho ^b, José Ribeiro ^b

^a Polytechnic Institute of Viana do Castelo, Portugal

^b Research Centre in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto, Portugal

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ABSTRACT

Type 2 diabetes mellitus has emerged as a major non-communicable chronic diseases in many countries. The importance of exercise in the prevention and management of this disease is evident. This paper briefly reviews the effects of combining aerobic and resistance exercises on glycemic control, and details the training and characteristics of various interventions in adults with type 2 diabetes mellitus. Literature searches were performed using electronic databases between the 1st of January 1950 and the 15th of September 2011. Of the 403 articles retrieved, 28 studies met our inclusion criteria. Combined exercise protocols seem to improve glycemic control to a greater extent than isolated forms of exercise. Nevertheless, length, duration, intensity, mode, number of exercises, sets and repetitions varied markedly among studies. Supervised training sessions, recommended structured exercises, and splitting aerobic and resistance training in separate sessions may be relevant for best results. Future studies should analyze the effects of different aerobic and resistance training modes, different training and progression methods, and whether one type of exercise is optimal, as these issues are likely to convey greater knowledge on type 2 diabetes mellitus management through combined exercise.

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Contents

1. Introduction	188
2. Methods	188
2.1. Search strategy	188
2.2. Inclusion and exclusion criteria	188
2.3. Statistical analyses	189
3. Results	189
3.1. Combined exercise	189
3.1.1. Glycemic control	189
3.1.2. Dietary control	191
3.1.3. Medication changes	191

* Corresponding author at: Escola Superior de Desporto e Lazer de Melgaço, Rua da Calçada, 4960-529 Melgaço, Portugal.

Tel.: +351 912545570; fax: +351 229512278.

E-mail addresses: cesarchaves@esdl.ipvc.pt, cesarchaves@mail.com (C. Oliveira), msimoes@esdl.ipvc.pt (M. Simões), jcarvalho@fade.up.pt (J. Carvalho), jribeiro@fade.up.pt (J. Ribeiro).

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3.2.	Exercise training characteristics	191
3.2.1.	Supervised versus non-supervised intervention	191
3.2.2.	Structured exercise training or physical activity advice only	191
3.2.3.	Exercise frequency	191
3.2.4.	Intensity/duration.	194
3.2.5.	Intervention length.	194
3.2.6.	Aerobic exercise mode	194
3.2.7.	Resistance exercise mode.	195
3.3.	Methodological issues	195
4.	Conclusions	196
	Acknowledgements	196
	References	196

1. Introduction

Diabetes mellitus (DM) is a leading cause of morbidity and mortality globally, and despite medical breakthroughs and treatment innovations, the number of adults with this condition is raising at a faster pace than previously expected [1]. In addition, diabetes-related costs are projected to double in the next 25 years, leading to a significant increase in the economic burden for patients and for healthcare systems [2]. However, type 2 diabetes mellitus (T2DM), the most common form of this disease, is also considered to be mainly preventable, especially via pharmacological treatment and/or significant lifestyle changes [3].

Exercise is recognized as a cornerstone for T2DM prevention and treatment due to its ability to regulate blood sugar levels, with minimal undesired side effects [4]. Along with glycemic control, exercise has a large number of benefits, such as improving aerobic capacity, muscular strength, body composition and endothelial function [5,6]. Despite these general benefits and low-cost, exercise is also vastly under-used in diabetes management [7]. There is a gap in the knowledge regarding how to optimize adequate exercise intervention in order to achieve maximal enhancements with lowest risks, such that exercise can be used in a primary care recommendation [8].

Recent evidence suggests that a combination of aerobic and resistance training (combined exercise) is more beneficial than either training modality alone [9]. It is postulated that while aerobic exercise enhances insulin sensitivity, resistance training improves blood glucose uptake by increasing muscle mass and Glut-4 expression, and that these mechanisms appear to be synergistic. Thus, combined

exercise is currently recommended for T2DM patients [4]. However, a detailed analysis of the exercise features of combined interventions is lacking. Therefore, we propose to review all interventions that used a combination of aerobic and resistance exercise on T2DM patients, and to further analyze specific exercise characteristics and their effects on glycemic control. To our knowledge, this is the first study to directly address these two topics.

2. Methods

2.1. Search strategy

Searches of the PubMed database were performed for studies published in English from the 1st of January 1950 up to, and including, the 15th of September 2011. Search terms used were “diabetes”, “exercise”, “combined”, “training”, “aerobic”, “resistance”, “strength”, “circuit”, “walking”, “HbA1c” and “A1c” in article title and abstract (Fig. 1). Reference lists of review articles and all included articles identified by the search were also examined for other potentially eligible studies.

2.2. Inclusion and exclusion criteria

Studies that met the following criteria were included in this review: (I) published in English, (II) subjects comprising human adults with T2DM, (III) performance of combined exercise (aerobic and resistance training executed in the same session or during the same week) and (IV) with glycated hemoglobin A (A1c) data as the glycemic control marker. In order to analyze the training characteristics of

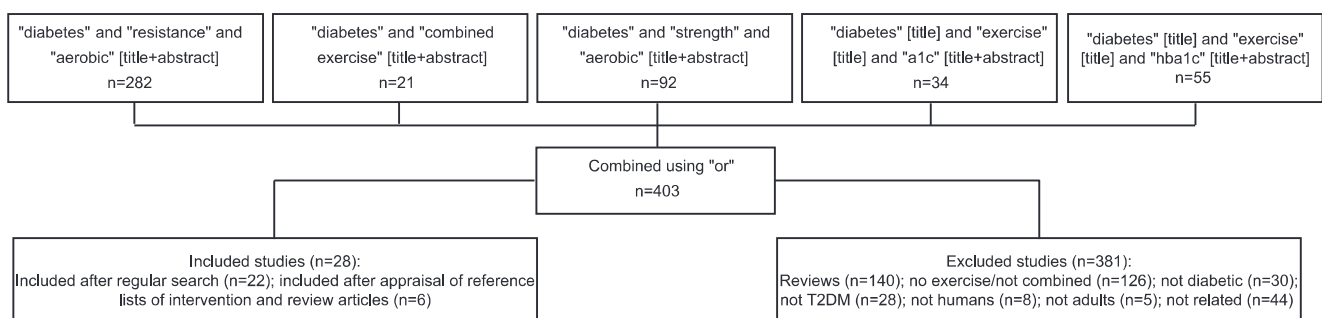


Fig. 1 – Search flow and results.

Table 1 – General characteristics of combined exercise interventions.

Author (year) [Ref.]	n				R	D	M	S
	c	com	aer	res				
Tessier et al. (2000) [31]	20	19			Y	Y	na	Y
Maiorana et al. (2001) [52]		16			Y	na	Y	na
Loimaala et al. (2003) [39]	24	24			Y	N	na	P
Cuff et al. (2003) [13]	9	10	9		Y	Y	na	Y
Balducci et al. (2004) [32]	58	62			Y	Y	Y	Y
Tokmakidis et al. (2004) [22]		9			N	na	Y	Y
McGavock et al. (2004) [27]	7	11			P	na	na	Y
Wagner et al. (E) (2006) [12]		17			Y	na	N	Y
Wagner et al. (E + A) (2006) [12]	17	14						
Sigal et al. (2007) [19]	63	64	60	64	Y	Y	Y	Y
Krousel-Wood et al. (2008) [29]	49	37			Y	N	N	N
Praet et al. (BWP) (2008) [10]		49			Y	na	N	N
Praet et al. (MFP) (2008) [10]		43						
Lambers et al. (2008) [14]	11	17	18		Y	N	na	Y
Marcus et al. (2008) [15]		7	8		N	na	na	Y
Aylin et al. (2009) [33]	18	18			Y	na	Y	P
Christos et al. (2009) [26]	10	10			na	na	Y	Y
Loimaala et al. (2009) [40]	24	24			Y	N	na	Y
Fatone et al. (2010) [25]		8			N	N	N	Y
Balducci et al. (2010) [16]	20	22	20		Y	na	na	Y
Balducci et al. (2010) [36]	288	277			Y	N	N	Y
Kluding et al. (2010) [23]		6			N	na	na	Y
Gram et al. (2010) [17]	22	24	22		Y	na	na	Y
Okada et al. (2010) [34]	17	21			Y	na	N	Y
Church et al. (2010) [20]	41	62	52	60	Y	Y	N	Y
Segerström et al. (LV) (2010) [11]		11			na	na	na	Y
Segerström et al. (HV) (2010) [11]		11						
Jorge et al. (2011) [21]	12	12	12	12	Y	N	N	Y
Touva et al. (2011) [24]		10			N	na	Y	Y
Ferrer-Garcia et al. (2011) [41]	40	44			Y	na	na	na
Lucotti et al. (2011) [18]		20	27		Y	N	na	Y

R: randomized controlled interventions; D: dietary assessment; M: medication change restricted; S: supervised; c: control group; com: combined exercise group; aer: aerobic exercise group; res: resistance exercise group; Y: yes; N: no; P: partially; na: non available; E: exercise only; E + A: exercise + acarbose; BWP: brisk walking programme; MFP: medical fitness programme; LV: low volume; HV: high volume. n refers to subjects that met compliance criteria (if data is available).

the highest number of combined exercise studies, no restrictions were made in relation to randomization and length of intervention. Reviews, comments and/or opinion/editorial papers were excluded.

2.3. Statistical analyses

Due to the vast methodological differences in terms of frequency, intensity, duration, length and mode of exertion measures of the exercises, we could not conduct a meta-analysis and thus only reported a summary of the presented data.

3. Results

Twenty-two articles met the search criteria. After appraising reference lists, we included six additional studies that also met inclusion criteria but were missed through regular search (Fig. 1). The resulting twenty-eight studies comprised thirty-one combined exercise groups (Table 1), which included two different exercise arms in two studies [10,11] and one compared combined exercise with and without acarbose

treatment [12]. The majority of the papers involved control groups (19), six papers compared combined exercise with aerobic exercise only [13–18], and three compared combined exercise with both aerobic and resistance exercises alone [19–21]. The total number of subjects enrolled was 2093 (n = 979 for the combined exercise). Twenty studies were randomized controlled trials, five were not randomized [15,22–25], two did not provide information [11,26], and, in one case, the sample comprised subjects that were both randomized and not randomized [27].

3.1. Combined exercise

3.1.1. Glycemic control

The selected measure of glycemic control was A1c, which is formed by the non-enzymatic attachment of glucose to the N-terminal valine of the β -chain of hemoglobin [28]. As the life span of an erythrocyte is around 120 days, this indicator represents the average glucose concentration over the preceding 8–12 weeks. A1c is associated with several diabetic-related complications and lowering A1c values significantly reduces the rate of progression of microvascular complications [28].

Table 2 – Combined exercise interventions and related glycated hemoglobin A (A1c) changes.

Author (year) [Ref.]	A1c					
	Control			Combined		
	Before	After	dif	Before	After	dif
Tessier et al. (2000) [31]	7.3 ± 1.7	7.8 ± 1.5	0.5	7.5 ± 1.2	7.6 ± 1.2	0.1
Maiorana et al. (2001) [52]				8.5 ± 0.4	7.9 ± 0.3	−0.6*
Loimaala et al. (2003) [39]	8.0 ± 1.3	8.3 ± 1.4	0.3	8.2 ± 2.1	7.6 ± 1.4	−0.6*
Cuff et al. (2003) [13]	6.9 ± 0.4	6.87 ± na	−0.03	6.9 ± 0.4	6.8 ± na	−0.1
Balducci et al. (2004) [32]	8.28 ± 1.73	na	na/ns	8.31 ± 1.73	7.1 ± 1.16	−1.2*
Tokmakidis et al. (2004) [22]				7.7 ± 1.7	6.9 ± 1.0	−0.8*
McGavock et al. (2004) [27]	7.4 ± 1.1	7.4 ± 0.8	0	6.6 ± 0.9	6.4 ± 0.6	−0.2
Wagner et al. (E) (2006) [12]				6.6 ± na	6.1 ± na	−0.5
Wagner et al. (E + A) (2006) [12]	5.8 ± na	5.2 ± na	−0.6	5.9 ± na	5.5 ± na	−0.4*
Sigal et al. (2007) [19]	7.44 ± 1.38	7.51 ± 1.47	0.7	7.46 ± 1.48	6.56 ± 1.55	−0.9*
Krousel-Wood et al. (2008) [29]	8.0 ± 1.5	7.2 ± 1.3	−0.7	7.4 ± 1.5	6.7 ± 1.4	−0.7
Praet et al. (BWP) (2008) [10]				7.18 ± 1.42	7.08 ± 1.37	−0.10
Praet et al. (MFP) (2008) [10]				7.08 ± 1.29	6.89 ± 1.13	−0.19
Lambers et al. (2008) [14]	6.7 ± 0.97	7.0 ± 0.88	0.3	7.4 ± 1.45	6.9 ± 1.20	−0.6*
Marcus et al. (2008) [15]				7.1 ± 1.2	6.5 ± 1.3	−0.6
Aylin et al. (2009) [33]	6.75 ± 0.27	6.88 ± 0.29	0.13	7.67 ± 0.44	6.38 ± 0.18	−1.29*
Christos et al. (2009) [26]	7.3 ± 0.8	7.3 ± 0.7	0	7.9 ± 1.5	6.7 ± 0.9	−1.2*
Loimaala et al. (2009) [40]	8.0 ± 0.3	8.3 ± 1.4	0.3	8.2 ± 2.1	7.6 ± 1.4	−0.6*
Fatone et al. (2010) [25]				6.38 ± 0.72	5.93 ± 0.64	−0.45*
Balducci et al. (2010) [16]	7.08 ± 1.28	6.93 ± 1.29	−0.15	7.74 ± 1.72	6.65 ± 1.10	−1.09*
Balducci et al. (2010) [36]	7.15 ± 1.4	7.02 ± 1.2	−0.13	7.12 ± 1.4	6.7 ± 1.1	−0.42*
Kluding et al. (2010) [23]				6.7 ± 0.6	6.2 ± 0.5	−0.5
Gram et al. (2010) [17]	7.8 ± 1.3	7.9 ± 0.3	0.1	7.2 ± 0.9	7.2 ± 0.2	0.0
Okada et al. (2010) [34]	7.9 ± 1.1	6.8 ± 0.8	−1.1*	8.5 ± 1.8	7.0 ± 1.3	−1.5*
Church et al. (2010) [20]	7.61 ± 0.1	7.72 ± 0.1	0.11	7.54 ± 0.08	7.27 ± 0.08	−0.27
Segerström et al. (LV) (2010) [11]				6.5 ± 1.4	6.8 ± 1.0	0.3
Segerström et al. (HV) (2010) [11]				6.6 ± 1.2	6.1 ± 1.0	−0.5*
Jorge et al. (2011) [21]				7.6 ± 1.12	7.53 ± 1.05	0.07
Touura et al. (2011) [24]	6.94 ± 0.74	7.07 ± 0.70	0.13	7.2 ± 1.5	6.7 ± 0.8	−0.5*
Ferrer-Garcia et al. (2011) [41]	6.51 ± 0.78	6.45 ± 1.49	−0.06	6.35 ± 1.5	6.0 ± 0.83	−0.35*
Lucotti et al. (2011) [18]				7.9 ± 1.9	7.3 ± 1.9	−0.6

dif: absolute difference; E: exercise only; E + A: exercise + acarbose; BWP: brisk walking programme; MFP: medical fitness programme; LV: low volume; HV: high volume; A1c values refer to subjects that met compliance criteria (if data is available).
 * Statistically significant.

Table 2 shows that seventeen combined exercise groups resulted in statistically significant reductions in A1c and three others attained a clinically significant change [15,18,29] (interpreted as a 0.6% improvement in A1c [30]). In six of these studies, combined exercise interventions produced more pronounced absolute A1c changes than aerobic or resistance exercises alone [14–16,18–20]. In these six studies, only two were powered to compare the between-group changes and both demonstrated that combined exercise resulted in significantly lower A1c than aerobic or resistance only [19,20]. However, the combined exercise from one study [19] had a higher energy expenditure than aerobic and resistance only exercises (in “Supplements” section).

In contrast, two studies, an aerobic only [17] and both aerobic only and resistance only exercises [21] produced a more noticeable absolute A1c change than a combined regimen. Study results varied, with some studies showing either no difference between combined versus aerobic exercises alone [13], no difference between combined exercise versus control groups [29], or even a greater absolute reduction in A1c in the control group [12], while the results from all the other studies favored the combined intervention.

3.1.2. Dietary control

Dietary modifications confound potential A1c changes as a result of exercise interventions. In fifteen of the twenty-eight papers, no information on subjects' caloric intake before and after interventions was reported, and eight stated that a dietary evaluation was not performed (Table 1). Only five papers described a dietary control: in two of them, authors reported no differences on energy intake before and after interventions [13,31], a slightly lower level of overall energy intake after intervention (requested as part of the intervention), but no difference within groups [19], and the last two did not provide additional information related to dietary changes [20,32]. Only the study performed by Sigal et al. [19] demonstrated that A1c changes occurred due to the exercise intervention were independent from the changes in total energy intake.

3.1.3. Medication changes

Since A1c is also affected by medication use, changes in medication use throughout the exercise intervention should be controlled or measured. In our review, seven papers generally described the diabetic medication used by participants at baseline but did not always take appropriate measures to limit drug changes (Table 1). As a result, A1c was significantly reduced from -0.5% [24] to -1.29% [33]. The highest A1c reduction by a combined exercise intervention was found by Okada et al. (-1.5%), which implemented the restriction on medication change; however, the control group also reduced A1c significantly, by -1.1% [34]. The finding of this study, together with another by Church et al. [20], confirmed that participants in control groups were more likely to increase their use of diabetes medications while participants of the combined exercise interventions were more likely to reduce medication use, which tended to reduce the effect size of A1c impact by exercise versus control groups.

3.2. Exercise training characteristics

3.2.1. Supervised versus non-supervised intervention

A recent review performed by Gordon et al. [35] analyzed the metabolic health effects of resistance training and found that when exercise supervision was removed, compliance to exercise and glucose control decreased. These results are in accordance with the Italian Diabetes and Exercise Study [36], that also confirmed greater improvements on blood glucose control and several other cardiovascular risk factors were associated with supervised exercise. Table 1 shows that most studies found in our review were partially to totally supervised and the two unsupervised groups did not produce statistically significant results [10,29]. Of these, the intervention conducted by Krousel-Wood et al. [29] manages to achieve a clinically significant A1c reduction of 0.7%, although this was not different from the control group.

3.2.2. Structured exercise training or physical activity advice only

Recently, Umpierre et al. [37] reviewed twenty-three studies with structured exercise training and twenty-four studies with physical activity advice only. While the structured exercise reduced A1c levels by an average of 0.67%, physical activity advice reduced A1c levels only when complemented with dietary advice and still to a lesser extent (0.43%).

All the combined groups gathered for this review were structured exercise interventions.

3.2.3. Exercise frequency

The effects of training frequency on glucose control are currently unknown as, to our knowledge, studies comparing different frequencies in T2DM patients are not available. Glucose uptake enhancement may last up to 72 h [38], with its maximal impact shortly after an exercise bout and decreasing during the following hours to days. It is hypothesized that a higher training frequency (at least 3 days/week) may be necessary to maintain its effects on daily glucose control. For this reason, it seems plausible to recommend that exercise should be performed on most days of the week. However, it is also essential to consider the higher risk of overtraining or injury in the habitually sedentary T2DM patients. These concerns can be addressed by careful exercise planning that adequately alternates intensity, duration and mode of exertion on different training sessions.

Thirteen of the interventions (Table 3) opted to perform aerobic and resistance training on the same exercise session, 3 times a week, and are in accordance with the most recent recommendations on minimum number of weekly sessions for aerobic and resistance training (3 and 2 times a week, respectively) [4]. Only two studies used 5 sessions/week frequency [18,29], while another one started with 2 sessions/week and progressed to a single weekly session of exercise [17]. In contrast, seven studies used a different approach and their subjects performed aerobic and resistance training on separate days, in a total of 4 days/week [22,26,33,39,40], or at least 3 days/week [23,41]. Although these seven studies did not match the recommended minimum amount of aerobic exercise frequency, all but one [23] produced statistically significant A1c reductions. This may

Table 3 – Combined exercise characteristics.

Author (year) [Ref.]	Len.	Freq.	Aerobic				Resistance																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																									
			Duration (min)	Intensity (%)	Mode	Other(s)	Leg press	Chest press	Lat pull-down	Leg extension	Leg curl	Abdominal crunch	Back extension	Arm curl	Arm extension	Seated row	Other(s)																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															
Tessier et al. (2000) [31]	16 w	3	20	35–59→60–79 HRmax	×	×	20	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na</

Table 3 (Continued)

Table 3 (Continued)																						
Author (year) [Ref.]	Len.	Freq.	Aerobic					Resistance														
			Duration (min)	Intensity (%)	Mode			Duration (min)	Intensity (%1RM)	No. exe	Mode											
					Walking	Cycling	Elliptical				Rowing	Stepper	Other(s)	Leg press	Chest press	Lat pull-down	Leg extension	Leg curl	Abdominal crunch	Back extension	Arm curl	Arm extension
Fatone et al. (2010) [25]	1 y	2	na	55–70 VO ₂ max	×	×	×	na	60	4	×	×	×	×	×	×	×	×	×	2	15	
Balducci et al. (2010) [16]	7 mo	2	40	70–80 VO ₂ max	×	×	×	20	80	4	×	×	×	×	×	×	×	×	×	3	8	
Balducci et al. (2010) [36]	1 y	2	na	na	×	×	×	×	na	4	×	×	×	×	×	×	×	×	×	na	na	
Kluding et al. (2010) [23]	10 w	3–4 (alt)	20–50	50–70 VO ₂ peak	×	×	×	×	na	10	×	×	×	×	×	×	×	×	×	na	10	
Gram et al. (2010) [17]	4 mo	2–1	na	>40 VO ₂ max	×	×	×	×	na	5	×	×	×	×	×	×	×	×	×	na	na	
Okada et al. (2010) [34]	3 mo	3–5	20 + 20	Karvonen's equation (0.6)	×	×	×	×	20	na	na	na	na	na	na	na	na	na	na	na	na	
Church et al. (2010) [20]	9 mo	2 + 1 aer	33–42	50–80 VO ₂ max	×	×	×	na	na	9	×	×	×	×	×	×	×	×	×	1	10–12	
Segerström et al. (LV) (2010) [11]	6 mo	2 + 1 aer	15–25	65% HRr	×	×	×	15→10	na (BW, RB, DB)	na	na	na	na	na	na	na	na	na	na	15–20		
Segerström et al. (HV) (2010) [11]	6 mo	2 + 1 aer	15–25	72% HRr	×	×	×	15→10	na (BW, RB, DB)	na	na	na	na	na	na	na	na	na	na	15–20		
Jorge et al. (2011) [21]	12 w	3	na	Lactate threshold	×	×	×	na	na	7	×	×	×	×	×	×	×	×	×	na	na	
Touvrá et al. (2011) [24]	8 w	4	30	70–80% HRmax	na	na	na	30	60	6	×	×	×	×	×	×	×	×	×	3	15	
Ferrer-García et al. (2011) [41]	24 w	≥2 res + 1 aer (alt)	na	na	×	×	×	na	75–95	na	na	na	na	na	na	na	na	na	na	na	na	
Lucotti et al. (2011) [18]	3 w	5	30	70% HRmax	×	×	×	15	40–50	9	×	×	×	×	×	×	×	×	×	1	10–20	
Len.: length; Freq.: frequency; 1RM: 1 repetition maximum; no. exe.: number of different exercises; Reps.: repetitions; w: week; y: year; mo: month; alt: aerobic and resistance training performed on alternate sessions; →: progressing to; aer: aerobic only; res: resistance only; ma: more exercises available; HRmax: maximal heart rate; HRpeak: peak heart rate; VO ₂ max: maximal oxygen consumption; VO ₂ peak: peak oxygen consumption; HRr: heart rate reserve; BW: body weight; EB: elastic bands; DB: dumb bells; na: non available; BWP: brisk walking programme; MFP: medical fitness programme; LV: low volume; HV: high volume.																						

Len.: length; Freq.: frequency; 1RM: 1 repetition maximum; no. exe.: number of different exercises; Reps.: repetitions; w: week; y: year; mo: month; alt: aerobic and resistance training performed on alternate sessions; →: progressing to; aer: aerobic only; res: resistance only; na: more exercises available; HRmax: maximal heart rate; HRpeak: peak heart rate; VO₂max: maximal oxygen consumption; VO₂peak: peak oxygen consumption; HRr: heart rate reserve; BW: body weight; EB: elastic bands; DB: dumb bells; na: non available; BWP: brisk walking programme; MFP: medical fitness programme; LV: low volume; HV: high volume.

be relevant when compared with interventions that used aerobic and resistance training on the same session, where only eleven out of twenty-four studies reached similar results. Whether this is due to unique benefits of separate training or greater exercise volume remains to be explored in the future. Moreover, the studies conducted by Krousel-Wood et al. [29] and Lucotti et al. [18] which used a 5 times/week routine, only achieved clinical significance. This may be attributable to other intervention characteristics such as unsupervised home-based low to moderate intensity exercises, low (38%) adherence to exercise recommendations [29], and short intervention length (3 weeks) [18]. Nevertheless, lower training frequencies (twice weekly) were also able to improve glycemic control [16,25,36].

3.2.4. Intensity/duration

Intensity and duration are considered as important variables in exercise training that clearly affect glucose control and insulin sensitivity in T2DM patients [42], most likely through the means of a greater muscle glycogen usage at higher intensities or longer durations and subsequent glycogen repletion rate [43,44]. In fact, higher exercise intensities appear to convey greater cardio-protective benefits than moderate exercise intensities, even after total energy expenditure adjustments [45]. One meta-analysis showed that exercise intensity predicts improvements in overall blood glucose control to a greater extent than exercise volume (intensity $\times$ duration) [46]. However, Segerström et al. [11] recently highlighted the singular interaction between exercise intensity and its duration, and found that while insulin sensitivity is more related to exercise intensity, reductions in A1c seem to be more strongly linked to training volume. The special relationship between these variables is further emphasized when using interval training, a form of exercise where subjects perform successive bouts of relatively short duration at high intensity workloads (usually 1–4 min at 90% VO_2peak or higher), alternated with relatively small periods of active rest (generally 1–4 min at 50–60% of VO_2peak). This alternative to a continuous exercise training is believed to promote faster physiological muscle adaptations and metabolic control [47]. Nevertheless, concerns about compliance and safety issues may arise due to the higher intensities used in interval training [48], and may currently restrain its widespread endorsement for T2DM patients.

Current recommendations state that T2DM individuals should engage in a minimum of 150 min/week of aerobic exercise, performed at least at moderate intensity, which translates into 40% of heart rate (HR) reserve/ VO_2 reserve, 55% of HRmax or “12” on Borg’s scale [4]. In absolute terms, this would correspond to about 4.0 METs (metabolic equivalents) for a middle-aged man (40–64 years old) [49]. As for strength training, it is advised to perform a minimum of 1 set of 5–10 exercises for large muscle mass groups and the recommended intensity is “moderate to vigorous” [4], which translates to 50–84% of a maximal voluntary contraction or one repetition maximum (1RM) [49]. In turn, this would allow subjects to perform between 6 and 20 repetitions to fatigue, but training status, exercise selection and ultimately the maximal strength prediction formula used, may influence the number of prescribed repetitions [50].

In our review, several different markers (VO_2max , HRmax, HRreserve, lactate threshold and Borg’s scale) were used to quantify aerobic exercise intensity, and two markers were used for resistance exercise intensity (% of 1RM and Borg’s scale) (Table 3). Adding to the different indicators, exercise intensities and durations were also distinct among studies and, while some authors prescribed a broader spectrum of these variables, others recommended patients to exercise at specific values. Most of the analyzed papers maintained the recommended parameters throughout the entire length of the intervention, but eleven increased during the interventions at some point [10,11,14,15,22,23,26,27,31,33,40]. Interventions recommended at an intensity of at least 60% of HRpeak/HRmax or 55% of VO_2max for aerobic training and 50% of 1RM for resistance training generally showed statistically significant results. The only exception was the intervention of Balducci et al. [32], in which the minimum recommended intensity was 40% of HRr and 40% of 1RM, for aerobic and resistance training, respectively. However, subjects were instructed to exercise between 40 and 80% of their HRreserve, and from 40 up to 60% of 1RM. Since no actual average intensity data was provided at the end of the intervention, one cannot exclude the assumption that most of the participants exercised at a higher intensity than the recommended minimum. The high volume group of the intervention conducted by Segerström et al. [11] showed that a minimum of 15 min of continuous aerobic session, progressing to 25 min per session, may be enough for statistical significant A1c reductions. As for resistance training, clinical significant A1c changes may be achieved by starting with 5 min per session, progressing to 20 min per session [15].

3.2.5. Intervention length

Current guidelines stress the importance of an adequate lifestyle for optimal glucose control and strongly advise T2DM patients to engage in lifelong exercises [4,51]. In a recent review by Hansen et al. [51], two of five studies reported an improvement in glycemic control with a longer program duration, one found no effect on A1c in either intervention length, and two others found no further reductions on A1c after 12 or 84 weeks of intervention.

In our review, although studies did not compare different intervention lengths, both short 8 weeks [24,33,52], and long 1 or 2-year interventions [25,32,36,39,40] attained statistically significant A1c changes (Table 2). After only 3 weeks (the shortest intervention analyzed) Lucotti et al. [18] produced a clinically significant A1c change. Praet et al. [10] conducted a carefully planned intervention with 2 combined exercise groups for 1 year but found no changes in relation to baseline A1c. Intensity-related issues may have contributed for this outcome (see Section 3.2).

3.2.6. Aerobic exercise mode

Currently, no studies have analyzed the effects of different exercise modes on glucose control. This may be of significant importance for T2DM patients since exercise modes differ substantially in terms of total recruited muscle mass, type of impact or energy expenditure, among others. Since aerobic training seems to benefit blood glucose control by blood glucose uptake and improved muscular insulin sensitivity [4],

it seems reasonable to speculate that exercise modes that require higher amounts of muscle mass and energy expenditure may result in better health improvements for T2DM patients. Of the many different aerobic exercise modes (cycling, rowing, stepping and others), running seems to produce the highest caloric expenditure [53]. However, for this exercise mode, greater energy contributions are only possible with higher intensities, which may not be maintained by most patients (at least during adaptation/earlier intervention stages). Furthermore, special attention should be focused to minimize foot injuries or ulcerations caused by the direct impact to the feet during running. Another popular exercise ergometer/mode that requires a near full body muscle mass activation is the elliptical trainer and its impact-free characteristics and ease of use may be particularly useful in motor and peripheral neuropathy individuals, as they might eliminate coordination, balance and sensitivity concerns [54] that could impair proper treadmill usage.

In our review, twelve studies used just one exercise mode (10 walking/running and 2 cycling) and all others interventions used two or more exercise modes. Of the seventeen statistically significant studies, seven used a walking/running only exercise mode [12,22,26,33,39,41,55] and four used a combination of walking/running and cycling modes [16,19,25,52]. A combination of cycling and aerobic dance was also found to elicit significant glucose control improvements [34]. Although a very popular activity, swimming was not used as an aerobic exercise mode in any of the studies reviewed. All but three interventions used a continuous aerobic training method: Maiorana et al. [52] used a supercircuit (seven resistance exercises alternated with eight aerobic (cycling) stations, each performed for 45 s + 5 min walking on a treadmill), Lambers et al. [14] used an adapted circuit (walking or jogging (10 min), elbow flexion and extension (10 min), cycling (10 min), knee flexion and extension (10 min), stepping (10 min)) and Okada et al. [34] used a combination of 20 min of cycling (stationary bicycle) and 20 min of aerobic dancing. All these last referred studies produced significant statistical changes on A1c.

3.2.7. Resistance exercise mode

No study has analyzed the influence of different resistance exercise modes on glucose control. Current recommendations advise subjects to select large muscle mass exercises [4], as they provide greater energy expenditure and are time-efficient. Eight studies did not describe what specific resistance exercises were used and in five cases even the number of prescribed exercises was missing [11,12,31,34,41]. Overall, the number of different exercises performed ranged from 3 to 10 per session, but interventions with only 1 exercise (1 set) [15] as those up to 24–32 exercises (8 exercises multiplied by 3–4 sets) [40] were able to produce clinical or statistical significant results on A1c. Of the eighteen detailed interventions, “chest press” was present in fourteen studies, “leg curl” in thirteen, and “leg extension” in twelve papers. Almost all authors prescribed mainly large muscle mass exercises, except Lambers et al. [14], who used 2 large and 2 small muscle groups exercises, with significant results. A standard/traditional sets method was used by most researchers. The supercircuit used by

Maiorana et al. [52] and the adapted circuit used by Lambers et al. [14] (described in Section 4.6) were the sole exceptions and both attained significant A1c improvements. Clarifications about the reasons for specific exercise modes or methods selected were not routinely done, although we believe them to be related to materials available at sports facilities/home and the will to comply with standard exercise recommendations.

3.3. Methodological issues

Some concerns about the methods used by the different studies are raised: (1) not all authors provide information on how HRmax, HRr, VO₂max or 1RM were assessed or derived. On at least four occasions, the maximal aerobic test was accomplished in a different exercise mode (cycling) than that of intervention (brisk walking or home trainer, elliptical trainer, rowing ergometer [10]; nordic walking or cycling, rowing, stepping [17]; treadmill, cycling, elliptical, steppers [23]; cycling and stepping [11]). As maximal heart rates differ substantially among exercise modes [56], establishing an intensity for a different exercise mode than that of evaluation can lead to erroneous (non-corresponding) values; (2) whenever possible, authors should state the actual average exercise intensity at the end of the study, in addition to the recommended one. For example, in the study conducted by Church et al. [20], subjects were advised to exercise between 50 and 80% of VO₂max, but they actually exercised between 56 and 66% of VO₂max. To avoid misinterpretation and to allow a better comparison between studies, results should be analyzed in face of actual/real exercise intensities and not the ones prescribed; (3) Praet et al. [10] recommended a 7 times cycle that alternated active exercise for 3 min at 70–80% of HRmax and active rest for 45 s at 45% of HRmax (10th month), but unless HR dropped and raised instantly, this could not be achieved (e.g. in normal circumstances, a HR descent from 80 to 45% of HRmax may take even longer than 45 s). To minimize inaccuracies, it may be preferable to use speed over heart rate as an intensity indicator, whenever short exercise durations in interval training are prescribed; (4) resistance training intensity and the number of repetitions that can be performed until fatigue are strongly related [50]. However, in some of the analyzed studies, prescribed intensities (% of 1RM) do not match prescribed repetitions [22,26,32,33]. For example, Aylin et al. [33] recommend an intensity of at least 50% of 1RM and progressing to 60% of 1RM. This would allow participants to perform 15–20 repetitions to fatigue [50], but the authors opted to recommend only 8–10 repetitions. Resistance/strength training may be described as “training that in an efficient manner induces a measurable increase in muscle strength or/and hypertrophy” [57]. Hypertrophy is valuable for increases in glut-4 expression and although it may arise from a wide range of intensities, evidence suggests that the greatest increases occur at least at 75–80% of 1RM (or 8–10 repetitions to fatigue or near) [58]. If the intensity is too low (low % of 1RM or repetitions are not accomplished to fatigue or near fatigue), resistance training may not generate the expected physiological effects. Studies that used body-weight resistance exercises may also not pose the required intensity for significant strength and hypertrophy developments [11,12].

4. Conclusions

In an extensive review of the published studies, we found that combined resistance and aerobic exercise regimens improve glycemic control to a greater extent than either aerobic or resistance interventions alone. Our review analyzed twenty-eight studies with a total of thirty-one groups and found that nineteen of these achieved clinically or statistically significant A1c reductions. However, the plethora of different methods used in the different studies and the occasional lack of detailed training characteristics limited our ability to delineate the optimal exercise strategy for the management of T2DM. Nevertheless, the data collected seems to indicate that: (1) it is desirable to supervise all training sessions and to recommend a structured exercise training program; (2) restrictions on medication change and the inclusion of dietary assessments would be useful to assess the independent contribution of exercise to A1c changes; (3) minimum exercise intensity, duration and frequency needed for A1c reductions through combined exercise are not fully understood. Our review also suggests that splitting aerobic and resistance training on different days might have additional benefits for glycemic control. Analyzing the effects of different aerobic and resistance training modes (for examples, treadmill versus cycling; free weights versus own weight), different training and progression methods (for example, continuous to interval aerobic training; standard/traditional sets to supersets), and whether if one type of exercise should be more evident than the other (such as two aerobic and one resistance training sessions per week or vice versa) are issues that should be addressed in future studies as they are likely to convey greater knowledge on T2DM management through combined exercise.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.diabres.2012.08.004>.

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Paper II

[Submitted – *under review*]

Nutrition and physical activity characteristics of Portuguese older individuals with type 2 diabetes: compliance with recommendations.

Oliveira, CC¹; Abreu, S²; Carvalho, J²; Ribeiro, JC².

¹ MsC, Instituto Politécnico de Viana do Castelo, Escola Superior de Desporto e Lazer

² PhD, Research Centre in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto

Corresponding author:

César Oliveira

Escola Superior de Desporto e Lazer de Melgaço

Rua da Calçada

4960-529 Melgaço, Portugal

cesarchaves@esdl.ipv.pt

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Abstract

Objectives: The aim of this study was to analyze the daily physical activity and nutritional characteristics of Portuguese older individuals with type 2 diabetes mellitus and check for their compliance to international recommendations. **Design:** Cross sectional study. **Setting:** Exercise facilities of community swimming pools of Famalicão, Portugal. **Participants:** 101 older individuals with type 2 diabetes. **Measurements:** Daily physical activity was accessed through 1-week accelerometer use and the dietary intake by a 3-day dietary record that included 2 weekdays and 1 weekend day, completed by participants. Hematological and anthropometric data was also gathered. **Results:** Time spent on moderate and vigorous activities was $26,6 \pm 19$ and $0,8 \pm 2,1$ min/day, respectively, but only 22% of the participants performed at least 150 min/week of such activities. None of the participants was engaged in strength training. In respect to dietary intake, we found that many individuals are consuming less fiber and more protein, saturated fat and cholesterol than recommended (100%, 60%, 50% and 48% of all participants, respectively). None of the participants complied with all recommendations for daily dietary intake. **Conclusion:** We provide evidence that most Portuguese older individuals from our sample are not following international physical activity and dietary recommendations. Future research should focus on improving adherence to these critical lifestyle features in order to convey better health outcomes for individuals with type 2 diabetes.

Key-words: Type 2 diabetes, daily physical activity, nutrition, guidelines, compliance.

Introduction

Diabetes Melitus is a fastly growing disease that already affects 347 millions of individuals worldwide (1). Its prevalence increases with age and is highest in those over 65 years of age, where more than 25% of the population may not be able to control their glycemic levels without glucose-lowering drugs (2). Both life expectancy and quality of life are reduced in people with this condition, as they are at a higher risk of developing a broader range of complications like dyslipidemia, nephropathy, blindness, high blood pressure and other cardiovascular diseases (3). Fortunately, it has been shown that many of such ailments can be modulated by lifestyle changes and better health outcomes are expected for those who follow specific physical activity and dietary endorsements (4).

A joint statement between the American Diabetes Association (ADA) and the American College of Sports Medicine (ACSM) recommends that people with type 2 diabetes mellitus undertake a minimum of 150 minutes/week of moderate to vigorous aerobic exercise, spread out at least three days during the week, with no more than two consecutive days between bouts of aerobic activity (5). In addition, moderate to vigorous resistance training at least 2 to 3 days each week should also be engaged.

On the other hand, both the ADA and the International Diabetes Federation (IDF) have also issued dietary guidelines for individuals with type 2 diabetes. Among the expected similarities, the latter institution provides a more specific range for the different macronutrient intake proportions: 45 to 65% of the dietary energy intake (DEI) should be provided by carbohydrates, 10-20% of DEI by protein and 20-35% of DEI by FAT (6). IDF also endorses that saturated fat, cholesterol and sodium intakes should be lower than 7% of DEI, 200 mg/day and 2300 mg/day, respectively. Finally, the amount of recommended daily fiber intake is set to 25-50 grams.

However, despite the known relationship between healthy lifestyle choices and improved glycemic control, data on both daily physical activity and

dietary profile for a given sample of the population is scarce, particularly in Portugal. Therefore, we propose to evaluate the daily physical activity and the dietary profile of a Portuguese population with type 2 diabetes and determine if they comply with international recommendations.

Methods

Sample

Participants were recruited from a community-based exercise intervention for the elderly, taking place in Famalicão, Portugal. Diabetic subjects were identified and asked to participate in the study by telephone, if criteria inclusion was met. These involved being type 2 diabetic for more than 1 year, with no history of past or current insulin therapy, muscular and skeletal limitations, any known cardiovascular diseases, recent change in drug medication or usual diet, creatinin $\geq 200 \mu\text{m/l}$ or proteinúria $\geq 1 \text{ g/dl}$. At the time of evaluation, participants had not exercised for at least 5 months (not involved in supervised exercise of moderate to vigorous intensity for 20 minutes or more at least twice a week). All participants received a complete explanation of the purpose, risks and procedures of the investigation, and provided written informed consent. The investigation was in full compliance with the Helsinki declaration and all methods and procedures were approved by the Institutional Review Board.

Daily Physical Activity

Daily physical activity levels were assessed through the use of accelerometers (Actigraph LLC GT3X), for one week, according to standard procedures (7). Participants were asked to maintain their usual levels of physical activity. Accelerometry cut-points for moderate to vigorous physical activity are described elsewhere (8). Data for resistance training characteristics was accessed through a questionnaire, applied to each of the subjects, after

being given an explanation/definition of resistance training and a description of some resistance exercises.

Dietary intake

Dietary intake was accessed by a 3-day dietary record that includes 2 weekdays and 1 weekend day, completed by participants. Portion sizes of foods and beverages consumed was estimated using household measures (cups, glasses, spoons, slices, etc.) and other props (cups, glasses, food wrappers or containers) as an aid in determining serving sizes. The nutrient analysis was performed using the software Food Processor SQL (ESHA Research Inc., Salem, OR, USA). This software uses nutritional information from the USA that was adapted for typical Portuguese foods and beverages. Nutrient means of the 3 day of diet record was used in the analysis. To evaluate nutritional inadequacy, IDF recommended intake goals were used (6). The 3-day dietary record is often used as the gold standard for characterization of current and usual diet in groups or individuals (9, 10). All subjects completed the dietary record during the same month of the year (November).

Body Composition

Body composition was evaluated by Dual Energy X-ray Absorptiometry - DXA, (model "Hologic 4500 Explorer"), and anthropometric methods (weight, height and body mass index – BMI). All evaluations were performed by the same individuals (one for all radiological evaluations and other for all anthropometric evaluations).

Biochemical analyses

Plasma concentrations of HbA1c (ADAMS A1c HA-8160; A. Menarini diagnostics; high performance liquid chromatography method), insulin (IMMULITE 1000 SYSTEMS; Siemens; chemiluminescence immunoassay method), fasting glucose, C-reactive protein (CrP), total cholesterol, high-density lipoprotein (HDL-c), low-density lipoprotein (LDL-c) and triglycerides (COBAS INTEGRA 800; Roche; fasting glucose – enzymatic method; total

cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides – colorimetric method; CrP – immunoturbidimetric method) were collected. Insulin resistance and β -cell function were derived from fasting plasma glucose and insulin concentrations by standard homeostasis model assessment (HOMA-is and HOMA-bcf) (11). Blood samples were collected after a 12-hour fasting period.

Resting heart rate and blood pressure

Resting blood pressure and heart rate were measured using an automated blood pressure monitor (Colin, DP 8800). After 15 minutes at rest in a quiet, temperature and humidity-controlled room (circa 22 degrees Celsius and 50% of humidity), measurements were taken with the subjects seated in an upright position with an arm comfortably placed at heart level. The average of three measures for systolic and diastolic blood pressure and heart rate were entered as data. All evaluations followed current guideline recommendations (12) and were conducted by the same experienced individual.

Statistical analysis

Data is presented as means $\pm$ (standard deviation). Carbohydrate, protein, fat, alcohol, saturated, mono and polyunsaturated fats are expressed as percentage of DEI. A detailed analysis of participant's nutrient and daily physical activity was also conducted to check for individual compliance to recommendations. All analyses were performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL).

Results

General data

Table 1 shows participants main characteristics. We collected information on 101 individuals (64 women and 37 men), with a mean age of 65 years. Mean duration of time living with diagnosed diabetes was 11 years. 58% of the participants were obese (mean BMI of 31 kg/m²) and body fat accounted for

38,1% of their body weight (42,4% in women and 30,6% in men). According to the original prediction equation of Harris and Benedict (13), subject's resting metabolic rate (RMR) should be 1402 kcal/day, but individuals with diabetes seem to show a higher resting metabolic rate than their non-diabetic counterparts (14). When using a formula designed for obese type 2 diabetic patients, RMR was estimated at 1561 kcal/day (14). Mean systolic and diastolic blood pressure was 145 and 77 mmHg, respectively. Mean fasting plasma glucose was 150 mg/dl and glycated hemoglobin 6,6%. Total cholesterol was 193 mg/dl, HDL cholesterol 52 mg/dl and LDL cholesterol 103 mg/dl. Triglycerides levels were 137 mg/dl and hs C-reactive Protein was evaluated at 0,42 mg/dl. Insulin was detected at 11,4 uIU and HOMA-is and HOMA-bcf was 4,3 and 60, respectively. Hypoglycemic drugs were used by almost all participants, while consumption of anti-hypertensive, cholesterol lowering and other types of medication were used by 71, 57 and 75% of participants.

Table 6 – Participant's main characteristics.

	mean±sd
Gender (M/F)	37/64
Age (years)	65,4±6,5
W/diabetes	10,8±9,5
BMI (kg/m ²)	31±4,2
%FAT	38,1±7,1
RMRh&b (kcal)	1402±159
RMRhuang (kcal)	1561±202
Mean SBP (mm/Hg)	145±17
Mean DBP (mm/Hg)	77±9
A1c (%)	6,6±1,4
FPG (mg/dl)	150±46,6
Total cholesterol (mg/dl)	193±36
HDL cholesterol (mg/dl)	52±14
LDL cholesterol (mg/dl)	103±29
Tryglycerides (mg/dl)	137±66
hsCrP (mg/dl)	0,42±0,72
Insulin (uIU)	11,4±7,8
HOMA-is	4,3±3,5
HOMA-bcf	60±54,3
Hypoglycemic drugs	89 (88%)
Anti-hypertensive drugs	72 (71%)
Cholesterol-lowering	58 (57%)

M= male; F= female; BMI= body mass index; h= height (m); RMR= resting metabolic rate; SBP= systolic blood pressure; DBP= diastolic blood pressure; A1c= glycated hemoglobin A1c; FPG= fasting plasma glucose; HDL= high density lipoprotein; LDL= low density lipoprotein; hsCrP= high sensitivity c-reactive protein; HOMA-is=

insulin sensitivity accessed by
homeostasis model assessment;
HOMA-bcf= beta cell function accessed
by homeostasis model assessment.

Dietary intake

Total energy intake and selected nutrient and fiber intake are shown in table 2. DEI was found to be 1443,5 kcal/day. When analyzed as a whole, the relative intake of macronutrients generally followed IDF's dietary recommendations. Fat and carbohydrate consumption was within 25-35% and 45-60% of total dietary intake, respectively, and protein intake was slightly above the upper limit recommendation of 20%.

Table 2 – Participant's dietary intake characteristics.

Macronutrient	Amount (gr)	%DEI
Protein	73,2±17,7	21,5±3,9
Carbohydrate	159,1±44,4	46,0±7,1
Fat	44,9±14,6	29,0±5,8
Saturated	11,3±5,1	7,3±2,6
Monounsaturated	17,3±6,0	11,3±2,8
Polyunsaturated	6,7±3,1	4,3±1,4
Omega-3	0,6±0,6	
Omega-6	5,2±2,6	
O6-03 ratio	16±11	
Trans	0,7±0,7	0,2±0,4
Alcohol	13,1±12,8	3,4±5,2
Total energy intake (Kcal)	1444±339	
Cholesterol (mg)	203,7±70,2	
Sodium (g)	1,297±0,473	
Caffeine (mg)	107,8±76,5	
Artificial Sweeteners (mg)	16,9±69,7	
Fiber (gr)	12,5±5,2	

Data shown as mean±sd; %DEI= percent of dietary energy intake.

However, when individually analyzed, 43% of participants consumed less than the lower limit for carbohydrate intake and 60% consumed more than the upper recommended limit for protein intake (fig.1). As for fat intake, most of the participant's intake was within recommendations. The mean amount of saturated fat intake marginally exceeds the proposed IDF limit of 7%, but half of the participants consumed more than this recommended limit. Among lipids, monounsaturated fats were the most consumed (11,3% of DEI) and the omega-

6:omega-3 polyunsaturated fatty acids ratio was 16:1. Daily cholesterol intake was of 204 mg, marginally above recommended upper limit. Nevertheless, nearly half of participants (48%) consumed more than 200 mg/day of cholesterol. Fiber intake was of 12,5 gr/day, which is far lower than IDF's recommendation (25-50 gr/day). In fact, none of the individuals from our sample achieved the minimum recommendation of 25 gr/day. Mean sodium intake was just under 1,3 gr/day, which is in line with recommendations that limit the amount of this nutrient to 2,3 gr/day. Only 4% of the individuals consumed more than this upper limit. Alcohol consumption was slightly above 3% of DEI. Caffeine and artificial sweeteners intake was of 108 and 17 mg/day, respectively. Finally, vitamin D intake was of 22 IU/day.

None of the evaluated individuals complied with all the different nutrient recommendations but most were able to follow recommendations for at least 4 nutrient intakes.

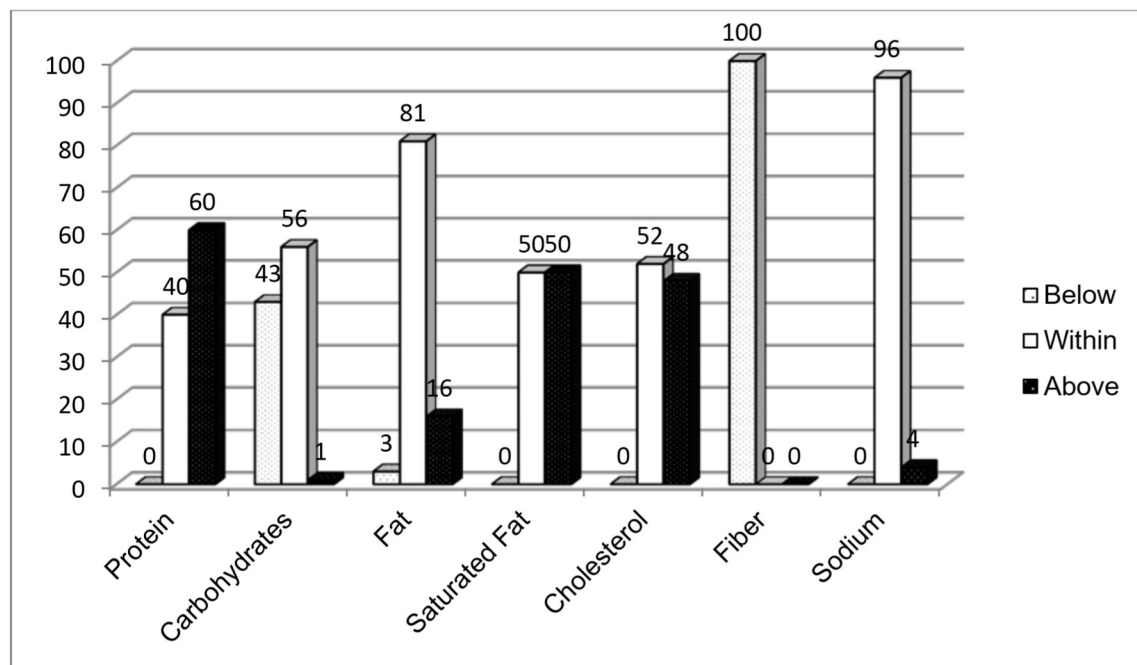


Fig. 2 – Percent of participants below, within or above recommendations of selected nutrients and fiber intakes.

Physical activity

Table 3 presents the data for the daily physical activity. Time spent on moderate activities was 26,6 min/day and in vigorous physical activities was less than 1 min/day. This approaches the recommended 150 min/week of moderate to vigorous activities, but the percentage of individuals that actually complied with these recommendations was only 22%. Furthermore, none of the participants reported being involved in any strength training exercises or activities.

Table 3 – Participant's daily physical activity characteristics.

Type of activity	Time (min/day)
Moderate activities	26,6±19,0
Vigorous activities	0,8±2,1
Very Vigorous activities	0,03±0,07

Data shown as mean±sd;

Discussion

One of the major medical nutrition therapy recommendation concerns weight loss in obese patients, as this likely increases insulin sensitivity and improves glycemic control (grade “A” evidence) (15). It is possible that some of the diabetic patients were trying to lose weight at the time of evaluation and therefore, consuming fewer calories. On the other hand, underreporting of caloric intake is a very well know phenomenon, especially among individuals with higher BMIs (16) or with diabetes (17, 18), and this could partially explain the self-reported reduced caloric intake results. In fact, the perceived social pressure to adopt a diabetes-recommended diet may prompt individuals to intentionally omit some food or food groups that are not in line with those recommendations, thus leading to underreporting of the total energy intake.

In relation to the dietary data, we found that when analyzed as a whole, the relative intake of macronutrients generally followed IDF's dietary

recommendations, but individual analysis revealed that most patients failed to comply with recommendations on most nutrients. This was specially observed for fiber intake (one of the staple premises of nutrition in type 2 diabetes), were none of them were able to reach the lower limit of recommended daily fiber intake.

Failing to adhere with dietary recommendations may compromise glycemic control in people with type 2 diabetes. The poor dietary adherence observed in our sample reflects similar findings across other European countries, either among individuals with type 1 (19) or type 2 diabetes (20, 21). Translation from the scientific basis of established recommendations into the daily routine of patients with type 2 diabetes has been challenging. A recent review analyzed the adherence outcomes of 38 dietary interventions and found that most of those outcomes were no different from the results in the control groups (22). As such, the authors conclude that it is not yet possible to identify the interventions that should be used in practice to enhance adherence to dietary recommendations.

As for physical activity, we found that the majority of the participants do not met recommendations for aerobic exercise and none complied with the strength training advice. This is especially relevant, as both forms of exercise are currently endorsed by the ACSM/ADA joint statement (5). In addition, a recent publication highlights the relevance of an exercise intervention that focus on both aerobic and strength components, concluding that this approach is more effective than either isolated forms of exercise to prevent/delay the onset of diabetes (23) or even control it when it is already installed (24, 25). Furthermore, exercise capacity can predict the mortality risk of diabetic patients independently of body mass index (26). It is known that unfit and sedentary diabetic individuals generally exhibit an increased cardiovascular disease risk. However, the dose–response relationship for physical activity/fitness is such that when they undertake high levels of activity (or have high fitness), the level of risk becomes similar to that of their normal weight or non-diabetic peers (27). Despite this, individuals with diabetes are less active than their non-diabetic

counterparts (28) and we can argue that low levels of regular physical activity contribute to an accelerated disease onset and progression (29). Furthermore, exercise, despite all of its well-known benefits, is the least used strategy on diabetes management (30), which clearly is a limitation for an optimal glycemic control. Of special interest to us, was the fact that none of the participants was involved in strength training activities. These are well-known for their glucose lowering effects (31) but their impact on people's quality of life (32, 33) and life expectancy (34) far exceeds simple changes in blood glucose levels. In particular, prevention, attenuation or reversal of sarcopenia (muscle mass loss) is critically relevant for the age group of our sample, as muscle mass maintenance can exert beneficial effects on glycemic control but also in the functional fitness and independence of older individuals (35, 36).

Lifestyle interventions have proven to be highly effective in preventing and controlling type 2 diabetes (37-39). However, individuals with this condition seem to have many difficulties following dietary and physical activity recommendations. Interventions aiming to improve dietary habits and increase physical activity specifically in older individuals can generate positive results (40, 41). Unfortunately, the beneficial effects of such interventions may be markedly reduced after intervention is completed (42), which indicates that a continuous intervention may be needed to sustain the related positive outcomes. Therefore, while there is no doubt that non-pharmacologic treatments are a key priority in glucose management of older individuals with diabetes (43), the optimal strategy to increase patient's adherence to recommendations is not yet fully understood.

A possible limitation for this study concerns its design (cross sectional) and the method used to assess patient's dietary intake. The latter was acquired through questionnaires, completed by participants, and it is possible that the patients under-estimated their dietary intakes, due to social desirability and eating restraint factors (44). Medication use can also mask the detrimental effects on glycemic control due to a poor nutrition or low daily physical activity. In an exercise-based intervention study, it has been shown that the control

group tends to increase medication usage, while the exercise group tends to decrease the use of glucose lowering-drugs (45). This study did not evaluate the effect of the types and dosages of medications used and their relationship with patient's glycemic control, so it is possible that the effects on glycemic control of a poor diet and a sedentary lifestyle may be masked by an increase in medication usage.

In summary, our data provides further evidence that individuals with type 2 diabetes do not follow available dietary and daily physical activity recommendations. As this can result in a compromised diabetes management response, future research should focus on improving adherence to these critical lifestyle features in order to convey better health outcomes for people with type 2 diabetes.

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Paper III

[Submitted – under review]

Title

Combined exercise in individuals with type 2 diabetes: emphasis on the aerobic component. A Randomized, Controlled Trial.

Oliveira, C¹; Carvalho, J²; Abreu, S²; Chen, KY³; Ribeiro, J².

¹ MsC, Instituto Politécnico de Viana do Castelo, Escola Superior de Desporto e Lazer

² PhD, Research Centre in Physical Activity, Health and Leisure, Faculty of Sport, University of Porto

³ PhD, Human Energy & Body Weight Regulation Core; Diabetes, Endocrinology, and Obesity Branch; Intramural Research Program/NIDDK, Bethesda Maryland, USA

Corresponding author:

César Oliveira

Escola Superior de Desporto e Lazer de Melgaço

Rua da Calçada, 4960-529 Melgaço, Portugal

cesarchaves@esdl.ipv.pt

Abstract

Aims: The aim of this study was to compare the efficacy of two different combined exercise interventions in reducing hemoglobin A1c levels in patients with type 2 diabetes. **Materials and methods:** 35 sedentary individuals with type 2 diabetes were randomly assigned to a combined exercise group with emphasis on the aerobic component (A+, n=10, 45 minutes aerobic, 15 minutes resistance), a combined exercise group with emphasis on the resistance component (R+, n=12, 15 minutes aerobic, 45 minutes resistance), or to a control group (n=13). Interventions took place 3 days/week for 20 weeks, at Famalicão, Portugal. Aerobic exercise intensity was set to a minimum of 55% of predicted maximal heart rate and resistance exercise intensity at 70% of 1 maximum repetition. **Results:** Glycated hemoglobin (A1c) levels were only significantly reduced in group A+ [-0.68%, 95% CI (-1.16% to -0.20%), p=0.007]. A+ and R+ exercise groups significantly reduced fasting glucose [-26.8 mg/dl, 95% CI (-46.5 to -7.1mg/dl), p=0.009; -19.3 mg/dl, 95% CI (-37.2 to -1.3 mg/dl), p=0.036, respectively] and insulin levels [-2.3 µIU/ml, 95% CI (-3.8 to -0.8 µIU/ml), p=0.005; -1.8 µIU/ml, 95% CI (-3.1 to -0.4 µIU/ml), p=0.015], and improved insulin sensitivity index [-1.6, 95% CI (-2.5 to -0.7), p=0.001; -1.95% CI (-1.8 to -0.2), p=0.021, respectively]. **Conclusions:** A 20-week combined exercise regimen that favors the aerobic component was more efficient to reduce A1c levels in patients with type 2 diabetes.

Keywords: type 2 diabetes, combined exercise, A1c, aerobic, resistance

Introduction

A strong body of evidence highlights the beneficial effects of exercise and physical activity for type 2 diabetes mellitus prevention and management [1]. Substantial research has been conducted to identify the specific impact by different types of exercise (aerobic vs. resistance exercise), and more recently a combination of both types of exercise [2-4]. Since these effects seem to be synergistic, evidence suggests that combined exercise improves glycemic control to a greater extent than practicing separately. As a result, the most recent joint statement between the American College of Sports Medicine (ACSM) and the American Diabetes Association (ADA) encourages individuals with type 2 diabetes to engage in both aerobic and resistance-type exercises for optimal glycemic control [5].

We recently reviewed the training characteristics of combined exercise interventions and found a plethora of different methods used by investigators. However, the lack of detailed training characteristics limit the ability to evaluate the differences in managing type 2 diabetes via combined exercise [6]. Of the 28 studies using combined exercise protocols, none identified the relative contribution of aerobic and resistance exercise on glycemic control. Therefore, in the current study, Diabetes Combined Exercise trial (DICE), we compared two combined exercise regimens with different ratios of the aerobic and resistance components to evaluate the subsequent effects on glycemic control, as reflected by fasting plasma hemoglobin A1c concentrations.

Materials and Methods

Design Overview

We conducted a 20-week randomized controlled trial with a parallel group design. Sedentary individuals with type 2 diabetes were randomly assigned to one of the two exercise groups (group A+ performed 45 min of aerobic exercise followed by 15 minutes of resistance exercise; group R+ performed 15 min of aerobic exercise followed by 45 minutes of resistance exercise), or a control group with no intervention (group C). Alongside with intervention, all groups performed one hydrogymnastics class (45 minutes) once a week. Exercise intervention took place 3 times a week (non-consecutive days) and each session was supervised by at least one exercise specialist.

Setting and Participants

Sample was acquired from a community-based exercise facility in Famalicão, Portugal. Subjects with type 2 diabetes were identified and asked to participate in the study by telephone, if the following inclusion criteria were met: confirmed diagnosis of type 2 diabetes for more than 1 year, being between 40 and 80 years-old, and without muscular and skeletal limitations for aerobic or resistance exercise. Exclusion criteria consisted of any history of insulin therapy, any known heart diseases, recent change in medication or usual diet, creatinin $\geq 200 \mu\text{m/l}$ or proteinuria $\geq 1 \text{ g/dl}$. At the time of evaluation, participants had not participated in a formal exercise program for at least 5 months (defined as moderate to vigorous intensity for 20 minutes or more at least twice a week). Before the study, all participants received a complete explanation of the

purpose, risks and procedures of the investigation, and provided written informed consent. The investigation was in full compliance with the Helsinki declaration and all methods and procedures were approved by the Institutional Review Board at the University of Porto. All individuals were cleared to participate in the intervention by their general practitioner. Participant's flow diagram is presented in figure 1.

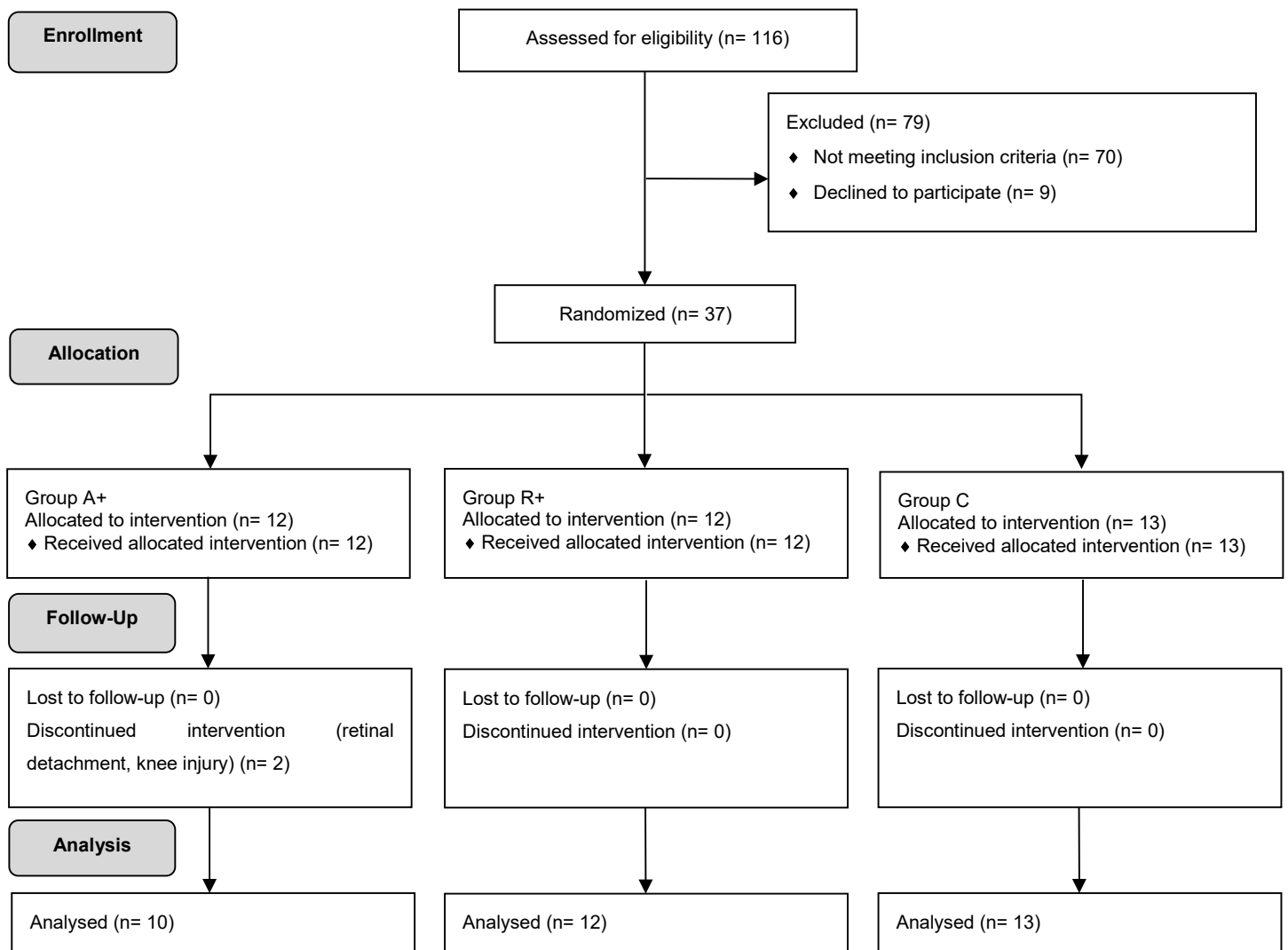


Figure 1. Participant's flow chart.

Randomization and intervention

37 individuals were randomly assigned to take part in one of the two exercise group arms or in a control group (simple randomization).

Aerobic exercise consisted in walking/running on a leveled indoor surface with a 100 meter perimeter. Participants were asked to achieve the highest number of laps in the assigned exercise time (15 or 45 minutes, respectively). Immediately after finishing aerobic exercise, participants recorded the number of achieved laps in their individualized exercise plan. As they were asked to improve their running/walking distance at each exercise session, adjustments for aerobic exercise were made at each session. Subjects used a heart rate monitor (POLAR Electro OY, Finland; Team System) throughout the entire exercise session. All participants were instructed to exercise at a minimum of 55% of their predicted maximal heart rate (pHR_{max}) [7], which is considered as “moderate intensity” [8]. We set no upper limit for exercise intensity and encouraged participants to exercise at the highest intensity that was still subjectively comfortable. After each session, we would analyze heart rate data to check for compliance. If the intensity was $<55\%$ of pHR_{max} , we would advise participants to increase walking or running speed. This mode of aerobic exercise (walking/running) was selected for being the most familiar aerobic activity and also the most related to everyday activities of our sample.

Resistance training consisted of 7 exercises, starting with large muscle mass groups and continuing to smaller muscle mass groups: leg press, chest press, lat pulldown, standing shoulder press, standing biceps curl, abdominal

crunch, and lumbar extension. Resistance exercise machines were used for the first four exercise modes and free weights for the rest at the exercise facility. Exercise selection was made based on current guidelines (both large and small muscle mass groups) and availability of strength training machines. An intensity of 70-80% of 1 repetition maximum (1RM) was used for increases in strength, muscle mass and insulin action [9], which generally allows participants to perform between 8 to 12 repetitions [10]. This intensity is classified as “hard” [8]. Once participants were able to perform more than 12 repetitions, they were instructed to increase exercise load in a manner that they were able to perform between 8-12 repetitions with the new weight load. Each new load was recorded on their individualized exercise plan. Subjects would perform 1 or 3 sets per exercise, according to group allocation. Since 30 seconds were needed to complete each set, and rest intervals between sets were fixed at 90 seconds, performing 1 set of each of the 7 exercises would take around 14-15 minutes and 42-45 minutes for 3 sets, respectively.

Compliance rate was set to completing at least $\frac{2}{3}$ of scheduled exercise sessions.

Maximal strength was evaluated using the submaximal exercise test of Lombardi [11] on leg press, chest press, lat pulldown, standing shoulder press, standing biceps curl, abdominal crunch and lumbar extension. Evaluated exercises and those selected for intervention were the same. Aerobic power was evaluated through Balke’s maximal physical fitness test [12]. All evaluations were made after two familiarization exercise sessions.

Body composition and bone mineral density were evaluated by Dual Energy X-ray Absorptiometry - DXA (Hologic QDR 4500a, Bedford, MA), and anthropometric methods, including weight and height (SECA 708, Hamburg, Germany). The same experienced study staff that was blinded to treatment groups performed all the evaluations.

Resting heart rate and blood pressure (Pressmate BP-10, Omrom Health Care Co., Ltd, Kyoto, Japan) were measured in a temperature and humidity controlled room (22 degrees Celsius and 50% of humidity) [13]. Before and after evaluations were performed at the same hour of the day, by the same experienced study staff.

participants were asked to maintain their normal levels of physical activity throughout the intervention. To assess if they complied with this recommendation, we recorded their daily physical activity levels using accelerometers (GT3X Actigraph LLC, Florida, USA) for one week before and one week after the intervention, according to standard procedures [14]. Accelerometry cut-points for moderate to vigorous physical activity are described elsewhere [15].

A letter sent to physicians of respective patients asking them not to change their medication throughout the 20-week intervention period, unless it was judged critically important to their health, controlled the medication usage. Informing the researchers of any drug modification or adjustment was mandatory.

Dietary intake was accessed by a 3-day dietary record that included 2 weekdays and 1 weekend day, completed by participants, before and after intervention [16, 17]. Portion sizes of foods and beverages consumed were estimated using household measures (cups, glasses, spoons, slices, etc.) and other props (cups, glasses, food wrappers or containers) as an aid in determining serving sizes. The nutrient analysis was performed using the software Food Processor SQL (ESHA Research Inc., Salem, OR, USA). This software uses nutritional information from the USA that was adapted for typical Portuguese foods and beverages. Nutrient means of the 3 days of diet record was used in the analysis. All subjects completed the dietary record during the same month of the year (November and June, before and after intervention, respectively). Participants were asked to maintain their usual dietary patterns throughout intervention.

Outcomes and Follow-up

Blood samples were collected after a 12-hour fasting period. To avoid interactions with acute exercise effects, final analyses were performed one week after the last bout of exercise. The main outcome was the plasma concentration of HbA1c (ADAMS A1c HA-8160; A. Menarini diagnostics; high performance liquid chromatography method). Secondary outcomes were insulin (IMMULITE 1000 SYSTEMS; Siemens; chemiluminescence immunoassay method), fasting glucose, C-reactive protein (CrP), total cholesterol, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and triglycerides (COBAS INTEGRA 800; Roche; fasting glucose – enzymatic method; total cholesterol, HDL-c, LDL-c and triglycerides –

colorimetric method; CrP – immunoturbidimetric method). Insulin sensitivity index and β -cell function were derived from fasting plasma glucose and insulin concentrations by standard homeostasis model assessment (HOMA-is and HOMA-bcf) [18].

Statistical analysis

All values are expressed as means (SD). Treatment effects were determined by General Linear Model (GLM – repeated measures ANOVA) with Bonferroni's post-hoc adjustments for multiple comparisons for main effects between intervention groups (interaction). All analyses were performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL), with a significant level set at 0.05.

Results

A total of 35 Caucasian patients (A+, n=10; R+, n=12; C, n=13) were considered for analyses (per-protocol). Dropout consisted of only 2 subjects, both in group A+ and during the first week of intervention (retinal detachment and knee injury, both unrelated to exercise intervention). There were no differences between groups at baseline (Table 1). Medication use was high across all groups. At least half of the participants consumed lipid-lowering or antihypertensive agents and almost all were treated with antidiabetic medications. Both exercise groups showed a compliance rate of >80%. Adverse effects were rare and related to minor delayed onset of muscle soreness. Medication use was unaltered throughout intervention.

Table 1. Baseline characteristics.

	A+	R+	C
n	10	12	13
Men/Women	4/6	3/9	6/7
Mean age (years)	66,7±6,3	65,7±8,6	65,5±5,6
Weight (kg)	70,0±7,0	71,1±10,4	75,9±10,4
BMI	29,6±2,9	30,3±4,1	30,8±4,3
Mean duration of diabetes (years)	13,3±11,0	6,1±4,5	11,3±8,5
Systolic blood pressure (mm/hg)	154,1±22,8	139,5±15,6	142,9±16,6
Diastolic blood pressure (mm/hg)	76,1±9,1	73,6±8,6	82,5±9,6
Medication use (n (%))			
Oral hypoglycemic agents	10 (100%)	10 (83%)	11 (85%)
Antihypertensive agents	8 (80%)	9 (75%)	9 (69%)
Lipid-lowering agents	6 (60%)	8 (67%)	8 (62%)

A+ = 45 minutes aerobic plus 15 minutes resistance exercise group; R+ = 15 minutes aerobic plus 45 minutes aerobic exercise group; C = control group; BMI = body mass index.

There was a significant main effect of intervention on A1c ($F=4.42$; $p=0.043$), fasting glucose ($F=9.22$; $p=0.005$), fasting insulin ($F=18.45$; $p<0.001$), and HOMA-is ($F=18.45$; $p<0.001$). There was a significant interaction effect between baseline and final evaluation and the groups on A1c ($F=3.49$; $p=0.043$). Results for baseline and final evaluation of hematological variables are shown in table 2. When compared to baseline evaluations, A1c, the primary outcome, was only significantly reduced in group A+, after intervention [-0.68%, 95% CI (-1.16% to -0.20%), $p=0.007$]. A+ and R+ exercise groups significantly reduced fasting glucose [-26,8 mg/dl, 95% CI (-46.5% to -7.1%), $p=0,009$; -19,3 mg/dl, 95% CI (-37.2 mg/dl to -1.3 mg/dl), $p=0,036$, respectively] and insulin levels [-2,3 μ IU/ml, 95% CI (-3.8 μ IU/ml to -0.8 μ IU/ml), $p=0,005$; -1,8 μ IU/ml, 95% CI (-3.1 μ IU/ml to -0.4 μ IU/ml), $p=0,015$], and improved insulin sensitivity [-

1,6, 95% CI (-2.5 to -0.7), $p=0,001$; -1, 95% CI (-1.8 to -0.2), $p=0,021$, respectively]. CrP was only reduced in group A+ [-0,65 mg/dl, 95% CI (-1.29 mg/dl to -0.01 mg/dl), $p=0,047$]. There were no significant changes in the control group.

Table 2. Hematologic data before and after intervention.

	A+			R+			C		
	Bef.	Aft.	Sig.	Bef.	Aft.	Sig.	Bef.	Aft.	Sig.
A1c (%)	7,1±1,2	6,5±0,8	0,007*	6,8±1,3	6,5±1,4	0,23	6,5±2,0	6,6±2,0	0,49
Glucose (mg/dl)	166,2±50,6	139,4±23,2	0,009*	147,7±31,6	128,4±31,4	0,036*	145,6±65,6	144,4±66,4	0,89
Insulin (µIU/dl)	9,6±5,2	7,3±4,7	0,005*	10,1±3,9	8,3±3,3	0,015*	8,5±3,7	7,3±2,5	0,088
HOMA IS	4,0±2,8	2,5±1,6	0,001*	3,6±1,3	2,6±1,0	0,021*	3,2±2,1	2,7±1,6	0,24
HOMA BCF	37,7±21,7	38,2±27,6	0,93	49,7±25,5	55,3±27,0	0,24	53,8±37,1	46,6±27,7	0,115
Total chol. (mg/dl)	177,6±26,5	178,1±25,2	0,97	200,5±39,9	187,8±34,7	0,27	186,9±40,9	193,2±55,2	0,56
HDL-c (mg/dl)	46,6±11,0	44,8±11,3	0,40	50,9±8,7	51,8±9,0	0,67	52,1±20,3	53±18,5	0,62
LDL-c (mg/dl)	91,3±23,1	101,9±17,6	0,28	113,0±32,8	110,4±32,3	0,77	97,9±33,6	111,5±48,2	0,112
Triglycerides (mg/dl)	150,3±91,6	145,4±90,1	0,74	120,5±35,8	117,3±55,2	0,81	142,4±88,9	117,3±63,1	0,058
CrP (mg/dl)	0,95±1,46	0,30±0,22	0,047*	0,25±0,17	0,22±0,15	0,91	0,53±1,21	0,27±0,26	0,35

A+ = 45 minutes aerobic plus 15 minutes resistance exercise group; R+ = 15 minutes aerobic plus 45 minutes aerobic exercise group; C = control group; Bef. = before intervention; Aft. = after intervention; Sig. = significance; * = statistically significant after intervention; A1c = glycated hemoglobin A1c; HOMA IS = insulin sensitivity accessed by homeostasis model assessment; HOMA BCF = beta cell function accessed by homeostasis model assessment; CrP = c-reactive protein.

Changes in body composition are depicted in table 3. After intervention, there was a significant reduction of fat mass percentage in group R+ [-1.3%,

95% CI (-2.2% to -0.3%), $p=0.011$] and a significant increase of bone mineral content on group A+ [90.5 g, 95% CI (23.1 g to 157.9 g), $p=0.010$].

Table 3. Body composition changes.

	A+			R+			C		
	Bef.	Aft.	Sig.	Bef.	Aft.	Sig.	Bef.	Aft.	Sig.
Weight (kg)	70,0±7,0	69,5±6,5	0,35	71,1±10,4	70,4±10,7	0,22	75,4±10,7	75,3±11,0	0,80
BMI	29,6±2,9	29,3±2,6	0,34	30,3±4,1	30,0±4,2	0,21	30,7±4,5	30,6±4,7	0,84
Fat (%)	36,2±7,4	35,3±7,3	0,094	39,0±6,9	37,8±6,5	0,011*	37,1±6,9	36,4±6,5	0,109
FFM (kg)	44,6±6,4	45,0±7,2	0,35	43,4±8,8	43,9±8,9	0,20	47,1±6,8	47,6±6,7	0,23
BMC (g)	1855±243	1945±298	0,010*	1897±459	1881±458	0,58	2120±383	2091±399	0,34
BMD (g/cm ²)	1,039±0,076	1,050±0,069	0,25	1,034±0,129	1,028±0,130	0,51	1,094±0,136	1,078±0,134	0,087
Z-score	-0,36±0,74	-0,19±0,61	0,103	-0,24±0,83	-0,27±0,82	0,79	-0,06±1,32	-0,17±1,26	0,25

A+ = 45 minutes aerobic plus 15 minutes resistance exercise group; R+ = 15 minutes aerobic plus 45 minutes aerobic exercise group; C = control group; Bef. = before intervention; Aft. = after intervention; Sig. = significance; * = statistically significant after intervention; BMI = body mass index; FFM = fat free mass; BMC = bone mineral content; BMD = bone mineral density.

Mean aerobic exercise intensity was 69% of pHR_{max} in A+ group and 73% of pHR_{max} in R+ group. Resistance exercise intensity remained at the scheduled 70-80% of 1 RM. Significant improvements on all strength measures and aerobic power were seen for both exercise groups after intervention (table 4).

Table 4. Physical fitness changes.

	A+				R+			
	Bef.	Aft.	%ch	Sig.	Bef.	Aft.	%ch	Sig.
Leg press (kg)	39,3±14,1	85,9±34,0	119	0,000*	30,5±14,0	76,6±33,4	151	0,000*
Chest Press (kg)	10,9±6,3	22,6±12,1	107	0,001*	14,6±7,3	24,7±11,9	69	0,001*
Lat Pulldown (kg)	29,4±8,6	49±15,4	67	0,000*	27,3±11,2	48,6±16	78	0,000*
Standing Shoulder Press (kg)	12,9±7,9	27,3±17,2	112	0,000*	16,8±13,1	27,8±17,4	65	0,000*
Standing Biceps Curl (kg)	5,3±2,6	15,2±7,5	187	0,000*	6,8±2,9	14,7±5,6	116	0,001*
VO ₂ max (ml/kg/min)	23,3±2,5	27,5±3,1	18	0,001*	22,0±2,7	27,6±3,9	25	0,000*

A+ = 45 minutes aerobic plus 15 minutes resistance exercise group; R+ = 15 minutes aerobic plus 45 minutes aerobic exercise group; Bef. = before intervention; Aft. = after intervention; %ch = percent change from baseline; Sig. = significant; * = statistically significant after intervention; A1c = glycated hemoglobin A1c; HOMA IS = insulin sensitivity accessed by homeostasis model assessment; HOMA BCF = beta cell function accessed by homeostasis model assessment; CrP = c-reactive protein.

Compared to baseline, there was no change on energy intake or daily physical activity levels after the intervention (data not shown).

Discussion

In this study, we tested the hypothesis that, within a 20-week combined exercise intervention program to improve glucose control in patients with type 2 diabetes, the difference in the amount of aerobic and resistance exercises may matter. In relation to the primary outcome (A1c), we found that 45-min aerobic + 15-min resistance exercise (group A+) achieved a higher reduction (0,68%) as compare to 15-min aerobic + 45-min resistance exercise (group R+, 0,3%). It's worth noting that both intervention groups achieved improvements in several secondary outcome measures such as fasting glucose levels, insulin, and

HOMA-IR. Since many of these parameters are found to be closely related [19], these findings collectively support the notion that combined exercise program benefit overall glycemic control and insulin sensitivity.

The different physiological mechanisms by which aerobic and resistance training operate and the nature of A1c may partially explain this finding. Aerobic exercise has traditionally been regarded for its acute effects on whole-body insulin sensitivity, even after a single bout of exercise, which lowers blood glucose levels and reduces the prevalence of hyperglycemic episodes throughout the subsequent day and up to 72 hours [20]. Improvements in glycemic control following aerobic exercise are essentially attributed to the acute and cumulative effects of transitory improvements in glucose uptake following each successive bout of exercise, rather than to the chronic structural adaptive changes to prolonged exercise training. After one bout of aerobic exercise, several cellular pathways, mainly AMP-activated protein kinase, calcium signaling and p38 mitogen-activated protein kinase, stimulate glucose uptake by muscular cells [21, 22]. Meanwhile, a relative chronic effect of aerobic exercise should not be discarded, as it has been shown that depending on exercise protocol (longer duration, 200 min/week), improved insulin sensitivity may persist to at least 15 days after exercise cessation [23]. However, these changes seem to occur on more distal components of insulin signaling, since insulin receptor expression is generally unaltered with aerobic exercise training [24].

On the other hand, resistance exercise has conventionally been noted for its chronic effects, which are related to increases in glucose transporter-4 (glut-

4) and skeletal muscle mass via activation of the mammalian target of rapamycin/serine (mTOR) kinase 6 pathway, increasing protein synthesis [25]. Insulin receptor substrate-1 expression is increased by resistance and combined training [26], but not by isolated aerobic training [27, 28]. Along with glut-4 increments, resistance training also increases protein kinase B and glycogen synthase expression, even without changes in total muscle mass [29]. However, this type of exercise also seems to display acute effects on insulin and non-insulin mediated glucose uptake after one bout of exercise, similar to those found for aerobic exercise, obviously without changes in muscle mass [30].

This intervention only lasted 20 weeks. It could be rationalized that combined exercise with a larger aerobic component might benefit glucose control from earlier stages of intervention as compared to an identical duration and frequency exercise regimen with a larger resistance component. We cannot discount that the latter regimen could produce equal or better results in a delayed fashion owing to muscle adaptations that take longer to occur. This was evident that group R+, although with a non-significant A1c reduction, managed to reduce fasting plasma glucose and insulin levels and improve insulin sensitivity, in a significant manner. By nature, HbA1c represents the average glucose concentration over the preceding 8–12 weeks [31], and therefore is a good indicator of glycemic control during, but not at the end of, the intervention. One can accept that combined exercise that favors the aerobic component might reduce A1c levels to a greater extent than other that favors the resistance component, by improving glucose control from the start of the intervention, but

we cannot assume that at the end of the intervention, group A+ individuals are more able to control acute glucose level changes than individuals from group R+. Studies with longer interventions and comparing the effects of unaltered groups (maintaining the characteristics of A+) to one that shifts from an emphasis on the aerobic component at initial stages to an emphasis on the resistance component at latter stages of the intervention (A+ converting to R+) should provide further clarification on the subject.

Due to the different training characteristics, one could expect A+ subjects to achieve higher VO₂max values and R+ subjects more pronounced strength gains. However, it is recognized that simultaneously training for both strength and aerobic power (also known as concurrent training) can result in a compromised adaptation of both features, compared with training for either exercise mode alone [32, 33], and impairments are especially marked for strength and hypertrophy developments [34]. This is known as the concurrent training effect or interference effect. The genetic and molecular mechanisms of adaptation induced by resistance and aerobic training are distinct, with each mode of exercise activating and (or) repressing specific subsets of genes and cellular signaling pathways [35-37]. In particular, aerobic training seems to inhibit mTOR expression when a combined exercise intervention is undertaken. With a reduced aerobic component but without an increase in muscle mass, glucose control on group R+ may have been proportionally limited. In a recent review, we highlighted that all combined interventions that prescribed aerobic and resistance training on separate days produced significant A1c improvements on individuals with diabetes [6]. However, we do not know if

undertaking such training methodology may attenuate the inhibition of strength and hypertrophy developments associated with concurrent exercise.

According to the latest energy requirements for selected activities, walking at 3.5-4.0 mph (average speeds in our intervention) requires 4.3-5.0 metabolic equivalents (METs) (about 5.2 to 6.1 kcal/min), and performing resistance exercises ranging from small to large muscle mass groups requires 3.5-5.0 METs (about 4.2-6.1 kcal/min) [38]. That would translate to an energy expenditure between 296 to 367 kcal/hour in group A+ (average 332) and 274 to 372 kcal/hour (average 323) in group R+, with the approximate difference between the two groups being negligible. Energy expenditure from Excess Post-exercise Oxygen Consumption (EPOC) was not measured in this study.

There were no significant changes on the lipid profile of the different groups. Serum levels of the inflammatory marker CrP were significantly reduced only in group A+.

Finally, both strength and aerobic power improvements are very marked but similar among exercise groups.

To our knowledge, this study was the first to demonstrate the different metabolic effects between aerobic + resistance exercise regimens within a combined intervention trial. We did not evaluate daily physical activity during intervention to discard between-groups differences. Nevertheless, had there been any differences due to changes in strength activities outside protocolled exercises, the accelerometry method used would not be able to detect them. After intervention, daily physical activity was similar to baseline levels, even in

the exercise groups. Despite being sample size limited, this intervention was controlled for several confounding factors, such as medication, daily physical activity and caloric intake changes.

In summary, recent evidences support the usefulness of combined exercise to both prevention [39] and management of type 2 diabetes [2], not only due to glycemic control improvements but also in terms of efficient use of resources [40]. In the DICE trial, we provide evidence that after 20 weeks of intervention, a combination of 45 minutes of aerobic exercise and 15 minutes of resistance training produces greater A1c improvements than a combination of 15 minutes of aerobic exercise and 45 minutes of resistance training. Future studies should delineate such differences from other physiological responses such as insulin action or EPOC. Longer intervention studies, larger trial size, and changing the order of exercises can also be tested with the overall goal to benefit the quality of exercise interventions for patients with type 2 diabetes.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Overall discussion

This research was designed to extend the available knowledge of some of the most critical aspects of type 2 diabetes management: exercise, diet and daily physical activity.

We started by identifying the most up-to-date scientific evidence on the general characteristics of an exercise intervention for individuals with type 2 diabetes. Recommendations from renowned institutions pointed that both resistance and aerobic activities should integrate every exercise regimen. Based on this assumption, we performed a systematic review of the effects of combined exercise interventions on the glycemic control of people with type 2 diabetes, using changes on A1c as the primary outcome. The findings from this research strengthen the concept of recommending a combined exercise intervention, as these seem to be more effective at lowering blood glucose levels than isolated forms of exercise. Although with different physiological pathways, performing both strength and aerobic exercises exert synergistic effects in such populations. Nevertheless, some of the combined interventions failed to improve glycemic control. The reasons for success or failure of such interventions can be partially explained by the training characteristics adopted in those studies. To our knowledge, this was the first time that a detailed analysis of such features was conducted. In summary, supervision by exercise specialists and recommendation of a structured combined exercise regimen seem critical for better outcomes. In contrast, lower exercise intensities are frequently associated with interventions with poorer results. Nevertheless, the training characteristics are not always fully described and the conceptual design of some interventions is far from optimal, hindering applicability and replication of such methods in a real life context. Still, beneficial effects are possible by means of very different training methodologies in regard to variables like *length*, *duration*, *intensity*, *mode*, *number of exercises*, *sets* and *repetitions*.

This review study also raised several doubts. Whether performing aerobic and resistance exercise on separate days is preferable to performing them on

the same exercise session, the most effective exercise mode and method, and whether one type of exercise should be emphasized are some examples of future lines of research. Furthermore, most of the studies analyzed compared the effects of traditional aerobic (continuous) and resistance training (standard sets) methodologies. However, many people enjoy participating in a variety of group exercise classes that can emphasize the aerobic or the resistance components. As the effects of these on glycemic control are still unknown, future research should address the effectiveness of such group classes on blood glucose improvements. Moreover, as motivation is a critical aspect of long term adherence to an exercise regimen, some of these popular classes may (and should) be used as a part of the exercise prescription for many individuals with diabetes. In addition, all combined exercise interventions reviewed reproduced a model of *one-size-fits-all*, in the sense that the exercise mode, exercise intensity, number of sets and other variables are identical to all participants of a given intervention. Although this is adequate (and perhaps required) to a scientific research, designing a training programme that is individualized to the unique characteristics, needs and motivations of each individual with diabetes should provide better results than applying a generalized, non-specific formula. In this sense, future studies should also compare the effects of two different training methods, one where all participants perform a standardized protocol (same exercises, sets, intensity, etc.) to another where all participants are given an individual exercise planning. The latter would obviously be more time-consuming but the overall health benefits gained by the participants should overcome that limitation.

In a logical sequence of our work, we proceeded to identifying the daily physical activity and dietary characteristics of a Portuguese sample of individuals with type 2 diabetes. There was a three-fold relevance for such step: firstly, we wanted to check for the population's compliance to the most recent recommendations for daily physical activity and dietary intakes; secondly, we wanted to provide additional information on these important health topics, as Portuguese data on these features is scarce; finally, from this sample we would

randomly select individuals to participate in our combined exercise intervention and in order to exclude possible confounders, participants were asked to maintain their usual dietary and daily physical activity patterns. As such, knowing their baseline characteristics (and comparing them after intervention) was mandatory. Subsequently, in our second paper, we accessed the dietary and daily physical activity characteristics of a Portuguese sample of individuals with type 2 diabetes. Data was collected from a community-based exercise intervention taking place at Famalicão, Portugal. It was found that when regarded as a whole, sample's compliance with recommendations seemed acceptable, but a different scenario emerged when an individual analysis was performed. In relation to diet, the most striking data revealed that none of the individuals consumed the advised minimum amount of fiber, and consequentially, none of the participants followed all dietary recommendations. In fact, individual compliance to most dietary recommendations remained sub-optimal. As for daily physical activity, it was found that less than ¼ of the individuals performed the recommended minimum of 150 min/week of aerobic activities and remarkably, none was involved in strength activities.

It was concluded that despite having a disease that can be effectively controlled by an adequate lifestyle, most individuals from our sample were sedentary and had a poor diet. These results mirror others attained in studies conducted in different European countries. As such, we believe that improving compliance to dietary and physical activity recommendations should be a top priority of future interventions designed to prevent and manage type 2 diabetes.

Furthermore, from the several issues raised in our review of combined exercise interventions, we decided to analyze the effects of two different combined exercise regimens on the glycemic control of individuals with type 2 diabetes. In the DICE intervention, one group performed 45 minutes of aerobic exercise and 15 minutes of resistance exercise, while the other performed 15 minutes of aerobic exercise and 45 minutes of resistance exercise. All other variables were kept identical (intensity, mode, number, selection and sequence of exercises, etc.) and both groups were compared to a control group. Our

intervention showed that in sedentary, older individuals with type 2 diabetes, combined exercise with emphasis on the aerobic component produced the best results for A1c reductions, at 5 months. It was hypothesized that emphasis on aerobic exercise may prove to be more effective, since it improves glycemic control from the start of the intervention. Such glycemic control may take longer to occur while emphasizing the resistance component, since muscle adaptations, as muscle mass increases, are generally needed. On the other hand, simultaneously training for both aerobic power and muscular strength (concurrent training) is known to inhibit the development of such features, when compared to isolated training. Combined exercise seems to especially attenuate increases on strength and muscle mass (but not aerobic power), suggesting that in combined exercise interventions, emphasizing the resistance component may not be a time-effective procedure to improve A1c scores. Nevertheless, both exercise groups from our intervention achieved significant improvements in other glycemic related variables (fasting glucose, insulin, insulin sensitivity) at 5 months. These glucose lowering effects of combined exercise are even more relevant, as they occurred in a population with poor dietary and daily physical activity lifestyles. Additionally, based on the low drop-out rates, we can hypothesize that both methods are easily endured by participants.

However, some questions remain for clarified. For example, we cannot speculate about the effects of a longer intervention or the potential effects of shifting from an emphasis on the aerobic component at early stages of intervention to an emphasis to the resistance component at latter stages of intervention (or vice-versa). In addition, we speculate that performing the aerobic and the resistance exercise on separate days may attenuate the inhibition of strength and hypertrophy developments associated with concurrent exercise, and thus, improve glycemic control. All these issues should be addressed in future studies.

Overall, our work provided a unique and comprehensive view on some of the main features of type 2 diabetes management. To our knowledge, this was the first time that a collection of data on the dietary, daily physical activity and

the optimal combined exercise intervention was conducted within the same sample. There are however, a few limitations in our work: sample sizes for dietary and daily physical activity, as well as for the combined exercise intervention could be larger; and the exercise machines used by participants do not accurately represent today's more sophisticated models found in most exercise facilities. Naturally, the latter *weakness* can also turn out to be a *strength*, as we demonstrated that improved glycemic control in individuals with type 2 diabetes is possible despite the usage of low-technology exercise equipment. In addition, although we certainly acknowledge the reduced sample size as a significant limitation, we have designed our intervention to control for several potential confounders, as changes in energy intake, daily physical activity and medication usage, which give strength to our results.

In summary, our main findings suggest that:

- the best results for glycemic control are achieved through a combination of both aerobic and resistance training;
- patients with type 2 diabetes exhibit poor dietary and daily physical activity compliance to recommendations;
- a combined exercise intervention for sedentary individuals with type 2 diabetes should emphasize the aerobic component.

We expect these results to be easily available and replicable by researchers, people with diabetes and others interested in the prevention and management of such disease, and that our work may have contributed to the increase in the knowledge of this important area of expertise.

Some final but utterly important words go to the people from so many different backgrounds that contributed to this work. Their help has been fundamental to the concept and development of this project and we feel that such tasks can only be implemented if a large number of responsible and willing professionals from different areas of expertise are involved. This is really the biggest challenge that diabetes management faces in the present days. It is

very rare to find a project where nutritionists, general practitioners, endocrinology specialists, exercise specialists and other related professionals work together with the same patients. It is our strong belief that diabetes prevention and management is a holistic endeavor and that individuals with this disease should receive simultaneous treatment and counseling from professionals of multiple areas. Within our abilities, we will work to make this the standard procedure of diabetes prevention and management in order to improve the quality of life of people with type 2 diabetes, starting from now!

Chapter 4

Conclusions

Based on the purpose and findings of the present dissertation, we highlight the following conclusions:

1. Combined exercise is more effective at improving the glycemic control of individuals with type 2 diabetes than isolated forms of exercise;
2. Many individuals do not comply with the recommendations for dietary intakes and daily physical activity;
3. Combined exercise interventions for previously sedentary individuals should emphasize the aerobic component.

In summary, performing a combination of aerobic and resistance exercises improves glycemic control of individuals with poor dietary and daily physical activity lifestyles.

Exercise, and specifically combined exercise, is a key feature of glucose management and should be a top priority of every intervention designed to improve the quality of life and life expectancy of individuals with type 2 diabetes.

Perspectives for future research

The results of this dissertation emphasize the need for more research on the effects of combined exercise with different methodologies and adherence to dietary and daily physical activity recommendations in individuals with type 2 diabetes, in order to improve their glycemic control. Specifically, we point the following main lines of research:

- Effects of performing aerobic and resistance exercise on separate days;
- Effects of participation in group classes;
- Effects of a generalized versus an individualized exercise planning;

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Attachments

Obrigado pelo seu interesse neste estudo! O nosso objectivo é compreender qual o tipo de exercício mais indicado para os pacientes **diabéticos do tipo 2**. Esta é uma investigação pioneira, que conta com a colaboração da Faculdade de Desporto da Universidade do Porto, Câmara Municipal de Famalicão, Associação de Diabéticos de Vila Nova de Famalicão e Centro de Saúde de Famalicão.

Para aqueles aceitem participar, ofereceremos gratuitamente:

Avaliação da densidade óssea (coluna e colo do fémur);

Avaliação da composição corporal;

Análises sanguíneas específicas;

Avaliação do perfil psicológico;

Avaliação da condição física (força, flexibilidade, agilidade, resistência);

Avaliação nutricional;

Avaliação da atividade física diária (por acelerometria);

Acesso às instalações desportivas nas piscinas municipais de Famalicão;

Acompanhamento profissional.

Se desejar aumentar a sua saúde através do exercício físico, poderá participar neste estudo, cumprindo o único requisito necessário (**treinar 3x/semana, durante 5 meses**).

Para tal, deve deslocar-se às piscinas de Famalicão e inscrever-se no programa dos diabéticos (**o mais cedo possível**) e posteriormente contactar o responsável pela investigação, professor César Chaves para informações acerca dos passos seguintes.

Obrigado pela sua colaboração!

César Chaves

912 545 570

Obrigado pela sua participação neste estudo!

O nosso objectivo é compreender qual o tipo de exercício mais indicado para os pacientes diabéticos. Esta é uma investigação pioneira que terá uma duração aproximada de 5 meses. Após a sua adesão ao programa, ser-lhe-á atribuído um grupo de treino específico. A recolha inicial de informações incluirá testes de condição física, realização de inquéritos, determinação da densidade mineral óssea e composição corporal, bem como análises sanguíneas.

Parte das avaliações envolvem uma deslocação à Faculdade de Desporto da Universidade do Porto (almoço ou lanche incluído), sendo solicitado que traga **equipamento desportivo e lista de todos os medicamentos actualmente consumidos**.

Para a determinação da actividade física habitual, ser-lhe-á entregue um acelerómetro, pequeno aparelho que deverá ser usado durante todo o dia, na cintura, sendo apenas retirado para dormir ou realizar actividades como hidroginástica, natação ou simplesmente tomar banho, dado que **não é à prova de água**. O aparelho deverá ser sempre utilizado do mesmo lado da cintura, com a **seta a apontar para baixo**. Enquanto o usar, deve fazer tudo o que costuma fazer habitualmente. Ele entrará automaticamente em funcionamento no dia seguinte à entrega e recolherá dados durante uma semana, inactivando-se automaticamente após esse período. Durante essa semana deve completar o quadro seguinte. Após essa semana, o acelerómetro deverá ser entregue o mais rapidamente possível à professora Marta ou outro professor responsável.

Nome: _____ Código: _____

Data de início: _____ Hora: _____ Data do fim: _____ Hora: _____

Dia da semana	Ao levantar	Antes de ir dormir	Só se realizou uma <u>actividade aquática (nadar, hidroginástica)</u>	
	Hora a que colocou	Hora a que retirou	Hora a que retirou (antes da actividade)	Hora a que colocou (depois da actividade)
2ª Feira				
3ª Feira				
4ª Feira				
5ª Feira				
6ª Feira				
Sábado				
Domingo				

Todos os procedimentos (recolha de dados, transporte, refeições, utilização de acelerómetro, etc.) serão **inteiramente gratuitos**. Em caso de qualquer dúvida, pf. contacte-me.

César Chaves 912 545 570

Obrigado pela sua colaboração!

DECLARAÇÃO DE CONSENTIMENTO

Conforme a “Declaração de Helsínquia” da Associação Médica Mundial (Helsínquia 1964; Tóquio 1975; Veneza 1983).

Designação do Estudo: **“Combined exercise in individuals with type 2 diabetes: mainly aerobic or resistance training? The DICE intervention”, com vista à obtenção do grau de doutoramento do candidato César Filipe Chaves de Oliveira, bolseiro financiado pelo Ministério da Ciência, Tecnologia e Ensino Superior através da Fundação para Ciência e Tecnologia.**

Eu, abaixo assinado, (nome completo), _____

compreendi a explicação que me foi fornecida acerca da minha participação no estudo que se tenciona efectuar, tendo-me sido dada oportunidade de fazer as perguntas que julguei necessárias.

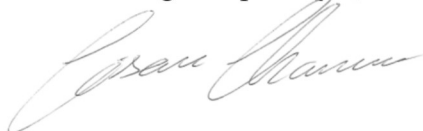
Tomei também conhecimento de que, de acordo com as recomendações da declaração de Helsínquia, a informação ou explicação que me foi prestada versou os objectivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto, além disso foi-me afirmado que tenho o direito de recusar a todo o tempo a minha participação no referido estudo, sem que isso possa ter como efeito qualquer prejuízo na assistência que me foi prestada.

Tendo em conta o atrás exposto autorizo a minha participação no projecto de investigação da Faculdade de Desporto da Universidade do Porto, efectuando duas medições de todos os testes referidos.

Porto, ____ de _____ de 2010

O investigador principal,

O participante,



Exmo(a). Dr(a).,

O seu paciente encontra-se a participar num estudo pioneiro que pretende determinar a melhor metodologia de treino para o indivíduo diabético do tipo 2. Esta intervenção abrange diversos aspectos relacionados com o controlo da glicemia, mas aborda igualmente variáveis psicológicas e nutricionais, bem como outras relacionadas com os hábitos e os estilos de vida. A sua participação de todos os intervenientes foi voluntária e informada, tendo os mesmos preenchido a declaração de consentimento informado, conforme a “Declaração de Helsínquia” da Associação Médica Mundial (Helsínquia 1964; Tóquio 1975; Veneza 1983).

Dado que as alterações na dosagem ou tipo de medicação podem confundir os resultados, comprometendo-os definitivamente, **solicito que não altere a medicação do seu utente, a não ser que seja estritamente necessário**, durante o período do estudo em causa (Janeiro a Junho de 2011). Pelo facto agradeço a sua compreensão e colaboração.

Para o esclarecimento de qualquer dúvida, pf não hesite em contactar-me.

Com os melhores cumprimentos,
César Chaves

Docente no Instituto Politécnico de Viana do Castelo
Doutorando na Faculdade de Desporto da Universidade do Porto
Bolseiro PROTEC
e-mail: cesarchaves@mail.com
tlm: 912545570

Ex.^{mo(a)} Senhor(a):

Sendo um estudo da máxima importância para a Região, gostaríamos de contar com a sua colaboração. Neste sentido, solicitamos o preenchimento do questionário em anexo.

Os resultados obtidos neste estudo serão **confidenciais** e nessa medida, apenas e só, poderão ser utilizados pela equipa de investigação para a realização do trabalho referido.

Gratos pela sua colaboração e compreensão subscrevemo-nos atenciosamente




Instruções de preenchimento do questionário:

Preencha, por favor, os campos em letras maiúsculas com uma letra por ☐, deixando um ☐ entre cada palavra. Por exemplo:

Nome ☐ M ☐ A ☐ R ☐ I ☐ A ☐ ☐ J ☐ O ☐ S ☐ É ☐ ☐ S ☐ I ☐ L ☐ V ☐ A ☐

Rendimento mensal ☐ 1 ☐ 0 ☐ 5 ☐ 0 ☐ 0 ☐ 0 ☐ euros/mês

Assinale cada ☐ com uma X. Por exemplo:

Preencha assim:

☒

Não preencha assim:

☒ ☒

Se se enganar risque completamente a opção incorrecta e escolha a opção correcta

☐ ☒

Os dados recolhidos serão processados automaticamente e destinam-se à realização deste estudo, sendo mantido o anonimato. No caso de não pretender novo contacto para eventuais esclarecimentos ou futuros estudos assinale aqui, por favor ☐

Morada ☐

☐

Localidade (freguesia)

☐

☐

Concelho

☐

☐

Código Postal

☐

- ☐

Telefone ou Telemóvel

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Data de Nascimento

☐ D ☐ D ☐ / ☐ M ☐ M ☐ / 1 9

Idade

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Anos

Sexo

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F

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M

Profissão

☐

Escolaridade

☐

Anos

(nº de anos completos)

Rendimento mensal

(líquido)

☐ 0 0

euros/mês

Estado civil ☐ Solteiro ☐ Casado/
União de facto ☐ Divorciado(a)/
Separado(a) ☐ Viúvo(a)

Qual o seu peso á nascença? Kg Qual o seu peso actual? Kg

Qual a sua altura? m Quantas horas dorme em média por dia? H/dia

Fuma ou alguma vez fumou? não ☐ sim ☐ (Se não passe à questão seguinte)

Se sim: 1. ☐ Fumava regularmente e deixei de fumar, há anos

2. ☐ Fumo menos de 1 cigarro /dia

3. ☐ Fumo regularmente - nº cigarros por dia

Que refeições costuma fazer por dia?	Todos os dias	4-5 vezes/ semana	2-3 vezes /semana	Nunca
a. Pequeno almoço	1 ☐	2 ☐	3 ☐	5 ☐
b. Lanche da manhã	1 ☐	2 ☐	3 ☐	5 ☐
c. Almoço	1 ☐	2 ☐	3 ☐	5 ☐
d. Lanche da tarde	1 ☐	2 ☐	3 ☐	5 ☐
e. Jantar	1 ☐	2 ☐	3 ☐	5 ☐
f. Ceia	1 ☐	2 ☐	3 ☐	5 ☐

a. Qual o meio de transporte que utiliza para ir para o trabalho?

1 ☐ Automóvel/mota 2 ☐ Autocarro 3 ☐ Bicicleta 4 ☐ A pé

Se vai a pé ou de bicicleta quanto tempo demora? h min

b. Qual o meio de transporte que utiliza para vir do trabalho?

1 ☐ Automóvel/mota 2 ☐ Autocarro 3 ☐ Bicicleta 4 ☐ A pé

Se volta a pé ou de bicicleta quanto tempo demora? h min

Alguma vez o médico o/a informou que tem (ou teve):

	Sim (x)	Há Quanto Tempo		Sim (x)	Há Quanto Tempo	
a. Ataque Cardíaco	☐		Anos	I. Outras doenças cardiovasculares	☐	
b. Angina de Peito	☐		Anos			
c. Trombose	☐		Anos			Quais?
d. Tensão arterial alta	☐		Anos			
e. Diabetes tipo I	☐		Anos	m. Doenças Respiratórias	☐	
f. Diabetes tipo II	☐		Anos			
g. Osteoporose	☐		Anos	Quais?		
h. Artrite	☐		Anos			
i. Depressão	☐		Anos	n. Cancro	☐	
j. Doença de Parkinson	☐		Anos	Tipo		
o. Outros problemas de saúde	☐		Anos	Qual?		
p. Outros problemas de saúde	☐		Anos	Qual?		
q. Toma algum medicamento	☐		Anos	Qual?		
r. Toma algum medicamento	☐		Anos	Qual?		
s. Toma algum medicamento	☐		Anos	Qual?		
t. Toma algum medicamento	☐		Anos	Qual?		

+

ESTADO DE SAÚDE

As questões que se seguem pedem-lhe a opinião sobre a sua saúde, a forma como se sente e sobre a sua capacidade de desempenhar as actividades habituais.

Pedimos que leia com atenção cada pergunta e que responda o mais honestamente possível. Se não tiver a certeza sobre a resposta a dar, dê-nos a que achar mais apropriada e, se quiser escreva um comentário a seguir à pergunta.

Coloque uma cruz no número que melhor descreve a sua saúde.

1. Em geral, a sua saúde é?

Ótima	Muito Boa	Boa	Razoável	Fraca
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

2. Comparando com o que acontecia há um ano, como descreve o seu estado geral actual?

Muito melhor	Com algumas melhoras	Aproximadamente igual	Um pouco pior	Muito pior
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

3. As perguntas que se seguem são sobre as actividades que executa no seu dia-a-dia. Será que a sua saúde o/a limita nestas actividades? Se sim, quanto?

		Sim, muito limitado/a	Sim, um pouco limitado/a	Não, nada limitado/a
a.	Actividades Vigorosas , tais como, correr, levantar pesos, participar em desportos extenuantes.	1 ☐	2 ☐	3 ☐
b.	Actividade Moderadas , tais como, deslocar uma mesa ou aspirar a casa.	1 ☐	2 ☐	3 ☐
c.	Levantar ou pegar nas compras de mercearia	1 ☐	2 ☐	3 ☐
d.	Subir vários Lanços de escadas	1 ☐	2 ☐	3 ☐
e.	Subir um lanço de escadas	1 ☐	2 ☐	3 ☐
f.	Inclinar-se, ajoelhar-se ou baixar-se	1 ☐	2 ☐	3 ☐
g.	Andar mais de 1 Km	1 ☐	2 ☐	3 ☐
h.	Andar várias centenas de metros	1 ☐	2 ☐	3 ☐
i.	Andar uma centena de metros	1 ☐	2 ☐	3 ☐
j.	Tomar banho ou vestir-se sozinho/a	1 ☐	2 ☐	3 ☐

4. Durante as últimas 4 semanas, no seu trabalho ou actividades diárias, teve algum dos problemas apresentados a seguir como consequência do seu estado de saúde físico?

Quanto tempo, nas últimas quatro semanas...	Sempre	A maior parte do tempo	Algum tempo	Pouco tempo	Nunca
a. Diminuíu o tempo gasto a trabalhar ou noutras actividades	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Fez menos do que queria?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Sentiu-se limitado/a no tipo de trabalho ou outras actividades	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. Teve dificuldades em executar o seu trabalho ou outras actividades (por exemplo foi preciso mais esforço)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

5. Durante as últimas 4 semanas, teve com o seu trabalho ou actividades diárias, algum dos problemas apresentados a seguir devido a quaisquer problemas emocionais (tal como sentir-se deprimido/a ou ansioso/a)?

Quanto tempo, nas últimas quatro semanas...	Sempre	A maior parte do tempo	Algum tempo	Pouco tempo	Nunca
a. Diminuiu o tempo gasto a trabalhar ou noutras actividades	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Fez menos do que queria?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Executou o seu trabalho ou outras actividades menos cuidadosamente do que era costume	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

6. Durante as últimas quatro semanas, em que medida é que a sua saúde física ou problemas emocionais interferiram no seu relacionamento social normal com a família, amigos, vizinhos ou outras pessoas?

Absolutamente nada	Pouco	Moderadamente	Bastante	Imenso
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

7. Durante as últimas quatro semanas teve dores?

Nenhumas	Muito fracas	Ligeiras	Moderadas	Fortes	Muito fortes
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

8. Durante as últimas quatro semanas, de que forma é que a dor interferiu com o seu trabalho normal (tanto no trabalho fora de casa como no trabalho doméstico)?

Absolutamente nada	Pouco	Moderadamente	Bastante	Imenso
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

9. As perguntas que se seguem pretendem avaliar a forma como se sentiu e como lhe correram as coisas nas últimas quatro semanas.
Certifique-se que responde a todas as perguntas.

Quanto tempo, nas últimas quatro semanas...	Sempre	A maior parte do tempo	Algum tempo	Pouco tempo	Nunca
a. Se sentiu cheio/a de vitalidade?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Se sentiu muito nervoso/a?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Se sentiu tão deprimido/a que nada o/a animava?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. Se sentiu calmo/a e tranquilo/a?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
e. Se sentiu com muita energia?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
f. Se sentiu deprimido/a?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
g. Se sentiu estafado/a?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
h. Se sentiu feliz?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
i. Se sentiu cansado/a?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

10. Durante as últimas quatro semanas, até que ponto a sua saúde física ou problemas emocionais limitaram a sua actividade social (tal como visitar amigos ou familiares próximos)?

Sempre	A maior parte do tempo	Algum tempo	Pouco tempo	Nunca
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

11. Por favor, diga em que medida são verdadeiras ou falsas as seguintes informações.

	Absolutamente verdade	Verdade	Não sei	Falso	Absolutamente falso
a. Parece que adoeço mais facilmente do que os outros	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Sou tão saudável como qualquer outra pessoa	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Estou convencido/a que a minha saúde vai piorar	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. A minha saúde é óptima	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

QUESTIONÁRIO INTERNACIONAL DE ACTIVIDADE FÍSICA (IPAQ)

Estamos interessados em conhecer os diferentes tipos de actividade física, que as pessoas fazem no seu quotidiano. Este questionário faz parte de um estudo alargado realizado em vários países. As suas respostas vão-nos ajudar a conhecer o nosso nível de actividade física, quando comparado com o de pessoas de outros países.

As questões que lhe vou colocar, referem-se à semana imediatamente anterior, considerando o tempo em que esteve fisicamente activo/a. Por favor, responda a todas as questões, mesmo que não se considere uma pessoa fisicamente activa. Vou colocar-lhe questões sobre as actividades desenvolvidas na sua actividade profissional e nas suas deslocações, sobre as actividades referentes aos trabalhos domésticos e às actividades que efectuou no seu tempo livre para recreação ou prática de exercício físico / desporto.

Ao responder às seguintes questões considere o seguinte:

Actividades físicas vigorosas referem-se a actividades que requerem um esforço físico intenso que fazem ficar com a respiração ofegante.

Actividades físicas moderadas referem-se a actividades que requerem esforço físico moderado e tornam a respiração um pouco mais forte que o normal.

Ao responder às questões considere apenas as actividades físicas que realize durante pelo menos **10 minutos seguidos**.

Q.1 Diga-me por favor, nos últimos 7 dias, em quantos dias fez actividades físicas vigorosas, como por exemplo, levantar objectos pesados, cavar, ginástica aeróbica, nadar, jogar futebol, andar de bicicleta a um ritmo rápido?

Dias

Q.2 Nos dias em que pratica actividades físicas vigorosas, quanto tempo em média dedica normalmente a essas actividades ?

Horas Minutos (por dia)

Q.3 Diga-me por favor, nos últimos 7 dias, em quantos dias fez actividades físicas moderadas como por exemplo, carregar objectos leves, caçar, trabalhos de carpintaria, andar de bicicleta a um ritmo normal ou ténis de pares? Por favor não inclua o “andar”.

Dias

Q.4 Nos dias em que faz actividades físicas moderadas, quanto tempo em média dedica normalmente a essas actividades?

Horas Minutos (por dia)

Q.5 Diga-me por favor, nos últimos 7 dias, em quantos dias andou pelo menos 10 minutos seguidos?

Dias

Q.6 Quanto tempo no total, despendeu num desses dias, a andar/caminhar?

Horas Minutos (por dia)

Q.7 Diga-me por favor, num dia normal quanto tempo passa sentado? Isto pode incluir o tempo que passa a uma secretária, a visitar amigos, a ler, a estudar ou a ver televisão.

Horas Minutos (por dia)

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O seguinte conjunto de questões referem-se às diversas estruturas existentes na sua área residencial e áreas envolventes. Referimo-nos a toda a área envolvente acessível a pé, no espaço de 10-15 minutos.

Assinale, por favor, a resposta que lhe parece mais correcta para o seu caso individual

1. Qual o tipo de habitação predominante na sua área residencial?

1. ☐ Moradias independentes.
2. ☐ Casas geminadas, prédios de apartamentos de 2-3 andares.
3. ☐ Uma combinação de moradias independentes, casas geminadas e prédios de apartamentos.
4. ☐ Prédios de apartamentos com 4 -12 andares.
5. ☐ Prédios de apartamentos com mais de 12 andares.
77. ☐ Não sabe / não tem a certeza

2. Muitas lojas, comércio, mercados ou outros estabelecimentos onde faço compras estão a uma distância de rápido acesso a pé. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

3. De minha casa, a pé, demoro 10 – 15 minutos a chegar a uma paragem de transportes públicos. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

4. A maior parte das ruas na minha área residencial têm passeios. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

QA	ID								
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5. Nas estradas da minha área residencial, ou muito próximo, existem caminhos ou faixas de circulação próprios para ciclistas. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

6. Nas minha área residencial existem várias zonas de recreação e lazer, de acesso gratuito ou a preços baixos, tais como: parques, caminhos só para peões, faixas de circulação só para ciclistas, centros recreativos, parques infantis, piscinas públicas etc. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

7. A taxa de criminalidade na minha zona não permite fazer passeios nocturnos por falta de segurança. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza



8. Há tanto trânsito nas ruas que se torna desagradável ou perigoso andar a pé na minha área residencial. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

9. Vejo muitas pessoas praticando exercício físico na minha área residencial. Isto é: caminham, correm, andam de bicicleta, praticam desportos e jogos. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza



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10. Na minha área residencial há muitas coisas interessantes para se apreciar enquanto se passeia. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

11. Quantos veículos motorizados em funcionamento existem no seu agregado familiar?

- 4. Veículos motorizados
- 77. ☐ Não sabe / não tem a certeza

12. Há muitos cruzamentos na minha área residencial. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza
- 88. ☐ Não há ruas nem estradas na minha área residencial

13. Na minha área residencial os passeios estão em bom estado de conservação (pavimentos com poucas fendas) e não estão obstruídos. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

14. Na minha área residencial e nos arredores as faixas para ciclistas estão em bom estado de conservação e não estão obstruídos. Diria que...

- 1. ☐ Discorda completamente
- 2. ☐ Discorda de certa forma
- 3. ☐ Concorda de certa forma
- 4. ☐ Concorda completamente
- 77. ☐ Não sabe / não tem a certeza

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QA	ID	
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15. Na minha área residencial há tanto trânsito que se torna difícil e desagradável andar de bicicleta. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

16. A taxa de criminalidade na minha área residencial não permite fazer passeios diurnos em segurança. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

17. Há muitos sítios próximos da minha casa onde posso ir facilmente a pé. Diria que...

1. ☐ Discorda completamente
2. ☐ Discorda de certa forma
3. ☐ Concorda de certa forma
4. ☐ Concorda completamente
77. ☐ Não sabe / não tem a certeza

PAR-Q		Não	Sim
1.	Alguma vez o seu médico lhe disse que tem algum problema cardíaco e que só deveria fazer actividade física recomendada por um médico?	1 ☐	2 ☐
2.	Quando faz actividade física sente dores do peito?	1 ☐	2 ☐
3.	No último mês, teve dores no peito mesmo quando não estava a fazer actividade física?	1 ☐	2 ☐
4.	Perde o equilíbrio por sentir tonturas ou já alguma vez desmaiou?	1 ☐	2 ☐
5.	Tem algum problema ósseo ou articular (por exemplo nas costas, nos joelhos ou na anca) que poderá piorar com a actividade física?	1 ☐	2 ☐
6.	O seu médico receitou-lhe algum medicamento para a tensão arterial ou para o coração?	1 ☐	2 ☐
7.	Existe alguma outra razão para não fazer actividade física?	1 ☐	2 ☐

+

ID: _____

INSTRUÇÕES PARA O PREENCHIMENTO DO DIÁRIO ALIMENTAR DE 3 DIAS

Este diário alimentar tem como objectivo avaliar a sua ingestão alimentar e consiste no registo de tudo aquilo que comeu e bebeu ao longo do dia. Procure preencher o registo de uma forma sincera, indicando aquilo que realmente come e não o que pensa que seria correcto comer.

Por favor, anote tudo o que comer ou beber durante 3 dias desta semana (2 dias da semana e 1 dia de fim-de-semana).

Faça descrições pormenorizadas dos alimentos e bebidas consumidos como, por exemplo, o tipo de pão (trigo, mistura, integral, etc.) ou o tipo de leite (gordo, meio-gordo ou magro). Mencione também o tipo de confecção culinária como, por exemplo, carne de vaca grelhada, ovo estrelado, lombo assado, costeletas de porco frita em margarina. No caso de pratos compostos tente mencionar a quantidade aproximada de cada alimento. Mencione sempre que possível a marca do alimento. Quando ingerir chá ou outros alimentos em que adicione açúcar ou outro edulcorante, não se esqueça de os referir, bem como as suas quantidades. Inclua sempre tudo aquilo que comeu e/ou bebeu fora de casa (p.ex, num café ou em casa de um amigo). Não se esqueça, também, de registar tudo o que comeu e/ou bebeu no intervalo das refeições como, por exemplo, bolachas, sumos, açúcar, bolos, etc.

Como fazer o registo: inicie com a página correspondente ao dia de registo; assegure-se, por favor, que preencheu todas as partes correspondentes à – HORA, LOCAL, ALIMENTOS E BEBIDAS CONSUMIDOS, QUANTIDADE.

Quanto às quantidades e aos tamanhos das porções

Use medidas caseiras como, por exemplo, 1 colher de chá, 4 colheres de sopa, 1 tigela, 1 chávena almoçadeira. Seguidamente é apresentado um quadro sumário de como pode ser efectuada a descrição da quantidade de alimentos/bebida.

Alimento	Medidas (exemplos)
Sopa	1 concha de sopa ou 1 tigela ou 1 prato cheio
Massa, arroz, leguminosas (feijão, grão, lentilhas, etc.)	1 colher de sopa ou 1 colher de servir ou 1/2 prato
Batata	1 batata média (tamanho de um ovo), grande ou pequena
Carne, peixe	1 posta média, grande, pequena ou 1 sardinha, faneca, dourada, etc.
Legumes cozidos ou crus	1, 1/2, 3/4 prato ou 1 chávena almoçadeira
Fruta	1 peça média, grande, pequena ou 1 rodela ou 1 fatia
Fiambre, queijo, mortadela, chouriço	1 fatia grossa, fina
Pão	1 pão, 1 baguete pequena
Cereais de pequeno-almoço	1 mão de cereais ou 1 colher de sopa
Açúcar, adoçante	1 colher de sopa, sobremesa ou chá ou 1 pastilha ou 1 pacotinho

Chocolate em pó, cevada, café	1 colher de sopa ou 1 colher de sobremesa ou 1 colher de chá
Leite, chá	1 chávena (280ml) ou 1 copo
Iogurte sólido ou líquido	1 iogurte sólido, 1 iogurte líquido
Bebidas (água, refrigerantes, sumo natural)	1 copo, 1 lata (330ml), 1 pacote (200ml)
Molhos (ketchup, maionese, mostarda)	1 colher de sopa ou 1 colher de sobremesa
Chocolates	1 Twix, 1 Kit-Kat, 1 quadrado de chocolate
Azeite, óleo, margarina, manteiga	1 colher de sopa ou 1 colher de sobremesa ou 1 colher de chá
Pizza, hambúrguer, cachorro	1 fatia de pizza, 1 hambúrguer, 1 cachorro
Doces (gelatina, mousse, bolo de chocolate, etc.)	1 fatia ou 1 bolo ou 1 taça

EXEMPLO: Dia da semana: Sexta Dia: 17/10/2010

Pequeno-Almoço

Hora	Local	Alimento	Quantidade
8h	Casa	Leite meio-gordo com cevada (Mokambo®) sem açúcar	180ml de leite 3 colheres de chá de cevada
		Pão integral com fiambre	1 pão médio (40g) 1 fatia fina de fiambre

Meio-da-manhã

Hora	Local	Alimento	Quantidade
10h30	Casa	Iogurte líquido de morango + Bolacha Maria	180g + 3 bolachas

Almoço

Hora	Local	Alimento	Quantidade
12h30	Casa	Sopa de legumes (cenoura, batata, couve, cebola)	1 prato (2 conchas)
		Bife de vaca grelhado	1 bife médio 100g
		Arroz de ervilhas	2 colheres de sopa de arroz + 1 colher de sopa de ervilhas
		Alface sem adição de azeite	1/4 prato
		Maçã + água	1 maçã média + 1 copo

Meio-da-tarde

Hora	Local	Alimento	Quantidade
16h	Café	Pão de trigo com manteiga	1 pão médio + 1 colher de chá de manteiga

Jantar e Ceia

Hora	Local	Alimento	Quantidade
19h	Casa	Sopa de legumes (cenoura, batata, couve, cebola)	1 prato (2 conchas)
		Massa com costeleta de porco grelhada	1 costeleta média (100g) + 4 colheres de sopa de massa
		Morango com açúcar	6 morangos + 1 colher de chá de açúcar
		Sumo (néctar de pêra)	200ml
22h	Casa	Leite meio-gordo simples	1 copo (170 ml)

ID	Nome				Idade		Peso	Altura	
TA	SYS1	DIA1	FC1	SYS2	DIA2	FC2	SYS3	DIA3	FC3
Med	PERcint	PERanc	PERbt	PERbr					
FULL	ARMc	BACKs	CHAIRs	SITreach	TUG	6 MIN			
ACEI	ID								
CONDIÇÕES				MEDICAÇÃO					
CL	Ficha/acelerómetro	Declaração	SF-36	DHP-18	Inquérito alimentar				

Nome: _____ Identificação: _____

Musculação: realizar 8 a 12 repetições; assim que seja possível realizar mais que 12 repetições, deve-se aumentar a carga e registá-la.

	Séries	Carga (s)							
Leg press									
Chest press									
Compound row									
Bíceps curl									
Shoulder press									
Abdominal crunch									
Lumbar extensions									

Cárdio: realizar o maior n.º de voltas no intervalo de tempo estipulado. Tentar melhorar em cada sessão. Registrar n.º de voltas conseguidas em cada sessão.

Nome: _____ Identificação: _____

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Lumbar extensions									

Cárdio: realizar o maior n.º de voltas no intervalo de tempo estipulado. Tentar melhorar em cada sessão. Registrar n.º de voltas conseguidas em cada sessão.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
J																															
F																															
M																															
A																															
M																															
J																															

X - treino combinado

H - hidroginástica

Eventos anómalos	
Data	Ocorrência

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
J																															
F																															
M																															
A																															
M																															
J																															

X - treino combinado

H - hidroginástica

Eventos anómalos	
Data	Ocorrência

**SEGURO DE ACIDENTES PESSOAIS
ESPAÇOS PÚBLICOS****CONDIÇÕES PARTICULARES****RAMO:** ACIDENTES PESSOAIS (SEGURO DE GRUPO NÃO CONTRIBUTIVO)**APÓLICE:** PA11AH0532**TIPO:** NOVO**INÍCIO:** 01/05/2012**RENOVAÇÃO:** 01/05/CADA ANO**PAGAMENTO:** SEMESTRAL**TOMADOR DE SEGURO:** MUNICÍPIO DE VILA NOVA DE FAMALICÃO**MORADA:** PRAÇA ÁLVARO MARQUES
4764-502 VILA NOVA DE FAMALICÃO**NIF:** 506663264**CORRETOR:**
SABSEG

Entre a CHARTIS EUROPE, SA e a entidade indicada como Tomador do Seguro, é estabelecido o presente contrato que se regula pelas presentes Condições Particulares, Gerais e Especiais aplicáveis.

1. OBJECTO DO CONTRATO

O objecto do presente contrato é a garantia do pagamento de indemnizações, em consequência de Acidente, de acordo com as coberturas e limites adiante designados e nos termos das Condições Gerais da Apólice.

2. PESSOAS SEGURAS

Todas as Pessoas que se encontrem nos Locais de Risco Seguros durante o regular horário de funcionamento dos mesmos e em observância às regras de segurança existentes.

Não são consideradas Pessoas Seguras os Funcionários do Tomador de Seguro ou outras pessoas ao serviço deste.

3. BENEFICIÁRIOS EM CASO DE MORTE

Os Beneficiários em caso de Morte serão os constantes das Declarações Individuais a subscrever pelas Pessoas Seguras e em poder da Seguradora. Na falta desta Declaração, serão beneficiários os herdeiros legais de harmonia com a legislação vigente.

4. LOCAL DE RISCO

Complexo Desportivo Municipal de Oliveira S. Mateus
Complexo Desportivo Municipal de Joane
Complexo Desportivo Municipal de Ribeirão

5. ÂMBITO TERRITORIAL

O Seguro é válido em Portugal.

6. LIMITE DE IDADE

75 Anos

7. ACTIVIDADE SEGURA

A apólice garante os danos corporais causados às Pessoas Seguras em consequência de Acidentes ocorridos durante a realização das seguintes actividades promovidas e/ou organizadas pelo Tomador de Seguro:

- Natação
- Hidroginastica
- Hidroterapia

8. COBERTURAS E CAPITALS SEGUROS

A presente Apólice garante nos termos e condições previstos nas Condições Gerais, as seguintes coberturas e capitais respectivamente indicados:

8.1. Morte ou Invalidez Permanente por Acidente:	25.000 Euros (Por Pessoa)
8.2. Despesas Médicas e Repatriamento por Acidente: Franquia de 50 Euros por sinistro e por pessoa segura	4.000 Euros
8.3. Despesas de Funeral:	2.000 Euros
Limite Máximo indemnizável por sinistro e por periodo seguro	Limite Máximo 5.000.000 Euros

Condições

Os riscos de Morte e o de Invalidez Permanente não são cumuláveis, pelo que, se o Segurado falecer, em consequência de Acidente, no decurso de 2 (dois) anos a contar da data do sinistro, a indemnização por Morte será abatido o valor da indemnização por Invalidez Permanente que eventualmente lhe tenha sido atribuída e paga relativamente ao mesmo acidente.

9. DECLARAÇÕES

De acordo com o estipulado nas Condições Gerais do Seguro de Acidentes Pessoais Grupo.

Derrogando o que em contrário se encontrar exarado nas Condições Gerais, este seguro deverá garantir as consequências de sinistros que se traduzam em:

- a) Roturas e/ou distensões musculares, de ligamentos, articulações e/ou tendões;
- b) Implantação, reparação ou substituição de próteses e/ou ortóteses.
- c) Despesas de transporte que se adequem à natureza da lesão, ocorridas em Portugal e no estrangeiro pelas pessoas seguras, incluídas no capital seguro da cobertura de Despesas de Tratamento e Repatriamento.