



UNIVERSITÀ DI PARMA

Dottorato di ricerca in Scienze degli Alimenti

Ciclo XXX

***Carbohydrate quality and health:
new evidence for driving dietary choices***

Ph.D. Coordinator
Prof. Furio Brighenti

Ph.D. Tutors
Prof.ssa Francesca Scazzina
Prof.ssa Nicoletta Pellegrini

Ph.D. Student
Marta Cossu

Table of contents

Abstract	1
Chapter 1. Introduction	5
The importance of lifestyle and dietary behaviour in the management and prevention of chronic diseases.....	6
The importance of carbohydrates	8
Carbohydrate quantity or quality?.....	10
Parameters to define carbohydrate quality	11
References	16
Chapter 2. Aim of the Doctoral Thesis	23
Chapter 3. Experimental sections	26
Study 1. <i>A nutritional evaluation of various typical Italian breakfast products: a comparison of macronutrient composition and glycaemic index values</i>	27
Introduction	28
Material and methods	28
Study Population	29
Foods/Meals	29
Experimental procedures.....	29
Sample collection and analysis.....	30
Data analysis.....	30
Statistical analysis	30
Results	31
Discussion	31
References	38
Study 2. <i>The importance of glycaemic index in the context of the addition of fat to carbohydrate foods: A randomized controlled trial on spaghetti versus rice as mixed meals</i>	41
Introduction	42
Materials and methods.....	43
Study design and participants.....	43
Study meals	44
Blood samples collection.....	45
Statistical analysis	45
Results	46
Discussions and conclusions	51

References	53
Study 3. Pasta consumption in the context of a hypocaloric diet: a dietary intervention study in obese patients	56
Introduction	57
Methods	59
Study design	59
Dietary intervention.....	60
Biochemical analysis.....	61
Dietary analysis	61
Statistical analysis	61
Results	62
Anthropometric characteristics.....	62
Blood parameters.....	65
Prescribed diet and 24-h dietary recall	65
7-day carbohydrate food record.....	67
Discussions and conclusions	68
Supplemental material.....	72
References	112
Study 4. Long-term effect of a low glycaemic index diet and a high cereal fibre diet on BMI in overweight and obese with type 2 diabetes	115
Introduction	116
Methods	118
Design of the study.....	118
Participants	119
Dietary intervention.....	119
Biochemical and dietary analysis	119
Statistical analysis	120
Results	121
BMI changes.....	122
Blood parameters.....	124
Dietary intake	126
Discussions and conclusions	129
Supplemental material.....	132
References	136
Chapter 4. General conclusions	139

Abstract

The growing prevalence of chronic diseases, such as obesity and type 2 diabetes (T2D), is an important public health concern and the development of strategies for reducing and preventing this real epidemic is of primary importance. Among the factors able to modulate the reduction of risk of chronic diseases and mortality, diet is certainly among the most relevant and modifiable. Carbohydrates play a fundamental role in this framework, as they are the major components in our diet. Recently, carbohydrates have received some negative publicity and their link to human health has been largely questioned. However, evidence suggests that the carbohydrates role in the incidence of chronic diseases depends both on their quantity and quality. In this scenario, the carbohydrate-quality concept needs to be considered as parameter to follow within the jungle of healthy dietary choice. Different tools have been proposed to classify carbohydrate foods based on their quality. Among them, the content of dietary fibre, the solid or liquid form, the ratio whole grain/refined, the glycaemic index (GI) and the glycaemic load (GL) emerge as the most investigated. Despite being one of the most studied and applied, the use of GI is still under debate, and its contribution to weight management still needs some robust confirmation. For this reason, more studies, and in particular long-term studies, are needed to evaluate the effect of carbohydrate quality toward human health to identify the best dietary recommendations for the population.

On the basis of these considerations, the aim of this Doctoral Thesis were: i) to provide data on GI, GL, and macronutrient composition of breakfast foods commonly consumed in Italy; ii) to explore whether the addition of fat-rich sauces (tomato sauce and pesto) may affect GI values and glycaemic responses of low GI (spaghetti) and medium-high GI (rice) carbohydrate-rich foods, and to infer if the health effects of low GI foods may be preserved also in the context of mixed meals; iii) to investigate the role of pasta consumption (as an easily implementable low GI carbohydrate dietary choice) on weight loss and weight loss maintenance in healthy obese

adults, in the framework of a hypocaloric diet; iv) to investigate the effect of a long-term low GI or high cereal fibre diets on weight reduction and on the subsequent maintenance of a reduced weight in overweight and obese adults with T2D.

The evidence from these studies suggests that high quality carbohydrate foods may have a positive impact on health. In particular, i) the substitution of commonly consumed Italian low-medium GI breakfast items, high in saturated fat and sugar and low in fibre, with other low-GI, low-saturated fat breakfast alternatives would help the population to meet nutritional recommendations; ii) the difference in postprandial glycaemic response and GI between a low GI foods (spaghetti) and a higher GI food (rice) was preserved when tomato sauce and olive oil were added as a source of fat, but not after the addition of pesto, where the quantity of fat was higher. However, lowering the postprandial response with the addition of fat, which lead to an increase in energy, should not be considered as a viable strategy; iii) the consumption of high quality carbohydrate foods, such as pasta, in the framework of a hypocaloric diet was effective in a 6-month weight loss program in healthy obese adults, as well as in improving glycaemic and lipidemic profiles, iv) ad libitum consumption of a low GI or a high cereal fibre diet resulted effective in a 3-year BMI reduction in T2D overweight and obese subjects. In the short period, the low GI diet induced a more relevant reduction in BMI, and a greater benefit on glycaemic control, when compared to the high cereal fibre diet.

In conclusion, the findings of this Doctoral Thesis contribute to shed light on the importance of selecting high quality carbohydrate foods as one of the possible strategy to increase the overall quality of the diet. The evidence emerging from this thesis links the consumption of low GI and high fibre foods, such as fruits, vegetables, legumes and wholegrain products, to a strong positive impact on health. In particular, the choice of high quality carbohydrate foods influences

acute post-prandial glycaemic control, and may represent a valuable strategy in the framework of weight loss and weight management in healthy obese, and in overweight and obese type 2 diabetics.

Chapter 1

Introduction

The importance of lifestyle and dietary behaviour in the management and prevention of chronic diseases

During the years, the world has seen a notable change in food behaviour as a consequence of demographic and socioeconomic aspects, technological innovations, migrations, rapid urbanization and globalization. It is nowadays well known that an unhealthy diet, in association with wrong habits, i.e. tobacco smoking, alcohol consumption and physical inactivity, is related to higher risk of chronic diseases and mortality (Ezzati and Riboli 2013).

If in the past one of the main concern used to be dealing with problems such as infections and undernutrition, we are now facing new and in some case opposite problems. In the developed countries first, and a decade later in the developing countries, cardiovascular diseases (CVD), diabetes and cancer have been recognized as the primary causes of death. These types of diseases are grouped under the name of non-communicable diseases (NCDs), not being caused by infectious agents. NCDs currently cause more deaths than all other diseases combined. The United Nations and the World Health Organization (WHO) estimate that NCD deaths will increase from 38 million in 2012 to 52 million by 2030. Approximately 48% of NCD deaths in low and middle-income countries and 28% in high income countries involve individuals aged under 70 years. This is the reason why, with the slogan “25 by 25”, the WHO has called for a 25% reduction in mortality from NCDs, among person aged from 30 to 70 years by 2025. (WHO 2014).

Similarly, the prevalence of overweight and obesity has increased rapidly during recent decades, in both developed and developing countries. In 2014, more than 1.9 billion adults, 18 years and older, were overweight, and, of these, over 600 million were obese (WHO 2016). Excessive body weight causes approximately 3.4 million deaths every year, representing one

of the five primary causes of death worldwide. Obesity has important consequences for morbidity, disability, quality of life, and increase the risk of developing type 2 diabetes (T2D), CVD, several common forms of cancer, and other health problems (Finer 2015).

To classify overweight and obesity, the most used indicator is the body mass index (BMI), calculated by dividing body weight (in kilograms) by the square of the body height (in meters). Overweight is defined as a BMI of ≥ 25 , whereas obesity as a BMI ≥ 30 . Compared to normal body weight, a higher BMI is associated with a reduction in life expectancy due to a higher risk of all-cause mortality. In particular, BMI values within the upper limit of normal weight (22.5 to 25 kg/m²) have been associated to the lowest overall mortality risk, with a 30% increase in all-cause mortality with every 5% increase in BMI, in the adult population of both genders (MacMahon et al. 2009).

Some specific behaviours have been recognized as effective targets for strategies aimed at reducing the incidence of some chronic diseases. For instance, elimination or substantial reduction of tobacco smoking may decrease the incidence of multiple cancer, CVD, diabetes, chronic respiratory disease, whereas elimination or substantial reduction of alcohol use has an effect in the prevention of liver cirrhosis, gastrointestinal diseases, CVD and cancers (Ezzati and Riboli 2012).

Diet is one of the factors that could be modified in order to reduce the risk of chronic diseases and mortality. It is now well accepted that a healthy diet is essential in preventing early death and disability worldwide (Lim et al. 2012). However, establishing an association between diet and the incidence of chronic diseases is not easy. If in the past a single-nutrient approach was applied, during the last decades a “dietary pattern” approach has taken hold, together with the use of diet quality indexes to evaluate the adherence to specific dietary patterns (Hu 2002;

Jacobs Jr and Tapsell 2007; Schwingshackl and Hoffmann 2015). Dietary patterns represent the combination of foods habitually consumed. Each food item contains energy, nutrients, and a multitude of bioactive compounds that may interact with each other. Moreover, people do not eat individual nutrients, but meals consisting of a variety of foods. For these reasons, it seems more reasonable focusing on overall dietary patterns, rather than on individual nutrients, and this approach facilitates individual behavioural therapy and dietary recommendations, since it is easier for people to adopt a whole dietary pattern than incorporating or eliminating specific nutrients (Sievenpiper and Dworatzek 2013; Mozaffarian 2016).

Most of the dietary patterns identified and proposed - such as the Prudent patterns (in contrast to the Western patterns) (Hu 2002), the Dietary Approaches to Stop Hypertension (DASH) (Sacks et al. 2001) and the Mediterranean diet (Willett et al. 1995) - are usually rich in wholegrain cereals, fruits, vegetables, nuts and legumes, with moderate consumption of dairy products, fish and poultry, and low consumption of processed foods, refined grains, red and processed meats, and sugar-sweetened beverages (Medina-Remón et al. 2017). High adherence to these dietary patterns has been recognized to be beneficial in preventing and reducing the incidence of several chronic diseases, such as T2D (Knowler et al. 2002; Salas-Salvadó et al. 2011; Ley et al. 2014), CVD, obesity (Estruch et al. 2013; Estruch et al. 2016; Soltani et al. 2016), and coronary heart diseases (CHD) (Mente et al. 2009).

The importance of carbohydrates

Carbohydrates play an important role in this relationship, as they represent the major components of the diet. International and national official public health institutions recommend that carbohydrates should represent from 45% to 75% of our daily energy intake, with less than

10% being simple sugars, and they suggested a dietary fibre intake greater than 25 g/die (WHO/FAO 2003, EFSA 2010, SINU 2014).

Carbohydrate rich foods, and in particular cereal products, represent the basis of most diets. Among the possible explanations behind the widespread consumption of cereal products, the wide variety of available edible species and the wide variety of ways to prepare and consume them (in grain form, such as rice, in flakes or as flours) may be the most relevant. Wheat, rice and maize are the most commonly grown cereals in the world, and, among these, wheat is the most important source of carbohydrates in a vast majority of countries. The relevance and abundant use of wheat are mainly due to its agronomic adaptability and to the relative facility of converting grains into flour and semolina, that are the basic ingredients for bread, pasta, and other bakery products production.

Cereals, and in particular whole grain products, represent an important source of indigestible carbohydrates, namely dietary fibre, resistant starch, and oligosaccharides (Slavin 2004). Dietary fibre plays a role in intestinal function regulation through its ability in increasing stool weight, speeding intestinal transit, getting fermented to short chain fatty acids, and modifying the gut microbiota (Slavin 2010). Furthermore, by prolonging gastric emptying and satiety, whole grain products may play a role in weight management (Wanders et al. 2011). A diet rich in wholegrain and cereal fibre-based foods has been associated with a reduced risk of developing chronic diseases, such as CVD (Giacco et al. 2010), T2D (Chanson-Rolle et al. 2015), and some types of cancer (Bingham et al. 2003; Zhang et al. 2013).

Carbohydrate quantity or quality?

In the last decade, the health effects of carbohydrates have been questioned in many occasions. There is a general belief that their intake should be reduced for weight loss and, as a consequence, there is increasing interest in the efficacy of diets that are high in proteins with a low to moderate carbohydrate content (Paddon-Jones et al. 2008; Claessens et al. 2009). In addition, the results of a very recent prospective cohort study, the PURE study, that investigated the association of fat and carbohydrates intake with CVD mortality, were interpreted as follows:

“High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke. Global dietary guidelines should be reconsidered in light of these findings.” (Dehghan et al. 2017).

This conclusion leaves small room to discussion: carbohydrates must surely be harmful for our health. However, some considerations need to be made. Indeed, if fats were considered both in their total intake and based on their individual characteristics, carbohydrates were considered only as total, with no distinctions whatsoever. Similarly, Jakobsen and colleagues investigated the substitution of saturated fatty acids with mono, polyunsaturated fatty acids and carbohydrates to prevent CHD. They concluded that polyunsaturated fatty acids rather than monounsaturated fatty acids and carbohydrates (in general) represent a healthier substitution to decrease the risk of CHD (Jakobsen et al. 2009). However, this is yet another case where carbohydrates were considered as a total, even if the authors comment that the effect of carbohydrate substitution may vary depending on the quality of the specific carbohydrate sources consumed. In another study, the same authors compared the intake of carbohydrates vs.

saturated fatty acids and the risk of myocardial infarction, but this time they made a distinction between carbohydrates with low and high glycaemic index. The result was that replacing saturated fat with low glycaemic index foods was associated with a lower risk of myocardial infarction, whereas the substitution with high glycaemic index foods was associated with higher risk (Jakobsen et al. 2010).

This last and other observations present in the literature clearly highlight the importance of quality in the health effects attributable to carbohydrates in the framework of a specific dietary pattern, generalization being obviously incorrect and potentially bringing to wrong conclusions. Carbohydrate quality, besides quantity, may have important health implications in obesity, T2D and CVD risk (Blaak 2016).

Parameters to define carbohydrate quality

To evaluate the quality of carbohydrates, different parameters have been suggested. There are parameters that take into account specific food characteristics, like the content of dietary fibre, the solid or liquid form, and the ratio whole grains /refined grains in a product. Furthermore, quality measures, such as the Glycaemic Index (GI) and the Glycaemic Load (GL) have been proposed and are used to evaluate the physiological effect of carbohydrates.

GI and GL have been largely used in epidemiological studies to evaluate the association of a diet rich in carbohydrates with chronic diseases. The GI, introduced in 1981 by Jenkins and colleagues, represents a way to rank carbohydrates according to the extent to which they increase postprandial glycaemia (Jenkins DJ et al. 1981). The mathematical product of the GI of a given food item by its carbohydrate content provides the GL, which integrates the quantity and the quality of carbohydrates consumed (Salmerón et al. 1997).

Foods with a GI of 55 or less are considered “low GI”, foods with a GI between 56 and 70 are considered “medium GI”, and foods with a GI above 70 are considered “high GI”. In general, in low GI foods starch is digested and glucose absorbed slowly along the small intestine compared to medium or high GI foods (Jenkins DJA et al. 2002).

The GI takes into account also the complex interaction of factors concurring to determine glycaemic response, including not only the rate of carbohydrate digestion, but also food-mediated effects on both gastrointestinal events and post-adsorptive metabolism (Englyst KN and Englyst 2005). Indeed, the GI of foods may vary depending on their composition and physical/chemical state. The presence of physical barriers such as intact plant cell-wall structures (Englyst KN et al. 2003), the nature of starch (e.g. ungelatinised starch granules and the ratio amylose/amylopectin) (Lehmann and Robin 2007), the presence of viscous and soluble fibre, the protein network in pasta products (Petitot et al. 2009) or the parboiling process of rice (Boers et al. 2015) are some examples of food-related factors generally lowering the GI.

To date, several studies have been carried out to investigate the effects of GI and GL on human health. Many studies clearly showed the benefits of a low GI diet on glycemic control, as well as on postprandial insulin and C-peptide levels, blood lipids, inflammatory and thrombolytic factors, endothelial function and the regulation of body weight (Rahelić et al. 2011). These low GI diets have been reported to improve the control of diabetes (Brand-Miller et al. 2003), to increase high density lipoprotein cholesterol (HDL-C) (Ford and Liu 2001), to lower serum triglyceride, plasminogen activator inhibitor 1 and high-sensitivity C-reactive protein concentrations (Liu et al. 2001; Liu et al. 2002), and to generally reduce diabetes incidence (Salmerón et al. 1997; Bhupathiraju et al. 2014) and overall cardiovascular events (Liu et al., 2000). A meta-analysis of prospective observational studies has shown that higher dietary GL and GI significantly increased the risk of CHD among women, and that the effect was more

pronounced in overweight and obese subjects (Dong et al. 2012), whereas low GI and/or low GL diets were independently associated with a reduced risk of certain chronic diseases and the protection offered by these diets was comparable or higher with that seen for whole grain and high fibre intakes (Barclay et al. 2008). Based on this literature, it could easily be concluded that adopting a low GI diet could be useful to prevent or treat a number of chronic conditions. Beside *in vivo* parameters, different *in vitro* methods have been developed to determine the rate and absorption of carbohydrates. *In vitro* studies have indicated that glycaemic response and the rate of starch digestion are closely correlated. Englyst and colleagues suggested an *in vitro* digestion method which allows to discriminate carbohydrate foods based on the amount of rapidly digestible starch (RDS) and slowly digestible starch (SDS), generating, in turn, rapidly available glucose (RAG) and slowly available glucose (SAG). A positive correlation between RAG and GI has been reported (Englyst HN et al. 1996), and foods containing a high content of RDS and a low content of SDS are likely to have higher GI compared to foods with a high content of SDS and a low content of RDS.

The ratio SDS/available starch has been recently accepted as valid measure to characterize cereal food products for a health claim related to “slowly digestible starch in starch-containing foods and reduction of postprandial glycaemic responses”. Studies demonstrated a cause and effect relationship between the consumption of SDS in cereal products, as compared to the consumption of RDS, and reduced postprandial glycaemic responses, without disproportionately increased postprandial insulinemic responses (EFSA 2011).

This last point highlights that an important aspect that should be considered is the insulinemic response. Indeed, blood glucose responses are not always proportional to the corresponding insulinemic responses. This is because, although carbohydrates are the major stimulus for insulin secretion, there are other dietary factors, such as the content of protein and fat, that may

play a role in the process of insulin secretion. For instance, high protein or high fat levels in a carbohydrate containing foods have been demonstrated to induce low postprandial glycaemic responses, but not a reduction in insulin secretion (Collier et al. 1988; Gannon et al. 1988; Normand et al. 2001). High insulinemic postprandial responses have been associated with an increased risk of overweight and hyperlipidaemia (Ostlund et al. 1990), T2D (Weyer et al. 2001), and cancer (Onitilo et al. 2014). Therefore, the evaluation of both glycaemic and insulinemic postprandial responses is necessary in order to demonstrate the true beneficial effect of the consumption of low GI foods.

Despite all the existing evidence suggesting a beneficial health effect of low GI diets, the use of GI as a measure of diet quality, at least when it comes to carbohydrates based foods, is still under debate. The FAO/WHO Scientific update on carbohydrates in human nutrition, highlighted some of the weaknesses of GI, and suggested caution regarding the use of GI as the sole determinant of the quality of carbohydrate foods (Mann et al. 2007). The scientific opinion of the European Food Safety Authority on Dietary Reference Values for carbohydrates and dietary fibre was that: “Although there is some support for a role of GI and GL in the treatment of type-2 diabetes and some evidence suggesting that lowering GI and GL may have favourable effects on some metabolic risk factors such as serum lipids, the evidence regarding their role in the prevention of diet-related diseases is still inconclusive” (EFSA 2010).

Nevertheless, international guidelines, especially diabetes guidelines, suggest the use of a low GI diet. The American Diabetes Association (ADA) (Evert et al. 2014), the Canadian Diabetes Association (CDA) (Dworatzek et al. 2013), the International Diabetes Federation (IDF 2014), the Diabetes UK (Dyson et al. 2011) advise to choose food sources with a low GI and to substitute high GI with lower GI foods. The Italian society of Human Nutrition (SINU) recommends to prefer starchy food sources with low GI, particularly when the intake of

carbohydrates is approaching the upper limit of intake, i.e. 60% of the energy (SINU 2010). In 2015, a scientific consensus from the International Carbohydrate Quality Consortium (ICQC) has recognized the importance of postprandial glycaemia in the framework of overall health, and the GI as a valid measure to classify carbohydrate foods (Augustin et al. 2015).

Beside these conventional quality indexes, novel measures have been suggested. For instance, the carbohydrate to dietary fibre ratio ($\leq 10:1$) was introduced as recommendation for CVD health promotion and disease reduction by the American Heart Association (Lloyd-Jones et al. 2010). AlEssa and colleagues, instead, proposed the starch/cereal dietary fibre ratio as novel metric for assessing carbohydrate quality in relation to T2D. They found that the ratio carbohydrates/total dietary fibre, carbohydrates/cereal fibre, starch/total fibre and starch/cereal fibre were all positively associated with the risk of T2D, but the strongest association was found with starch/cereal dietary fibre. This ratio identifies a novel metric for assessing carbohydrate quality in relation to T2D (AlEssa et al. 2015). Therefore, their conclusion was that eating whole grains and having a low GI diet is associated with lower carbohydrate/fibre or starch/fibre ratios and a lower risk of T2D. Later, they investigated the effect of carbohydrate on biomarker related to T2D. They found that carbohydrate quality but not carbohydrate quantity was associated with HbA1c, adiponectin and C-reactive protein. In particular, higher starch/total fibre intake was associated with lower adiponectin and higher HbA1c concentration, and higher starch/cereal fibre intake was associated with lower adiponectin (AlEssa et al. 2016).

Recently, another index, named carbohydrate quality index (CQI), was used to evaluate weight change and incidence of obesity (Santiago et al. 2015) and risk of CVD (Zazpe et al. 2016) in a Mediterranean cohort. The CQI takes into consideration dietary fibre intake, GI, whole grain/total grain ratio (to take into account the degree of processing) and solid

carbohydrates/total carbohydrates ratio. In the study of Zazpe and colleagues, the ratio carbohydrates from whole grain/carbohydrates to total grain was used instead of whole grain/total grain ratio to specifically assess the quality of carbohydrates. CQI at baseline was significantly inversely associated with the incidence of overweight, obesity (Santiago et al. 2015) and CVD (Zazpe et al. 2016).

In light of all this evidence, recommendations should be focused more on improving the quality of carbohydrates (i.e. substituting refined grain with whole grain, increasing dietary fibre, preferring foods with low GI) rather than limiting the quantity. The quality parameters that have been recently developed, and mentioned above, could be useful in dietary advice related to prevention or treatment of chronic diseases.

References

- AlEsa HB, Bhupathiraju SN, Malik VS, Wedick NM, Campos H, Rosner B, Willett WC, Hu FB. 2015. Carbohydrate quality and quantity and risk of type 2 diabetes in US women. *American Journal of Clinical Nutrition*. 102(6):1543-1553.
- AlEsa HB, Ley SH, Rosner B, Malik VS, Willett WC, Campos H, Hu FB. 2016. High fiber and low starch intakes are associated with circulating intermediate biomarkers of type 2 diabetes among women. *Journal of Nutrition*. 146(2):306-317.
- Augustin LSA, Kendall CWC, Jenkins DJA, Willett WC, Astrup A, Barclay AW, Björck I, Brand-Miller JC, Brighenti F, Buyken AE et al. 2015. Glycemic index, glycemic load and glycemic response: An International Scientific Consensus Summit from the International Carbohydrate Quality Consortium (ICQC). *Nutrition, Metabolism and Cardiovascular Diseases*. 25(9):795-815.
- Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P, Brand-Miller JC. 2008. Glycemic index, glycemic load, and chronic disease risk - A metaanalysis of observational studies. *American Journal of Clinical Nutrition*. 87(3):627-637.
- Bhupathiraju SN, Tobias DK, Malik VS, Pan A, Hruby A, Manson JE, Willett WC, Hu FB. 2014. Glycemic index, glycemic load, and risk of type 2 diabetes: Results from 3 large US cohorts and an updated meta-analysis. *American Journal of Clinical Nutrition*. 100(1):218-232.

Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, Clavel-Chapelon F, Kesse E, Nieters A, Boeing H et al. 2003. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): An observational study. *Lancet*. 361(9368):1496-1501.

Blaak EE. 2016. Carbohydrate quantity and quality and cardio-metabolic risk. *Current Opinion in Clinical Nutrition and Metabolic Care*. 19(4):289-293.

Boers HM, Seijen Ten Hoorn J, Mela DJ. 2015. A systematic review of the influence of rice characteristics and processing methods on postprandial glycaemic and insulinaemic responses. *British Journal of Nutrition*. 114(7):1035-1045.

Brand-Miller J, Hayne S, Petocz P, Colagiuri S. 2003. Low-glycemic index diets in the management of diabetes: A meta-analysis of randomized controlled trials. *Diabetes Care*. 26(8):2261-2267.

Chanson-Rolle A, Meynier A, Aubin F, Lappi J, Poutanen K, Vinoy S, Braesco V. 2015. Systematic review and meta-analysis of human studies to support a quantitative recommendation for whole grain intake in relation to type 2 diabetes. *PLoS ONE*. 10(6).

Claessens M, Van Baak MA, Monsheimer S, Saris WHM. 2009. The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight loss maintenance and metabolic risk factors. *International Journal of Obesity*. 33(3):296-304.

Collier GR, Greenberg GR, Wolever TM, Jenkins DJ. 1988. The acute effect of fat on insulin secretion. *J Clin Endocrinol Metab*. 66(2):323-326.

Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, Iqbal R, Kumar R, Wentzel-Viljoen E, Rosengren A et al. 2017. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): A prospective cohort study. *The Lancet*.

Dong JY, Zhang YH, Wang P, Qin LQ. 2012. Meta-analysis of dietary glycemic load and glycemic index in relation to risk of coronary heart disease. *American Journal of Cardiology*. 109(11):1608-1613.

Dworatzek PD, Arcudi K, Gougeon R, Husein N, Sievenpiper JL, Williams SL. 2013. Nutrition Therapy. *Canadian journal of diabetes*. 37(SUPPL.1):S45-S55.

Dyson PA, Kelly T, Deakin T, Duncan A, Frost G, Harrison Z, Khatri D, Kunka D, McArdle P, Mellor D et al. 2011. Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes. *Diabetic Medicine*. 28(11):1282-1288.

EFSA. 2010. Scientific Opinion on Dietary Reference Values for carbohydrates and dietary fibre. *EFSA Journal* 8(3):1462.

EFSA. 2011. Scientific Opinion on the substantiation of a health claim related to “slowly digestible starch in starch-containing foods” and “reduction of post-prandial glycaemic responses” pursuant to Article 13(5) of Regulation (EC) No 1924/2006. *EFSA Journal* 9(7):2292.

Englyst HN, Veenstra J, Hudson GJ. 1996. Measurement of rapidly available glucose (RAG) in plant foods: A potential in vitro predictor of the glycaemic response. *British Journal of Nutrition*. 75(3):327-337.

Englyst KN, Englyst HN. 2005. Carbohydrate bioavailability. *British Journal of Nutrition*. 94(1):1-11.

Englyst KN, Vinoy S, Englyst HN, Lang V. 2003. Glycaemic index of cereal products explained by their content of rapidly and slowly available glucose. *British Journal of Nutrition*. 89(3):329-339.

Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Fitó M, Chiva-Blanch G, Fiol M, Gómez-Gracia E, Arós F, Lapetra J et al. 2016. Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial. *The Lancet Diabetes and Endocrinology*. 4(8):666-676.

Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J et al. 2013. Primary prevention of cardiovascular disease with a Mediterranean diet. *New England Journal of Medicine*. 368(14):1279-1290.

Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, Neumiller JJ, Nwankwo R, Verdi CL, Urbanski P et al. 2014. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care*. 37(SUPPL.1):S120-S143.

Ezzati M, Riboli E. 2012. Can noncommunicable diseases be prevented? Lessons from studies of populations and individuals. *Science*. 337(6101):1482-1487.

Ezzati M, Riboli E. 2013. Behavioral and dietary risk factors for noncommunicable diseases. *New England Journal of Medicine*. 369(10):954-964.

Finer N. 2015. Medical consequences of obesity. *Medicine (United Kingdom)*. 43(2):88-93.

Ford ES, Liu S. 2001. Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. *Archives of Internal Medicine*. 161(4):572-576.

Gannon MC, Nuttall FQ, Neil BJ, Westphal SA. 1988. The insulin and glucose responses to meals of glucose plus various proteins in type II diabetic subjects. *Metabolism*. 37(11):1081-1088.

Giacco R, Clemente G, Cipriano D, Luongo D, Viscovo D, Patti L, Di Marino L, Giacco A, Naviglio D, Bianchi MA et al. 2010. Effects of the regular consumption of wholemeal wheat foods on cardiovascular risk factors in healthy people. *Nutrition, Metabolism and Cardiovascular Diseases*. 20(3):186-194.

Hu FB. 2002. Dietary pattern analysis: A new direction in nutritional epidemiology. *Current Opinion in Lipidology*. 13(1):3-9.

IDF. 2014. International Diabetes Federation Guideline Development Group. Guideline for management of postmeal glucose in diabetes. *Diabetes research and clinical practice*. 103:256-68.

Jacobs Jr DR, Tapsell LC. 2007. Food, not nutrients, is the fundamental unit in nutrition. *Nutrition Reviews*. 65(10):439-450.

Jakobsen MU, Dethlefsen C, Joensen AM, Stegger J, Tjønneland A, Schmidt EB, Overvad K. 2010. Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: Importance of the glycemic index¹⁻³. *American Journal of Clinical Nutrition*. 91(6):1764-1768.

Jakobsen MU, O'Reilly EJ, Heitmann BL, Pereira MA, Bälter K, Fraser GE, Goldbourt U, Hallmans G, Knekt P, Liu S et al. 2009. Major types of dietary fat and risk of coronary heart disease: A pooled analysis of 11 cohort studies. *American Journal of Clinical Nutrition*. 89(5):1425-1432.

Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. 1981. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr*. 34(3):362-366.

Jenkins DJA, Kendall CWC, Augustin LSA, Franceschi S, Hamidi M, Marchie A, Jenkins AL, Axelsen M. 2002. Glycemic index: Overview of implications in health and disease. *American Journal of Clinical Nutrition*. 76(1):266S-273S.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM. 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*. 346(6):393-403.

Lehmann U, Robin F. 2007. Slowly digestible starch - its structure and health implications: a review. *Trends in Food Science and Technology*. 18(7):346-355.

Ley SH, Hamdy O, Mohan V, Hu FB. 2014. Prevention and management of type 2 diabetes: Dietary components and nutritional strategies. *The Lancet*. 383(9933):1999-2007.

Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, Amann M, Anderson HR, Andrews KG, Aryee M et al. 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 380(9859):2224-2260.

Liu S, Manson JE, Buring JE, Stampfer MJ, Willett WC, Ridker PM. 2002. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women ¹⁻³. *American Journal of Clinical Nutrition*. 75(3):492-498.

Liu S, Manson JE, Stampfer MJ, Holmes MD, Hu FB, Hankinson SE, Willett WC. 2001. Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *American Journal of Clinical Nutrition*. 73(3):560-566.

Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF et al. 2010. Defining and setting national goals for cardiovascular health

promotion and disease reduction: The American Heart Association's strategic impact goal through 2020 and beyond. *Circulation*. 121(4):586-613.

MacMahon S, Baigent C, Duffy S, Rodgers A, Tominaga S, Chambless L, De Backer G, De Bacquer D, Kornitzer M, Whincup P et al. 2009. Body-mass index and cause-specific mortality in 900 000 adults: Collaborative analyses of 57 prospective studies. *The Lancet*. 373(9669):1083-1096.

Mann J, Cummings JH, Englyst HN, Key T, Liu S, Riccardi G, Summerbell C, Uauy R, van Dam RM, Venn B et al. 2007. FAO/WHO Scientific Update on carbohydrates in human nutrition: Conclusions. *European Journal of Clinical Nutrition*. 61:S132-S137.

Medina-Remón A, Kirwan R, Lamuela-Raventós RM, Estruch R. 2017. Dietary patterns and the risk of obesity, type 2 diabetes mellitus, cardiovascular diseases, asthma, and neurodegenerative diseases. *Critical Reviews in Food Science and Nutrition*. 1-35.

Mente A, De Koning L, Shannon HS, Anand SS. 2009. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Archives of Internal Medicine*. 169(7):659-669.

Mozaffarian D. 2016. Dietary and Policy Priorities for Cardiovascular Disease, Diabetes, and Obesity. *Circulation*. 133(2):187-225.

Normand S, Khalfallah Y, Louche-Pelissier C, Pachiaudi C, Antoine JM, Blanca S, Desagea M, Rioua JP, Laville M. 2001. Influence of dietary fat on postprandial glucose metabolism (exogenous and endogenous) using intrinsically ¹³C-enriched durum wheat. *British Journal of Nutrition*. 86(1):3-11.

Onitilo AA, Stankowski RV, Berg RL, Engel JM, Glurich I, Williams GM, Doi SA. 2014. Type 2 diabetes mellitus, glycemic control, and cancer risk. *European Journal of Cancer Prevention*. 23(2):134-140.

Ostlund RE, Staten M, Kohrt WM, Schultz J, Malley M. 1990. The ratio of waist-to-hip circumference, plasma insulin level, and glucose intolerance as independent predictors of the HDL₂ cholesterol level in older adults. *New England Journal of Medicine*. 322(4):229-234.

Paddon-Jones D, Westman E, Mattes RD, Wolfe RR, Astrup A, Westerterp-Plantenga M. 2008. Protein, weight management, and satiety. *American Journal of Clinical Nutrition*. 87(5):1558S-1561S.

Petitot M, Abecassis J, Micard V. 2009. Structuring of pasta components during processing: impact on starch and protein digestibility and allergenicity. *Trends in Food Science and Technology*. 20(11-12):521-532.

Rahelić D, Jenkins A, Božikov V, Pavić E, Jurić K, Fairgrieve C, Romić D, Kokić S, Vuksan V. 2011. Glycemic index in diabetes. *Collegium Antropologicum*. 35(4):1363-1368.

Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller III ER, Simons-Morton DG et al. 2001. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (dash) diet. *New England Journal of Medicine*. 344(1):3-10.

- Salas-Salvadó J, Bulló M, Babio N, Martínez-González MÁ, Ibarrola-Jurado N, Basora J, Estruch R, Covas MI, Corella D, Arós F et al. 2011. Reduction in the incidence of type 2 diabetes with the mediterranean diet: Results of the PREDIMED-Reus nutrition intervention randomized trial. *Diabetes Care*. 34(1):14-19.
- Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. 1997. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care*. 20(4):545-550.
- Santiago S, Zazpe I, Bes-Rastrollo M, Sánchez-Tainta A, Sayón-Orea C, De La Fuente-Arrillaga C, Benito S, Martínez JA, Martínez-González MÁ. 2015. Carbohydrate quality, weight change and incident obesity in a Mediterranean cohort: The SUN Project. *European Journal of Clinical Nutrition*. 69(3):297-302.
- Schwingshackl L, Hoffmann G. 2015. Diet Quality as Assessed by the Healthy Eating Index, the Alternate Healthy Eating Index, the Dietary Approaches to Stop Hypertension Score, and Health Outcomes: A Systematic Review and Meta-Analysis of Cohort Studies. *Journal of the Academy of Nutrition and Dietetics*. 115(5):780-800.
- Sievenpiper JL, Dworatzek PD. 2013. Food and dietary pattern-based recommendations: an emerging approach to clinical practice guidelines for nutrition therapy in diabetes. *Canadian journal of diabetes*. 37(1):51-57.
- SINU, Società Italiana di Nutrizione Umana (2014). LARN – Livelli di Assunzione di Riferimento di Nutrienti ed energia per la popolazione italiana IV Revisione. Milano (IT): SICS Editore.
- Slavin J. 2004. Whole grains and human health. *Nutrition Research Reviews*. 17(1):99-110.
- Slavin J. 2010. Whole grains and digestive health. *Cereal Chemistry*. 87(4):292-296.
- Soltani S, Shirani F, Chitsazi MJ, Salehi-Abargouei A. 2016. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: A systematic review and meta-analysis of randomized controlled clinical trials. *Obesity Reviews*. 17(5):442-454.
- Wanders AJ, van den Borne JJGC, de Graaf C, Hulshof T, Jonathan MC, Kristensen M, Mars M, Schols HA, Feskens EJM. 2011. Effects of dietary fibre on subjective appetite, energy intake and body weight: A systematic review of randomized controlled trials. *Obesity Reviews*. 12(9):724-739.
- Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley RE, Tataranni PA. 2001. Hypoadiponectinemia in obesity and type 2 diabetes: Close association with insulin resistance and hyperinsulinemia. *Journal of Clinical Endocrinology and Metabolism*. 86(5):1930-1935.
- WHO. 2014. Global status report on noncommunicable diseases 2014. World Health Organization (pp 298).
- WHO. 2016. Obesity and overweight. *In Fact sheet: obesity and overweight* (Vol. 2016): World Health Organization.

WHO/FAO Expert Consultation 2003. Diet, nutrition and the prevention of chronic diseases. World Health Organization, Technical Report Series;916:1-149.

Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, Trichopoulos D. 1995. Mediterranean diet pyramid: A cultural model for healthy eating. *American Journal of Clinical Nutrition*. 61(6 SUPPL.):1402S-1406S.

Zazpe I, Santiago S, Gea A, Ruiz-Canela M, Carlos S, Bes-Rastrollo M, Martínez-González MA. 2016. Association between a dietary carbohydrate index and cardiovascular disease in the SUN (Seguimiento Universidad de Navarra) Project. *Nutrition, Metabolism and Cardiovascular Diseases*. 26(11):1048-1056.

Zhang Z, Xu G, Ma M, Yang J, Liu X. 2013. Dietary fiber intake reduces risk for gastric cancer: A meta-analysis. *Gastroenterology*. 145(1):113-120.e113.

Chapter 2

Aim of the Doctoral Thesis

We are facing a dramatic increase in the incidence of serious health problems such as obesity, diabetes, cardiovascular disease and cancer, worldwide. Among the many possible plans to counteract these epidemics, promoting high-quality diets and physical activity seem to be the most valuable and viable strategies.

Carbohydrate foods, being the major component of our diet, play a fundamental role in the association between nutrition and the risk of chronic diseases. Recently, the health impact of carbohydrates has been questioned, and there is a general belief that their intake should be reduced in the framework of weight loss programs. However, the most recent evidence suggests that the impact of carbohydrates in the context of human health may depend on the quality more than on the quantity of carbohydrate rich sources. The overall hypothesis is that it may be more beneficial to focus on selecting high quality carbohydrate foods, rather than focus on reducing quantity consumed.

The aim of this Doctoral Thesis was to better understand the relation between carbohydrates and health, with a main focus on glycaemic index (GI) as a quality parameter, with the final goal to identify the best dietary choices for the population.

The following four actions were carried out and discussed to pursue this aim.

- ❖ Providing data on the GI and GL values, as well as on macronutrient composition, of a number of breakfast foods commonly consumed in Italy to assist in the selection of healthier breakfast options. (*Study 1: A nutritional evaluation of various typical Italian breakfast products: a comparison of macronutrient composition and glycaemic index values*).

- ❖ Exploring whether the addition of fat in the form of commonly consumed sauces, i.e. tomato sauce and pesto, affects the difference in glycaemic responses and glycaemic index between a commonly consumed low GI (spaghetti) and a high GI (rice) carbohydrate based food, hence if the beneficial effects of the low GI food is preserved also in the context of mixed meals. (*Study 2: The importance of glycaemic index in the context of the addition of fat to carbohydrate foods: A randomized controlled trial on spaghetti versus rice as mixed meals*).

- ❖ Investigating the effect of pasta consumption, in the context of a hypocaloric diet, on weight loss and consequent weight loss maintenance in healthy obese and overweight adults. (*Study 3: Pasta consumption in the context of a hypocaloric diet: a dietary intervention study in obese patients*).

- ❖ Investigating if following a low GI diet or a diet rich in cereal dietary fibre, over a long period (3 years), results in weight reduction and in the subsequent weight loss maintenance in overweight and obese adults with type 2 diabetes. (*Study 4: Long-term effect of a low glycaemic index diet and a high cereal fibre diet on BMI in overweight and obese with type 2 diabetes*).

Chapter 3

Experimental sections

Study 1

A nutritional evaluation of various typical Italian breakfast products: a comparison of macronutrient composition and glycaemic index values

Laura Chiavaroli[§], Marta Cossu[§], Margherita Dall'Asta, Veronica Francinelli,
Francesca Scazzina and Furio Brighenti

Department of Food and Drug, University of Parma, Parma

[§] these authors contributed equally

This paper has been submitted to "International Journal of Food Science and Nutrition"

Introduction

Foods that elicit a lower postprandial glycaemic response, especially if consumed in the morning, may be beneficial to manage body weight (Schwingshackl and Hoffmann 2013; Smith et al. 2015), which is of great interest in Italy due to the rising prevalence of obesity. The glycaemic response that follows the consumption of a carbohydrate-containing food depends on the amount of carbohydrate consumed as well as its glycaemic index (GI) (Jenkins et al. 1981). The carbohydrates in low-GI foods are more slowly digested and absorbed and are thus beneficial in controlling postprandial blood glucose excursions (Jenkins et al. 2002). Both low-GI foods and the consumption of breakfast have been associated with better body weight management (Ma et al. 2003; Slavin 2005; Marin-Guerrero et al. 2008).

Typical Italian breakfast foods included milk, coffee, tea, yogurt, crispbread, breakfast cereals, pastries, biscuits, honey, sugar and jam (di Giuseppe et al. 2012), however how the use of common additions/spreads on bread affect the glycaemic response and a comparison of the macronutrients of these options has not yet been undertaken. Therefore, with the need to find effective strategies to manage body weight, and with breakfast being one such possible strategy, the aim of the present study is to provide data on the GI and GL values, as well as on macronutrient composition, of a number of breakfast foods commonly consumed in Italy to assist in the selection of healthier breakfast options.

Material and methods

A total of 20 breakfast food items were considered in this work for both glycaemic index values and macronutrient composition. The glycaemic index of 5 breakfast food combinations were directly analysed using the same methods as previously reported (Scazzina et al. 2016), while the glycaemic index of the other 15 foods were analysed in a previous publication (Scazzina et

al. 2016). Briefly, the GI of the foods were analysed at the Department of Food and Drug at the University of Parma following the method described by the Food and Agriculture Organization/World Health Organization (FAO/WHO 1998) applying the guidelines set up by the International Standards Organization (ISO 2010).

Study Population

A total of 88 healthy subjects were recruited during 2005–2015 who were 18-69y, with a BMI $\leq 30\text{kg/m}^2$ and generally healthy. They participated in a total of 16 GI sub-studies, each with an average of 10 participants, and each sub-study was approved case-by-case by the ethical committee of the University of Parma and written consent was obtained from all participants in accordance with the Declaration of Helsinki.

Foods/Meals

For all foods/meals tested in each sub-study, foods were purchased in a single batch at the local market or directly obtained by the producer in sufficient amounts for the entire sub-study. Portion sizes were calculated according to manufacturers' nutrition information. All foods/meals were portioned to provide 50 g of available carbohydrate in total and the ratio of each ingredients in mixed meals was calculated based on how the meal is commonly consumed in Italy.

Experimental procedures

After a 12-hour overnight fast, subjects consumed the test food/meal within 15 minutes, with 500 ml of water. The reference meal, glucose monohydrate, was dissolved in 500 ml of water and consumed by the subjects on two or three independent sessions.

Sample collection and analysis

Capillary whole blood samples were collected by finger prick in heparin/fluoride vials (Microvette CB 300 FH, Sarstedt, Germany) in the fasting state and at 15, 30, 45, 60, 90 and 120 minutes after consumption of the test food/meal. Whole blood samples were stored at -20°C until analysis. Blood glucose concentration was measured with an automatic analyser (YSI 2300 STAT PLUS, Yellow Spring Instruments, OH, U.S.A.).

Data analysis

The incremental area under the blood glucose response curve (IAUC) was calculated geometrically using the trapezoid rule, ignoring the area below the fasting baseline. For each test food/meal, the IAUC was expressed as a percentage of the mean IAUC of the iso-carbohydrate glucose reference food (average of 2-3 tests) consumed by the same subject. The GI of each food/meal was then calculated as the mean value across all subjects consuming that food/meal. Glycaemic load (GL) was calculated as the product of the GI and the available carbohydrate, divided by 100.

Statistical analysis

The GI value for each food/meal is reported as mean (\pm SEM). Individual values exceeding the mean by at least 2 standard deviations (SD) were excluded from the mean calculation, as per ISO methodology (ISO 2010).

Results

Overall, subjects were 27.4 ± 0.8 y, with a BMI of 22.5 ± 0.2 kg/m² and 54% were men.

The GI values for the foods/meals tested are presented in Table 1, along with the macronutrients and calculated GL values for one typically consumed portion. Food items categorized as breads had medium GI (59-64) (except for one with a high GI of 76) and low-medium GL (5.5-13.8), with 0.9-1.9g of fibre, 1.4-2.3g of sugar (0.3-0.5% kcal, based on a 2000kcal diet) and 0.1-0.3g of saturated fat (0.05-0.1% kcal); those categorized as breads with added spreads, were low-medium GI (47-66) and medium-high GL (17.6-22.8), with 0.9-1.1g of fibre, 19.8-22.0g of sugar (4.0-4.4% kcal) and 0.1-5.7g of saturated fat (0.05-2.6% kcal); those categorized as muesli cereals, were all medium GI (62-66) and GL (19.8), with 3.6-4.3g of fibre, 7.4-12.2g of sugar (1.5-2.4% kcal) and 0.2-0.4g of saturated fat (0.1-0.2% kcal); those categorized as cookies, were low-medium GI (49-58) and GL (6.3-11.2), with 0.7-2.4g of fibre, 3.3-6.1g of sugar (0.7-1.2% kcal) and 0.6-1.0g of saturated fat (0.3-0.5% kcal); and those categorized as cakes and pastries, were low-medium GI (44-60) and GL (7.8-11.3), with 0.4-1.2g of fibre, 6.9-15.3g of sugar (1.4-3.1% kcal) and 0.6-6.2g of saturated fat (0.3-2.8% kcal).

Discussion

The mixed meals analysed in the present study assessed the addition of spreads to bread and generally demonstrated lower glycaemic responses. These results may be partly explained by the contribution of fat and protein from the spreads, as these have been demonstrated to affect glycaemic response (Nuttall and Gannon 1991; Gannon et al. 1993). Previous studies have used additions of these macronutrients generally greater than 30g and found reductions in glycaemic responses (Gulliford et al. 1989; Henry et al. 2006). For example, Henry et al. (Henry et al. 2006) added 120g of cheddar cheese to bread, contributing an additional 35g of fat and 20g of

protein, significantly reducing the glycaemic response (GI of 35 versus 50 for bread alone). The present study used quantities of spreads typical of what is commonly consumed for breakfast in Italy, falling within a range much lower and yet lower glycaemic responses were still observed for most mixed meals. For example, the addition of butter and jam, contributing an addition of 7g of fat, resulted in a GI of 55, whereas bread alone had a GI of 76. Similarly, with the addition of chocolate hazelnut spread, contributing an addition of 8g of fat and 2g of protein, the GI was 47. The addition of ham and cheese to bread did not seem to have an effect on the glycaemic response, however, this may be because the quantities used were small and contributed too little protein and fat (2-3g of each). Therefore, moderate additions of fat may contribute to a lower glycaemic response, possibly through a reduction in gastric emptying (Collier et al. 1988).

Although certain foods may have a lower glycaemic response, it is important to assess the potential health effects of the food as a whole. Pastries and cookies, which are among the most commonly consumed breakfast foods in Italy (di Giuseppe et al. 2012), were demonstrated in the present study to generally have low-medium GI and GL. However, they are high in sugar and saturated fat and low in fibre. Conversely, foods categorized as muesli and breads were generally higher in terms of GI and GL, but had lower saturated fat, higher fibre (muesli) and lower sugar (breads). The addition of spreads to breads bring their nutritional profiles closer to those in the categories of cakes and pastries, by increase sugar and saturated fat, although also lower the GI, which is not surprising since previous studies have shown the addition of fat to a meal can lower the glycaemic response (Frost et al. 2003; Henry et al. 2006). Therefore, caution should be taken in considering the overall nutritional profile, including carbohydrate quality, of the actual food combination most likely consumed to correctly assess overall benefit.

Since the majority of commonly consumed Italian breakfast foods are higher in sugar and saturated fat and low in fibre, there may be interest in encouraging alternative low-GI breakfast foods which have a better nutritional profile, including natural oatmeal, yogurts and fruits (especially temperate climate). Although this may be challenging since added sugar and chocolate in breakfasts arise from a strong cultural history deeply rooted in Italian food traditions (Affinita et al. 2013), it may be a suggestion to limit portions, e.g. limit to one biscuit, one slice of bread with one level tablespoon or less of spread, and follow with yogurt and fruit. Progressive introduction may thus displace a source of saturated fat and added sugars in the diet.

Furthermore, since Italian breakfasts are usually carbohydrate-rich, choosing high-quality (high-fibre and low-GI) carbohydrates can help control body weight and glycaemia (Slavin 2005; Wang et al. 2015), reducing the risk of type 2 diabetes (Livesey et al. 2013; Bhupathiraju et al. 2014) and cardiovascular disease (Ma et al. 2012; Mirrahimi et al. 2012). Indeed, studies have highlighted specific breakfast food components including fruits, whole grain, and fibre were associated with a lower BMI (Brighenti et al. 1999; Cho et al. 2003). How breakfast choices can affect the overall nutritional profile is additionally important since the most recent national food consumption survey in Italy demonstrated that Italians generally have low intakes of fibre, fruits and vegetables, calcium and yogurt, and high intakes of saturated fat and meat (Sofi et al. 2006; Leclercq et al. 2009; Sette et al. 2011). Thus, low-GI/high-fibre carbohydrate breakfasts may also help Italians to meet recommendations.

Overall, the present study demonstrated that cakes/pastries/cookies, as the most commonly consumed breakfast items in Italy, have a low-medium GI, however are higher in saturated fat and sugar and lower in fibre compared to other breakfast items like bread and muesli cereal which have medium GIs. Due to generally low population intakes of fibre and high saturated

fat, reduction in the frequency in which pastries are consumed for breakfast, and substitution with other low-GI, low-saturated fat breakfast alternatives non-commonly consumed, such as low-fat yogurt, fruit and whole grains, would help the population to meet national recommendations for nutritional intakes and possibly help target obesity reducing the risk of chronic diseases.

Table 1. Nutritional information of commonly consumed Italian breakfast items

	Food/Meal ^a	Serving ^b	GI ^c	GL ^d	Calories (kcal)	CHO ^e (g)	Fiber (g)	Sugar (g)	Pro (g)	Fat (g)	SFA (g)
Non-commercially available; typically made at home											
Bread+Spreads/Toppings	White bread (Harry's) + hazelnut chocolate spread (Nutella)	1 slice (35g) +1.75tbsp* (33g)	47±5	17.6	246.8	37.6	1.1	22.0	4.8	9.7	3.6
	White bread (Harry's) + apricot jam	1 slice (35g) + 2tbsp* (30g)	66±4	22.8	144.9	34.5	0.9	19.8	2.6	0.1	0.1
	White bread (Harry's) + apricot jam + butter	1 slice (35g) +2tbsp* (30g) + 2tsp (11g)	55±5	19.0	263.2	34.5	0.9	19.8	2.6	9.2	5.7
	White bread (Pane Bauletto Bianco) + cooked ham (Prosciutto Cotto, lean) + sliced cheese (Sottilette Classiche)	1 slice (23.6g), 1 slice (6g), ½ slice (14.3g)	61±7	7.3	105.2	12.0	1.1	2.3	5.7	3.5	1.7
Pastry+coffee	Pastry (Nastrine) + Milk (Latte Intero) and coffee	125g whole milk + 25ml espresso + 1 (40g)	44±7	10.7	273.0	24.5	1.2	12.6	7.0	16.1	9.0

Commercially Available Foods

Breads	Bread, sliced, wheat flour (Harry's) ^f	1 slice (35g)	76±1 4	13. 8	102.0	18.2	1.0	2.3	2.9	1.8	0.1
	Bread, sliced, wheat flour (Pan Bauletto Bianco) ^f	1 slice (23.6g)	59±7	7.4	69.3	12.6	0.9	1.4	2.0	1.2	0.1
	Bread, sliced, whole-meal wheat flour (Pan Bauletto Integrale) ^f	1 slice (23.6g)	59±5	5.5	59.4	9.3	1.9	1.4	2.6	1.3	0.1
	Melba toast, wheat flour (Fette Biscottate Le Dorate) ^f	3 pieces (26.4g)	64±1 1	12. 8	100.6	19.9	1.0	1.9	3.0	1.0	0.3
Muesli	Muesli (Cereali croccanti classic) ^f	1 serving (45g)	66±6	19. 8	167.6	29.8	4.3	7.4	4.8	3.2	0.4
	Muesli, with concentrated fruit juices (Cereali croccanti frutta) ^f	1 serving (45g)	62±8	19. 8	161.5	32.2	3.6	12.2	3.6	2.0	0.2
Cookies/Biscuits	Biscuits, wheat flour, butter, cream (Macine) ^f	2 biscuits (26g)	52±7	8.8	125.6	17.2	0.7	4.5	2.0	5.5	1.0
	Biscuits, wheat flour, oat flour, whole-meal buckwheat flour (6.2%) (Molinetti) ^f	2 biscuits (30g)	58±7	11. 2	143.7	19.4	0.8	6.1	2.4	6.3	1.0
	Biscuits, rolled oat, whole-meal wheat flour, wheat fiber (Gran Cereale Classico) ^f	2 biscuits (22g)	49±4	6.3	97.6	12.8	2.4	3.3	1.8	4.4	0.6

Cakes/Pastries	Plumcake, wheat flour, yogurt (Plumcake) ^f	1 piece (33g)	47±6	7.8	136.7	16.5	0.4	8.3	2.4	6.8	1.6
	Puff pastry, wheat flour, sugar (Nastrine) ^f	1 piece (40g)	47±6	9.2	186.5	19.6	0.9	8.0	2.8	10.8	5.8
	Sponge cake with cocoa, milk cream-filled, coated with chocolate (Kinder Délice) ^f	1 piece (42g)	58±8	10. 6	192.1	18.3	1.2	15.3	2.4	12.2	6.2
	Sponge cake, wheat flour, rolled barley and oat (2.5%), filled with apricot jam (Brioss Albicocca e cereali) ^f	1 piece (28g)	60±7	10. 5	100.0	17.5	1.0	10.5	1.6	2.6	0.6
	Sweet bread, with chocolate chips (Pangoccioli) ^f	1 piece (42g)	50±5	10. 2	153.5	20.4	0.8	6.9	3.4	6.5	2.1
	Tarte, wheat flour, apricot jam (Crostatina all'albicocca)	1 piece (40g)	44±4	11. 3	164.9	25.8	0.8	11.5	2.2	5.9	2.3

*level tablespoons, equivalent to one “heaping” tablespoon typically consumed (Turconi and Roggi 2007)

a macronutrients determined using packaging available at the time

b serving sizes based on one commonly consumed portion while maintaining proportions used in GI determination

c GI, glucose scale; ≤55 low, 56-70 medium, ≥71 high

d the product of GI and available carbohydrate portion divided by 100; ≤10 low, 11-19 medium, ≥20 high

e available carbohydrate

CHO, carbohydrate; GI, glycemic index; GL, glycemic load; Pro, protein; SFA, saturated fatty acids

f IG value previously published in Scazzina et al. 2016

References

- Affinita A, Catalani L, Cecchetto G, De Lorenzo G, Dilillo D, Donegani G, Fransos L, Lucidi F, Mameli C, Manna E et al. 2013. Breakfast: a multidisciplinary approach. *Ital J Pediatr.* 39:44.
- Bhupathiraju SN, Tobias DK, Malik VS, Pan A, Hruby A, Manson JE, Willett WC, Hu FB. 2014. Glycemic index, glycemic load, and risk of type 2 diabetes: results from 3 large US cohorts and an updated meta-analysis. *Am J Clin Nutr.* 100(1):218-232.
- Brighenti F, Casiraghi MC, Canzi E, Ferrari A. 1999. Effect of consumption of a ready-to-eat breakfast cereal containing inulin on the intestinal milieu and blood lipids in healthy male volunteers. *Eur J Clin Nutr.* 53(9):726-733.
- Cho S, Dietrich M, Brown CJ, Clark CA, Block G. 2003. The effect of breakfast type on total daily energy intake and body mass index: results from the Third National Health and Nutrition Examination Survey (NHANES III). *J Am Coll Nutr.* 22(4):296-302.
- Collier GR, Greenberg GR, Wolever TM, Jenkins DJ. 1988. The acute effect of fat on insulin secretion. *J Clin Endocrinol Metab.* 66(2):323-326.
- di Giuseppe R, Di Castelnuovo A, Melegari C, De Lucia F, Santimone I, Sciarretta A, Barisciano P, Persichillo M, De Curtis A, Zito F et al. 2012. Typical breakfast food consumption and risk factors for cardiovascular disease in a large sample of Italian adults. *Nutr Metab Cardiovasc Dis.* 22(4):347-354.
- FAO/WHO. 1998. Carbohydrates in human nutrition. Report of a joint FAO/WHO expert consultation. *FAO Food and Nutrition Paper.*
- Frost GS, Brynes AE, Dhillo WS, Bloom SR, McBurney MI. 2003. The effects of fiber enrichment of pasta and fat content on gastric emptying, GLP-1, glucose, and insulin responses to a meal. *Eur J Clin Nutr.* 57(2):293-298.
- Gannon MC, Nuttall FQ, Westphal SA, Seaquist ER. 1993. The effect of fat and carbohydrate on plasma glucose, insulin, C-peptide, and triglycerides in normal male subjects. *J Am Coll Nutr.* 12(1):36-41.
- Gulliford MC, Bicknell EJ, Scarpello JH. 1989. Differential effect of protein and fat ingestion on blood glucose responses to high- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. *Am J Clin Nutr.* 50(4):773-777.
- Henry CJ, Lightowler HJ, Kendall FL, Storey M. 2006. The impact of the addition of toppings/fillings on the glycaemic response to commonly consumed carbohydrate foods. *Eur J Clin Nutr.* 60(6):763-769.
- ISO. 2010. Food products e determination of the glycaemic index (GI) and recommendation for food classification. *ISO 26642- 2010.*
- Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkins AL, Axelsen M. 2002. Glycemic index: overview of implications in health and disease. *Am J Clin Nutr.* 76(1):266S-273S.

Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. 1981. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr.* 34(3):362-366.

Leclercq C, Arcella D, Piccinelli R, Sette S, Le Donne C, Turrini A, Group I-SS. 2009. The Italian National Food Consumption Survey INRAN-SCAI 2005-06: main results in terms of food consumption. *Public Health Nutr.* 12(12):2504-2532.

Livesey G, Taylor R, Livesey H, Liu S. 2013. Is there a dose-response relation of dietary glycemic load to risk of type 2 diabetes? Meta-analysis of prospective cohort studies. *Am J Clin Nutr.* 97(3):584-596.

Ma Y, Bertone ER, Stanek EJ, 3rd, Reed GW, Hebert JR, Cohen NL, Merriam PA, Ockene IS. 2003. Association between eating patterns and obesity in a free-living US adult population. *Am J Epidemiol.* 158(1):85-92.

Ma XY, Liu JP, Song ZY. 2012. Glycemic load, glycemic index and risk of cardiovascular diseases: meta-analyses of prospective studies. *Atherosclerosis.* 223(2):491-496.

Marin-Guerrero AC, Gutierrez-Fisac JL, Guallar-Castillon P, Banegas JR, Rodriguez-Artalejo F. 2008. Eating behaviours and obesity in the adult population of Spain. *Br J Nutr.* 100(5):1142-1148.

Mirrahimi A, de Souza RJ, Chiavaroli L, Sievenpiper JL, Beyene J, Hanley AJ, Augustin LS, Kendall CW, Jenkins DJ. 2012. Associations of glycemic index and load with coronary heart disease events: a systematic review and meta-analysis of prospective cohorts. *J Am Heart Assoc.* 1(5):e000752.

Nuttall FQ, Gannon MC. 1991. Plasma glucose and insulin response to macronutrients in nondiabetic and NIDDM subjects. *Diabetes Care.* 14(9):824-838.

Scazzina F, Dall'Asta M, Casiraghi MC, Sieri S, Del Rio D, Pellegrini N, Brighenti F. 2016. Glycemic index and glycemic load of commercial Italian foods. *Nutr Metab Cardiovasc Dis.* 26(5):419-429.

Schwingshackl L, Hoffmann G. 2013. Long-term effects of low glycemic index/load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: a systematic review and meta-analysis. *Nutr Metab Cardiovasc Dis.* 23(8):699-706.

Sette S, Le Donne C, Piccinelli R, Arcella D, Turrini A, Leclercq C, Group I-SS. 2011. The third Italian National Food Consumption Survey, INRAN-SCAI 2005-06--part 1: nutrient intakes in Italy. *Nutr Metab Cardiovasc Dis.* 21(12):922-932.

Slavin JL. 2005. Dietary fiber and body weight. *Nutrition.* 21(3):411-418.

Smith JD, Hou T, Ludwig DS, Rimm EB, Willett W, Hu FB, Mozaffarian D. 2015. Changes in intake of protein foods, carbohydrate amount and quality, and long-term weight change: results from 3 prospective cohorts. *Am J Clin Nutr.* 101(6):1216-1224.

Sofi F, Innocenti G, Dini C, Masi L, Battistini NC, Brandi ML, Rotella CM, Gensini GF, Abbate R, Surrenti C et al. 2006. Low adherence of a clinically healthy Italian population to nutritional

recommendations for primary prevention of chronic diseases. *Nutr Metab Cardiovasc Dis.* 16(6):436-444.

Turconi G, Roggi C. 2007. *Atlante fotografico alimentare: uno strumento per le indagini nutrizionali.* EMSi Editrice.

Wang Q, Xia W, Zhao Z, Zhang H. 2015. Effects comparison between low glycemic index diets and high glycemic index diets on HbA1c and fructosamine for patients with diabetes: A systematic review and meta-analysis. *Prim Care Diabetes.* 9(5):362-369.

Study 2

The importance of glycaemic index in the context of the addition of fat to carbohydrate foods: A randomized controlled trial on spaghetti versus rice as mixed meals

Laura Chiavaroli[§], Marta Cossu[§], Margherita Dall'Asta, Veronica Francinelli,
Francesca Scazzina and Furio Brighenti

Department of Food and Drug, University of Parma, Parma,

[§] these authors contributed equally

Introduction

Carbohydrate-containing foods elicit a variety of postprandial glycaemic responses based on both the quantity consumed and their quality. They can be classified according to their digestibility, which is generally characterized by the rate and duration of the glycaemic response expressed by the glycaemic index (GI). The GI, introduced in 1981 by Jenkins and colleagues, represents a way to rank carbohydrates according to the extent to which they increase postprandial glycaemia. Starchy foods included in the low GI category are absorbed more slowly across the intestine compared to medium or high GI foods (Jenkins et al. 1981). Low GI foods have been demonstrated to improve glycaemic control, insulin sensitivity and diabetes management (Thomas and Elliott 2009; Ajala et al. 2013), and have been associated with reduced risk of chronic disease (Barclay et al. 2008), including coronary heart disease (Mirrahimi et al. 2012) and cardiovascular disease (Ma et al. 2012). Therefore, a diet composed of low GI foods could be a strategy to reduce postprandial glycaemia and could be useful to prevent or treat a number of chronic conditions. However, since the GI was proposed, it has received several criticisms. This could be a consequence of a misunderstanding of the GI concept and a wrong use of the terminology. For example, in the context of mixed-meals, it is possible to read “fat or protein eaten with carbohydrates reduces the GI of the carbohydrates”. The term glycaemic index in this case is mistakenly used to refer to glycaemic response. Indeed, it is the glycaemic response that is reduced by protein or fat (Wolever 2013), and not the GI, which is a characteristic property of the carbohydrate containing food.

Pasta and rice are two of the most commonly consumed grains worldwide, where the former has a low GI (e.g. spaghetti) and the latter, usually has a higher GI (e.g. white rice). The most typical ways in which pasta and rice are consumed are with the addition of oil and tomato sauce or herbs, and are recommended to be consumed in this way in the Mediterranean diet (Estruch

et al. 2013). The main factors modifying the glycaemic response to mixed meals are the amount of fat and protein. Fat and protein reduce glycaemic responses by delaying gastric emptying and stimulating insulin secretion (Nuttall and Gannon 1991). Gastric emptying is known to be a major determinant of postprandial glycaemia where small changes can have a substantial effect (Rayner et al. 2001). Fat, in particular, may modulate the gut hormones cholecystokinin (CCK) and peptide YY, which delay gastric emptying (Pironi et al. 1993; Moran and Kinzig 2004).

There is a lack of data on whether the difference in glycaemic response between a commonly consumed low GI food and higher GI food can be maintained with the addition of fat to the meal, particularly in the context of how it may typically be consumed. Some studies have demonstrated that the addition of protein and fat to a high and low GI food results in reductions in glycaemic responses, which are still significantly lower for the low GI food (Gulliford et al. 1989; Matsuo et al. 1999). However, these studies are quite old, and used foods that are not commonly consumed in our diet. Therefore, this study aims to explore whether the addition of fat in the form of commonly consumed sauces, i.e. tomato sauce and pesto, affects the difference in glycaemic response between a commonly consumed low GI (spaghetti) and a higher GI (rice) carbohydrate food.

Materials and methods

Study design and participants

The study had a randomized controlled crossover design and included 13 healthy subjects that were recruited from advertisements posted on university, hospital and public message boards in Parma. Volunteers who decided to participate, after obtaining a written informed consent, attended a screening visit to determine eligibility. Volunteers were not eligible to participate if

they were <18 or >75 years old, were obese ($BMI \geq 30 \text{ kg/m}^2$), had any health conditions (including anaemia and metabolic conditions such as hypertension, dyslipidaemia, impaired glucose intolerance or diabetes), if they had celiac disease, performed intense physical activity ($LAF \geq 2.10$ – LARN 2014), or were taking any prescription medication for chronic diseases. Women who were pregnant or breastfeeding were also excluded.

Study meals

The study included nine meals (6 test meals and 3 reference test meals) containing 50g of available carbohydrates to consume on 9 occasions, each separated by at least 1 day (minimum washout). The test meals were: i) spaghetti (No. 5, durum wheat flour); ii) spaghetti with tomato sauce (“Sugo al basilico”) and extra virgin olive oil; iii) spaghetti with pesto (“Pesto alla genovese senza aglio”); iv) rice (“Originario”); v) rice with tomato sauce and extra virgin olive oil; vi) rice with pesto; vii-ix) glucose solution. Spaghetti and rice were cooked for 9 and 17 minutes, respectively (according to package instructions) in 1 L of boiling water with 5 g of salt for each portion. When tomato sauce and olive oil or pesto were part of the meal, they were added at room temperature to the cooked portions of rice and spaghetti, without any additional manipulation. The reference meal, glucose monohydrate, was prepared the day before each test by dissolving 50g available carbohydrate portion (55g, dry weight) in 250 ml of water and refrigerated overnight. Test meals were administered according to a randomized block design. Each block consisted of one reference test meal and one set of comparison test meals (rice and spaghetti without sauce, or rice and spaghetti with tomato sauce, or rice and spaghetti with pesto). At each visit, a test record was completed by study staff in the presence of the participant to record information including the dinner consumed the evening prior, time of dinner, length of fast, and any unusual events.

Blood samples collection

On test days, volunteers attended the laboratory between the hours of 8:00 and 10:00am after a 10-12 hour overnight fast. Two fasting capillary blood samples were taken 10 minutes apart (time point -10' and 0'). A timer was started with the first bite of the test meal which they were asked to consume within 12-15 minutes. The capillary blood was taken and collected by the participants with the assistance of study staff following the procedure described by the WHO Guidelines (2010). Capillary whole blood samples were collected by finger prick in an Eppendorf tube (Microvette CB 300, Sarstedt) containing EDTA (Sigma E5134) (5 μ L) and glyceraldehyde (Sigma G5001) (5 μ L) in the fasting state and at 15, 30, 45, 60, 90 and 120 minutes after consumption of the test meal. The Eppendorf tubes collected for glucose analysis were stored in a refrigerator until the end of the test and then stored at -20°C until analysis. Prior to analysis, the samples were thawed to room temperature and then analysed using the 2900 STAT Plus™ biochemical analyser (Yellow Springs Instrument Company, USA). A second Eppendorf tube was collected for insulin and c-peptide analyses at the same time points and were kept at room temperature and centrifuged within 30 minutes of collection (10,000 x g, 2 min, room temperature) and stored at -20°C until analysis. Prior to analysis, the samples will be thawed to room temperature and analyse using the Bio-Plex MAGPIX™ multiplex reader and the specific kit for the determination of insulin and c-peptide (Merk Milipore).

Statistical analysis

Data are presented as means \pm standard error of the mean (SEM), unless otherwise indicated. Incremental area under the curve (IAUC) of test foods were calculated using the trapezoid rule, ignoring the area beneath the curve. For each subject, the IAUC for each of the 3 glucose tests was averaged and used in the GI calculations. GI was calculated by the ratio of the average

IAUC of the glucose tests divided by the IAUC of each test food, multiplied by 100, for each subject. For analyses, paired students t-tests were used for the comparisons between the spaghetti and rice for both the IAUCs and GI, in each of the 3 contexts (without sauce, with tomato sauce and olive oil, and with pesto). P-value <0.05 was considered statistically significant. The comparisons within the meal groups (meals with the same carbohydrate source but with different condiments) were subjected to repeated measures general linear model (GLM) ANOVA (SPSS software version 24.0). After demonstration of significant heterogeneity, the significance of differences among individual meals was determined using Bonferroni post-hoc analyses with $p < 0.05$ (where Bonferroni adjustments are already included for multiple comparisons).

Results

Characteristics of participants included in the preliminary analyses are presented in Table 1 and are reported as mean \pm SD. The mean age of the participants was 31 \pm 10 years (22-55y), 60% were female; the mean BMI was 21.2 \pm 2.5 kg/m² with 90% within normal weight (BMI value from 18.5 to 25 kg/m²) and 10% overweight (BMI value from 25 to 30 kg/m²).

Characteristics (n=10)	
Sex	
Male	4
Female	6
Age	31 \pm 10
Weight, kg	63 \pm 12
Height, m	1.72 \pm 0.1
BMI, kg/m ²	21.2 \pm 2.5
Blood pressure, mm Hg	
Systolic	115 \pm 11
Diastolic	70 \pm 9

Table 1. *Characteristics of study participants (Mean \pm SD).*

The nutritional compositions of the meals, as well as of the different condiments, are shown in Table 2. The total energy intake of the meal was greater when pesto was used as a source of fat compared to tomato sauce and olive oil. This was a consequence of the higher amount of fat in rice and spaghetti meals with pesto (39% and 41% of the total energy, respectively). In the meals containing tomato sauce and olive oil the fat accounted for 31% of the total energy in both meals.

Meals		Amount (g)	Energy (kcal)	AvCHO (g)	Fibre (g)	Sugar (g)	Protein (g)	Fat (g)	Saturated fat (g)
Spaghetti without sauce									
	Spaghetti	71.0	254.9	49.8	2.1	2.5	9.6	1.4	0.4
Rice without sauce									
	Rice	62.0	222.0	49.9	0.6	0.1	4.0	0.6	0.2
Spaghetti + tomato sauce + olive oil									
	Spaghetti	64.5	231.6	45.3	1.9	2.3	8.7	1.3	0.3
	Tomato sauce	64.5	39.3	4.4	1.0	3.9	1.0	1.7	0.3
	Olive oil	10.0	82.2	0.0	0.0	0.0	0.0	9.1	1.4
	Total		353.1	49.7	3.0	6.2	9.7	12.1	2.0
Rice + tomato sauce + olive oil									
	Rice	57.0	204.1	45.9	0.6	0.1	3.6	0.5	0.2
	Tomato sauce	57.0	34.8	3.9	0.9	3.5	0.9	1.5	0.2
	Olive oil	10.0	82.2	0.0	0.0	0.0	0.0	9.1	1.4
	Total		321.0	49.8	1.5	3.6	4.6	11.2	1.8
Spaghetti + pesto									
	Spaghetti	68.0	244.1	47.7	2.0	2.4	9.2	1.4	0.3
	Pesto	34.0	174.8	1.9	0.7	1.4	1.7	17.7	1.9
	Total		418.9	49.6	2.7	3.7	10.9	19.0	2.2
Rice + pesto									
	Rice	60.0	214.8	48.3	0.6	0.1	3.8	0.5	0.2
	Pesto	30.0	154.2	1.7	0.6	1.2	1.5	15.6	1.7
	Total		369.0	50.0	1.2	1.3	5.3	16.1	1.8

Table 2. Nutritional composition of the meals and condiments. AvCHO=available carbohydrates.

Postprandial capillary glucose responses for the three meal comparisons are presented in Figure 1 (a, b, c). When consumed without sauce, spaghetti elicited a glycaemic response significantly lower compared to that elicited by rice at 30 and 45 minutes ($P=0.004$, $P=0.048$, respectively) (Fig 1a). When tomato sauce and olive oil was added as a condiment and source of fat, the glucose response was significantly lower at 15 minutes ($P=0.013$) after spaghetti consumption compared to rice (Fig 1b). After the consumption of the meals containing pesto, the glucose

response elicited by spaghetti was significantly lower compared to rice at 30 minutes ($P=0.027$) (Fig 1c).

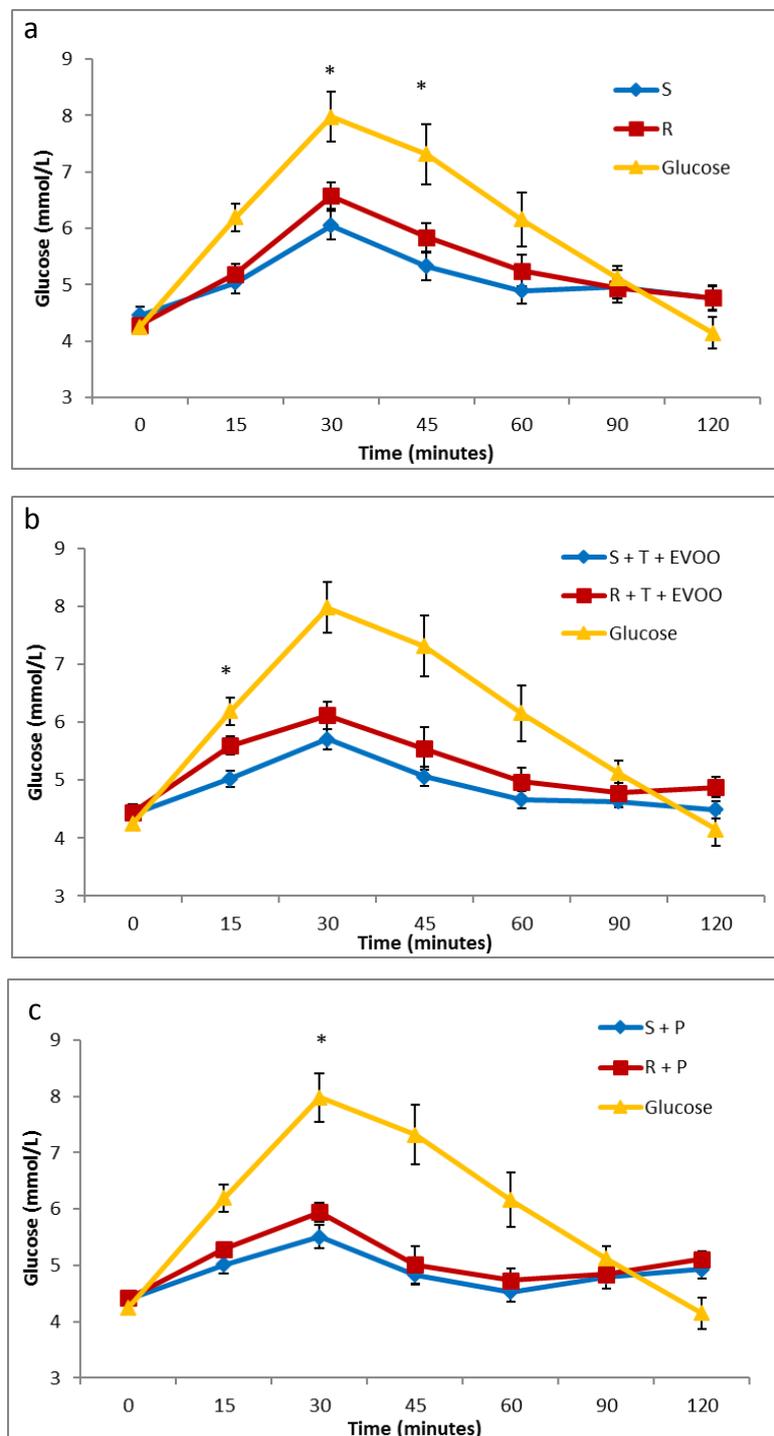


Figure 1. Capillary glucose response and capillary glucose IAUC after the consumption of the meals (mean \pm SEM): a) capillary glucose response after spaghetti and rice without sauce, b) capillary glucose response after spaghetti and rice with tomato sauce and olive oil, c) capillary glucose response after spaghetti and rice with pesto. S=spaghetti without sauce; R=rice without sauce; S+T+EVOO=spaghetti with tomato sauce and olive oil; R+T+EVOO=rice with tomato sauce and olive oil; S+P=spaghetti with pesto; R+P=rice with pesto. * $p<0.05$ (comparison between spaghetti and rice meals, glucose is not considered in the statistical analysis).

The average maximum peak of the 2-hour blood glucose response was reached for each test meal at 30 minutes. The peak value in response to the plain rice (6.6 ± 0.2 mmol/L) was significantly higher than the peak value for plain spaghetti (6.1 ± 0.3 mmol/L) ($P=0.006$). When tomato sauce and olive oil was added to the meals, the peak value in response to the rice (6.4 ± 0.2 mmol/L) was higher than the peak value for spaghetti (5.7 ± 0.2 mmol/L), however, was not significantly different ($P=0.051$). When pesto was added to the meals, the peak value in response to the rice (5.9 ± 0.2 mmol/L) was significantly higher than the peak value for spaghetti (5.6 ± 0.2 mmol/L) ($P=0.029$).

The IAUCs for the meals were calculated and are reported in Figure 2. The IAUC for the plain rice (120.2 ± 8.4 mmol*min/L) was significantly greater compared to the plain spaghetti (78.3 ± 14.6 mmol*min/L) ($P=0.024$). When tomato sauce and olive oil were added, the IAUC for the rice meal (89.6 ± 11.9 mmol*min/L) was significantly greater compared to the spaghetti meal (55.4 ± 8.2 mmol*min/L) ($P=0.009$). When pesto was used as condiment, the IAUC for the rice meal (80.1 ± 13.1 mmol*min/L) was not significantly greater compared to the spaghetti meal (59.2 ± 8.7 mmol*min/L) ($P=0.071$).

Post-hoc analyses within carbohydrate source showed that there was not a main effect of condiment on the IAUC of the meals containing spaghetti ($P=0.163$). Conversely, a main effect of condiment was found within the meals containing rice ($P=0.004$). The IAUC was significantly lower after the addition of pesto as a source of fat compared to the meals where rice was consumed without sauce ($P=0.036$) (Figure 2).

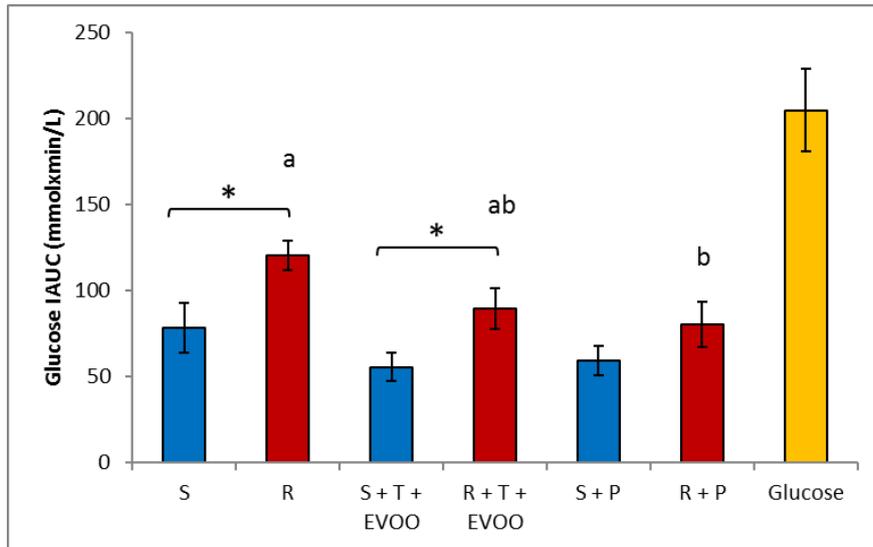


Figure 2. Capillary glucose IAUC (mean±SEM). S=spaghetti without sauce; R=rice without sauce; S+T+EVOO=spaghetti with tomato sauce and olive oil; R+T+EVOO=rice with tomato sauce and olive oil; S+P=spaghetti with pesto; R+P=rice with pesto. * $p<0.05$ (comparison between spaghetti and rice meals); different letters indicate $p<0.05$ (comparison within carbohydrate source). Glucose is not considered in the statistical analysis.

The GI (glucose scale) of spaghetti and rice consumed without sauce and in the context of mixed meals were calculated and are reported in Figure 3. The GI values of the meals ranged from 30.1 to 65.2. The average GI of plain rice was 65.2 ± 2.9 while the average GI of plain spaghetti was 43.2 ± 8.0 . According to the generally convention, they ranked as a medium and low GI food, respectively. The GI of the plain rice was significantly greater compared to the GI of plain spaghetti ($P=0.010$). When tomato sauce and olive oil were added, the GI for the spaghetti meal was significantly lower (31.0 ± 5.7) compared to the rice meal (46.8 ± 6.8) ($P=0.014$). According to the generally convention, they both ranked as low GI foods. When genovese pesto was added, the GI of the spaghetti meal (30.1 ± 4.3) was not significantly different compared to the GI of the rice meal (40.4 ± 7.4) ($P=0.159$). According to the generally convention, they both ranked as low GI foods.

Post-hoc comparison within carbohydrate source showed that there was a main effect of condiment on GI in the meals containing rice ($P=0.002$) but not in the meals with spaghetti ($P=0.098$). The GI was significantly reduced when both tomato sauce and pesto were added as source of fat when compared to the meal where rice was consumed without sauce ($P=0.017$ and $P=0.022$, respectively) (Figure 3).

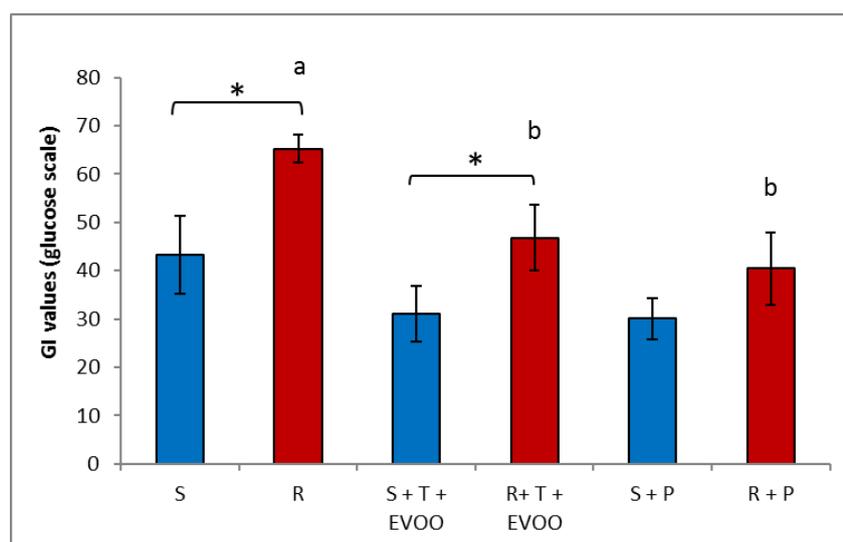


Figure 3. GI of the meals (mean±SEM). S=spaghetti without sauce; R=rice without sauce; S+T+EVOO=spaghetti with tomato sauce and olive oil; R+T+EVOO=rice with tomato sauce and olive oil; S+P=spaghetti with pesto; R+P=rice with pesto. * $p<0.05$ (comparison between spaghetti and rice meals); different letters indicate $p<0.05$ (comparison within carbohydrate source).

Discussions and conclusions

The preliminary results of the present study demonstrated that the difference in glycaemic response between spaghetti and rice was preserved and remained significantly lower even when tomato sauce and olive oil were added as condiment. However, when pesto was added as source of fat, although there was a trend in IAUC and GI reduction, there was no longer a statistically significant difference between spaghetti meal vs. rice meal.

The fat content of the meals was different and nearly twice when pesto was used as condiment and source of fat compared to tomato sauce and olive oil. Furthermore, the addition of pesto determined a significantly reduction in both the IAUC and GI in the meal containing rice but not in the meal containing spaghetti.

Therefore, the lack of significance between spaghetti vs. rice with pesto, could be due to the fact that the addition of larger amount of fat, had a greater effect in lowering the glycaemic response of the higher GI food (rice) compared to a lower GI food (spaghetti).

This is consistent with a previous study where the glucose-lowering effect of the addition of fat was quantitatively smaller for the slowly absorbed carbohydrate food compared (lentils) to rapidly absorbed carbohydrate food (potatoes) (Collier et al. 1984).

Pasta is known to have a low glycaemic response and a low GI; its compact structure, the physical structure of starch granules and the encapsulation of starch in the gluten matrix play a major role in reducing the rate of starch digestibility. On the other hand, rice come in a variety of forms which have a wider range of GIs (48-93), largely attributable to intrinsic factors, i.e. starch characteristic, and extrinsic factors, such as post-harvesting and consumer processing (Boers et al. 2015). In the present study “Originario” white rice had a medium GI (GI=65.2) and spaghetti had a low GI (GI=43.2). The greater reduction in blood glucose response to the rice meals induced by the addition of fat compared to the spaghetti meals, might suggests that gastrointestinal motility is an important factor limiting the glycaemic response to rice and that this is not necessarily additive to the low starch hydrolysis already present with pasta (Wong and O'Dea 1983). However, although increasing the fat content of a meal can delay glucose absorption from the small intestine (Collier and O'Dea 1983), the effect of increased energy intake from the addition of fat is an important consideration, particularly since obesity is a global issue.

The GI values calculated for the mixed-meals were lower compared to the GI of the spaghetti and rice consumed without sauce. However, since GI is a property of the food, it is important to remark that the addition of fat does not reduce the GI of spaghetti and rice. The addition of fat to a meal affects instead its glycaemic response. The GI value (which depends on the carbohydrate quality) is only one of the parameters that influence the glycaemic response of a mixed-meal, which is also influenced by both amount and type of fat and protein added.

We were not able to demonstrate a statistical difference in glycaemic response and GI between the spaghetti and rice meals containing pesto. However, these are preliminary data based on a lower number of subjects, thus limiting the statistical power to detect differences.

It is anticipated that the complete results of the study will give more clarity and consistency, and determine if there is a continued glycaemic and insulinemic benefit of pasta as a low GI food, compared to a higher GI food, white rice, in the context of how they are commonly encouraged to be consumed. These results may be useful to encourage the use of low GI foods for greater improvements in glycaemic and insulinemic control, which is an important public health concern in global society.

References

- Ajala O, English P, Pinkney J. 2013. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes 1-3. *American Journal of Clinical Nutrition*. 97(3):505-516.
- Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P, Brand-Miller JC. 2008. Glycemic index, glycemic load, and chronic disease risk - A metaanalysis of observational studies. *American Journal of Clinical Nutrition*. 87(3):627-637.
- Boers HM, Seijen Ten Hoorn J, Mela DJ. 2015. A systematic review of the influence of rice characteristics and processing methods on postprandial glycaemic and insulinaemic responses. *British Journal of Nutrition*. 114(7):1035-1045.

Collier G, McLean A, O'Dea K. 1984. Effect of co-ingestion of fat on the metabolic responses to slowly and rapidly absorbed carbohydrates. *Diabetologia*. 26(1):50-54.

Collier G, O'Dea K. 1983. The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein. *American Journal of Clinical Nutrition*. 37(6):941-944.

Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J et al. 2013. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 368(14):1279-1290.

Gulliford MC, Bicknell EJ, Scarpello JH. 1989. Differential effect of protein and fat ingestion on blood glucose responses to high- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. *American Journal of Clinical Nutrition*. 50(4):773-777.

Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. 1981. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr*. 34(3):362-366.

Ma, Liu JP, Song ZY. 2012. Glycemic load, glycemic index and risk of cardiovascular diseases: meta-analyses of prospective studies. *Atherosclerosis*. 223(2):491-496.

Matsuo T, Mizushima Y, Komuro M, Sugeta A, Suzuki M. 1999. Estimation of glycemic and insulinemic responses to short-grain rice (Japonica) and a short-grain rice-mixed meal in healthy young subjects. *Asia Pac J Clin Nutr*. 8(3):190-194.

Mirrahimi A, de Souza RJ, Chiavaroli L, Sievenpiper JL, Beyene J, Hanley AJ, Augustin LS, Kendall CW, Jenkins DJ. 2012. Associations of glycemic index and load with coronary heart disease events: a systematic review and meta-analysis of prospective cohorts. *J Am Heart Assoc*. 1(5):e000752.

Moran TH, Kinzig KP. 2004. Gastrointestinal satiety signals. II. Cholecystokinin. *American Journal of Physiology - Gastrointestinal and Liver Physiology*. 286(2 49-2):G183-G188.

Nuttall FQ, Gannon MC. 1991. Plasma glucose and insulin response to macronutrients in nondiabetic and NIDDM subjects. *Diabetes Care*. 14(9):824-838.

Pironi L, Stanghellini V, Miglioli M, Corinaldesi R, De Giorgio R, Ruggeri E, Tosetti C, Poggioli G, Morselli, Labate AM et al. 1993. Fat-induced meal brake in humans: A dose-dependent phenomenon correlated to the plasma levels of peptide YY. *Gastroenterology*. 105(3):733-739.

Rayner CK, Samsom M, Jones KL, Horowitz M. 2001. Relationships of upper gastrointestinal motor and sensory function with glycemic control. *Diabetes Care*. 24(2):371-381.

Thomas D, Elliott EJ. 2009. Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. *Cochrane Database of Systematic Reviews*.

Wolever TM. 2013. Is glycaemic index (GI) a valid measure of carbohydrate quality? *Eur J Clin Nutr*. 67(5):522-531.

Wong S, O'Dea K. 1983. Importance of physical form rather than viscosity in determining the rate of starch hydrolysis in legumes. *American Journal of Clinical Nutrition*. 37(1):66-70.

Study 3

Pasta consumption in the context of a hypocaloric diet: a dietary intervention study in obese patients

Alice Rosi¹, Marta Cossu¹, Beatrice Biasini¹, Margherita Tesan², Annalaura Cremonini², Elisabetta Dall'Aglio², Francesca Scazzina¹

¹*Department of Food and Drug, University of Parma;* ²*Department of Medicine and Surgery, University of Parma*

Introduction

Most of the world's population lives in countries where overweight and obesity kill more people than underweight. In 2014, more than 1.9 billion adults, 18 years and older, were overweight (Body Mass Index (BMI) ≥ 25 kg/m²) and of these over 600 million were obese (BMI ≥ 30 kg/m²) (WHO, 2015). The common health consequences of overweight and obesity are mainly type 2 diabetes, which represents one of the most significant global health issue of the twenty-first century (Rahelić et al. 2011), and CVD, which remains the most common cause of death in industrialized countries (Wolf-Maier et al. 2003). The causes of obesity are complex and include genetic, environmental, physiological, social and economic factors. The adoption of a sedentary lifestyle and a reduction in physical activity, the occurrence of eating disorder, the consumption of high energy density foods and the increase in portion size are some of the major risk factors for obesity development (Yumuk et al. 2015). Lifestyle factors, and in particular the combination of physical activity and healthy diet, have been recognized as the most effective strategies in overweight and obesity prevention, management and treatment.

Results from meta-analysis and systematic review of randomized controlled trials have shown that the combination of diet and exercise results in a significantly more pronounced reduction in body weight and fat mass when compared with only diet or exercise intervention (Curioni and Lourenço 2005; Schwingshackl et al. 2015); furthermore, dietary intervention resulted more efficient when compared to exercise intervention (Schwingshackl et al. 2015). Many dietary approaches have been proposed to promote weight loss, however, regardless of the macronutrient they emphasize (e.g. low-carbohydrate or low-fat diet), a hypocaloric diet results in clinically meaningful weight reduction, as a consequence of a negative energy balance. However, about 40% of the weight lost is regained over the first year of treatment and much of the rest over the following 3 years after a lifestyle intervention (Cooper and Fairburn 2001).

The reason of weight regain could be due to the fact that changing an individual's behaviour is not necessarily successful at changing an individual's habits (Cleo et al. 2017). Indeed, most of the people are able to change toward a new healthy habit, but only for a short period after which there is a tendency to come back to the usual unhealthy habit.

There is a general belief that carbohydrate foods, and in particular pasta, are dietary factors that should be restricted in a weight loss program. Evidence suggests that a low-carbohydrates diet is more efficient in reducing body weight compared to a low-fat diet during the first 6 month of intervention. However, after 12 months, there is no more significant difference among dietary interventions (Nordmann et al. 2006).

In Italy, pasta is one of the most consumed staple food. Pasta is a traditional component of the Mediterranean diet, which has been recognize as healthy eating behaviour model and that has been associated with several health benefit (Sofi et al. 2008; Estruch et al. 2013). Pasta is known to be a low-medium glycaemic index food (Atkinson et al. 2008) and its consumption rather than other carbohydrate rich-foods might be useful in reducing postprandial glycaemia, which has been associated with many chronic diseases, including obesity, type 2 diabetes and cardiovascular disease (Blaak et al. 2012). Recently, pasta consumption has been negatively associated with BMI, waist circumference and waist-to-hip ratio and with a lower prevalence in overweight and obesity in two large Italian cohorts (Pounis et al. 2016).

To our knowledge, there are no intervention studies that have investigated the effect of pasta consumption in a context of a hypocaloric diet. Therefore, this study aimed to investigate if a hypocaloric diet where food preferences and the habitual diet, hence also pasta consumption, are considered and preserved could be a valuable strategy to stimulate a better

compliance in following a dietary treatment, to improve patients' adherence to a healthier diet, to stimulate weight loss and to maintain the weight loss during time.

Methods

Study design

Participants were recruited from the clinic "U.O. SSD malattie del ricambio e diabetologia" located in the hospital of Parma, where they entered voluntarily to follow a dietary treatment. They were not eligible if were less than 18 years old, with a BMI <30 or >45 kg/m², if they had diabetes, hepatic or kidney diseases and with eating disorder. Participants who decided to participate, after obtaining a written informed consent, and before starting the dietary intervention, attended a screening visit where a dietary assessment of habitual food intake and a 24h recall were collected to monitoring their food consumption. Patients were divided in two groups based on weekly pasta consumption: High Pasta group (HP) (n=21) and Low Pasta group (LP) (n=23), where pasta consumption was ≥ 5 and ≤ 3 times per week, respectively. The primary outcome of the study is a weight loss >8% at 12 months.

Study design are graphically represented in Figures 1. Anthropometric measures (body weight, height, waist circumference) were collected every month for the first 6 months and after 1 year. In addition, at baseline and after 3, 6 and 12 months, a 7-day carbohydrate food record was collected and a 24-h food recall was completed the day of the visit in presence of study staff. Blood samples were collected at baseline and at 6 and 12 months to analyse glucose, insulin, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and uric acid. HOMA-IR index was calculated as well. Furthermore, participants attended a visit with a psychologist to ascertain the absence of eating disorder.

The study was approved by Parma Ethical Committee (n.37171 13/10/15).

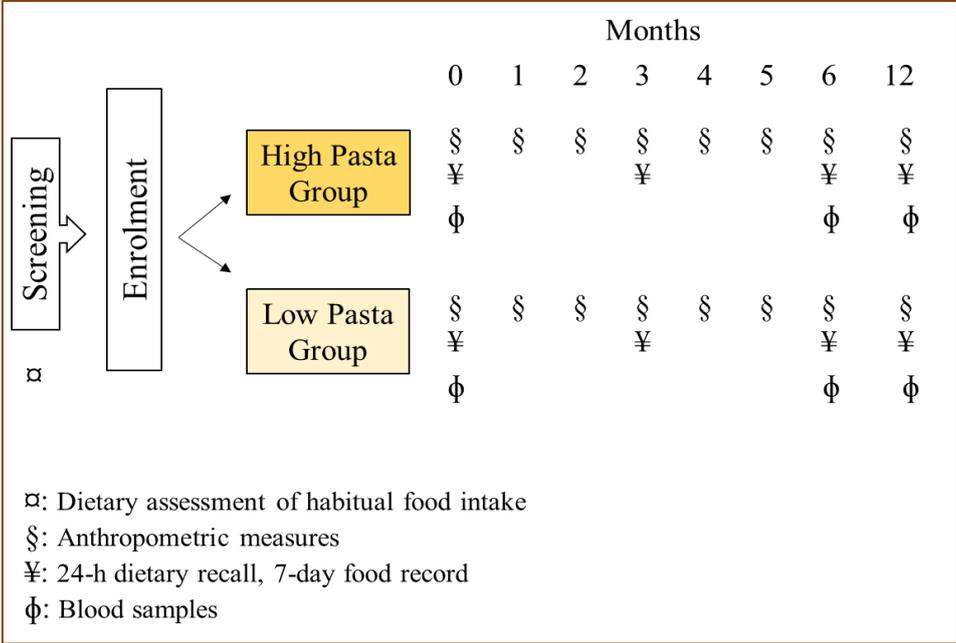


Figure 1. Study protocol representation.

Dietary intervention

All participants received a dietary plan that was personalized considering their food preferences and eating behaviour and that was in agreement with the Italian guidelines for a healthy diet in accordance with the principles of Mediterranean diet and with the reference values of energy and nutrients intake (INRAN 2007, SINU 2014).

Participants received dietary advice monthly during the visit and they were provided with several recipes proposed by a nutritionist in collaboration with a chef. This was done to encourage participants to prepare healthy meals by using high quality raw materials. The recipes differed for the use of pasta as main carbohydrate food. However, for both group, recipes

emphasized the consumption of legumes, vegetables and fruits. The recipe books are attached as supplemental material (S1).

Biochemical analysis

Blood was obtained from an intravenous catheter into tubes containing EDTA, heparin or nothing depending on the analysis. Analyses were performed in a single-blind manner by the personnel of the Laboratory of Clinical Chemistry and Haematology, University Hospital of Parma (Italy). Fasting plasma glucose, insulin, total cholesterol, HDL cholesterol, triglycerides, and uric acid were assessed by a central laboratory using standard methods. LDL cholesterol was calculated by using the Friedewald formula.

Dietary analysis

Dietary data were collected and analysed by means of the Automated Self-Administered 24-hour dietary recall ASA24 which is a free available online software developed by the U.S. National Cancer Institute (NHI) -Division of Cancer control and Population Science- (Subar et al. 2012).

Statistical analysis

Anthropometric data, blood parameters, and energy and nutrient intakes were expressed as mean \pm standard deviation (SD) or mean \pm standard error of the mean (SEM) by treatment groups. Normality of data distribution was verified through the Kolmogorov-Smirnov tests and not normally distributed variables (blood parameters and nutrient intakes) were transformed using the natural logarithm (ln). The effect of time, treatment, and time x treatment, and time by treatment groups on BMI was assessed using a repeated measure ANOVA model and a repeated measure ANCOVA model adjusted for gender, testing the sphericity through the

Mauchly's test and, when violated, using the corrected value with Greenhouse–Geisser if epsilon was lesser than 0.75 or Huynh–Feldt if epsilon was greater than 0.75. In addition, Bonferroni *post-hoc* tests were used for multiple comparisons if there was a main effect of time. Similarly, a repeated measure ANOVA model was used to assess the effect of time by treatment groups for all other variables, using Bonferroni *post-hoc* pairwise comparisons.

Between-group differences were explored, after checking for the homogeneity of the variance through Levene's test, using an independent-samples T-student test at each time point.

Qualitative variables (7-day carbohydrate-based food intake frequencies) were presented as median (interquartile range) and analysed using Friedman non-parametric tests to explore within-group differences among time points, and Wilcoxon non-parametric tests for between groups comparisons.

A *P*-value <0.05 was considered statistically significant. All statistical analyses were performed with IBM SPSS 24.0 Statistics (IBM SPSS, Inc., Chicago, IL, USA).

Results

Anthropometric characteristics

The mean age of participants was 49±9 years in the High Pasta (HP) group (31-61y) and 48±9 years in the Low Pasta (LP) group (23-58y); most participants were women, 71% (n=15) and 78% (n=18) in the HP and LP group respectively. The mean body weight, BMI and waist circumference (WC) at baseline and after 3 and 6 months are reported in Table 1. At baseline, participants in the HP group had a mean BMI of 37.4±4.6 kg/m², whereas in the LP group the mean BMI was 36.9±4.4 kg/m². The mean body weight was 98.1±12.7 kg in the HP and 99.9±14.5 kg in the LP group. The waist circumference was 106.4±9.2 cm and 105.8±10.7 cm

in the HP and LP group, respectively. There were no statistically significant differences between the two groups at the three time points.

	High Pasta	Low Pasta	P¶	High Pasta	Low Pasta	P¶	High Pasta	Low Pasta	P¶
	Months								
	0			3			6		
BMI, kg/m ²	37.4±4.6 ^a	36.9±4.4 ^A	0.703	34.3±4.7 ^b	34.6±4.4 ^B	0.833	33.5±5.2 ^c	34.2±4.3 ^B	0.664
Weight, kg	98.1±12.7 ^a	99.9±14.5 ^A	0.649	89.9±12.3 ^b	93.8±14.3 ^B	0.339	88.0±14.1 ^c	92.6±13.9 ^B	0.286
WC, cm	106.4±9.2 ^a	105.8±10.7 ^A	0.855	98.6±9.7 ^b	100.3±10.9 ^B	0.593	97.2±11.7 ^b	99.1±9.9 ^B	0.564

Table 1. Anthropometric characteristics of participants (mean±SD). ¶ P values for differences between the two groups. Different lowercase letters indicate $p<0.05$ within High Pasta group; different uppercase letters indicate $p<0.05$ within Low Pasta group. WC: waist circumference.

During the 6 months there was a decrease in BMI in both groups as shown in Figure 2. The mean changes in BMI after 3 months were -2.3 ± 1.4 in the HP group, and -3.1 ± 2.1 in the LP group, whereas at 6 months were -2.7 ± 1.6 and -3.9 ± 3.1 in the HP and LP groups, respectively. There were no significant differences between the two groups. However, there was a main effect of time on BMI ($P=0.000$): the BMI was different at 3 and 6 months compared to baseline ($P=0.000$), and between 3 and 6 months ($P=0.001$). There was not a main effect of time x treatments ($P=0.113$), and treatment ($P=0.922$) on BMI. The same results were obtained after adjustment for gender.

When the two groups were considered separately, there was a main effect of time on BMI ($P=0.000$), on body weight ($P=0.000$), and waist circumference ($P=0.000$) in the LP group as well as in the HP group.

The BMI in the LP group was significantly different after 3 months ($P=0.000$) and after 6 months ($P=0.000$) when compared to baseline, while BMI difference was not observed between 3 and 6 months ($P=0.097$). According to BMI results, the body weight at baseline was different from 3 months ($P=0.000$) and 6 months ($P=0.000$). Similarly, the waist circumference was significantly different after 3 months ($P=0.000$) and after 6 months ($P=0.000$) compared to baseline.

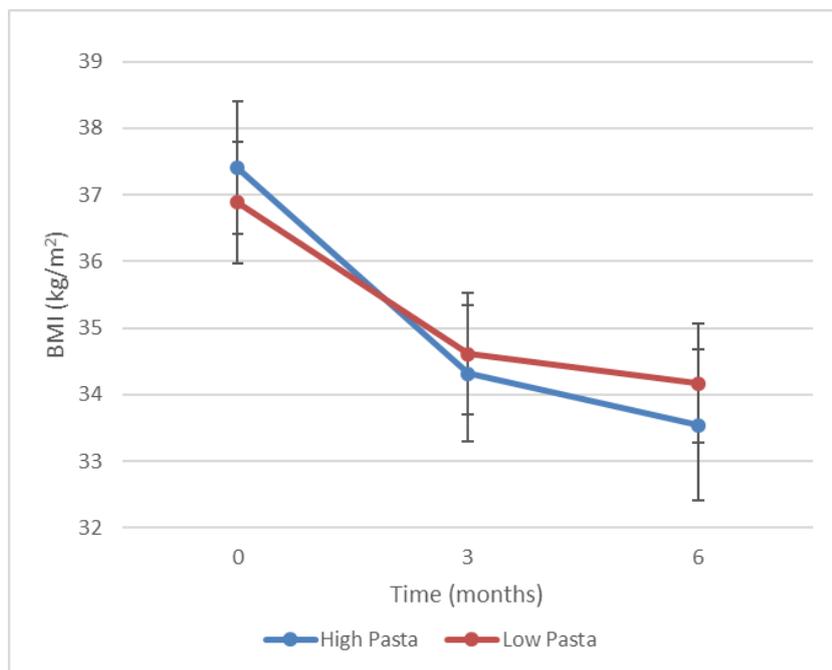


Figure 2. BMI of participants during 6 months in the two groups (mean \pm SEM).

In the HP group the BMI was significantly different after 3 months ($P=0.000$) and after 6 months ($P=0.000$) when compared to baseline, and also between 3 and 6 months ($P=0.023$). In line with the BMI results, the body weight at baseline was different from 3 and 6 months ($P=0.000$) and between 3 and 6 months ($P=0.035$). The waist circumference was significantly different after 3 and 6 months ($P=0.000$) compared to baseline, but not between 3 and 6 months ($P=0.211$).

Blood parameters

Blood parameters values at baseline and 6 months are presented in Table 2.

	High Pasta	Low Pasta	P¶	High Pasta	Low Pasta	P¶
	Months					
	0			6		
Glucose, mg/dl	96.7±10.2 ^a	99.6±11.5 ^A	0.391	90.5±9.3 ^b	86.7±9.9 ^B	0.262
Insulin, µU/ml	17.6±11.2 ^a	21.1±11.6 ^A	0.186	13.5±5.0 ^a	13.3±6.8 ^B	0.758
HOMA-IR index	4.3±3.2 ^a	5.2±3.0 ^A	0.148	3.0±1.3 ^b	2.9±1.7 ^B	0.593
Total cholesterol, mg/dl	213.2±41.9 ^a	199.6±33.0 ^A	0.298	198.9±34.5 ^b	192.6±33.1 ^A	0.624
HDL-C, mg/dl	56.3±18.1 ^a	50.0±9.3 ^A	0.221	60.4±16.4 ^a	54.4±7.7 ^A	0.262
LDL-C, mg/dl	131.8±33.7 ^a	120.4±24.4 ^A	0.292	116.1±33.0 ^b	116.8±26.6 ^A	0.839
Triglycerides, mg/dl	124.7±55.0 ^a	133.7±77.4 ^A	0.832	114.4±47.4 ^a	105.9±52.2 ^A	0.483
Uric acid, mg/dl	5.5±1.5 ^a	5.8±1.1 ^A	0.432	5.0±1.3 ^b	5.4±1.0 ^A	0.273

Table 2. Blood values at baseline and 6 months (mean±SD). ¶ P values for differences between the two groups. Different lowercase letters indicate $p < 0.05$ within High Pasta group; different uppercase letters indicate $p < 0.05$ within Low Pasta group. HOMA-IR, Homeostasis model assessment: insulin resistance; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

There were no significant differences between the two groups at baseline, as well as after 6 months of dietary intervention. However, at 6 months there was a reduction of all parameters' values and an increase in HDL in both groups.

In the LP group the reduction was significantly different for glucose ($P=0.001$), insulin ($P=0.000$), and HOMA-IR index ($P=0.000$), whereas in the HP there was a significant reduction in glucose ($P=0.007$), HOMA-IR index ($P=0.029$), total cholesterol ($P=0.002$), LDL ($P=0.004$), and uric acid ($P=0.002$).

Prescribed diet and 24-h dietary recall

Nutritional composition of the prescribed diet for the two groups are reported in Table 3. The recommended calories intake were 1618 ± 163 kcal and 1564 ± 150 kcal for the HP and LP group, respectively. The percentage of carbohydrate, fat and protein were: 48 ± 4 , 32 ± 3 and 21 ± 2 for

the HP group and 46±6, 33±3 and 22±6 for the LP group. There were no significant differences between the diet assigned to the two groups.

	High Pasta	Low Pasta	P¶
Calories, kcal	1618±163	1564±150	0.254
Carbohydrate, % of E	48±4	46±6	0.108
Fat, % of E	32±3	33±3	0.575
Protein, % of E	21±2	22±6	0.378

Table 3. *Nutritional composition (mean±SD) of the prescribed diet for the two groups.*

The dietary data intake at 0, 3 and 6 months are presented in Table 4.

	High Pasta	Low Pasta	P¶	High Pasta	Low Pasta	P¶	High Pasta	Low Pasta	P¶
	Months								
	0			3			6		
Calories, kcal	2245±839	2285±1211	0.902	2025±638	1752±530	0.129	1832±510	1934±510	0.511
CHO, % of E	44±9	47±12	0.691	42±8	43±13	0.208	48±11	48±11	0.525
Sugar, % of E	17±7	19±11	0.681	14±4	17±7	0.969	16±8	18±7	0.062
Fibre, g/1000 kcal	8±2	9±4	0.560	11±4	11±4	0.426	12±5	11±4	0.655
Fat, % of E	35±8	35±9	0.922	36±7	35±9	0.173	34±8	33±8	0.757
Protein, % of E	20±6	17±6	0.192	21±6	22±6	0.545	17±5	18±7	0.609

Table 4. *Dietary intake at baseline, 3 and 6 months (mean±SD). ¶ P values for differences between the two groups. CHO: total carbohydrates.*

At baseline, 3 and 6 months there were no significant differences in the composition of the diets consumed by participants assigned to the HP and LP groups. However, there was a main effect of time, independently of treatment, on calories intake (P=0.020), carbohydrates intake (P=0.011) and sugar intake (P=0.047). There was not a main effect of treatments and treatments x time, not even after adjustment for gender and age.

When the two groups were considered separately, there was a main effect of time, within the LP group, on carbohydrates intake ($P=0.010$), which was no longer significant after adjusting for gender and age. Within the HP group there was no effect of time in both unadjusted and adjusted model.

7-day carbohydrate food record

The results of the 7-day carbohydrates food record are presented in Figure 3. Among carbohydrate foods, only pasta consumption was different between the groups at baseline ($P=0.000$), 3 months ($P=0.001$), and at 6 months ($P=0.000$). The weekly consumption for the other carbohydrate foods was not statistically different between the two groups.

There was an increase in fruits and vegetables consumption that was significant in both LP group ($P=0.001$) and HP group ($P=0.001$).

The weekly consumption of fruits and vegetables in the HP group almost doubled from baseline to month 3 and 6. At baseline the consumption of fruits was 7 (3) times per week, whereas at 3 and 6 months, participants increased the consumption to 13 (5) and 12 (8) times per week, respectively. Similarly, the weekly consumption of vegetables was increased from 7 (0) times to 13 (5) at 3 months and 11 (5) at 6 months.

In the LP group, the consumption of fruits, from 7 (3) times per week, increased to 9 (8) and 10 (7) at 3 and 6 months respectively, whereas the weekly consumption of vegetables increased from 7 (2) times per week to 10 (5) at 3 months and 9 (4) at 6 months. Participants in the LP group reduced significantly the intake of legumes.

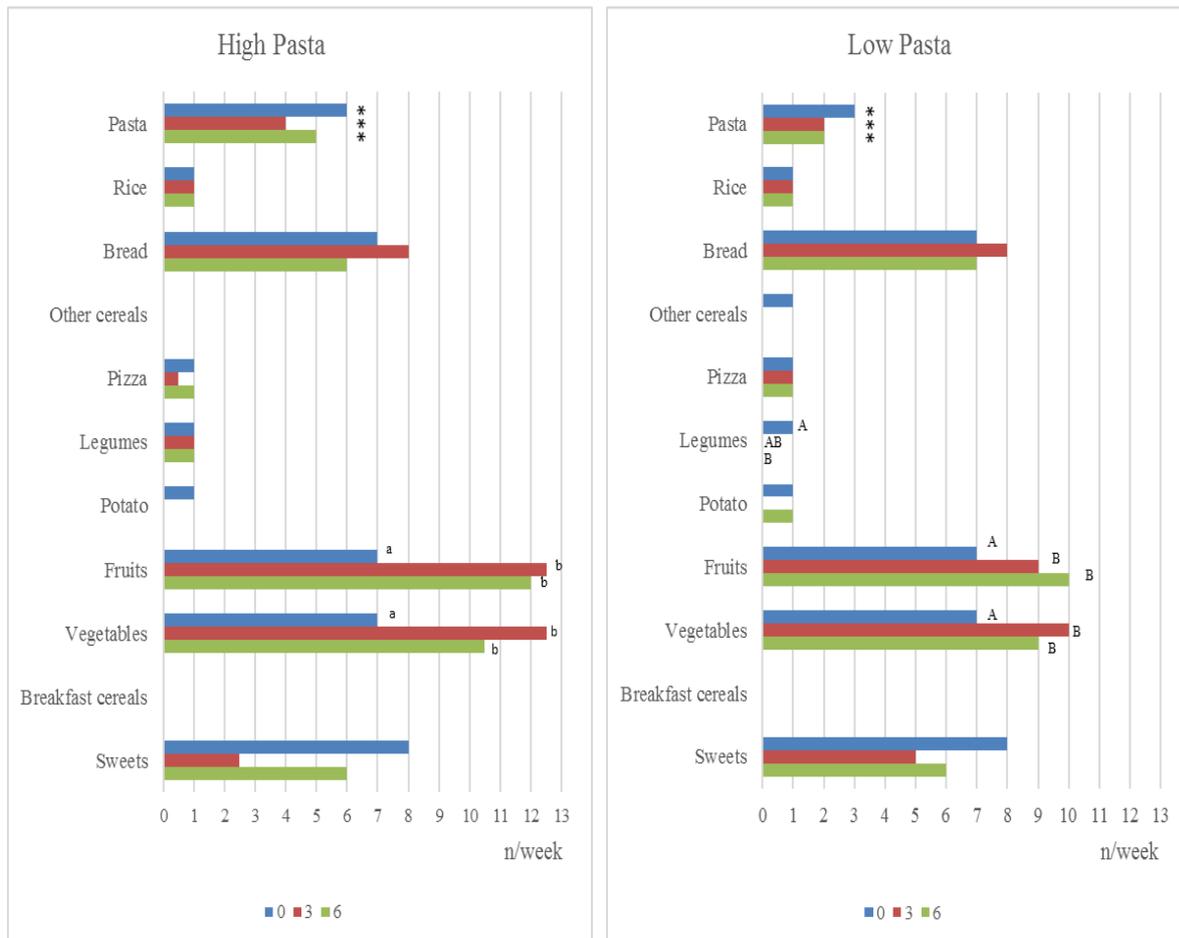


Figure 3. Weekly frequency consumption of carbohydrate foods. * indicated differences between the two groups ($p < 0.05$). Different lowercase letters indicate $p < 0.05$ within High Pasta group; different uppercase letters indicate $p < 0.05$ within Low Pasta group.

Discussions and conclusions

This study aimed to investigate if a hypocaloric diet, where food preferences and the habitual diet are considered and preserved, could be a valuable strategy to stimulate a better compliance to follow a dietary treatment, to improve patients' adherence to a healthier diet (in accordance with the principles of Mediterranean diet), to stimulate weight loss and to maintain the weight loss during time. In particular, obese patients were divided in two groups, based on weekly pasta consumption: High Pasta group and Low Pasta group, pasta consumption ≥ 5 and ≤ 3 times

per week respectively. This study took into consideration the first six months of one-year programmed intervention.

During the 6 months BMI progressively and significantly decreased in both groups respect to the baseline. It is interesting to note that, despite the lack of significance between the two groups in the same time point, there was a greater weight loss at 3 and 6 months in the HP group compared to the LP group. Participants in the HP group reached a body weight reduction >8% already after 3 months and ~10% after 6 months. In the LP the body weight reduction was ~6% and ~7% after 3 and 6 months. Our results are in agreement with other studies where Mediterranean diet was associated with body weight reduction and management, especially with a restricted calories intake (Shai et al. 2008; Esposito et al. 2011).

Besides body weight reduction, beneficial effects were observed on glycaemic control, given by improvement in glucose and HOMA-IR index in both groups after 6 months. Also insulin levels lowered strongly in both groups even if only in LP group significantly. Hypocaloric diets were previously seen effective in improving glycaemic control (De Luis et al. 2015) and this is of interest as overweight and obesity are associated with increased risk of diabetes (Guh et al. 2009) and other NCDs (Ogden et al. 2007). A beneficial effect was also found in blood lipid profile, but only in the HP group, probably as a consequence of the greater weight reduction compared to LP group. Previous studies demonstrated that a more pronounced reduction in body weight resulted in a greatest improvement in lipid profile (Schwingshackl et al. 2015).

Dietary intakes did not change for nutrients nor for energy in both groups during intervention period. Actually, it is possible to observe positive trends in both diets with calorie intake reductions and dietary fibre intake increases, however these values did not change significantly over time probably due to the huge variability within the same group at the different time points.

Regarding weekly frequency of consumption, groups resulted different for pasta: HP diet was significantly higher respect to LP diet in the three time points how expected and required. In both groups along the time fruit and vegetable frequency of consumption significantly increased. Maybe, dietary suggestion got stronger thanks to the recipes emphasizing use of fruit and vegetable. Providing recipes, not only dietary advices, resulted successful in supporting dietary intervention (Tovar et al. 2012).

Furthermore, the increased consumption of fruits and vegetables may have played a role in BMI and physiological improvements. Indeed, increased consumption of these foods, that are a rich source of dietary fibre, has been recommended as a key component of a healthy diet for the prevention of chronic diseases (WHO/FAO 2003). High consumption of fruits and vegetables has been associated with body weight reduction (Kim et al. 2016), and with lower risk of all-cause mortality, particularly cardiovascular mortality (Wang et al. 2014). However, although participants in both groups increased the weekly consumption of fruits and vegetable, they did not reach the recommendation of 5 serving/day. Similarly, the intake of dietary fibre, was below the recommended level of ~14-17 g/1000 kcal (LARN 2014).

One limitation of this study was the use of the 24-h dietary recall to collect food consumption, in addition, the 24-recall was collected only every three months. Maybe a food diary and/or a more frequent survey could be better representing the dietary intake during dietary interventions (Willett 2013).

A strength of the study was that the intervention diets has been chosen based on patients' food preference. This may have led to a better adherence to the dietary intervention and a concomitant improvement in the quality of the diet. In addition, providing several recipes, encouraging the participants to cook and to introduce high quality food in their diet, resulted

winning for the compliance, as reported by the patients themselves. Unfortunately, we did not renew the recipes during the 6 months, but we think that this could represent another good strategy to motivate and stimulate participants to continue in improving their diet.

In conclusion, a hypocaloric diet, in accordance with the principle of Mediterranean diet and considering participants' food preferences, was effective in reducing body weight overall 6 months in obese adults, as well as improving diet quality. Moreover, the consumption of pasta, as food allowed in the hypocaloric regimen, resulted not negatively interfering with the reduction of weight registered in the study. Dietary intervention is still ongoing and it will be very interesting to evaluate results at 12 months.

Supplemental material



*Dimagrire
con
gusto!*

*Dimagrire
con
gusto!*

Dimagrire con gusto!

Dipartimento di Scienze degli Alimenti
Università degli Studi di Parma
in collaborazione con Madegus s.r.l.
Marzo 2016.

Indice

Conchiglie in zuppa bicolore con verdure e tacchino	1
Ditalini con crema di zucca, salmone, rucola e tartufo nero	3
Ditalini in crema di carote e ceci	5
Fusilli con polpettine di pollo e verdure al pomodoro	7
Pasta mista con zuppa di lenticchie, basilico e pomodoro	9
Penne rigate con branzino e melanzane in crema di cipolla	11
Penne rigate con pesce spada e melanzane in crema di broccoli	13
Pennette con salmone ed erbe aromatiche	15
Risoni in zuppa di pollo e verdure	17
Sedanini con anatra, carciofi, fave, olive e pomodoro fresco	19
Spaghetti con carbonara di zucchine	21
Spaghetti rigati con verdure croccanti in pesto di rucola	23
Tagliatelle di semola con pesce spada, zucchine e radicchio rosso	25
Vermicellini con straccetti di tacchino e melanzane	27
Ziti al forno con polpettine, pomodoro fresco e pecorino	29

CONCHIGLIE IN ZUPPA BICOLORE CON VERDURE E TACCHINO



INGREDIENTI

Conchiglie di semola	80 g
Polpa di tacchino	60 g
Patate	25 g
Zucchine	60 g
Sedano	25 g
Carote	60 g
Cipolla	15 g
Brodo vegetale	75 ml
Olio extra vergine di oliva	15 g
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 559 kcal proteine 25 g
carboidrati 75 g lipidi 20 g



Tempo: 30'

Difficoltà: facile

Tritare la cipolla e rosolarla con 1 cucchiaio abbondante di olio.

Unire le patate pelate e tagliate a cubetti.

Quando è tutto ben rosolato aggiungere la polpa di tacchino tagliata a bastoncino, il brodo e portare a cottura per circa 25 minuti, aggiustando di sale e pepe.

Cuocere la pasta direttamente nella zuppa, allungandola con un mestolo di acqua se risultasse asciutta.

Per la presentazione del piatto guarnire aggiungendo il sedano, le zucchine e le carote tagliati a julienne e scottati in acqua bollente.



DITALINI CON CREMA DI ZUCCA. SALMONE. RUCOLA E TARTUFO NERO



INGREDIENTI

Ditalini di semola	80 g
Zucca	175 g
Salmone	90 g
Olio Extravergine di oliva	10 ml
Sedano	15 g
Brodo Vegetale	75 g
Rucola fresca	10 g
Tartufo nero	10 g
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 582 kcal proteine 29 g
carboidrati 71 g lipidi 22 g



Tempo: 40'

Difficoltà: media

Mettere in una casseruola il sedano tagliato a pezzetti con la zucca tagliata a dadini e coprire con il brodo.

Cuocere per 20 minuti finché la zucca risulterà tenera, infine passare il tutto al mixer aggiustando di sale e pepe.

Tagliare la polpa di salmone a cubetti e la rucola a pezzetti, spadellare con l'olio il salmone per 3 minuti.

Cuocere la pasta nella zuppa, allungandola se risultasse troppo asciutta con un goccio di acqua.

Servire guarnendo con rucola, il salmone e fettine sottili di tartufo.



DITALINI IN CREMA DI CAROTE E CECI



INGREDIENTI

Ditalini di semola	80 g
Porro	20 g
Carote	110 g
Pomodoro	30 g
Olio Extravergine di oliva	15 ml
Ceci	100 g
Sale	q.b.
Acqua	500 ml

VALORI NUTRIZIONALI

energia 567 kcal proteine 17 g
carboidrati 88 g lipidi 19 g



Tempo: 30'

Difficoltà: facile

Soffriggere il porro in un cucchiaio di olio, aggiungere le carote tagliate a rondelline, i ceci e il pomodoro privato dei semi e tagliato a pezzetti .

Aggiungere l'acqua, quindi cuocere per altri 20 minuti

Aggiustare di sale e frullare il tutto.

Cuocere la pasta all'interno della crema oppure a parte in acqua e servire aggiungendo un cucchiaino di olio a crudo.



FUSILLI CON POLPETTINE DI POLLO E VERDURE AL POMODORO

INGREDIENTI



Fusilli	80 g
Parmigiano	10 g
Polpa di pomodoro	50 g
Prezzemolo tritato	q.b.
Petto di pollo	70 g
Zucchine	50 g
Carote	25 g
Spinaci	40 g
Pangrattato	15 g
Cipolla	5 g
Olio Extravergine di oliva	15 ml
Sale	q.b.
Pepe	q.b.
Farina	q.b.

VALORI NUTRIZIONALI

energia 530 kcal proteine 33 g
carboidrati 81 g lipidi 10 g



Tempo: 25'

Difficoltà: media

Soffriggere la cipolla tritata in un cucchiaino di olio, aggiungere le carote tritate, la polpa di pomodoro e aggiustare di sale e pepe.

Rosolare il pollo tagliato a pezzetti in un cucchiaio di olio, frullare al mixer e unire il pangrattato, il formaggio e aggiustare di sale e pepe.

Tagliare le zucchine a cubettini piccoli, tritare gli spinaci finemente e unire all'impasto di pollo.

Fare piccole polpettine, infarinarle e unirle alla salsa cuocendo per 7 minuti circa.

Cuocere la pasta e mantecare con la salsa e il prezzemolo.



PASTA MISTA CON ZUPPA DI LENTICCHIE



INGREDIENTI

Pasta di semola mista	80 g
Lenticchie in scatola	150 g
Brodo vegetale	350 ml
Basilico	10 g
Melanzane	80 g
Carote	30 g
Cipolla	20 g
Pomodoro	50 g
Olio Extravergine di oliva	15 ml
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 597 kcal proteine 19 g
carboidrati 94 g lipidi 19 g



Tempo: 40'

Difficoltà: facile

Imbiondire la cipolla tritata con un cucchiaio di olio, unire le lenticchie e melanzane e carote a cubetti, bagnare con il brodo e cuocere per circa 25 minuti.

Frullare il tutto al mixer aggiustando di sale e pepe.

Macerare il pomodoro tagliato a cubetti con un cucchiaio di olio, il basilico tritato e un pizzico di sale e pepe.

Cuocere la pasta nella zuppa.

Guarnire con il pomodoro macerato e il basilico e servire con in goccio di olio extravergine crudo.



PENNE RIGATE CON BRANZINO E MELANZANE IN CREMA DI CIPOLLA



INGREDIENTI

Penne rigate	80 g
Polpa di branzino	80 g
Pomodorini ciliegia	50 g
Melanzane	80 g
Cipolla	40 g
Brodo vegetale	20 ml
Olio Extravergine di oliva	15 ml
Aglione	1 spicchio
Rosmarino	q.b.
Basilico	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 582 kcal proteine 26 g
carboidrati 71 g lipidi 23 g



Tempo: 40'

Difficoltà: media

Cuocere in forno il branzino con sale, pepe e rosmarino per 10 minuti a 200°circa. Lasciare raffreddare e togliere la polpa spezzettandola grossolanamente.

Cuocere le melanzane in un cucchiaio di olio per 3 minuti e scolarle su carta assorbente.

Unire i pomodorini pelati, svuotati e tagliati a listarelle, le melanzane e il branzino e cuocere 3 minuti a fuoco basso.

Rosolare la cipolla nel restante olio con sale, pepe e un mestolo di brodo cuocendo a fuoco basso per 10 minuti. Frullare al mixer.

Cuocere la pasta, scolare al dente, saltare in padella con la salsa di branzino.

Porre sul fondo del piatto la crema di cipolla, la pasta al centro e guarnire con basilico.



PENNE RIGATE CON PESCE SPADA E MELANZANE IN CREMA DI BROCCOLI



INGREDIENTI

Penne rigate	80 g
Pesce spada	80 g
Pomodorini ciliegia	50 g
Brodo vegetale	75 ml
Olio Extravergine di oliva	15 ml
Melanzane	50 g
Broccolo	75 g
Cipolla	10 g
Timo fresco	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 550 kcal proteine 26 g
carboidrati 70 g lipidi 20 g



Tempo: 40'

Difficoltà: media

Rosolare la cipolla in un cucchiaino di olio, unire il pesce spada tagliato a cubetti, il timo tritato, il sale e il pepe e cuocere per circa 5 minuti.

Cuocere le melanzane tagliate a cubetti in un cucchiaio di olio a fuoco alto.

Cuocere i broccoli tagliati a pezzetti nel brodo vegetale e frullare al mixer una volta cotti aggiustando di sale e pepe.

Tagliare i pomodorini a cubetti.

Cuocere le penne, scolare al dente e saltare con lo spada al timo, i pomodorini e un filo di olio extravergine.

Stendere la crema di broccoli sul fondo del piatto, mettere la pasta con lo spada al centro e guarnire con le melanzane.



PENNETTE CON SALMONE ED ERBE AROMATICHE



INGREDIENTI

Penne rigate	80 g
Salmone affumicato	75 g
Olio Extravergine di oliva	10 ml
Zucchine	120 g
Carote	60 g
Prezzemolo fresco	q.b.
Timo fresco	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 520 kcal proteine 30 g
carboidrati 71 g lipidi 15 g



Tempo: 20'

Difficoltà: facile

Rosolare il salmone tagliato a piccoli bastoncini con l'olio, unire le zucchine e le carote tagliate come il salmone e cuocere per 5 minuti, aggiungendo un mestolo di acqua all'occorrenza.

Tritare finemente il prezzemolo e il timo unendoli al salmone.

Cuocere la pasta, scolare e condire con la salsa di salmone ed erbe aromatiche, unire un mestolo di acqua di cottura della pasta per condire in modo uniforme.



RISONI IN ZUPPA DI POLLO E VERDURE

INGREDIENTI



Risoni di semola	80 g
Petto di pollo	80 g
Carote	80 g
Broccolo	80 g
Cipolla	30 g
Gambe di sedano	30 g
Brodo	200 ml
Olio Extravergine di oliva	10 ml
Buccia di limone	1/4
Sale	q.b.
Pepe	q.b.
Zenzero fresco	q.b.
Curry in polvere	q.b.
Rafano	q.b.

VALORI NUTRIZIONALI

energia 550 kcal proteine 33 g
carboidrati 79 g lipidi 14 g



Tempo: 30'

Difficoltà: media

Tagliare a bastoncini il pollo, le verdure, lo zenzero e la buccia di limone e tagliare a ciuffetti il broccolo.

Rosare nell'olio le verdure, unire il pollo, il rafano, lo zenzero e il curry.

Bagnare con il brodo e cuocere per 20/25 minuti a fuoco medio.

Aggiustare di sale e pepe.

Cuocere i risoni nella zuppa.

Servire la zuppa in una ciotolina e guarnire con la buccia di limone.



SEDANINI CON ANATRA. CARCIOFI. FAVE. OLIVE E POMODORO FRESCO



INGREDIENTI

Sedanini di semola	80 g
Petto di anatra	80 g
Carciofi	150 g
Fave	30 g
Olive nere	15 g
Pomodori a grappolo	100 g
Cipolla	30 g
Olio Extravergine di oliva	15 ml
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 652 kcal proteine 33 g
carboidrati 74 g lipidi 27 g



Tempo: 30'

Difficoltà: media

Pulire e tagliare a cubetti il petto d'anatra. Arrostitirlo in una casseruola con la cipolla tritata e un cucchiaio di olio.

Pelare le fave. Pulire i carciofi e tagliarli a lamelle. Sbollentare, pelare e svuotare dai semi i pomodori e tagliarli a cubetti.

Saltare con un cucchiaino d'olio i carciofi, aggiungere le olive, le fave ed i pomodori e cuocere per 5 minuti.

Incorporare l'anatra con le verdure e fare bollire ancora per alcuni minuti.

Cuocere la pasta, scolare al dente e saltare con il sugo precedentemente preparato.



SPAGHETTI CON CARBONARA DI ZUCCHINE



INGREDIENTI

Spaghetti	80 g
Tuorlo d'uovo	25 g
Zucchine	150 g
Porro	50 g
Parmigiano	10 g
Olio Extravergine di oliva	5 ml
Brodo vegetale	25 ml
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 480 kcal proteine 19 g
carboidrati 68 g lipidi 17 g



Tempo: 20'

Difficoltà: facile

Tagliare a listarelle fini le zucchine e il porro, saltarli in padella con un cucchiaino di olio e un pizzico di sale per 3 minuti.

Sbattere in una ciotola i rossi d'uovo, unire il parmigiano, il brodo vegetale e una macinata di pepe nero.

Cuocere la pasta, scolare e saltare con le zucchine e il porro.

Togliere dal fuoco e unire le uova al composto. Se risultasse leggermente liquido rimettere per 1/2 minuti sul fuoco.



SPAGHETTI RIGATI CON VERDURE CROCCANTI IN PESTO DI RUCOLA



INGREDIENTI

Spaghetti	80 g
Zucchine	100 g
Porro	30 g
Carote	30 g
Melanzane	80 g
Olio Extravergine di oliva	10 ml
Rucola fresca	5 g
Pinoli	3 g
Parmigiano	15 g
Sale	q.b.
Pepe	q.b.
Acqua	q.b.

VALORI NUTRIZIONALI

energia 494 kcal proteine 18 g
carboidrati 71 g lipidi 17 g



Tempo: 20'

Difficoltà: media

Saltare in padella con un cucchiaino di olio le melanzane per 1 minuto. Aggiungere le carote e saltare per 1 altro minuto. Infine, aggiungere le zucchine per 1 minuto e toglierle dal fuoco.

Tagliare il porro a rondelle, metterlo in padella, aggiungere un mestolo d'acqua e cuocere a fuoco basso per 5/6 minuti.

Frullare al mixer la rucola, un cucchiaino di olio, i pinoli e il parmigiano.

Cuocere la pasta, scolare e condire con le verdure e il porro.

Stendere sul fondo del piatto un velo di pesto alla rucola e mettere la pasta con le verdure al centro.



TAGLIATELLE DI SEMOLA CON PESCE SPADA, ZUCCHINE E RADICCHIO ROSSO



INGREDIENTI

Tagliatelle di semola	80 g
Pesce spada	100 g
Pomodorini ciliegia	50 g
Scalogno	10 g
Zucchine	125 g
Radicchio rosso	50 g
Olio Extravergine di oliva	15 ml
Prezzemolo	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 560 kcal proteine 29 g
carboidrati 69 g lipidi 21 g



Tempo: 25'

Difficoltà: media

Imbiondire lo scalogno tritato in padella con 1 cucchiaio abbondante di olio.

Unire il pesce spada tagliato a cubetti e lasciare rosolare.

Aggiungere i pomodorini pelati e tagliati a listarelle e cuocere per 4 minuti,aggiustando di sale e pepe.

Sbollentare in acqua le zucchine tagliate a listarelle e unirle alla salsa.

Cuocere le tagliatelle, scolare al dente e saltare in padella con la salsa.

Tagliare il radicchio rosso a listarelle finissime, stenderne sul fondo del piatto un velo e posizionare la pasta al centro guardando con prezzemolo tritato.



VERMICELLINI CON STRACCETTI DI TACCHINO E MELANZANE



INGREDIENTI

Vermicellini di semola	80 g
Fesa di tacchino	80 g
Melanzane	100 g
Zucchine	100 g
Olio Extravergine di oliva	10 ml
Prezzemolo	q.b.
Sale	q.b.
Pepe	q.b.
Origano	q.b.

VALORI NUTRIZIONALI

energia 487 kcal proteine 30 g
carboidrati 67 g lipidi 13 g



Tempo: 20'

Difficoltà: facile

Tagliare il tacchino a piccoli pezzetti lunghi 4 cm e di circa 1 cm di spessore.

Rosolare in padella con un cucchiaino di olio di oliva, unire il prezzemolo tritato e aggiustare di sale e pepe, cuocendo per 3/4 minuti.

Tagliare le melanzane e le zucchine a pezzetti come il tacchino, passarle in padella con un cucchiaino di olio a fuoco alto per 3 minuti girando continuamente.

Cuocere la pasta, scolare al dente e condire con la salsa di tacchino, guarnendo con le verdure e l'origano tritato.



ZITI AL FORNO CON POLPETTINE, POMODORO FRESCO E PECORINO



INGREDIENTI

Ziti napoletani	80 g
Macinato di manzo	70 g
Melanzane	80 g
Pomodori	100 g
Porro	25 g
Tuorlo d'uovo	1/2 g
Parmigiano grattugiato	10 g
Pangrattato	5 g
Olio Extravergine di oliva	15ml
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 608 kcal proteine 32 g
carboidrati 74 g lipidi 22 g



Tempo: 40'

Difficoltà: media

Impastare la carne con parmigiano, tuorlo d'uovo, sale e pangrattato. Formare delle polpettine, infarinare leggermente e cuocerle in padella con un cucchiaio di olio.

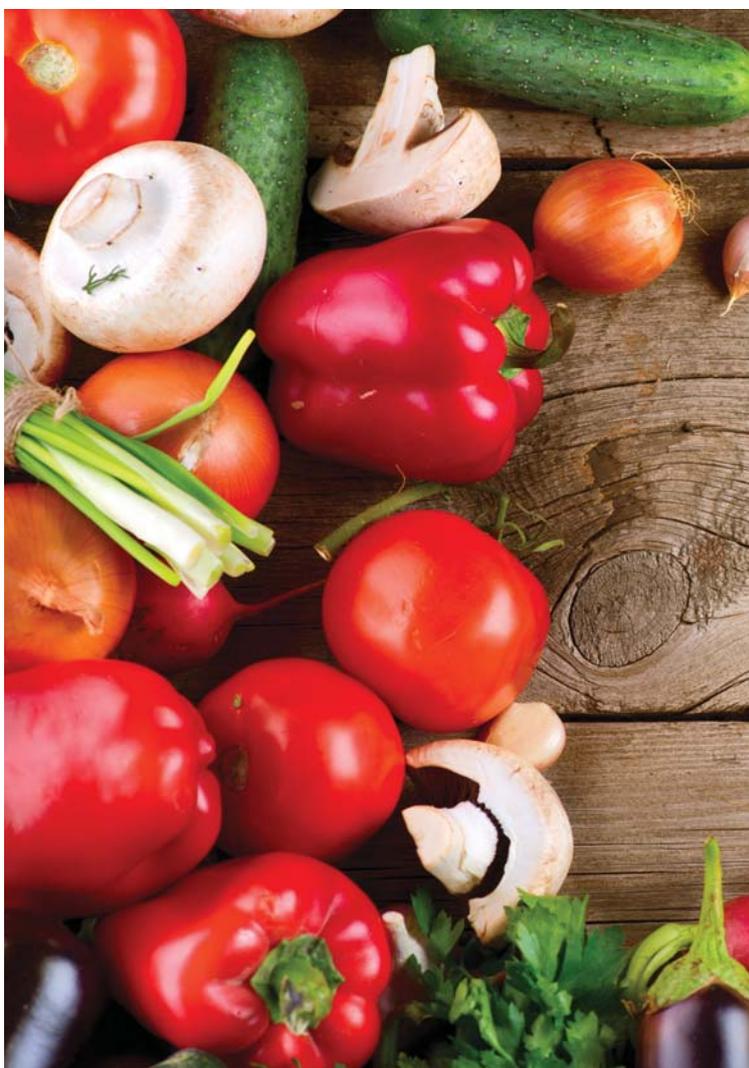
Tagliare il porro a rondelline, rosolarlo in padella con un cucchiaino di olio, unire il pomodoro pelato e tagliato a cubetti. Cuocere per 5 minuti e unire le polpettine.

Tagliare la melanzana a rondelle e passarla in padella senza olio per 4 minuti circa.

Cuocere la pasta 2 minuti in meno del suo tempo di cottura e scolarla.

Fare una teglia alternando uno strato di salsa, uno di pasta, uno di melanzane, etc.

Passare in forno a 220° per 10 minuti e servire con scaglie di pecorino stagionato.





*Dimagrire
con
gusto!*

*Dimagrire
con
gusto!*

Dimagrire con gusto!

Dipartimento di Scienze degli Alimenti
Università degli Studi di Parma
in collaborazione con Madegus s.r.l.
Marzo 2016.

Indice

Focaccia farcita con pomodorini e ricotta	1
Focaccia farcita con zucchine e salmone	3
Insalatona estiva con tonno, mais, spinaci, piselli e prosciutto	5
Pane con crema di pomodorini, tonno, capperi, olive e finocchio	7
Pane con patate e pesce spada affumicato	9
Pane con pollo e patate al prezzemolo	11
Pane con salsa e pollo al profumo di ginepro	13
Riso pilaf con calamari e verdure croccanti al profumo di timo	15
Riso pilaf con pollo e verdure saltate	17
Tortino casereccio ai carciofi	19
Tortino casereccio di verdure miste	21
Zuppa di riso al radicchio rosso	23
Zuppa di orzo con broccoli e porro	25
Zuppa di orzo e fagioli al pomodoro e basilico	27

FOCACCIA FARCITA CON POMODORINI E RICOTTA



INGREDIENTI

Farina	100 g
Lievito	2,5 g
Latte	50 ml
Zucchero	q.b.
Sale	q.b.
Patate	15 g
Olio di oliva extravergine	10 ml
Pomodorini	180 g
Ricotta	80 g

VALORI NUTRIZIONALI

energia 600 kcal proteine 26 g
carboidrati 78 g lipidi 23 g



Tempo: 2 h 40'

Difficoltà: medio

Intiepidire il latte e farvi sciogliere il lievito mescolando bene. Fare raffreddare e impastare con gli altri ingredienti.

Fare lievitare l'impasto per un'ora.

Stendere nella teglia leggermente unta e poi lasciare lievitare per un'altra ora.

Fare dei fori sopra l'impasto con la forchetta, unire un filo di olio per evitare che faccia la pelle sopra e cuocere in forno preriscaldato a 180° fino a cottura desiderata (circa 20/25 minuti).

A fine cottura guarnire aggiungendo la ricotta e i pomodorini.



FOCACCIA FARCITA CON ZUCCHINE E SALMONE



INGREDIENTI

Farina	100 g
Lievito	2,5 g
Latte	50 ml
Zucchero	q.b.
Sale	q.b.
Patate	15 g
Olio di oliva extravergine	10 ml
Zucchine	180 g
Salmone in salamoia	80 g

VALORI NUTRIZIONALI

energia 576 kcal proteine 35 g
carboidrati 72 g lipidi 19 g



Tempo: 2 h 40'

Difficoltà: medio

Sbollentare le zucchine tagliate a rondelle. Intiepidire il latte e farvi sciogliere il lievito mescolando bene. Fare raffreddare e impastare con gli altri ingredienti e fare lievitare l'impasto per un'ora.

Stendere nella teglia leggermente unta e poi lasciare lievitare per un'altra ora.

Fare dei fori sopra l'impasto con la forchetta, unire un filo di olio per evitare che faccia la pelle sopra e cuocere in forno preriscaldato a 180°.

Dopo circa 20/25 minuti, quando l'impasto ha quasi raggiunto la cottura desiderata, aggiungere le zucchine e il salmone e terminare la cottura in forno.



INSALATONA ESTIVA CON TONNO. MAIS. SPINACI. PISELLI E PROSCIUTTO



INGREDIENTI

Piselli surgelati	80 g
Tonno sott'olio sgocciolato	50 g
Prosciutto cotto	20 g
Mais	120 g
Spinaci	120 g
Olio extravergine di oliva	10 ml
Sale	q.b.
Pepe	q.b.
Pane	50 g

VALORI NUTRIZIONALI

energia 559 kcal proteine 33 g
carboidrati 56 g lipidi 23 g



Tempo: 20'

Difficoltà: facile

Sbollentare i piselli per 3 minuti.
Tagliare il prosciutto a cubetti.
Cuocere gli spinaci e frullarli al mixer con un goccio di acqua di cottura e un pizzico di sale.
Unire i piselli, il tonno, il prosciutto e il mais.
Condire con la crema di spinaci e un cucchiaio di olio.
Servire a temperatura ambiente guarnendo con il pane abbrustolito.



PANE CON CREMA DI POMODORINI, TONNO, CAPPERI, OLIVE E FINOCCHIO



INGREDIENTI

Pancarrè	100 g
Pomodorini ciliegia	120 g
Tonno in scatola	80 g
Olio extravergine di oliva	5 ml
Zucchero	3 g
Olive	10 g
Capperi	5 g
Finocchio	50 g
Timo	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 532 kcal proteine 30 g
carboidrati 55 g lipidi 20 g



Tempo: 1 h e 20'

Difficoltà: facile

Preparare una teglia con i pomodorini, l'olio, lo zucchero, il timo e un pizzico di sale e cuocere in forno per un'oretta a 120°.

Togliere dal forno e frullare al mixer ottenendo una crema.

Lavare molto bene i capperi sotto acqua corrente e tagliare a spicchi oppure a rondelle le olive, tagliare a fettine sottili il finocchio tenendolo in acqua gassata per evitare che diventi troppo scuro.

Cospargere le fette di pane con la salsa di pomodorini, aggiungere le olive, i capperi e il tonno ed in fine il finocchio crudo, che darà un'ottima consistenza.



PANE CON PATATE E PESCE SPADA AFFUMICATO



INGREDIENTI

Pancarrè	100 g
Patate	50 g
Olio di oliva extravergine	5 ml
Zucchine	150 g
Tuorlo d'uovo	10 g
Pesce spada affumicato	80 g
Prezzemolo	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 492 kcal proteine 26 g
carboidrati 59 g lipidi 16 g



Tempo: 40'

Difficoltà: facile

Cuocere le patate con la pelle, a cottura scolarle e metterle in una ciotola tagliandole a pezzi.

Tagliare le zucchine a piccoli cubetti e cuocerle leggermente in acqua salata.

Cuocere un uovo per 10 minuti in acqua salata, scolarlo e lasciarlo raffreddare. Pelarlo e tenere il rosso.

Mescolare le patate con il rosso dell'uovo, l'olio, il prezzemolo tritato, le zucchine, sale e pepe per ottenere una crema con pezzetti all'interno.

Affettare il pesce affumicato.

Spalmare la crema di patate sul pane e posizionare il pesce affumicato sopra.



PANE CON POLLO E PATATE AL PREZZEMOLO



INGREDIENTI

Pancarrè	100 g
Patate	50 g
Olio extravergine di oliva	10 ml
Pomodori maturi	150 g
Polpa di pollo	80 g
Prezzemolo	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 509 kcal proteine 30 g
carboidrati 61 g lipidi 15 g



Tempo: 40'

Difficoltà: facile

Tagliare a cubetti piccolini le patate, sbollentarle in acqua salata per 2 minuti circa a seconda della grandezza dei cubetti, scolarle e tenerle da parte.

Cuocere il pollo in forno a 180° con sale e un cucchiaio di olio, a cottura lasciare raffreddare e tagliare la polpa a cubetti della stessa dimensione delle patate.

Frullare i pomodori con un pizzico di sale. Unire ai pomodori le patate e la carne, mescolando bene e aggiustare di sale e pepe. Spalmare le fette di pane con la salsa ottenuta e finire con il prezzemolo tritato.



PANE CON SALSA E POLLO AL PROFUMO DI GINEPRO



INGREDIENTI

Pancarrè	100 g
Polpa di pollo	75 g
Passata di pomodoro	80 g
Carote	80 g
Gambo di sedano	50 g
Cavolo bianco	80 g
Cipolla	15 g
Olio extravergine di oliva	10 ml
Timo	q.b.
Ginepro	q.b.
Prezzemolo	q.b.

VALORI NUTRIZIONALI

energia 551 kcal proteine 34 g
carboidrati 70 g lipidi 15 g



Tempo: 40'

Difficoltà: facile

Tagliare a cubetti piccolini le carote, il sedano e la cipolla.

Fare rosolare in padella a fuoco basso con un cucchiaino di olio, aggiustare di sale e unire il ginepro e il timo.

Togliere dal fuoco, tritare con il mixer e unire la passata di pomodoro.

Cuocere il pollo in forno a 180° con sale e un cucchiaino di olio, a cottura lasciare raffreddare e tagliare la polpa a listarelle. Sbollentare il cavolo tagliato a pezzetti in acqua.

Spalmare la crema di verdure sul pane, aggiungere la polpa di pollo e il cavolo e guarnire con prezzemolo tritato.



RISO PILAF CON CALAMARI E VERDURE CROCCANTI AL PROFUMO DI TIMO



INGREDIENTI

Riso carnaroli	80 g
Ciuffi di calamaro	150 g
Carote	50 g
Zucchine	80 g
Porro	50 g
Brodo vegetale	125 ml
Olio Extravergine di oliva	15 ml
Pomodorini ciliegia	50 g
Timo fresco	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 559 kcal proteine 28 g
carboidrati 75 g lipidi 19 g



Tempo: 45'

Difficoltà: media

Mettere in teglia i pomodorini lavati, unire un pizzico di sale e il timo. Infornare a 100° per circa un'oretta. Togliere dal forno e frullare al mixer.

Tagliare a rondelle il porro, imbiondirlo leggermente con un cucchiaino di olio, unire due mestoli d'acqua e cuocere a fuoco basso fino a totale assorbimento dell'acqua (10 minuti circa). Tostare il riso con un cucchiaio di olio e coprire con il brodo. Cuocere in forno a 200° per 15 minuti circa, togliere dal forno e stenderlo in una teglia per farlo raffreddare.

Saltare le verdure tagliate a bastoncino in padella con sale e pepe a fuoco alto per 3 minuti.

Tagliare a metà i ciuffi di calamaro, cuocerli in padella per 2 minuti, salare e pepare.

Unire tutti gli ingredienti al riso mescolandoli bene. Saltare in padella e servire stendendo la crema di pomodorini sotto e il riso sopra.



RISO PILAF CON POLLO E VERDURE SALTATE



INGREDIENTI

Risoni carnaroli	80 g
Petto di pollo	100 g
Carote	80 g
Zucchine	80 g
Melanzane	50 g
Porro	20 g
Brodo vegetale	125 ml
Olio Extravergine di oliva	15 ml
Rosmarino	q.b.
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 558 kcal proteine 32 g
carboidrati 74 g lipidi 17 g



Tempo: 40'

Difficoltà: media

Tagliare a rondelle il porro, imbiondirlo leggermente con un cucchiaio di olio.

Unire il riso tostandolo, coprire con il brodo e cuocere in forno per 15/17 minuti circa a 190°. Togliere dal forno e stendere in una telia per farlo raffreddare.

Saltare in padella tutte le verdure tagliate a bastoncino con un cucchiaino di olio, sale e pepe a fuoco alto per 3 minuti circa. Tagliare a bastoncino anche la polpa di pollo, cuocerla in padella, salare e pepare leggermente e insaporire con un trito di rosmarino.

Unire tutti gli ingredienti al riso mescolandoli bene, saltarli in padella e servire dando a piacere una forma nel piatto.



TORTINO CASERECCIO AI CARCIOFI



INGREDIENTI

Pane	100 g
Carciofi	100 g
Uovo	1
Scalogno	10 g
Olio Extravergine di oliva	15 ml
Parmigiano reggiano	20 g
Latte	20 g
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 504 kcal proteine 27 g
carboidrati 42 g lipidi 25 g



Tempo: 25'

Difficoltà: media

Amalgamare e sbattere l'uovo con il parmigiano reggiano.

Pulire e tagliare a fettine sottili i carciofi.

Rosolare lo scalogno con un cucchiaio di olio, unire i carciofi e dopo circa 5 minuti aggiungere il latte e il preparato di uova e parmigiano, aggiustando di sale e pepe.

Ungere degli stampini per tartallete con il restante olio e riempirli con la crema preparata. Cuocere a 170° per 12 minuti.

Servire guarnendo a piacere con il pane abbrustolito.



TORTINO CASERECCIO DI VERDURE MISTE



INGREDIENTI

Pane	100 g
Zucchine	100 g
Cipollotti	50 g
Piselli	50 g
Melanzane	50 g
Uovo	1
Olio Extravergine di oliva	5 ml
Latte	20 ml
Aglione	1 spicchio
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 557 kcal proteine 22 g
carboidrati 58 g lipidi 25 g



Tempo: 20'

Difficoltà: facile

Pulire e lavare tutte le verdure. Tagliare le melanzane a cubetti e i cipollotti à julienne. Saltare tutto in padella con anche i piselli. Mettere un cucchiaino di olio in una padella a fuoco medio, aggiungere l'aglio e cucinare le zucchine tagliate a fette spesse 2 mm per la loro lunghezza.

Mescolare insieme il latte e le uova aggiungendo di sale e pepe.

Rivestire degli stampini monouso di alluminio con le fette di zuccina, riempirli con le verdure saltate e il latte e uovo.

Infernare lo sformatino per 20 minuti circa a 160° C. Sformare nel piatto e guarnire a piacere con il pane abbrustolito.



ZUPPA DI RISO AL RADICCHIO ROSSO



INGREDIENTI

Riso arborio	80 g
Gambi di sedano	30 g
Carote	50 g
Cipolla	30 g
Radicchio rosso	100 g
Patata	25 g
Brodo vegetale	250 ml
Olio Extravergine di oliva	10 ml
Parmigiano	30 g
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 550 kcal proteine 20 g
carboidrati 77 g lipidi 20 g



Tempo: 25'

Difficoltà: facile

Rosolare con l'olio le verdure tagliate a cubetti, aggiungere il radicchio tagliato a listarelle, la patata tagliata a cubetti, il brodo e aggiustare di sale e pepe. Cuocere fino a che le verdure saranno tenere.

Cuocere il riso direttamente nella zuppa avendo cura di aggiungere un goccio di brodo se risultasse troppo densa.

Servire cospargendo il piatto con il parmigiano grattato.



ZUPPA DI ORZO CON BROCCOLI E PORRO



INGREDIENTI

Orzo precotto	80 g
Porri	30 g
Broccoli	150 g
Olio extravergine di oliva	10 ml
Brodo vegetale	250 ml
Pinoli	30 g
Sale	q.b.
Pepe	q.b.

VALORI NUTRIZIONALI

energia 585 kcal proteine 24 g
carboidrati 65 g lipidi 28 g



Tempo: 30'

Difficoltà: facile

Rosolare leggermente il porro in un cucchiaio di olio, unire i broccoli tagliati a pezzetti e cuocere per 5 minuti insaporendo con sale e pepe.

Bagnare con il brodo vegetale e lasciare cuocere per circa 20 minuti. A cottura ultimata frullare il tutto al mixer ottenendo una crema densa e vellutata.

Cuocere l'orzo in acqua o direttamente nella crema.

Tostare leggermente i pinoli in padella antiaderente.

Servire guarnendo con pinoli e pasta direttamente sulla crema, profumando con un filo di olio extravergine di oliva.



ZUPPA DI ORZO E FAGIOLI AL POMODORO E BASILICO



INGREDIENTI

Orzo	80 g
Fagioli	100 g
Cipolla	30 g
Patate	50 g
Pomodori	80 g
Brodo vegetale	250 ml
Olio Extravergine di oliva	10 ml
Sale	q.b.
Pepe	q.b.
Basilico	q.b.

VALORI NUTRIZIONALI

energia 559 kcal proteine 22 g
carboidrati 94 g lipidi 14 g



Tempo: 20'

Difficoltà: facile

Rosolare in padella con un cucchiaino di olio la cipolla tritata finemente.

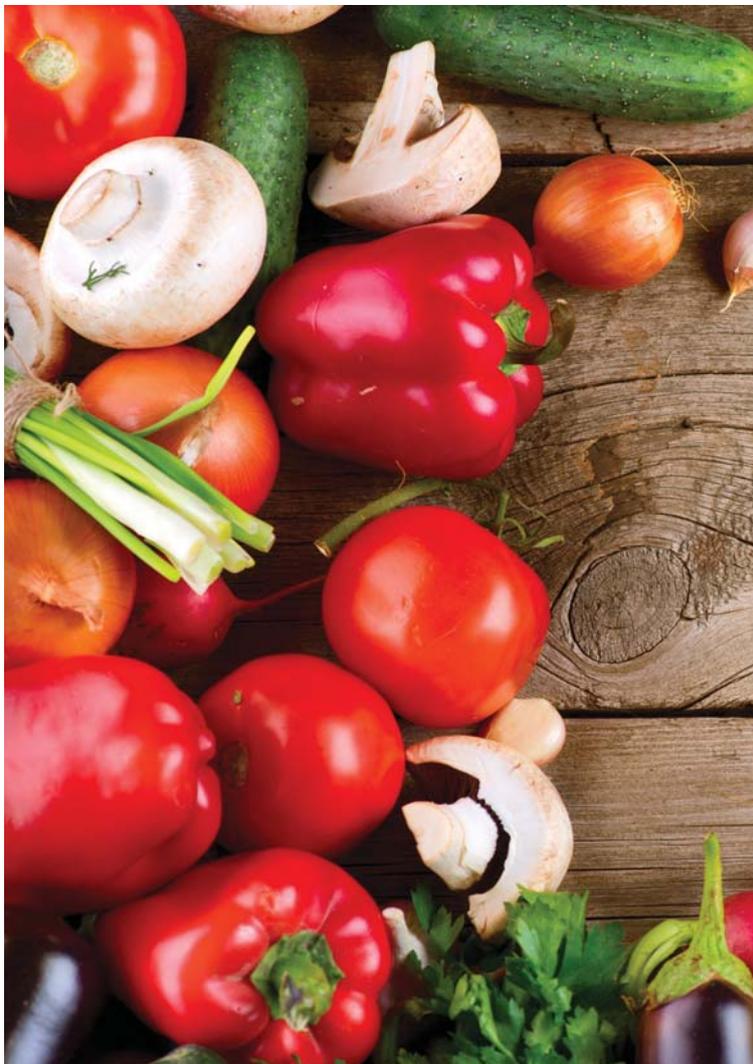
Unire i fagioli, le patate tagliate a pezzetti e bagnare con il brodo cuocendo per 15 minuti circa. Frullare nel mixer.

In una terrina mettere il pomodoro e il basilico con 1 cucchiaino di olio extravergine, lasciandolo macerare per 10 minuti.

Cuocere l'orzo in acqua leggermente salata e scolare.

Servire la zuppa di fagioli, guarnendo con il pomodoro e basilico e il farro.





References

- Atkinson FS, Foster-Powell K, Brand-Miller JC. 2008. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care*. 31(12):2281-2283.
- Blaak EE, Antoine JM, Benton D, Björck I, Bozzetto L, Brouns F, Diamant M, Dye L, Hulshof T, Holst JJ et al. 2012. Impact of postprandial glycaemia on health and prevention of disease. *Obesity Reviews*. 13(10):923-984.
- Cleo G, Isenring E, Thomas R, Glasziou P. 2017. Could habits hold the key to weight loss maintenance? A narrative review. *Journal of Human Nutrition and Dietetics*. 30(5):655-664.
- Cooper Z, Fairburn CG. 2001. A new cognitive behavioural approach to the treatment of obesity. *Behaviour Research and Therapy*. 39(5):499-511.
- Curioni CC, Lourenço PM. 2005. Long-term weight loss after diet and exercise: A systematic review. *International Journal of Obesity*. 29(10):1168-1174.
- De Luis DA, Izaola O, Aller R, De La Fuente B, Bachiller R, Romero E. 2015. Effects of a high-protein/low carbohydrate versus a standard hypocaloric diet on adipocytokine levels and insulin resistance in obese patients along 9 months. *Journal of Diabetes and its Complications*. 29(7):950-954.
- Esposito K, Kastorini CM, Panagiotakos DB, Giugliano D. 2011. Mediterranean diet and weight loss: Meta-analysis of randomized controlled trials. *Metabolic Syndrome and Related Disorders*. 9(1):1-12.
- Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J et al. 2013. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 368(14):1279-1290.
- Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. 2009. The incidence of comorbidities related to obesity and overweight: A systematic review and meta-analysis. *BMC Public Health*.
- INRAN (2007), LINEE GUIDA PER UNA SANA ALIMENTAZIONE ITALIANA.
- Kim SJ, De Souza RJ, Choo VL, Ha V, Cozma AI, Chiavaroli L, Mirrahimi A, Mejia SB, Di Buono M, Bernstein AM et al. 2016. Effects of dietary pulse consumption on body weight: A systematic review and meta-analysis of randomized controlled trials. *American Journal of Clinical Nutrition*. 103(5):1213-1223.
- Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy Jr WS, Brehm BJ, Bucher HC. 2006. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: A meta-analysis of randomized controlled trials. *Archives of Internal Medicine*. 166(3):285-293.
- Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. 2007. The Epidemiology of Obesity. *Gastroenterology*. 132(6):2087-2102.

Pounis G, Di Castelnuovo A, Costanzo S, Persichillo M, Bonaccio M, Bonanni A, Cerletti C, Donati MB, De Gaetano G, Iacoviello L. 2016. Association of pasta consumption with body mass index and waist-to-hip ratio: Results from Moli-sani and INHES studies. *Nutrition and Diabetes*. 6(7).

Rahelić D, Jenkins A, Božikov V, Pavić E, Jurić K, Fairgrieve C, Romić D, Kokić S, Vuksan V. 2011. Glycemic index in diabetes. *Collegium Antropologicum*. 35(4):1363-1368.

Schwingshackl L, Dias S, Hoffmann G. 2015. Impact of long-term lifestyle programmes on weight loss and cardiovascular risk factors in overweight/obese participants: A systematic review and network meta-analysis. *Systematic Reviews*. 3(1).

Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H et al. 2008. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *New England Journal of Medicine*. 359(3):229-241.

SINU, Società Italiana di Nutrizione Umana (2014). LARN – Livelli di Assunzione di Riferimento di Nutrienti ed energia per la popolazione italiana IV Revisione. Milano (IT): SICS Editore.

Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. 2008. Adherence to Mediterranean diet and health status: meta-analysis. *BMJ (Clinical research ed)*. 337.

Subar AF, Kirkpatrick SI, Mittl B, Zimmerman TP, Thompson FE, Bingley C, Willis G, Islam NG, Baranowski T, McNutt S et al. 2012. The Automated Self-Administered 24-Hour Dietary Recall (ASA24): A Resource for Researchers, Clinicians, and Educators from the National Cancer Institute. *Journal of the Academy of Nutrition and Dietetics*. 112(8):1134-1137.

Tovar J, Nilsson A, Johansson M, Ekesbo R, Åberg AM, Johansson U, Björck I. 2012. A diet based on multiple functional concepts improves cardiometabolic risk parameters in healthy subjects. *Nutrition and Metabolism*.

Wang X, Ouyang Y, Liu J, Zhu M, Zhao G, Bao W, Hu FB. 2014. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: Systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ (Online)*. 349.

WHO/FAO Expert Consultation 2003. Diet, nutrition and the prevention of chronic diseases. *World Health Organ Tech Rep Ser* 2003;916:1-149.

WHO, World Health Organisation (2015) Obesity and overweight fact sheet. <http://www.who.int/mediacentre/factsheets/fs311/en/> (accessed June 2015)

Willett W. 2013. *Nutritional Epidemiology*, pp. 1-552.

Wolf-Maier K, Cooper RS, Banegas JR, Giampaoli S, Hense HW, Joffres M, Katarinen M, Poulter N, Primatesta P, Rodríguez-Artalejo F et al. 2003. Hypertension Prevalence and Blood Pressure Levels in 6 European Countries, Canada, and the United States. *Journal of the American Medical Association*. 289(18):2363-2369.

Yumuk V, Tsigos C, Fried M, Schindler K, Busetto L, Micic D, Toplak H. 2015. European Guidelines for Obesity Management in Adults. *Obesity Facts*. 8(6):402-424.

Study 4

Long-term effect of a low glycaemic index diet and a high cereal fibre diet on BMI in overweight and obese with type 2 diabetes

Marta Cossu¹, Laura Chiavaroli^{2,3}, Arash Mirrahimi^{3,4}, Christopher Ireland^{2,3}, Sandra Mitchell^{2,3}, Sandhya Sahye-Pudaruth^{2,3}, Judy Coveney³, Darshna Patel^{2,3}, Russell J de Souza^{3,7}, Livia SA Augustin^{3,8}, Balachandran Bashyam^{2,3}, Sonia Blanco Mejia^{2,3}, Stephanie K Nishi^{2,3}, Lawrence A Leiter^{2,9}, Robert G Josse^{2,9}, Gail McKeown-Eyssen¹⁰, Alan Moody^{5,6}, Alan R Berger¹¹, Cyril WC Kendall^{3,12}, John L Sievenpiper^{2,3}, David JA Jenkins^{2,3}

¹Department of Food and Drug, University of Parma; ²Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; ³Clinical Nutrition and Risk Factor Modification Center, St. Michael's Hospital, Toronto, Ontario, Canada; ⁴Faculty of Health Sciences, School of Medicine, Queen's University, Kingston, Ontario, Canada; ⁵Department of Medical Imaging, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; ⁶Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada; ⁷Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada; ⁸National Cancer Institute "Fondazione G. Pascale", Naples, Italy; ⁹Division of Endocrinology and Metabolism, St. Michael's Hospital, Toronto, Ontario, Canada; ¹⁰Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; ¹¹Department of Ophthalmology, St. Michael's Hospital, Toronto, Ontario, Canada; ¹²College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

Introduction

The number of people with type 2 diabetes (T2D) is growing rapidly worldwide. The International Diabetes Federation predicts major growth in the global T2D prevalence from 415 million in 2015 to 642 million in 2040 (IDF 2015). The exact causes for the development of T2D are still unknown. Nevertheless, elevated blood glucose concentration, excess body weight, physical inactivity and poor nutrition have been recognised as modifiable risk factors (IDF 2015).

Changes to lifestyle, including adopting a specific dietary pattern, such as Mediterranean diet, low glycaemic index (GI) diet, or vegetarian diet, and increasing physical activity, have been recognized as effective at reducing the incidence of T2D in those at high risk and improving glycaemic control and blood lipids in those with diabetes (Knowler et al. 2002; Ley et al. 2014).

The prevalence of T2D is higher in obese compared to normal-weight adults. Excess body weight is associated with an increase in insulin resistance and blood glucose level, higher risk of hypertension, dyslipidaemia and cardiovascular disease, the latter of which is a major cause of death in those with T2D (Klein et al. 2004). Modest weight loss of about 5% of total body weight is recommended for overweight and obese people with T2D as it has been demonstrated to improve glycaemic control, insulin action and reduce the need for diabetes medications (Klein et al. 2004).

Although the consumption of low GI foods, whole grain products and a high intake of dietary fibre have been shown to be effective in the prevention and management of T2D (Brand-Miller et al. 2003; De Munter et al. 2007), their effect on body weight is not clear.

There is some evidence that the consumption of low GI foods may be beneficial for weight control. Some hypotheses suggest the mechanism may be within the ability of low GI foods to

promote satiety and delay hunger, to reduce fluctuations in glycaemia and insulinemia and promote higher rates of fatty acid oxidation (McMillan-Price and Brand-Miller 2006). While some reviews of low GI intervention studies have found no effect on satiety, hunger and food intake compared with high GI foods (Raben 2002), others have found convincing evidence of an increase in satiety (Bornet et al. 2007). Another review showed that acute studies demonstrate a more supportive effect of low GI foods on appetite control compared to long-term studies (Blaak et al. 2012).

In a meta-analysis of randomized control trials, Thomas and colleagues found that low GI and low GL diets were associated with greater weight loss in overweight and obese when compared to higher GI or GL diets or conventional weight loss diets (Thomas et al. 2007). Conversely, in a recent 6-month randomized controlled trial, there was no difference between the low GI and high GI diet on body mass index (BMI), although the low GI diet resulted in a more pronounced reduction compared to the low-fat diet in overweight and obese adults (Juanola-Falgarona et al. 2014). The 6-month DIOGENES study, however, showed a positive effect of a low GI diet in reducing weight regain after weight loss. Although the 12 month-follow up analyses no longer demonstrated a significant effect of GI, this may be because the data were based on only 2 of the 6 sites and food was no longer provided as it was in the first 6-months, possibly resulting in a reduction in compliance (Larsen et al. 2010; Aller et al. 2014).

Similarly, the consumption of whole grain products could have a positive effect on weight regulation by promoting satiety. The proposed mechanism is related to the dietary fibre content that influences food volume and energy density, may delay gastric emptying and suppress the glycaemic response (Pereira and Ludwig 2001). Observational studies have demonstrated that a high intake of dietary fibre, especially cereal fibre, and whole grain products is inversely associated with weight gain (Liu et al. 2003; Du et al. 2010). However, dietary intervention

studies have yielded mixed results. Recent systematic review and meta-analyses of randomized control trials have found no effect of dietary fibre and whole grain consumption on body weight (Pol et al. 2013), whereas another find that higher consumption of whole grain, compared to rare or never consumption, is associated with less weight gain (Ye et al. 2012).

The evidence suggesting a beneficial effect of low GI foods and high intake of dietary fibre on body weight control and management are mostly observational studies or short-term trials. Thus, the aim of the present study is to investigate if following a low GI diet or a high cereal fibre diet over a long term (3 years) results in weight reduction and the subsequent weight loss maintenance in overweight and obese adults with T2D.

Methods

Design of the study

Data were obtained from a randomized controlled, parallel, dietary intervention trial assessing the effect of GI on vascular disease in T2D over 3 years. The study was conducted at the Risk Factor of Modification Centre, St. Michael's Hospital, Toronto, Canada. Details of the study protocol have been previously published (Chiavaroli et al. 2016). Briefly, 169 participants were recruited and randomized to either a low GI diet (LGI) or a high-cereal fibre diet (HCF). During the 3 years, participants attended clinic visits every 3 months where 7-day dietary food records were obtained and reviewed by the dieticians in the presence of the participant. Every 3 months, anthropometric measures and blood samples were taken. The effect of the two diets on macrovascular and microvascular disease markers were also evaluated. Macrovascular disease was investigated by means of magnetic resonance imaging (MRI) and 2-D and 3-D carotid ultrasound scanning (CUS) of the carotid arteries. MRI and CUS were performed 3 times during the study (baseline, year 1 and year 3). Microvascular disease measures included assessments

of eye and kidney health through eye examinations and retinal photography and 24-hour urine collections, performed at baseline and years 1 and 3.

Participants

For this analysis only participants who were overweight or obese ($\text{BMI} \geq 25\text{kg/m}^2$) at baseline were considered ($n=55$ in the LGI diet and $n=55$ in the HCF diet). All participants had a diagnosis of T2D > 6 months prior to the start of the study, a glycated haemoglobin A1c (HbA1c) between 6.5% and 8.0% at screening, were on oral antidiabetic agents at a stable dose for ≥ 8 weeks, not on insulin, without gastrointestinal disease, clinically significant liver disease or history of cancer, and had not had a major cardiovascular event or major surgery in the past 6 months.

Dietary intervention

Participants were randomized to receive either dietary advice on a low GI or a high-cereal fibre diet. The low GI diet emphasized products such as steel cut or large flake oats, hot oatbran cereal, a specifically formulated low GI oat bran bread, parboiled rice, pasta, pulses/legumes and low GI temperate climate fruits (e.g. apples, oranges and berries). The high-cereal fibre group were encouraged to consume wholegrain products, including whole wheat bread, wheat fibre cereals, cream of wheat hot cereal, brown rice and tropical fruits (e.g. bananas, mangos and pineapples). Details of the recommended foods for the LGI and HCF diets are reported as supplemental material.

Biochemical and dietary analysis

The HbA1c value was analysed within 24 hours using whole blood collected in EDTA Vacutainer tubes (Vacutainer; Becton, Dickinson and Co) in the hospital routine analytical

laboratory by a turbidimetric inhibition latex immunoassay (TINIA Roche Diagnostics) with a coefficient of variation between assays of 3–4%. Blood glucose and serum lipid levels were also measured in the hospital routine analytical laboratory using a Random Access Analyzer and Beckman reagents (SYNCHRON LX Systems; Beckman Coulter), with a coefficient of variation of 1.6–2.3% for blood glucose level and 1.3– 3.0% for total cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C) levels. The low-density lipoprotein cholesterol (LDL-C) level was calculated by the method of Friedewald and colleagues (Friedewald et al. 1972) ($LDL-C \text{ level} = \text{total-C} - [(\text{triglycerides}/5) \times (\text{HDL-C level})]$).

Dietary assessments using participant completed 7-day food records were analysed using a computer program (ESHA Food Processor SQL V.10.9; ESHA, Salem, Oregon, USA) based on the USDA database, supplemented with data from the Canada Nutrient File, and with GI values from international GI tables (Atkinson et al. 2008). Glycaemic load (GL) was calculated as $GI \times \text{available carbohydrate} \div 100$. Product data were updated with manufacturers' nutrient information and relevant foods were analysed by Covance Laboratories (3301 Kinsman Blvd, Madison Wisconsin, USA).

Statistical analysis

Anthropometric data, blood parameters, and energy and nutrient intakes were expressed as mean \pm standard deviation (SD) or as mean \pm standard error of the mean (SEM) by treatment groups. Normality of data distribution was verified through the Kolmogorov-Smirnov tests and not normally distributed variables (blood parameters) were transformed using the natural logarithm (ln). The effect of time, treatment, and time x treatment, and of time by treatment groups on change in BMI was assessed using a repeated measure ANOVA model and a repeated measure ANCOVA model adjusted for gender and age, testing the sphericity through the

Mauchly's test and when violated using the corrected value with Greenhouse–Geisser if epsilon was lesser than 0.75 or Huynh–Feldt if epsilon was greater than 0.75. In addition, Bonferroni post-hoc tests were used for multiple comparisons if there was a main effect of time. Similarly, a repeated measure ANOVA model was used to assess the effect of time by treatment groups for all other variables, using Bonferroni post-hoc pairwise comparisons. Between-group differences were explored, after checking for the homogeneity of the variance through Levene's test, using an independent-samples T-student test at each time point. A P-value <0.05 was considered statistically significant. All statistical analyses were performed with IBM SPSS 24.0 Statistics (IBM SPSS, Inc., Chicago, IL, USA).

Results

Baseline characteristics of the participants are reported in Table 1. The mean age of the participants was 62±8 (43-82y), and 63±6 (50-76y) in the LGI and HCF diet groups, respectively. Of the participants, 61.5% were male in the LGI diet and 60.0% were male in the HCF diet. The mean body weight was 88.2±16.2 kg in the LGI diet and 84.9±13.4 kg in the

	LGI	HCF
Sex		
Male	40	33
Female	25	22
Age, year	62±8	63±6
Body weight, kg	88.2±16.2	84.9±13.4
BMI, kg/m²	31.2±4.7	30.2±4.5
Fasting glucose, mmol/L	7.7±1.6	7.3±1.7
HbA1c, %	7.1±0.6	7.1±0.5
Lipids, mmol/L		
Total cholesterol	3.9±1.0	4.0±1.0
LDL-C	2.1±0.8	2.2±0.9
HDL-C	1.1±0.3	1.2±0.3
Triglycerides	1.6±1.0	1.5±1.1

Table 1. Baseline characteristics of study participants (Mean±SD). BMI, body mass index; HbA1c, glycated haemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

HCF diet. Participants in the LGI diet group had a mean BMI of 31.2 ± 4.7 kg/m², whereas in the HCF group the mean BMI was 30.2 ± 4.5 kg/m².

At baseline, the nutritional composition of the diet of the two groups was similar (Table 2). The caloric intake was ~ 1800 kcal from which ~ 47% was from carbohydrates, ~ 34% from fat, ~ 19% from protein. The fibre intake was ~ 15g/1000 kcal. The baseline mean GI of the diet in both groups was ~ 56, with a range from 42 to 63, which falls in the low-medium GI (glucose scale). The mean GL of the diet was ~ 103 (40-224) for both groups.

	LGI	HCF
Calories, kcal	1781±516	1817±417
Carbohydrate, % of E	48±7	47±8
Sugar, % of E	15±5	15±5
Fat, % of E	34±7	34±6
Protein, % of E	19±3	19±4
Fibre, g/1000 kcal	15±5	14±5
Glycaemic index	56±4	56±4
Glycaemic load	103±33	103±29

Table 2. *Nutritional composition of the study participants at baseline (Mean ±SD).*

BMI changes

The changes in BMI over the 3 years are reported in Figure 1.

At the end of the 3 years, participants assigned to either the LGI or HCF diet, had a BMI reduction of 0.9 ± 1.3 kg/m². In the HCF diet, participants had an initial reduction in BMI, which was maintained over the 3 years. Contrarily, participants assigned to the LGI diet had a BMI reduction at 9 months of -1.3 ± 1.3 kg/m², that was twice as low compared to that in the HCF group (-0.6 ± 1.1 kg/m²).

There was a main effect of time ($P=0.000$) and time x treatment ($P=0.002$) on BMI change that was significantly different at each time point compared to baseline ($P<0.005$ for all). A main effect of time x treatment on BMI change was observed also after adjusting for age ($P=0.002$).

The mean BMI reduction was significantly different between the two groups at 3 months (-1.14 ± 1.00 kg/m² and -0.63 ± 0.81 kg/m² in the LGI and HCF group respectively; $P=0.003$), after 6 months (-1.34 ± 1.34 kg/m² and -0.69 ± 1.07 kg/m² in the LGI and HCF group respectively; $P=0.004$), and at 9 months (-1.31 ± 1.33 kg/m² and -0.62 ± 1.09 kg/m² in the LGI and HCF group respectively; $P=0.002$). After 9 months the BMI changes were no longer significantly different between the groups at any time point over the 3 years ($P>0.05$).

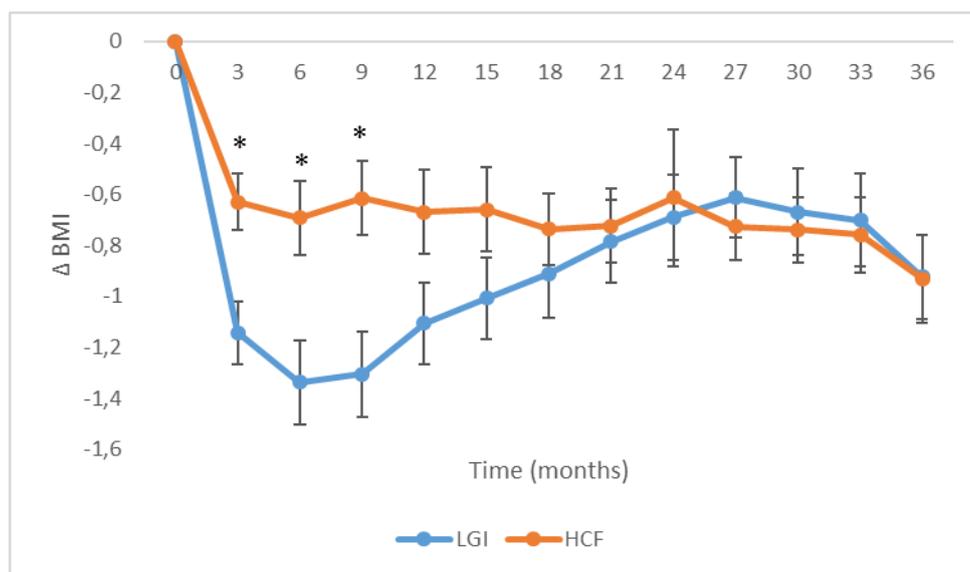


Figure 1. BMI changes over 3 years (mean \pm SEM). * $P<0.05$, comparison between LGI and HCF groups.

Within the LGI and HCF diet groups, there was a main effect of time on BMI change ($P=0.000$ and $P=0.005$, respectively).

In the LGI group, the BMI change was significantly different compared to baseline at each time point ($P<0.05$ for all). The change in BMI at 6 months was greater and significantly different

compared to that at 21 (P=0.019), 24 (P=0.005), 27 (P=0.005), and 30 months (P=0.039). Similarly, at 9 months the change in BMI was greater and significantly different when compared to 18 (P=0.017), 21 (P=0.001), 24 (P=0.000), 27 (P=0.001) and 30 months (P=0.013). At 12 months, the change in BMI was greater and significantly different compared to 24 and 27 months (P=0.039 and P=0.032, respectively).

In the HCF diet group, the BMI change was different at each time point (P<0.02 for all), except at 24 months (P>0.05), compared to baseline only.

After adjusting for sex, there was still a main effect of time on BMI change in the LGI (P=0.000) and HFC diet groups (P=0.002).

Blood parameters

The 3-year values of the blood parameters are showed in Figure 2. The comparison between the LGI and HCF diet groups at each time point showed that there was a significant difference in HbA1c after 3 months (6.6±0.6 % and 6.9±0.6 % in LGI and HCF groups, P=0.010), 6 months (6.5±0.7 % and 6.9±0.6 % in LGI and HCF groups, P=0.010) and 9 months (6.6±0.7 % and 6.9±0.7 % in LGI and HCF groups, P=0.006). HDL-C values between the groups were significantly lower in the LGI group over the 3 years including at baseline (P<0.05), except at 9, 12 and 21 months (P>0.05). Triglycerides were significantly higher in the LGI compared to HCF group at 24 months (P=0.023), 30 months (P=0.038), and 36 months (P= 0.037). No differences were found for fasting glucose, total cholesterol and LDL-C (P>0.05).

Within the LGI diet group, there was a main effect of time on HbA1c (P<0.001), fasting glucose (P<0.001) and triglycerides (P=0.008). HbA1c was lower and significantly different only at 3, 6, 9 months (P<0.001 for all) and 12 months (P=0.001) compared to baseline.

At 3 months, HbA1c was lower and significantly different compared to the study period from 21 to 36 months ($P < 0.001$ for all), whereas at 6 months, it was lower also compared to 15 months ($P = 0.008$) and 18 months ($P = 0.011$). HbA1c at 9 months was lower and significantly different compared to 15 months ($P = 0.013$) and from 21 to 36 months ($P < 0.001$ for all). At 12 months, HbA1c was lower and different compared to 21 and 24 months ($P = 0.010$ and $P < 0.001$, respectively), 33 months ($P = 0.006$) and 36 months ($P = 0.001$).

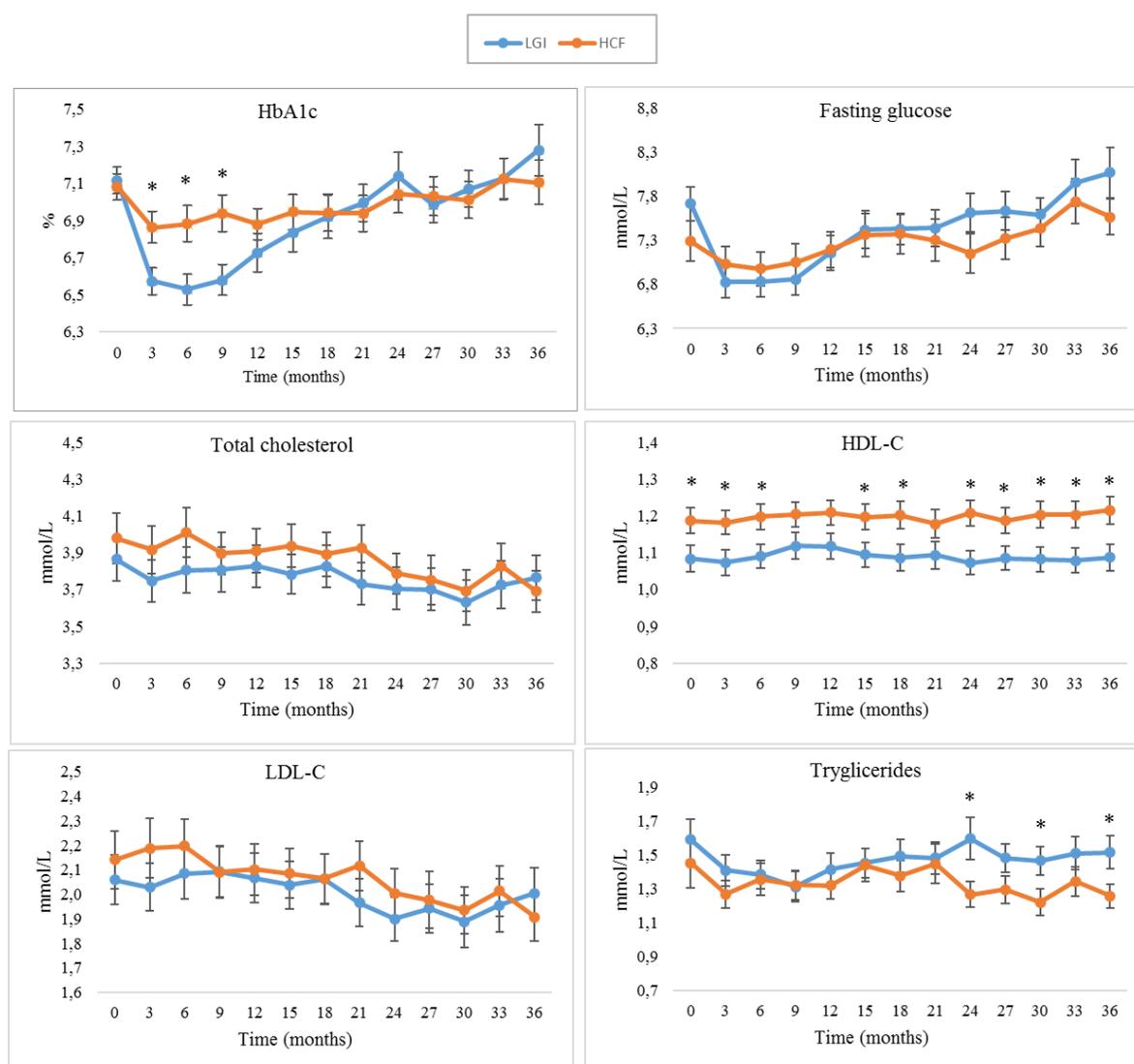


Figure 2. 3-year blood parameters values (mean ± SEM). * $p < 0.05$, comparison between LGI and HCF groups. HCF, high cereal fiber diet; LGI, low glycemic index diet; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

Fasting glucose was different at 3, 6 (P=0.001) and 9 months (P=0.012) compared to baseline. At 3 and 6 months fasting glucose was lower and different compared to 18-36 months (P<0.02 for all), whereas at 12 months was different from 33 and 36 months (P=0.021 and P=0.005, respectively). Triglycerides were lower and significantly different at 9 months compared to 24 months (P=0.019).

Within HCF group, there was a main effect of time on fasting glucose (P=0.006), total cholesterol (P=0.005), LDL (P=0.012) and triglycerides (P=0.026). Fasting glucose was lower and significantly different at 6 months compared to 33 months (P=0.033); at 6 months, total cholesterol and LDL were higher compared to 36 months (P=0.009 and P=0.011, respectively). Triglycerides at 15 months was higher and different compared to 30 months (P=0.028).

Dietary intake

The 3-year dietary intakes are graphically reported in Figure 3 for each diet group. There were no significant differences in caloric intake, % of calories from carbohydrate, protein and sugar between the two groups. Participants in the LGI group reduced the GI of the diet by ~9 units, whereas in the HCF group there was a GI increase of ~2 units. The GI of the diet was significantly different between the groups at each time point (P=0.000), as well as the GL (P=0.000).

There was an increase in dietary fibre intake. Participants' average intake was 22 g/1000 kcal and 19 g/1000 kcal in the LGI and HCF, respectively, over the 3 years. The fibre intake was significantly different between the groups at each time point (P<0.05), except at 21 months (P=0.064).

Within the LGI diet group, there was a main effect of time on caloric intake, % of calories from protein, total fibre intake (g/1000kcal), GI and GL (P<0.001 for all). The caloric intake was

lower and significantly different at 3 ($P=0.002$), 6 ($P=0.015$), 9 ($P=0.025$), 18 and 21 ($P=0.005$) and 30 months ($P=0.007$). The % of calories from protein and the total fibre intake was higher and significantly different at each time point compared to baseline ($P<0.001$ for all). The GI and GL of the diet were lower and significantly different at each time point compared to baseline ($P<0.001$).

Within the HCF diet group, there was a main effect of time on caloric intake ($P=0.000$), % of calories from fat ($P=0.008$) and protein ($P=0.013$), GI ($P=0.013$) and total fibre intake ($P<0.001$). Caloric intake was lower from 18 to 36 months when compared to baseline ($P<0.05$ for all). The % calories from fat was lower and significantly different at 12 ($P=0.002$) and 33 months ($P=0.001$) compared to baseline, whereas that from protein was higher at 15 months compared to baseline ($P=0.007$). The GI of the diet was higher at 12 ($P=0.042$) and 24 months ($P=0.001$) compared to baseline. The total fibre intake was higher and significantly different at each time point compared to baseline ($P<0.05$ for all).

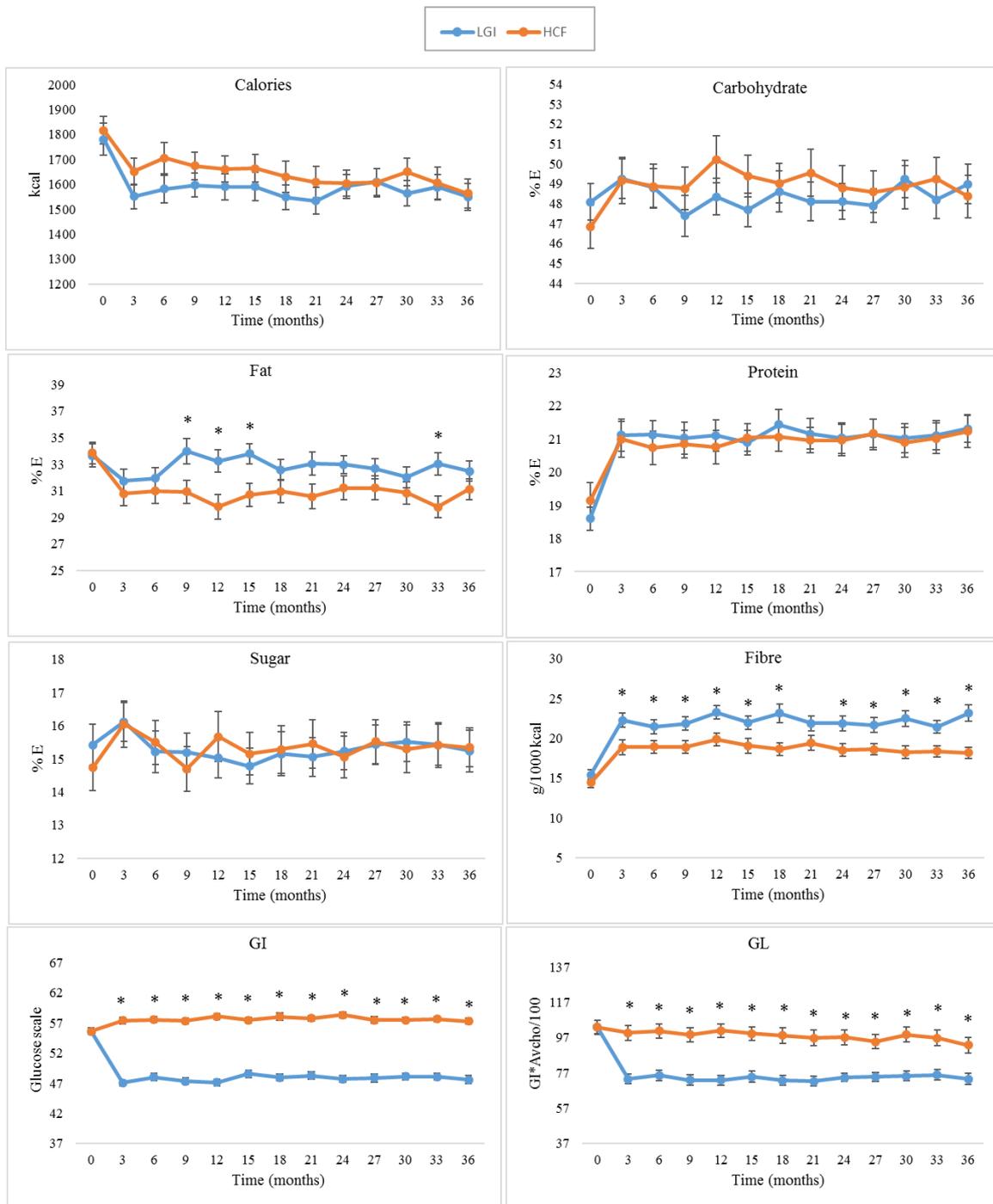


Figure 3. 3-year dietary intake (mean ± SEM). * $p < 0.05$, comparison between LGI and HCF groups. GI, glycemic index; GL, glycemic load.

Discussions and conclusions

This study aimed to investigate if a low GI diet or a high cereal fibre diet could be effective in long-term BMI reduction in overweight and obese adults with T2D. Participants in both dietary treatment groups received intense counselling and dietary advice without any restriction in term of calories, hence the consumption of the recommended foods was ad libitum. Both dietary treatments were characterised by consumption of high-quality carbohydrate foods, such as oat-containing products, parboiled rice, pasta and pulses/legumes, in the LGI diet and wholegrain products in the HCF diet.

Our findings showed that a LGI diet and a HCF diet were both effective in reducing the BMI of participants over the 3 years. In the short-term (0-9 months), the LGI diet resulted in a greater BMI reduction compared to the HCF diet. In the LGI group there was a decrease in the GI of the diet of ~10 units compared to baseline and a greater increase in fibre intake compared to the HCF group. The greater reduction in BMI in the first year of the LGI diet compared to the HCF diet group may be due to the ability of both low GI foods and higher dietary fibre to increase satiety (Bornet et al. 2007; Zijlstra et al. 2008).

During the 3 years, participants in both diets significantly increased their fibre intake compared to baseline. However, the consumption of high cereal fibre products was not as effective as the LGI diet in increasing the intake of fibre. In the two diets, the type of fibre consumed was different, and in particular the products in the LGI diet were high in soluble/viscous fibre, whereas the HCF diet was rich in insoluble fibre. Wanders and colleagues, in a systematic review of randomized controlled trials, found that viscous fibres were more effective in reducing appetite than those less viscous. However, their effects on energy intake and body weight were relatively small (Wanders et al. 2011).

To our knowledge, there are no other ad libitum dietary intervention studies of this duration. Nevertheless, our results are in agreement with other studies in which a diet characterized by low GI foods and/or wholegrain products is effective in reducing body weight (Larsen et al. 2010; Juanola-Falgarona et al. 2014).

The consumption of low GI foods and wholegrain products has been previously associated, in both intervention studies and observational studies, with an improvement in blood lipids (Bouché et al. 2002; Liu 2002; Sloth et al. 2004; Ajala et al. 2013). In our study, there was a main effect of time in total cholesterol and LDL-C reduction in the HCF group. However, we did not find any significantly change over time or difference between the LGI and HCF groups.

For both treatments, a trend in improvement in glycaemic control in the short-term (0-9 months) was observed, measured as fasting glucose and HbA1c. Participants in the LGI diet had a significant reduction in HbA1c levels compared to baseline, whereas those assigned to HCF diet did not. The short-term effect of a LGI vs. a HCF diet on lowering HbA1c levels has been previously reported (Jenkins et al. 2008). The increase in HbA1c back to initial levels after 1-year could be a consequence of regaining body weight, which also began to occur around the 1-year time point of the trial.

A strength of this study was the continuous counselling by dietitians over the 3 years and the use of participant completed 7-day food records every 3 months. Additionally, many foods recommended in the study were specifically tested for their GI, thus allowing for the most accurate GIs of the recommended foods to be available. A limitation of this study is the possible reduction in adherence to the diets over time and possibly a slacking in dietary recording, since in the LGI group, after 9 months, there was an increase in BMI despite the reported caloric intake not changing over the 3 years.

In conclusion, ad libitum consumption of a LGI and HCF diet resulted in an effective BMI reduction over 3 years, in overweight and obese adults with type 2 diabetes. Low GI diets in the short-term may be more effective at reducing BMI compared to a high cereal fibre diet.

Supplemental material

Foods for Low GI Diet

		Choose	Portion Size	AVOID
(_____) servings	Pulses	Beans -red, navy etc. Lentils – red, green Chick peas	½ c cooked or canned	
	Breads	Stonemill™ 3 Grain Bread Dempster's™ Ancient Grains Tortilla Clinic Oatbran Bread	1 slice 1 small Tortilla 1x ½ inch slice (65g)	All other breads Bagel, pita, tortilla, buns, rolls
	Cereal	Red River Cereal Oatmeal (large flake, steel cut) Oat Bran Kellogg's™ All Bran Buds with Psyllium	2 Tbsp. dry 1/3 c dry “ 1/3 c	All other cereal Instant oatmeal Pancakes, muffins, donuts
	Other Starchy Food	Pasta (al dente) Parboiled rice Bulgur Barley Quinoa	1/3 c cooked 1/3 c cooked ½ c cooked “ “	potatoes – baked, mashed, French fries White, brown rice Basmati rice Rice noodles Crackers, cookies
3 servings	Fruits	Apple Orange Blueberries, Raspberries Strawberries	1 small 1 1 cup 1.5 cups	Ripe banana Grapes, raisins Pineapple, mango Papaya, melon Canned fruit
5 or more servings	Vegetab les	All, especially eggplant, okra and zucchini, except potato	½ cup	potato
3 servings	Dairy	Low fat, low sugar yogurt Skim or 1% milk Soy Beverage, fortified Hard cheese <15%mf	1 cup 1 cup 1 cup 1 ½ oz. (45 g)	Cream, ice cream, Cheese > 15%mf
2 servings	Meat, fish and alternat es	Lean meat, poultry, fish, Soy, tofu, seitan Nuts (almonds, walnuts ...) Egg	2-3 oz. (60-90g) (deck of cards) 60-90g 10 1-2	Fatty meats, sausage
	Snacks, desserts	Fruit, vegetables Nuts yogurt	As listed above	Crackers, Cakes, cookies Chips, popcorn
	Spreads	Soft Margarine Peanut butter, natural Jam (reduced sugar) Low fat cottage cheese/ricotta Red pepper spread, Guacamole, hummus	1 tsp. 1 Tbsp. 1 tsp	Jam with sugar butter
	Drinks	Water, tea, coffee Sugar-free drinks, Vegetable juice (low salt)		Fruit juice Regular pop

Foods for High Fibre Diet

		Choose	Portion Size	AVOID
(— servings)	Breads	whole wheat breads or bagels, wheat Bran, Ryvita, Finn Crisp crackers	1 slice (40g) 3	White - bread, bagels, pita, buns
	Cereal	Bran flakes, Corn Bran, Fibre 1 Weetabix, Shredded Wheat Cream of wheat	$\frac{3}{4}$ cup 1 biscuit 2 Tbsp. dry	Pancakes, muffins, donuts Oatmeal, Red River, Bran buds
	Other Starchy Food	Potatoes – baked, boiled Brown rice Whole wheat Couscous	$\frac{1}{2}$ cup 1/3 cup 1/3 cup	French fries Pasta, Barley Beans/lentils/chickpeas
3 servings	Fruits	Banana Grapes Pineapple Mango, Papaya Watermelon Cantaloupe, honeydew Raisins guava	$\frac{1}{2}$ large, 4” 15 $\frac{3}{4}$ cup $\frac{1}{2}$ fruit 1 $\frac{1}{2}$ cups 1 cup cubed mini box 1 $\frac{1}{2}$	Apples, Pears Oranges, Citrus fruits Peaches All berries
5 servings or more	Vegetables	All vegetables except >	$\frac{1}{2}$ cup	Beans, lentils, chickpeas
3 servings	Dairy	Low fat yogurt Skim or 1% milk, soy beverage Hard cheese < 15% MF	1 cup 1 cup 45 g	Cream, Ice cream, Cheese (>15% MF)
2 servings	Meat, fish and alternates	Lean meat, poultry, fish Soy, Tofu, seitan egg	2-3 oz. (60-90g) 60-90g 1-2	Fatty meats, sausage nuts
	Snacks and Desserts	Raw vegetables (from list) WW bread with listed spreads Low fat plain yogurt	No limit 1 slice 1 cup	White crackers Potato chips Corn/tortilla chips Cakes/cookies/wafers Nuts
	Spreads	Soft margarine, Jam (low sugar) Low-fat cottage/ricotta cheese Red pepper spread Guacamole (avocado spread)	1 tsp. 1 tbsp	Jam with sugar Hummus Butter Peanut butter
	Drinks	Water, tea, coffee Sugar-free drinks Vegetable juice (low salt)		Fruit juice Regular soft drinks

References

- Ajala O, English P, Pinkney J. 2013. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes 1-3. *American Journal of Clinical Nutrition*. 97(3):505-516.
- Aller EEJG, Larsen TM, Claus H, Lindroos AK, Kafatos A, Pfeiffer A, Martinez JA, Handjieva-Darlenska T, Kunesova M, Stender S et al. 2014. Weight loss maintenance in overweight subjects on ad libitum diets with high or low protein content and glycemic index: The DIOGENES trial 12-month results. *International Journal of Obesity*. 38(12):1511-1517.
- Atkinson FS, Foster-Powell K, Brand-Miller JC. 2008. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care*. 31(12):2281-2283.
- Blaak EE, Antoine JM, Benton D, Björck I, Bozzetto L, Brouns F, Diamant M, Dye L, Hulshof T, Holst JJ et al. 2012. Impact of postprandial glycaemia on health and prevention of disease. *Obesity Reviews*. 13(10):923-984.
- Bornet FRJ, Jardy-Gennetier AE, Jacquet N, Stowell J. 2007. Glycaemic response to foods: Impact on satiety and long-term weight regulation. *Appetite*. 49(3):535-553.
- Bouché C, Rizkalla SW, Luo J, Vidal H, Veronese A, Facher N, Fouquet C, Lang V, Slama G. 2002. Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care*. 25(5):822-828.
- Brand-Miller J, Hayne S, Petocz P, Colagiuri S. 2003. Low-glycemic index diets in the management of diabetes: A meta-analysis of randomized controlled trials. *Diabetes Care*. 26(8):2261-2267.
- Chiavaroli L, Mirrahimi A, Ireland C, Mitchell S, Sahye-Pudaruth S, Coveney J, Olowoyeye O, Maraj T, Patel D, De Souza RJ et al. 2016. Low-glycaemic index diet to improve glycaemic control and cardiovascular disease in type 2 diabetes: Design and methods for a randomised, controlled, clinical trial. *BMJ Open*. 6(7).
- De Munter JSL, Hu FB, Spiegelman D, Franz M, Van Dam RM. 2007. Whole grain, bran, and germ intake and risk of type 2 diabetes: A prospective cohort study and systematic review. *PLoS Medicine*. 4(8):1385-1395.
- Du H, Van Der A DL, Boshuizen HC, Forouhi NG, Wareham NJ, Halkjær J, Tjønneland A, Overvad K, Jakobsen MU, Boeing H et al. 2010. Dietary fiber and subsequent changes in body weight and waist circumference in European men and women. *American Journal of Clinical Nutrition*. 91(2):329-336.
- Friedewald WT, Levy RI, Fredrickson DS. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*. 18(6):499-502.

IDF. 2015. IDF Diabetes Atlas (7th Edition). International Diabetes Federation. <http://www.idf.org/diabetesatlas>.

Jenkins DJA, Kendall CWC, McKeown-Eyssen G, Josse RG, Silverberg J, Booth GL, Vidgen E, Josse AR, Nguyen TH, Corrigan S et al. 2008. Effect of a low-glycemic index or a high-cereal fiber diet on type 2 diabetes: A randomized trial. *JAMA - Journal of the American Medical Association*. 300(23):2742-2753.

Juanola-Falgarona M, Salas-Salvadó J, Ibarrola-Jurado N, Rabassa-Soler A, Díaz-López A, Guasch-Ferré M, Hernández-Alonso P, Balanza R, Bulló M. 2014. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: A randomized controlled trial. *American Journal of Clinical Nutrition*. 100(1):27-35.

Klein S, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, Clark NG. 2004. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: Rationale and strategies - A statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. *Diabetes Care*. 27(8):2067-2073.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM. 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*. 346(6):393-403.

Larsen TM, Dalskov SM, Van Baak M, Jebb SA, Papadaki A, Pfeiffer AFH, Martinez JA, Handjieva-Darlenska T, Kunešová M, Pihlsgård M et al. 2010. Diets with high or low protein content and glycemic index for weight-loss maintenance. *New England Journal of Medicine*. 363(22):2102-2113.

Ley SH, Hamdy O, Mohan V, Hu FB. 2014. Prevention and management of type 2 diabetes: Dietary components and nutritional strategies. *The Lancet*. 383(9933):1999-2007.

Liu S. 2002. Intake of Refined Carbohydrates and Whole Grain Foods in Relation to Risk of Type 2 Diabetes Mellitus and Coronary Heart Disease. *Journal of the American College of Nutrition*. 21(4):298-306.

Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. 2003. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *American Journal of Clinical Nutrition*. 78(5):920-927.

McMillan-Price J, Brand-Miller J. 2006. Low-glycaemic index diets and body weight regulation. *International Journal of Obesity*. 30:S40-S46.

Pereira MA, Ludwig DS. 2001. Dietary fiber and body-weight regulation: Observations and mechanisms. *Pediatric Clinics of North America*. 48(4):969-980.

- Pol K, Christensen R, Bartels EM, Raben A, Tetens I, Kristensen M. 2013. Whole grain and body weight changes in apparently healthy adults: A systematic review and meta-analysis of randomized controlled studies. *American Journal of Clinical Nutrition*. 98(4):872-884.
- Raben A. 2002. Should obese patients be counselled to follow a low-glycaemic index diet? No [Review]. *Obesity Reviews*. 3(4):245-256.
- Sloth B, Krog-Mikkelsen I, Flint A, Tetens I, Björck I, Vinoy S, Elmståhl H, Astrup A, Lang V, Raben A. 2004. No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *American Journal of Clinical Nutrition*. 80(2):337-347.
- Thomas DE, Elliott EJ, Baur L. 2007. Low glycaemic index or low glycaemic load diets for overweight and obesity. *Cochrane Database of Systematic Reviews*.(3).
- Wanders AJ, van den Borne JJGC, de Graaf C, Hulshof T, Jonathan MC, Kristensen M, Mars M, Schols HA, Feskens EJM. 2011. Effects of dietary fibre on subjective appetite, energy intake and body weight: A systematic review of randomized controlled trials. *Obesity Reviews*. 12(9):724-739.
- Ye EQ, Chacko SA, Chou EL, Kugizaki M, Liu S. 2012. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. *Journal of Nutrition*. 142(7):1304-1313.
- Zijlstra N, Mars M, De Wijk RA, Westerterp-Plantenga MS, De Graaf C. 2008. The effect of viscosity on ad libitum food intake. *International Journal of Obesity*. 32(4):676-683.

Chapter 4

General conclusions

The aim of this Doctoral Thesis was to better understand the relation between carbohydrates and health, given a main focus on glycaemic index (GI) as a quality parameter, with the final goal to identify the best dietary choices for the population.

Two studies were performed for testing GIs of mixed meals for evaluating foods as consumed in a real-life scenario. Two studies were performed for evaluating the effects of high quality carbohydrates in the framework of intervention diets in patients with metabolic dysfunctions (obese or with diabetes), with the final aim of weight reduction.

The following general conclusion can be obtained.

- ❖ ***A nutritional evaluation of various typical Italian breakfast products: a comparison of macronutrient composition and glycaemic index values.*** The substitution of commonly consumed Italian breakfast items, such as cakes, pastries, and cookies, which are classified as low-medium GI, but are high in saturated fat and sugar and low in fibre, with other low-GI, low-saturated fat breakfast alternatives might represent a viable strategy for the population to meet the recommendations for nutritional intakes, and possibly help target obesity, reducing the risk of chronic diseases.

- ❖ ***The importance of glycaemic index in the context of the addition of fat to carbohydrate foods: A randomized controlled trial on spaghetti versus rice as mixed meals.*** The difference in postprandial glycaemic response and GI between a low GI foods (spaghetti) and a higher GI food (rice) was preserved when tomato sauce and olive oil were added as a source of fat, but not after the addition of pesto, where the quantity of fat was higher. However, lowering the postprandial response with the addition of fat, which lead to an increase in energy, should not be considered as a viable strategy.

- ❖ ***Pasta consumption in the context of a hypocaloric diet: a dietary intervention study in obese patients.*** A hypocaloric regimen, in accordance with the principle of the Mediterranean diet, and where food preferences and the habitual diet were considered and preserved, was a valuable strategy to improve patients' adherence to a healthier diet, and was effective in reducing body weight over 6 months, as well as to improve glycaemic control and blood lipid profile.

- ❖ ***Long-term effect of a low glycaemic index diet and a high cereal fibre diet on BMI in overweight and obese with type 2 diabetes.*** Ad libitum consumption of a low GI diet or ad libitum consumption of a high cereal fibre diet resulted effective in BMI reduction in a 3-year dietary intervention study. In the short period, the low GI diet induced a more relevant reduction in BMI, and a greater benefit on glycaemic control, as proved by a significant reduction of the levels of HbA1c and of fasting glucose, when compared to the high cereal fibre diet.

In conclusion, the findings of this Doctoral Thesis contribute to shed light on the importance of selecting high quality carbohydrate foods as one of the possible strategy to increase the overall quality of the diet. The evidence emerging from this thesis links the consumption of low GI and high fibre foods, such as fruits, vegetables, legumes and wholegrain products, to a strong positive impact on health. In particular, the choice of high quality carbohydrate influences acute post-prandial glycaemic control, and may represent a valuable strategy in the framework of weight loss and weight management in healthy obese, and in overweight and obese type 2 diabetics.