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Final Dissertation

Preferably not Necessarily: Whole Grain Recommendation in the Mediterranean Diet

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Abstract

Grain-based foods are the primary suppliers of carbohydrates and proteins also the dominant low-fat staple foods in the Mediterranean diet. The importance of their intake becomes more profound in the time of a worldwide crisis such as the coronavirus disease outbreak. They are essential regarding global food security due to providing around two-third of the total energy intake in the form of affordable, portable, versatile, and shelf-stable products. Moreover, they are rich sources of a wide range of bioactive compounds such as dietary fibers and phytochemicals. Above all, total grains consumption boosts the immune system through having antioxidant, anti-inflammatory, and immunomodulatory activities. Since most of these beneficial impacts are associated with the consumption of the whole portion of the grain-based products, the majority of dietary guidelines suggest the exclusive intake of whole-grain products and not their refined-grain counterparts. However, the Mediterranean diet stands out by recommending preferably and not necessarily consumption of whole-grain products. This review provides more insight into this recommendation by enlightening several issues and deliberations, including the lack of a universal standard definition of whole grains and a meaningful quantity of them that should be presented in a food product to be considered significantly health-promoting. These issues, later on, lead to a non-uniformity in the methodical calculation among studies that examined whole- and refined-grain intakes and their health outcomes and consequently make them incomparable and inconsistent. Other discrepancies exist, such as differences in the diet backgrounds of the population under examination and covariations between dietary variables themselves. All these confounding factors trigger a greater caution for interpretation of any research in the literature. Finally, some drawbacks of whole-grain products are explained that hinder the incorporation of such products by the overall population in their diets, for instance, not being widely available for all the types of products, having higher economics, and lesser palatability compared to other food choices. In conclusion, a more achievable goal is increasing the whole-grain intake by replacing some portions of refined grains rather than prohibiting all refined grains without considering nutritional and culinary impacts on the overall diet.

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1. Grains

The term ‘grain’ refers to plants from the *Poaceae* grass family which divided into cereal grains and pseudo-cereals. All species of this family are composed of three integral components namely starchy endosperm, the germ, and the outer bran layer. Pseudo-cereals including amarant, buckwheat and quinoa have a similar macronutrient composition to cereals. However pulses, nuts, and seeds are not included in this family. [1]

Annual cereal production, as it is reported by FAO on November 2021, was recorded as 2,793 million tons which stands as 0.8 % higher than previous record in 2020. [2]

1.1. Nutrient Compositions

Three main fractions of grains from inner part toward outer part can be described as the micronutrient-rich and lipid-rich germ, the starchy endosperm, and the multi-layered outer fiber-rich bran. [3] Considering wheat as one of the most typical staple grains of the Mediterranean regions, it is composed of 2·5-3·0 % germ, 80-85 % endosperm, and 10-14 % bran which may differ severely depending on the intensity of the milling process. Figure 1 depicts different and complex compositions of a whole-grain wheat. This heterogenous structure with uneven distribution of bioactive compounds among these three parts may vary accordingly with variety and geography. Whole grains are well-known for being a rich source of dietary fibers which are approximately 13 %. However, beyond this fiber content there are at least 2 % of other bioactive compounds which the most beneficial ones in wheat are n-3 fatty acids, sulfur amino acids, oligosaccharides, lignin, minerals, trace elements, vitamins B and E, carotenoids, polyphenols, alkylresorcinols, phytic acid, betaine, total choline-containing compounds, inositols, phytosterols, policosanol and melatonin. Although each of them is accounted for having health-promoting physiological functions, the positive effects linked to the consumption of whole grains are predominantly a result of synergy between the actions of compounds rather than each biological action separately. [4]

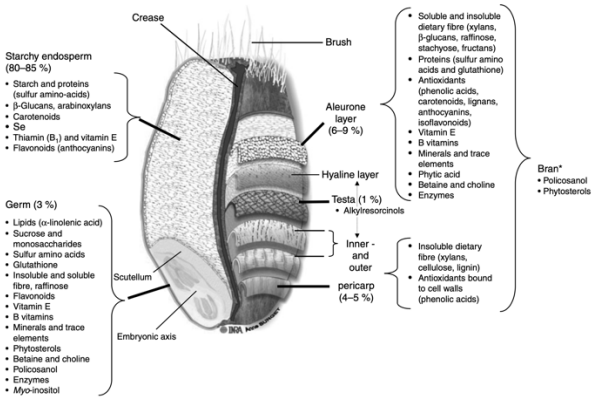


Figure 1: The three fractions of wheat (bran, germ and endosperm) with their main bioactive compounds [4]

1.2. Health Outcomes

Due to the presence of dietary fibers and other bioactive compounds, many potential protective physiological mechanisms are linked to the ingestion of whole grains. These mechanisms may be involved in the digestive tract (e.g., fibers), hormonal (e.g., Zn, Se), antioxidative (almost all micronutrients), anti-inflammatory (e.g., n-3 a-linolenic acid, Cu, and ferulic acid), anti-carcinogenic. They may also be associated with gene regulation (e.g., flavonoids), cell signaling (e.g., polyphenols), energy metabolism (e.g., the B-complex vitamins), and effects on enzymes (e.g., some minerals and trace elements). [4] Figure 2 illustrates the overall graphical connections presented for different compounds in grains and their health-promoting benefits studied for them.

While there is a bulk of evidence focusing on the importance of fibers (especially on digestive health), not enough attention is on other bioactive compounds in grains. The majority of these compounds have antioxidant activity. Grains' antioxidants vary depending on their mode of action. They can be indirect (such as minerals: Fe, Zn, Cu, and Se) that serve as co-factors of antioxidant enzymes or be direct actors as radical scavengers such as polyphenols. Among polyphenols of grains, the most commonly found are phenolic acids, which can be in free form (mainly in pericarp) or bounded by esterification to cell walls. Bound compounds are hard to digest and they require acid or base hydrolysis to be released from the cell matrices. Thus, these indigestible materials probably survive gastrointestinal digestion and reach the colon where through colonic digestion, they become available to perform their antioxidative functions. Their absorption in the colon is a part of the justification for the protective mechanisms of grains in preventing colon cancer and other digestive cancers. [5], [6]

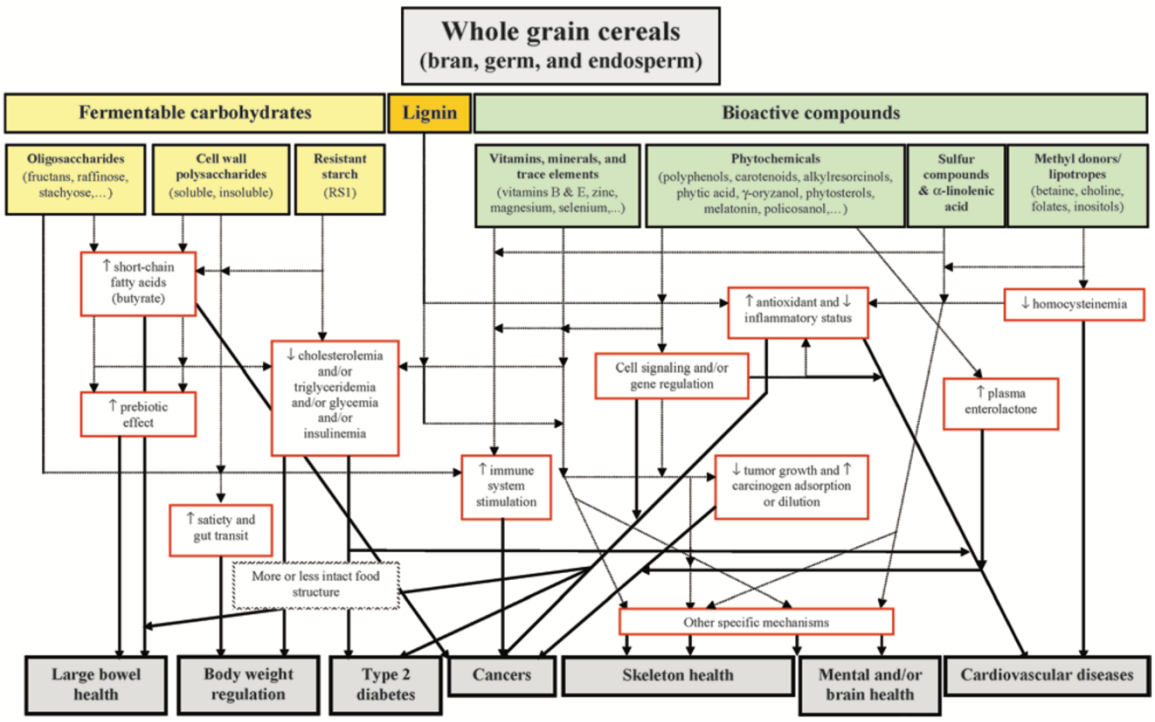


Figure 2: Schematic of potential physiological mechanisms contributed to health outcomes of whole grains consumption. Arrows with dotted tails indicate the link between bioactive compounds and protective physiological mechanisms, whereas the solid tails refer relationships with health outcomes.[7]

Although there are many mechanisms proposed for assessing the functionalities of each bioactive compound in grains and their associations with chronic diseases, the precise mechanisms are not yet understood completely. For example, fiber certainly plays a significant role in the cardioprotective effects of whole grains, while it is still debatable to what extent it is responsible. The reason is that many compounds may contribute to lower the risk of cardiovascular diseases, including Mg, vitamin E, and so on, and not fiber alone. Therefore, a holistic approach may explain the complete physiological mechanisms more effectively by considering the synergic effects of different compounds. [8] It is noteworthy to mention that cells are never in contact with only one isolated bioactive compound at a time but rather with a pool of compounds that act synergistically to provide a particular metabolic effect. Furthermore, the structure of grains has a profound role in their physiological effects, both on digestive physiology (e.g., satiety and gastric emptying rate) and the kinetics of which those compounds are released.

In this context, some authors proposed considering grains as a complex matrix including different bioactive packages, such as antioxidant packages. For example, whole-grain wheat contains more than 30 compounds with potential antioxidant effects which differ from other grains. [7] Each variety of grains with a different structure offers a unique polyphenols

composition besides other bioactive compounds. Hence, each provides different protective functions with different extents. Figure 3 indicates the total antioxidant activities of four common types of grains, namely wheat, corn, oat, and rice. The total amount is the sum of free and bound compounds expressed as micromoles of vitamin C equivalent per gram of grain. As it can be seen, the highest amount of the total antioxidant activity was calculated for corn (181.42 (0.86 µmol/g of grain)), followed by wheat (76.70 (1.38 µmol/g of grain), oats (74.67 (1.49 µmol/g of grain)), and finally rice (55.77 (1.62 µmol/g of grain)). Since each antioxidant plays its role exclusively, adequate amounts of each antioxidant from a wide variety of sources can maximize the health benefits. [5]

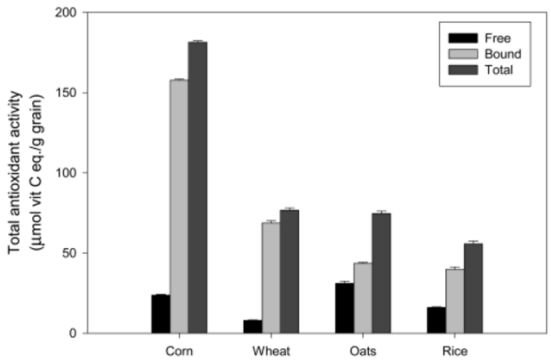


Figure 3: Total antioxidants activity (free + bound) of grains [5]

2. Dietary Guidance: definitions, issues, and deliberations

Increasing the intakes of whole grains and dietary fibers are recommended universally in dietary guidance. While recommendations depend on definitions and regulations, yet there are several issues still standing which require urgent considerations to be solved.

Efforts to determine the intake of whole-grain foods across the world are challenging since definitions for whole grains and tracking systems vary greatly. These definitions and regulations need to be globally well-established to ensure three-fold benefits. Namely, encouraging the food industry to add more whole-grain ingredients into their products, assisting scientists in measuring the whole-grain intake more accurately, and promoting consumption by providing practicable and understandable information to the public. [9]

2.1. Recommended Daily Intake of Whole Grains

Daily recommendations for consumption of whole grains all over the world vary greatly. These recommendations can be quantitative, qualitative, or a combination of both. For instance, the recommended intakes for Canada and the United States are 'make half your grains whole' which has the range of 48 - 85 g per day depending on age and gender. Less-specific recommendations are also present that only promote a greater consumption of whole grains without mentioning any quantifications by suggesting that 'eat a variety of grain (cereal) foods, mostly whole-grain and/or high cereal fiber varieties' or 'prefer wholegrain cereals' as it recommended in Food-Based Dietary Guidelines in Europe. According to European Commission, data on the intakes of whole grains are limited due to the lack of a consistent definition among European countries which will be explained further in details in section 2.2, but also because many of researchers limited their scopes of research to the intake of fiber but not the whole grain as a separated group of foods.

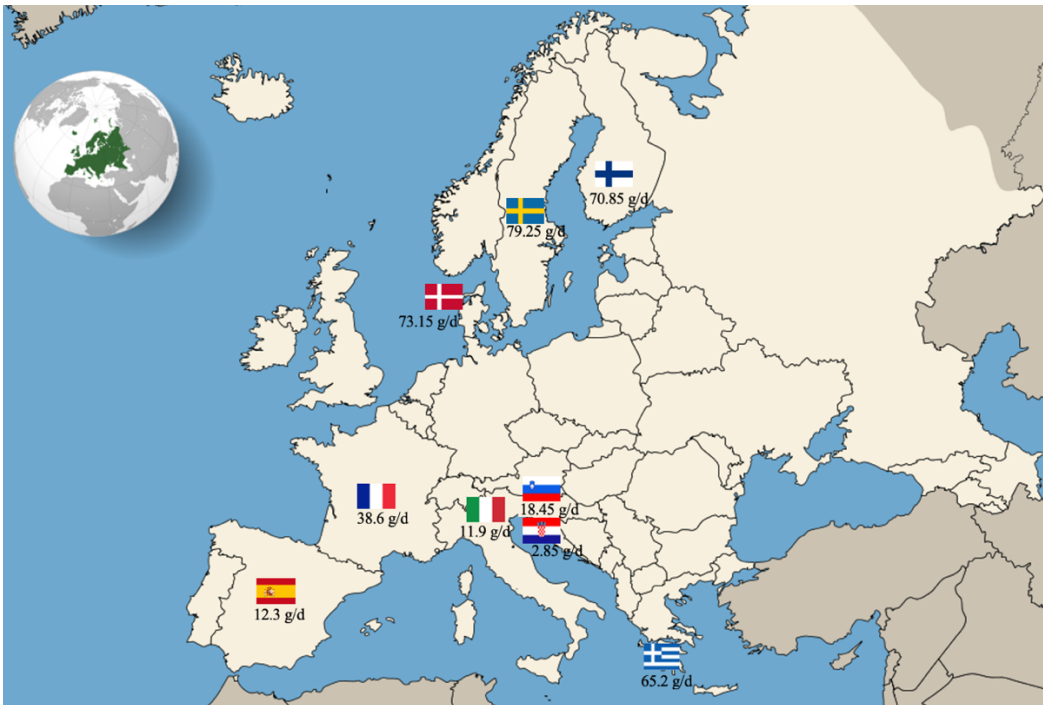


Figure 4: Examples of daily intakes of whole grain foods based on Global Dietary Guideline Database reported by the European Commission [10]

Figure 4 depicts the mean daily intakes in some Mediterranean and Scandinavian countries for adults older than 20 years old. Data are the arithmetic means among males and females consumptions extracted from the European Commission report based on Global Dietary

Database (GDD). In which 'the total intake of whole grains includes breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes etc. A whole grain food is defined as a food with ≥1.0 g of fibre per 10 g of carbohydrate'. [10]–[12]

A study reported the intakes of whole grains among the Italian population differently, even lower than the one by the GDD. The calculation has been done by using the national survey INRAN-SCAI 2005–06. In which by assessing a 3-day food record, mean intakes were 3.7 g/day in adults and 2.1 g/day in children and adolescents. Only one quarter of the total population (23 %) who participated in the survey reported the consumption of whole grains that reveals considerably low daily intakes in the Italian samples. Among the grain-based foods, bread was the main contributor accounted for about half of the intake in adults. While for children, breakfast cereals were calculated as the main source with 32 % of the overall intake. Substantially, biscuits contributed approximately 20 % of the total whole-grain intakes in both groups of children and adults. Interestingly, whole grain pasta was not present in the dietary patterns of children at all, and represented only 2 % of the total consumption of whole grains in the diets of adults. One of the reasons behind the different data reported by this study and the one by the GDD, could be due to the variation of methods they applied for definition and calculation of whole grain consumed by the different samples. As it mentioned in the Italian study, the definition of whole grain was in accordance with the one that outlined by HEALTHGRAIN, presented in Table 1. [13]

One of the driving forces for the consumption of whole grains is tradition. More probably, the availability of traditional foods made with whole grains in a given country has a more profound impact on the consumption of whole grains rather than the dietary recommendations themselves. Countries in which the majority of their grain-based foods are produced traditionally with whole grains reported higher mean intakes compared to others. For example, Scandinavian countries, as it is shown in Figure 4, have a strong tradition of consuming bread made of whole grain rye and wheat, as well as muesli cereals with whole grain oats that resulted in significant differences in intake accordingly. [14] However, this seems paradoxical to the traditional Mediterranean diet, considering that Italy was one of the first regions adopting this dietary pattern. According to food balance sheets, over the last 50 years, this tradition disappeared in Italy progressively by increasing the consumption of animal-based products at the expense of decreasing the consumption of grain-based ones. Moreover, the same study observed regional differences in the acceptance of whole grain foods across Italy. In which participants subjects living in North-Western and Central regions had greater preferences for the consumption of whole grains compared to the South and Islands. [13]

2.2.Nonuniform Definition

One of the challenges in reporting the whole grain intake is the lack of a standard definition of whole grains. Various definitions have been published by regulatory bodies, grain organizations, and others (Table 1). All agreed that whole grain should include three main components (bran, germ, and starchy endosperm), though some differences exist.
Regardless of the supporting evidence in favor of higher consumption of whole grains, there is no universal definition at the European level to quantify how much whole grains should be present in food products in order to provide significant health benefits. [14], [15]

Table 1: Several definitions of whole grains [10]

Source	Definition
AACC 2000	'Whole grains shall consist of the intact, ground, cracked or flaked caryopsis, whose principal anatomical components — the starchy endosperm, germ and bran — are present in the same relative proportions as they exist in the intact caryopsis'.
EU (Regulation No 1308/2013)	'Whole grain means grains from which only part of the end has been removed, irrespective of characteristics produced at each stage of milling'.
HEALTHGRAIN 2014	'Whole grains shall consist of the intact, ground, cracked, or flaked kernel after the removal of inedible parts such as the hull and husk. The principal anatomical components, the starchy endosperm, germ and bran are present in the same relative proportions as they exist in the intact kernel. Small losses of components that is less than 2% of the grain 10% of the bran that occur through processing methods consistent with safety and quality are allowed'.
FDA 2015	'Whole grains are cereal grains that consist of the intact, ground, cracked or flaked kernel, which includes the bran, the germ, and the inner most part of the kernel (the endosperm)'.

AACC: American Association of Cereal Chemists, FDA: American Food and Drug Administration

Since the first formal definition, controversies have been arisen to propose it more accurately. Initially, the European Food Safety Authority (EFSA 2010), in a whole-grain related health claim opinion, represented the definition of the American Association of Cereal Chemists (AACC) in 2000, which stated that a degree of processing is acceptable as long as three main

components of the grains (bran, germ, and endosperm) remain constant as their natural ratio in the intact kernel. While this definition emerged further difficulties in identifying what can be considered as a grain and to what extent the processing is allowable. [16]

Table 2: Grains included in the HEALTHGRAIN whole grain definition [9], [11]

Cereal	**Scientific Name**
Cereals	
Wheat, including spelt, emmer, faro, einkorn, Khorasan wheat[1], durums	*Triticum* spp.
Rice, including brown, black, red, and other colored rice varieties	*Oryza* spp.
Barley, including hull-less or naked barely, but not pearled	*Hordeum* spp.
Maize (corn)	*Zea mays*
Rye	*Secale* spp.
Oats, including hull-less or naked oats	*Avena* spp.
Millets	*Brachiaria* spp.; *Pennisetum* spp.; *Panicum* spp.; *Setaria* spp.; *Paspalum* spp.; *Eleusine* spp.; *Echinochloa* spp.
Sorghum	*Sorghum* spp.
Teff (tef)	*Eragrostis* spp.
Triticale	*Triticale*
Canary seeds	*Phalaris canariensis*[*]
Job's tears	*Coix lacryma-jobi*
Fonio, black fonio, Asian millet	*Digitaria* spp.
Pseudo-cereals	
Amaranth	*Amaranthus caudatus*
Buckwheat, tartar buckwheat	*Fagopyrum* spp.
Quinoa	*Chenopodium quinoa* Willd.
Wild rice**	*Zizania aquatica*

[1]Khorazan wheat – also known as Kamut (registered trademark).

[*]In the first version of the definition document two scientific names were erroneously mentioned: *Phalaris arundinacea* and *P. canariensis*. The former one is a noxious weed.

[**]In the first version Wild rice was – incorrectly – listed as a cereal and not as a pseudo-cereal.

For enlightening these issues, the European HEALTHGRAIN consortium provided an inclusive list of commonly available grains, pseudo-grains, and wild mentioned in Table 2 in detail. This list includes a greater variety of grains compared to the list provided by the FDA definition. For instance, Canary seeds, Job's tears, and Fonio are noted in the definition of the HEALTHGRAIN consortium,[10], [11], [17] but not in the FDA. However, FDA specifies that "products derived from legumes, oilseeds (sunflower seeds), and roots (e.g., arrowroot) should not be considered whole grains." [18] Moreover, as opposed to the AACC definition, it allows

for a minimal loss of the main three components during the processing, hence, up to 2% of the grain or 10% of the bran can be removed to ensure the elimination of some undesirable substances such as bacteria, molds, agrochemicals, and heavy metals. [17], [19]

2.3. Labeling of whole-grain products

The whole-grain health claims are linked to products that contribute a meaningful quantity of whole grains to the diet, however, there is no agreed-on definition of what a "significant amount" is in a food for a fair whole-grain labeling to guide consumers and for setting an industry standard. Regarding this goal, several authorities established quantifications based on how much whole grain should be presented in a food product to be considered significantly health-promoting.

In 1999, the American Food and Drug Administration (FDA) announced a definition following an authoritative statement of "Diets high in plant foods--i.e., fruits, vegetables, legumes, and whole-grain cereals--are associated with a lower occurrence of coronary heart disease and cancers of the lung, colon, esophagus, and stomach." States "For purposes of bearing the prospective claim, the notification defined "whole-grain foods" as foods that contain 51 percent or more whole grain ingredient(s) by weight per reference amount customarily consumed (RACC). It proposed that compliance with this definition could be assessed by reference to the dietary fiber level of whole wheat, the predominant grain in the U.S. diet. Whole wheat contains 11 grams of dietary fiber per 100 grams; thus, the qualifying amount of dietary fiber required for a food to bear the prospective claim could be determined by the following formula: 11 grams x 51% x RACC/100." [20]

The FDA definition was the starting point for all the discussions, and it was debated several times subsequently. The claim of > 51 % by weight per serving, implies that whole-grain foods could contain 49 % refined grains. This triggers the question that the benefits assigned to whole grains may be more accurately correlated with the combination of whole and refined grain foods rather than only whole grain ones. [21]

The European Whole Grain Task Force (WGTF) in 2008 announced that "supports the use of the term whole-grain for products of milling operations that divide the grain into germ, bran, and endosperm, but then recombine the parts into their original proportions before the flour leaves the mill". Although, a majority of the studies on the health benefits of whole grains are made of recombined whole-grain flour, which barely incorporates the same proportions of the

main components as the intact grain before milling. Since the germ fraction is usually removed because of its high lipid content (about 9 %) which may go rancid during storage. [4], [22]

The FDA definition was challenged by the WGTF explaining that "Using total weight gives an advantage to products sold by dry weight such as crackers and ready-to-eat cereal. Because foods like bread have a proportionally high water content, even some bread made with all whole grain flours but containing significant amounts of nuts, seeds, and fruit would fail to meet the 51 % by weight rule". Another example that has been discussed by the WGTF was considering a soup which more probably contains only whole grain barley and technically based on the FDA definition it can be called a whole-grain food, however, it would not deliver a significant amount of whole grain to the diet when it only consists of a few barley corns per serving. In response, the WGTF announced that it supports labeling based on foods which contain 8 g of whole grain per labeled serving. [22]

According to evidence provided by a research study, grain-based foods that outlined the FDA requirements (< 51 % of whole-grain content) provided 28 % of overall whole grain intake for young British people (aged between 4-18 years) and even a higher percentage for older adolescents. This implies that by considering the FDA cut-off, the overall intake has been underestimated by 28 %. Moreover, the study mentioned that with setting a lower cut-off point of whole-grain content of 25 %, whole grain intake would still have been underestimated by 15%. [23]

Following the FDA definition, there was a global call for defining what constitutes a whole-grain food. As a result, a roundtable of experts from the United States and Europe was held in 2012. In which the expert panel recommended that "8 g of whole grain/30 g serving (27 g/100 g), without a fiber requirement, be considered a minimum content of whole grains that is nutritionally meaningful and that a food providing at least 8 g of whole grains/30 g serving to be defined as a whole-grain food". This definition has been made considering the 2010 Dietary Guidelines for Americans (DGA) recommendation of "6–11 servings per day of grains based on an individual's energy needs, with at least one-half of those servings (at least 3 servings) as whole grains". Thirty grams was counted as a standard serving of a grain-based product. Hence, the minimum DGA recommendation of 48 g/d whole grains could be met with six 30 g servings of such foods included in the daily diet. [24]

Several concerns were raised with the previous definitions which were contested by the Oldways Whole Grains Council (a US-based non-profit educational organization funded by industry) in a letter to the FDA in 2014. The main issue was explained as such that the definition is lacking clarification about whether the wet weight shall be used or dry weight. Mentioning

that many ready-to-eat foods have a greater amount of moisture content which can set them below the threshold to be recognized as a whole-grain food. For instance, the bread which includes a moisture content of roughly 35–40%, essentially requires a greater whole-grain content than crispbreads and crackers (moisture content ~ 5%) to be labeled as "whole grain". Alternatively, three different levels of labeling have been proposed by the Whole Grains Council to provide light for consumers for easier identification of food with a greater source of whole grains.

- 100 % Whole Grain Foods (foods in which all the grain is whole; 16 g / serving; the term "100 %" shall be used on the label, e.g., 100 % whole wheat)
- Mostly Whole Grain Foods (foods where 50% of the grain is whole or more; minimum 8 g / serving; the term "whole grain" shall be used on the label, e.g., whole grain crackers)
- Foods Contributing Whole Grains (8 g or more of whole-grain ingredients per labeled serving; it provides factual statements about the amount of whole grain per serving e.g., 14 g / serving; but shall not be labeled as "whole grain" in their names.) [11], [19]

Undoubtedly this approach could provide comprehensive information for the consumers, however, it has been found that too many levels of labeling could be also confusing in a way that some consumers might not be able to distinguish them. Consequently, the Healthgrain Forum emphasized that there is still a strong necessity for a clearer definition, and it developed guidance for the industry upon labeling the whole-grain content of foods. In this definition foods shall be called whole grain only if they contain 30% or more whole-grain ingredients on a dry-weight basis, moreover, a greater quantity of whole-grain ingredients than refined ones. In addition to this definition, the Healthgrain Forum suggested some bullet points as there are listed below.

- If national regulations in respect of whole-grain labeling are present, they are foremost of this definition.
- Whole-grain foods shall meet accepted standards for healthy foods (e.g., not being high in sodium, saturated fat, and added sugars)
- Food manufacturers are advised to report the percentage of whole grain on front-of-pack labeling of all products.
- No need for restricting the type of processing applied on whole grains unless it leads to a more than 10 % reduction in dietary fiber content (the main indicator of beneficial components)

- According to observational evidence, foods with more than 25 % whole grain led to disease risk reduction. Considering an additional 5 % as the safety margin, 30 % has been proposed as the starting point for labeling. Although, the Healthgrain Forum acknowledged the purpose of this threshold is not health claims but rather providing suggestions for the industry. [11]

Table 3: Labeling statements for identifying a grain product as whole grain

Source	**Description**
FDA (1999)	"For purposes of bearing the prospective claim, the notification defined 'whole grain foods' as foods that contain 51 percent of total weight or more whole grain ingredient(s) by weight" [20]
Whole Grain Task Force (2008)	"To be labeled as a whole grain product, the food would contain 8 g of whole grain per labeled serving."[22]
AACCI (2012)	"8 g of whole grain/30 g serving (27 g/100 g), without a fiber requirement, be considered a minimum content of whole grains that is nutritionally meaningful and that a food providing at least 8 g of whole grains/30 g serving to be defined as a whole-grain food" [24]
Oldways Whole Grains Council (2014)	"FDA should support labeling for three different levels of whole-grain foods: 1. 100% Whole Grain Foods 2. Whole Grain Foods (foods where 50% or more of the grain is whole) 3. Foods Contributing Whole Grains" [19]
HEALTHGRAIN Forum (2017)	"A food may be labeled as 'whole grain' if it contains ≥ 30% whole-grain ingredients in the overall product and contains more whole grain than refined grain ingredients, both on a dry-weight basis."[11]
Whole Grain Initiative (2020)	"A whole grain food shall contain at least 50% whole-grain ingredients based on dry weight." [25]

2.4. Importance of structure

Another important consideration is the distinction between whole grains and whole-grain foods. The content of nutrients differs significantly based on the type and the percentage of whole grains contained in such foods. Moreover, the physical structure may affect the nutritional and functional properties of whole-grain foods. For instance, two terms of 'whole-grain' and 'wholemeal' are perceived interchangeably, while they can cause different physiological responses. A research study negotiated that the term 'whole-grain' is inadequate since it may refer to both products with intact or cracked kernels plus those with highly milled kernels (in which all the dietary fibers are present but none of them in their original forms). Particle size is a profound determinant of glycemic responses to cereals. As a role of thumb, the smaller the particle size of the food, the higher was the glycaemic-insulin response and the lower the satiety rating. The same study concluded the whole-grain bread produces significantly lower postprandial blood glucose profiles compared to the wholemeal bread. As a clarification, it has been suggested that the term wholemeal shall be used for products containing 100 % milled flour while the term whole-grain for those with a specified percentage of unmilled flour, such as 50 % whole-grain. These results highlight the importance of food structure on physiology. In general, these differentiations are not considered for establishing dietary guidelines. [4], [26]–[28] However, it should be mentioned that some researchers confer that the quantity and frequency of consumption of whole grains are foremost important rather than the type of processing for having a healthier diet. [22]

2.5. Studies regarding whole and refined grains with medical conditions

2.5.1 Inconsistent findings

For the last 20 years, health outcomes of ingesting whole grains have been the focal points of epidemiological analyses, randomized controlled trials (RCTs), reviews, and meta-analyses. Epidemiological studies and their meta-analyses consistently supported these biological outcomes. Although, results from RCTs that are a rigorous tool to examine cause-effect relationships between whole-grain intake and risk markers of diseases are less consistent. Among numerous studies that emphasized the health impacts of whole grains, only few underlined the effects of refined grains, and those who focused on them showed

a null association of refined grains and health risks. These findings trigger a greater caution for interpretation of any research that has examined whole- and refined-grain intakes and their health outcomes. These studies may have confounding factors such as various whole-grain definitions, methods to calculate the intake, diet backgrounds, and the covariance between dietary variables.

Whole grain is an ingredient of foods composed of several nutrients such as dietary fibers and phytochemicals. Hence the frequent chemical analyses are incompetent in the quantification of whole-grain contents in food products. Various procedures may be used to estimate the content of whole grains, such as calculation from an ingredient list per serving of a certain food product, though, they are hardly described in studies. [15], [21]

Furthermore, there are some uncertainties about the quality of whole grains consumed. One of the main contributors to the potential health impacts of whole grains is dietary fibers. However, different types of whole grains are composed of different nutritional profiles from others. As a role of thumb, "high fiber does not always equate with whole grain, just as whole grain does not always equate with high fiber". Thus, some varieties are better sources of dietary fibers than others. Fiber contents are listed on the Nutrition Facts Panels of products but not the whole-grain contents since a whole grain is an ingredient (not a nutrient), as mentioned before. Hence, due considerations are needed to ensure these two concepts are not mistakenly used one for another. Table 4 presents some examples of different grains with their fiber contents. [24]

Table 4: Examples of different fiber contents in different grain varieties [24]

Grain	**Fiber content**	
	g / 8 g Grain	*g / 100 g Grain*
Brown rice	0.3	3.5
Wild rice	0.5	6.2
Corn, yellow	0.6	7.3
Oats	0.9	10.6
Wheat	1.0	12.2
Amaranth	1.2	15.0
Rye	1.2	15.1
Barley	1.4	17.3

Meanwhile, it is essential to note that the beneficial impacts of whole grains consumption are beyond their dietary fiber contents. Considering brown rice as an example, as it can be seen in Table 4, it has the lowest fiber content though a high amount of unusual fatty acids that are

known to have significant roles in lowering serum cholesterol. Therefore, the health claims of whole-grain foods shall not be limited to only those grains with the highest fiber contents (e.g., wheat and barley). In addition, a variety of whole grains shall be recommended, especially for those with special dietary needs, such as celiac patients. [22]

An American study negotiated that the recommendation of the Dietary Guidelines Advisory Committee in 2015, which suggested the replacement of most refined grains with whole ones, was grounded on findings from studies that examined dietary patterns rather than separate food groups. A typical Western dietary pattern is mainly composed of animal-based foods and sweetened beverages, besides refined grains. The general eating pattern should be regarded as increasing the risk factors of many chronic diseases rather than grain-based foods solely. To provide a more accurate overview of the contribution of refined-grain intake and chronic diseases, eleven meta-analyses of prospective cohort studies, in which refined grains were analyzed as a distinct food category, were selected by the same American study. Results exhibited that the intake of up to 6–7 servings/day (each serving equal to 30 g) of refined grain was not associated with a higher risk of cardiovascular diseases, type 2 diabetes, hypertension, or all-cause mortality. Moreover, the definition of refined grains in most of these studies is debated to be biased. Since those grains defined as being whole were mostly staple grain foods (e.g., bread and pasta), while refined grains included both staple and indulgent (e.g., sweets). Indulgent refined-grain foods are inherently high in fat and sugar contents, which frequent consumption of them can counteract the favorable impacts of staple grain foods. As a result, this study hypothesized that disease risk factors are "a consequence of guilt by association with other foods within the Western dietary pattern, but not refined grains per se". [29]

Recently, a systematic review examined the potential divergence caused by different methods on calculating the whole grain intake and their associations with body weight measures in adults. From 6675 initial articles found in the literature, only 31 articles were included as eligible mainly due to their quantitative methods to measure the intake of whole grains, which proves a significant inconsistency among studies. Mostly, the U.S. studies prefer to use a minimum amount of 25 % as a serving of whole grains, whereas the European studies do not provide any definition. Both cases are problematic since even with defining a minimum proportion, all food items above 25% of whole grains as their ingredients are considered equally as a serving of whole grains. Finally, it has been concluded that mainly studies that used total grams of intake showed consistent beneficial effects of increasing whole grain intake on body weight, but not those with general lists of foods included as "whole-grain foods" without any specification. Consequently, the heterogeneity in the methods of identification and

calculation of whole-grain intakes leads to incomparable and more likely not credible findings.[30]

Table 5: Examples of some evidence-based studies for comparison of whole- and refined-grain intakes and their association with several diseases

Article	Outcomes	Results
Ampatzoglou et al. [31]	Blood biochemistry and body composition	Substitution of whole grains from 28 g/d to 168 g/d in low habitual consumers does not a statistically significant impact on body composition, fecal microbiota, blood lipid and glucose
Hosseini et al. [32]	Body Mass Index	No significant difference in adults' BMI across seven dietary patterns including ('other bread', 'cake and cookies', 'pasta', 'rice', 'mixed', 'white bread', and finally 'whole wheat and whole-grain bread')
Aune et al. [33]	Cardiovascular disease, total cancer, all-cause mortality	There was little evidence of an association between intake of refined grains and any of the outcomes
Sadeghi et al. [34]	Depression and anxiety	No link between refined grain consumption and depression in men; but among women the third quartile of refined-grain intake resulted in greater risk of having anxiety compared to the first quartile
Wu et al. [35]	Stroke	Consumption of refined grains was not linked to increased risk of strokes (neither hemorrhagic and ischemic nor incident and fatal) for both men and women
Pol et al. [36]	Weight gain, percentage of body fat, and waist circumference	Whole grain intervention did not result in a difference in body weight and waist circumference compared with control consumption (including refined-grain diet), but a small beneficial impact on body fat
Khosravi-Boroujeni et al. [37]	Cardiovascular disease	No significant correlation between white rice consumption and cardiovascular risk factors (fasting blood sugar and serum lipid profiles) among Iranian men

Table 5: Cont.

Article	Outcomes	Results
Schwingshackl et al. [38]	Colorectal cancer	No association between highest versus lowest intake of refined grains (15-585 g/d) and the risk of colorectal cancer
Williams [39]	Cardiovascular disease, diabetes, weight gain, and overall mortality	Results from 135 articles show that intake of up to half of refined grains from the overall grain consumption was not a risk factor for any of outcomes
Katcher et al. [40]	Cardiovascular disease and weight gain	Risk factors of cardiovascular diseases improved for obese adults with metabolic syndrome under both hypocaloric diets (all whole grains or all refined grains). Both groups have a moderate weight loss with a decrease in total, LDL, HDL cholesterol.
Kristensen et al. [27]	Post-prandial glucose responses	No significant differences between any whole products (bread or pasta) with their corresponding refined-wheat products. But significantly lower glucose response for refined-wheat pasta compared to refined-wheat bread and similarly for whole-wheat pasta compared with whole-wheat bread.
Hauner et al. [41]	Obesity, diabetes, blood pressure, metabolic syndrome	Lack of risk relations between the intake of refined grain products and any of outcomes
McKeown et al. [42]	Visceral adipose tissue (VAT)	There is a joint interaction between whole- and refined-grain intakes on VAT. The lowest VAT volume was observed for the ingestion of 3 whole- plus 2 refined-grain foods per serving per day.
Bazzano et al. [43]	Weight gain	An inverse association of ingestion of both refined- and whole-grain breakfast cereals (at least one serving per day) with weight gain among men over a follow-up period of 8 years in comparison with those who never or barely consumed breakfast cereals regardless of type of the grain

Another confounding factor is the dietary backgrounds of participants who have been evaluated in studies. Consumption of whole grains may not be the exact justification for health outcomes that have been observed. Generally, whole-grain consumers tend to have a healthier lifestyle, such as smoking less, doing more physical activities, and so forth. In addition, it has been reported that these participants with higher Healthy Eating Indexes (HEIs) are more conscious and knowledgeable about food labels and nutrients. [13], [21], [44]

Aside from the dietary backgrounds, there are co-variations among dietary variables. As if the intake of one certain food group may positively or negatively shift the intake of another. For instance, higher consumption of refined-grain products may lead to lower consumption of fruits and vegetables, which triggers confusion about whether the observed association is a result of greater consumption of refined grains or decreasing the one for fruits and vegetables. Accordingly, the interactions between specific food groups together shall be taken into account as well. [21], [30], [42]

These confounding factors can be used as an explanation for the inconsistency among studies. In spite of numerous studies that analyzed the beneficial impacts of higher whole-grain intake, there were only a few ones that focused on refined grains separately. Those that examined refined grains showed a null effect or a slight association with increasing the risk of disease that most of the time was not statistically significant. Some examples of such studies are presented in Table 5. Since there are few studies available, the evidence regarding the relevance of refined grain products as a risk marker of diseases is considered insufficient.

2.5.2 Some disadvantages of whole-grain products

In defiance of the beneficial impacts mentioned for whole-grain intake, some downsides exist. Considering the whole wheat bread as an example, it has some typical characteristics including, lower loaf volume, firmer texture, darker crust and crumb appearance, more bitter flavor, and shorter shelf-life in contrast with the refined wheat bread. These are due to the deleterious impacts of some endogenous wheat components in bran and germ proportions. The decrease in the loaf volume may be a result of a high amount of non-polar lipids in the germ proportion which tend to destabilizion of gas cells. Moreover, there is a competition among the water-soluble and water-insoluble fiber components for water that results in an inadequate hydration of gluten proteins and starch. To solve such difficulties, some process modifications are vital such as addition of oxidizing agents, emulsifiers, shortening and mold inhibitors, and enzymes

(Phytase, Xylanase, etc.). The concentrations of these additives are generally higher than those used for formulation of refined wheat bread. Interestingly, for achieving the level of sweetness equal to refined-grain alternative, a higher addition of sucrose is required since phenolic constitutes in bran have a strong flavor, mainly bitter-flavored. [45]

On the other hand, additional germ and bran proportions make whole-grain products more prone to have higher contaminant contents. Toxic residuals from soil and pesticides can remain particularly in outer layers of grains (i.e., bran). Heavy metals (e.g., Arsenic) and Mycotoxins are the most common contaminants in whole grains. Mycotoxins are toxins from secondary metabolites of filamentous fungi. They can accumulate in maturing cereals on the field or even during transportation. However, more accurate cleaning practices can reduce their concentrations. Arsenic, a neurotoxin with carcinogenic effects, can concentrate in the bran of cereals, commonly in rice. Since its concentration is intensively higher in bran than other components of the cereals, removing the bran, as it happens in refined grains, can solve the problem to a great extent.

Furthermore, processing procedures can be another source of contamination in whole grain products. Toasting is a process that is usually used to eliminate the possible contaminants that come from the soil such as, fungi, bacteria, yeasts, insect eggs, so forth. It also deactivates some enzymatic activities that are responsible for the deterioration of final products, for example, the Lipoxidase enzymes that can initiate fat rancidity. At high temperatures and long exposure times, the toasting process leads to the formation of acrylamides. The pathways for acrylamide formation start from asparagine, which is an amino acid mainly found in high concentrations in germ and bran. Acrylamides, known as processing contaminants, are carcinogenic. As prevention, lowering temperature and time of toasting with the addition of Asparaginase enzyme are usually carried out by manufacturing companies. [3], [46]

Apart from higher potential sources of contamination, several components are present in whole grains that are known as mineral antinutrients (namely phytic acid, polyphenols, and dietary fibers). These compounds can lead to mineral deficiencies by impairing their absorption. For instance, phytic acid is stored in bran as mixed salts of several cations (including iron, zinc, magnesium, calcium, and potassium) to serve as phosphor storage in the grains. These salts are not digestible for humans because of the lack of endogenous phytase enzymes. Moreover, phytic acid can have detrimental effects on protein digestibility since it also forms a complex with proteins and makes them less soluble. However, it is noteworthy to mention that, despite the negative impacts of phytic acid on mineral bio-accessibility and protein absorption, it also can have some positive ones, such as protective roles for cancers. [47]

Although disadvantages as such exist, they are manageable with applying stricter considerations in farming and processing practices of whole grains. Therefore, the overall advantages of whole grains may outweigh the disadvantages.

2.5.3 Adequacy of fortified refined grains

Grain-based foods are the best effective vehicles for improving diet quality either through fortification (i.e., adding nutrients to increase their concentrations more than their natural contents) or enrichment (i.e., substituting nutrients lost during processing steps). Their efficiency is because of their universal consumption and familiarity among consumers. Nutrients that are mainly used are vitamins and minerals such as thiamin, niacin, riboflavin, iron, magnesium, folic acid, and calcium. Mandatory or voluntary fortification of refined-grain products can enhance nutrient availability due to having a lower bran proportion that may impair some nutrient absorption, as it is mentioned before. Among these nutrients, folic acid and calcium are more of the concern of scientists than others. Folic acid fortification is widely known as an initiative for decreasing the prevalence of birth defects. As estimated, 4500 births per year are influenced by neural tube defects (such as spina bifida) all over Europe. Folate involves in DNA and RNA synthesis throughout fetal development, therefore, its presence in sufficient amounts is essential during pregnancy. Since the bioavailability of folic acid is approximately 70 % higher than its natural folate, grain-based foods can act as a potential carrier to ensure the overall population (especially women of child-bearing age) receives an adequate nutritional profile through their diets. [21], [32], [48]–[50] As for calcium fortification, an Italian study concluded that after fortification of flour (of any grain sources) with 156 mg per 100 g, the deficiency of calcium decreased from 1.7 % to 1 %, from 1.9 % to 0.3%, 37.2 % to 12.6 % in children less than one, four, and nine years, respectively. [51]

The importance of the consumption of fortified/enriched refined-grain products was debated several times. A scientific expert panel was held in 2018 in the U.S. regarding the question of "do refined grains provide meaningful contributions to nutrient adequacy in the dietary pattern?". In response, consensuses reached upon the significant values of such foods by stating that removing refined grains from the diet leads to nutrient shortfalls below the recommended amounts in the dietary guidelines among a considerable proportion of the population. Additionally, staple refined-grain products (not the indulgent ones) were identified as "leading contributors for dietary folate", after the regulation of mandatory folic acid

fortification by the FDA in 1998. The main refined-grain products that provided folic acid to the U.S. diet were breads, rolls, and crackers. They accounted for around 16 % of the total intake, which surpasses the one from vegetables. [52]

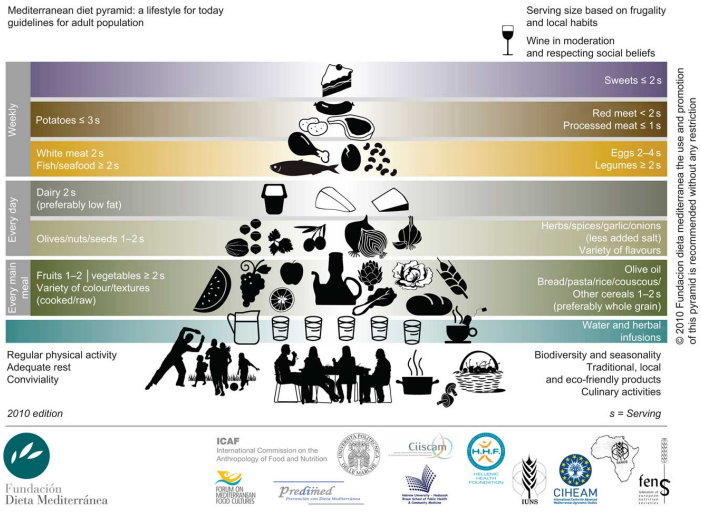
Another American study analyzed the role of fortified/enriched refined grain foods on the daily intake of nutrients by eliminating specific percentages (25, 50, and 100% of all grains consumed) from the diet of two groups (19-50 year old adults, N = 11,169; 51-99 year old adults, N = 9,641). In which the removal of all grains from the diet resulted in a reduction of 10 % of overall energy intake in both groups. Furthermore, by eliminating the percentage of grains' portion from the diet from 25, 50, and finally 100%, the adequate intake (AI) of dietary fibers decreased by 2.6 ± 0.3, 1.8 ± 0.2, and 0.7 ± 0.1%, respectively. Likewise, 11.0 and 13.8% of younger and older adults accounted for shortfalls of folate. [53]

2.6. Preferably not Necessarily

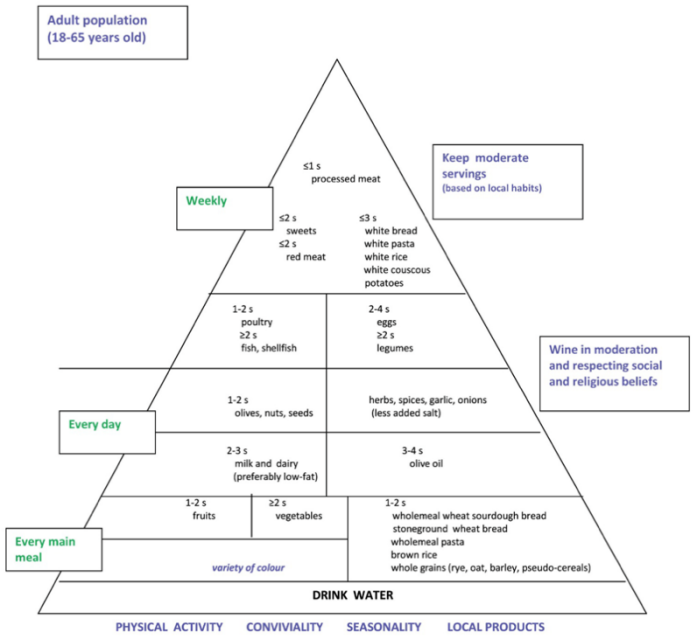
The traditional Mediterranean Diet Pyramid (MDP) was evolved several times after its recognition in 1995. Initially, an international conference titled “The Mediterranean diet as a sustainable diet model” was held on November 3, 2009, in Parma, Italy. Through which the 2010 edition of MDP was presented (Figure 5-I) with more emphasis on lifestyle activities including regular physical activity, adequate rest, and conviviality, as well as greater attention to the concept of sustainability (e.g., biodiversity and seasonality). Because the Mediterranean region covers the land from three continents, this version was developed as a simplified framework to be adopted by different countries based on their unique cultural and socio-economic contexts. Hence some countries such as Italy personalized this pyramid to provide dietary advice to their population based on their cultural heritage and tradition.

In 2014, the MDP version for Italian people was proposed with some significant modifications concerning cereals (Figure 5-II). According to the Italian pyramid, the serving frequencies of cereals are the same as the universal MDP, while the type of cereals changed significantly. The statement of 'preferably whole grains' for daily consumption of cereals was replaced with a specified list of necessarily whole-grain products, namely wholemeal wheat sourdough bread, stoneground wheat bread, wholemeal pasta, brown rice, and whole grains (rye, barley, pseudo-cereals). Moreover, the intakes of refined-grain products (e.g., white bread, white pasta, white rice, white couscous) and potatoes were shifted to the top of the pyramid with suggesting not more than three servings per week. The serving size was characterized as 30 g per meal of

whole grains, which implies the total intake of 90-180 g/day for three meals a day, each time 1-2 servings. 30 g was considered based on previous dose-response meta-analyses of prospective studies on whole-grain intake and cardiovascular disease, coronary heart disease, stroke, type 2 diabetes mellitus, and colorectal cancer extracted from the literature.



(I)



(II)

Figure 5: Mediterranean diet pyramid: I) universal version in 2010 [54], II) proposed version for Italian people in 2014 [55]

The importance of the structure of grains, explained in section 2.4, was considered in the proposed Italian pyramid by suggesting the daily consumption of stoneground wheat bread. The percentage of intactness has a direct effect on the glycemic index. Thus the traditional grounding with millstones leads to higher intact or partially milled kernels, which results in a lower glycemic response of bread.

Another interesting characteristic that has been listed in the pyramid is the use of sourdough whole bread. The reason is that sourdough bread was noted as the typical bread in the Mediterranean Diet during the early 1960s in Nicotera in Italy and more probably in Crete and Corfu in Greece. [55]–[57] Sourdough is called as such due to its peculiar lactic acid bacterial content, which distinguishes it from baker's yeast. The blend of flour and water is left at room temperature for several hours in order to let spontaneous fermentation takes place. The leavening agents are endogenous microorganisms namely yeast and lactic acid bacteria (LAB) which through a process called backslopping (addition of new flour and water to the dough) they stay in an active state. The most prominent effect of LAB metabolism is to acidify the dough and makes it sour. The range of pH is usually 3.8 - 4.5 in sourdough which acts as an inhibitor for spoilage and results in a delay in staling and longer shelf-life. However, this high level of acidity may affect adversely the consumers' perception and acceptability. On the other hand, the reduction of pH gradually is in favor of the activity of some enzymes such as amylase and proteinase. As a result, greater enzymatic activities improve the softness and extensibility of the dough. This is crucial especially for bread with high-fiber contents since the additional bran reduces loaf volume and elasticity, as mentioned in section 2.5.2. Interestingly, the high content of phytate in whole grains may degrade by the action of microorganisms in sourdough. As it is explained above, the low pH in sourdough is a prerequisite for the activity of some enzymes including the endogenous cereal phytase. Above all, the organic acids produced by bacteria lower the postprandial glycemic response in the blood. Lactic acid provokes interaction between starch and gluten and decreases starch availability. Moreover, it slows down the digestion of starch by inhibiting amylolytic enzymes. Meanwhile, acetic acid causes a lag in gastric emptying rate. [58]

Regarding glycemic response, whole- and refined- wheat bread induce the same glycemic Index (GI) of 71 and glycemic load (GL) of 9 and 10 for a 30 g serving size, respectively. Whereas in the case of sourdough wheat bread, the GI is 54, and the GL is 8 for the same serving size. [55] Another study analyzed the blood glucose responses in healthy participants after ingestion of 4 different types of bread with whole- or refined grains and leavened with sourdough or with Saccharomyces cerevisiae. As a result, both types of bread (whole and

refined) fermented with sourdough produced significantly lower glycemic responses when compared to those prepared with S. cerevisiae. By contrast, the presence of bran did not make any difference. [59]

Across Italy, 200 various types of bread are baked traditionally, of which around one-third of them are produced through sourdough leavening. [55] Some examples that are protected by European regulations are Pane di Altamura, Pagnotta del Dittaino, Pane di Matera, Pane di Genzano, and Coppia Ferrarese, which in compliance with their single documents they must be leavened through sourdough technique. [58]

Regardless of the attractiveness of the Italian pyramid by the beneficial medical outcomes that it can provide, its implementation is not feasible, as it is admitted by the authors as well. [55] The main reason is the low availability of such products in the market that can meet the need of the overall population. Moreover, the final products as such (stone-grounded and leavened by sourdough) are more expensive and time-consuming than conventional products. For instance, the fermentation by sourdough requires about 12-24 hours, and the maintenance of the starter is more labor-intensive. However, the industrial baker's yeast produces more uniform products with a shorter time and lower cost of production, which results in higher productivity. It is noteworthy to mention that there are some very recent techniques by which the sourdough application can spread more effectively on an industrial scale. For example, the drying technologies (e.g., freeze-drying and spray-drying) can reduce the difficulties in maintaining the starter. The procedure is the temporary inactivation of microorganisms by the mean of drying, which later the dried sourdough starter gets reactivated by rehydration to perform fermentation. Even though the drying process introduces a promising perspective for the sourdough market by reducing the time of production, but it is still costly. Therefore, it cannot be utilized for the overall population since the general desires of consumers are high-quality but low-price products. [60]

Lately, an up-to-date version of MDP has been released with greater attention on sustainability. The new pyramid is three-dimensional, and the third dimension highlights the corresponding environmental impacts related to those food groups (Figure 6).

Figure 6: The latest revision of MDP in 2020 [61]

The term 'serving' changed to 'portion size' depending on the energy needs of the modern lifestyle in compliance with moderation. Another concept that has been noted along with sustainability is affordability. Legumes intake is shifted down of the pyramid from weekly to daily consumption but not in every meal. Similarly, potatoes consumption is altered from ≤ 3 servings weekly to 1-2 portions with every main meal parallel with the consumption of cereals. Daily main meals are based on cereals, vegetables, fruits, and legumes in order to provide healthy dietary guidance for all classes of the population, even those in financial distress. In this way, the expenses of animal products which have potentially higher prices are cut off in favor of the environment as well as those in need. Interestingly, this updated version just like the previous one recommends preferred consumption of whole grains or partly refined grains not as a necessity, as it was recommended in the Italian MDP. [61]

The main reason behind recommending preferably but not necessarily intakes of whole grains is to provide dietary guidance for the overall population with various socioeconomic ranks. Diet quality is strongly affected by the economics of food choices, in a way that those social classes with lower income tend to choose energy-dense grains (i.e., refined grains), fats, and sweets that have potentially the lower cost than other dietary options. Mainly, the lower the income, the greater demand for starchy staples, whereas those with higher incomes are more likely diversity-seekers with a desire for unusual tastes. Similar findings have been found in a study on Italian people reporting that the risk of diet-related diseases is higher for those with lower socioeconomic status, not only lower incomes but also lesser education. [32], [62]–[64]

Despite of the economic barriers, another prohibitive factor may be palatability of food. Whole grains, like green vegetables, are usually not palatable due to the higher amount of polyphenolic compounds that make them bitter. Several strategies can be implemented to increase the acceptability and accordingly the intake of whole grains by consumers. First of all, the palatability of foods is not a static feature but rather dynamic. It is due to the concept of 'learning' that develops sensory preferences and eating habits toward the appreciation of unfamiliar tastes. Thus unpalatable foods can be perceived as more pleasant through repeated exposure. Subsequently, some studies suggested that whole-grain foods shall be introduced as early as possible, even during infancy, to shape eating habits more effectively. The profound learning ability of infants provides a unique opportunity for a greater acceptance of whole grains throughout the entire lifetime. An intervention study of cereals with 30 % of whole grains for infants, between the age of 4 - 24 months, reported that the bitter taste of whole grains is masked by the dilution and sweetness of the added milk, therefore, no significant changes were observed in sensory experiences compared to a similar cereal made from refined flour (2.30 ± 0.12 and 2.32 ± 0.11, $p = 0.606$, respectively). [3], [65], [66]

As a rule, the acceptability of new foods improves when they are introduced along with an already accepted food. Thereby refined grains can be used as an approach for enhancing likability and consequently greater intakes of whole grains. Likewise, dietary patterns such as the Mediterranean Diet are based their recommendations on a balanced intake of grain-based foods. Some researchers claimed that the positive health-promoting outcomes of grain-based foods are results of the right combination of refined- and whole grains and defined it as 35 % and 23 %, respectively. After all, it is noteworthy to mention that the whole grains may contain 49 - 74% of refined grains, depending on their definitions. [21], [66]

In conclusion, a more achievable goal is increasing the whole-grain intake by replacing some portions of refined grains rather than prohibiting all refined grains without considering nutritional and culinary impacts on the overall diet.

3. Coronavirus Disease 19 (COVID-19) and dietary changes

From March 2020, the entire world is confronting one of the most severe outbreaks in history. Coronavirus disease (COVID-19) is still spreading globally while no country has been spared.[67] Apart from its high fatality rate (the highest rate of 14.53% was recorded for Italy

on the 20th of June 2020 [68]), COVID-19 led to several catastrophic mental complications. Panic and anxiety triggered by uncertainty from the disease, isolation, and loss of income all promoted a severely stressful period.

In response to psychological distress during a crisis, people usually tend to change their eating behaviors, not only in terms of food choice but also quantity of intake. With this perspective, several studies examined the changes in dietary habits before and during COVID-19. One of the most considerable changes that frequently has been reported by most of the studies was an increase in the consumption of sweets. Sugary products are linked to a greater release of serotonin and dopamine that are both neurotransmitters responsible for mood regulation by boosting the sensations of happiness and pleasure. Stressful situations and boredom due to home confinement initiated a subliminal driving force in the majority of people to self-medicate through increasing their consumption of foods rich in sugar. This eating pattern is known as emotional eating in a way that it creates a vicious circle of constant craving for calorically dense foods such as those with higher sugar and fat contents which continues as long as the source of stress is still intense. [69], [70]

Among the Mediterranean countries, Italy was one of the pioneers for identifying the association of food-related behavioral changes during quarantine. The majority of studies also analyzed the correlation of observed changes with Adherence to the Mediterranean Diet (AMD) among Italian participants. Main findings by focusing on changes in consumption of two carbohydrate sources (namely sugary products and cereals) are represented in Table 6.

In Italy, there was a north-south gradient in the incidence of infection and the mortality rate. Figure 7 indicates the higher infection rates in northern regions compared to the southern ones. Numerous variables may cause the greater susceptibility of northern Italian inhabitants, which can be intrinsic (e.g., different genetic backgrounds and lifestyles) or extrinsic (e.g., population density, healthcare system, and air pollution). Among intrinsic factors, dietary habits play a significant role since a balanced healthy diet boosts the immune system in a way that it can act more efficiently as the first defense against infection [67].

With this logic, several studies hypothesized the potential protective effects of the Mediterranean Diet against the risk of virus infection. Generally, those participants with a low score of AMD were more likely to increase their intakes of the ultra-processed foods (UPFs) [71], reduce physical activity, have a higher level of distress [72], and a higher risk of infection. Furthermore, the southern areas tend to have a higher score of AMD than northern ones. Thus, the trend of Italian people to the AMD appears to be in the opposite direction of the infection gradient that is shown in Figure 7.

Table 6: Summary of several Italian studies on changes in eating habits during the COVID-19 pandemic

Authors	Sample Size	Study Group	Sugary products	Cereals Consumption	AMD*	Overall Findings
Grant et al. [73]	2678	≥ 18 years	Increased by 36.9%	Respondents with high AMD consumed 20.1% more whole grains, while those with low AMD consumed more of white bread and non-whole pasta and rice for 20.3% and 17.3% respectively.	62% had low score	Increased intakes of fruits (24.4%), vegetables (28.5%), legumes (22.1%), nuts (12%), and fish or shellfish (14%); while unfavorable changes were decreased physical activity (37.2%), and increased comfort foods (22.7%) and wine (16%) intakes.
Izzo et al. [74]	1519	All ages	Increased by 55.9%	60.1% of respondents had daily consumption of cereals while 22.6% had them twice a day. Daily intake of whole-grain products also was observed for 34%.	Medium score in 73.5% of respondents mainly with 18-30 years	81% of respondents decreased intake of alcohol, 81.3% of them increased intake of frozen foods, while 70.5% reported a decrease in physical activity, while 29% showed high distress.
Prete et al. [72]	604	16-62 years	Increased by 51%	30% of respondents increased intakes of bread/rice/pasta.	63% had low score	Increased intakes of 28% for fresh fruits and 27% for vegetables. 72% of respondents claimed to be more inactive, and 61% had low sleep quality. Lower AMD led to 3-times more risk of physical inactivity but no significant changes in sleep quality.
Ponzo et al. [67]	900	Active HCPs** with 20-65 years	-	-	Mean score was 10.5 out of 17	16.4% of HCPs who reported infection had low AMD score with low intake of cereals and high intakes of proteins and saturated fats.
Bonaccio et al. [71]	1501	≥ 18 years	Intake of chocolate increased by 11.1%	90% of respondents reported no changes in intakes of breakfast cereals and cereal bars, while overall 3.9% and 11.8% increased the intakes of bread substitutes and biscuits.	-	37.5% of respondents their increased intakes of UPFs***, while those Italians from south had a lower intake than northern ones. 37.6% of respondents gained weight. Food budget increased by 30.4%.

** Adherence to the Mediterranean Diet (AMD), ** Healthcare professionals (HCPs), *** Ultra-Processed Foods (UPFs): foods containing predominantly industrial substances (i.e., high amount of additives)*

Figure 7: North–South gradient of cumulative infected cases of COVID-19 in Italy by 27 June 2020. The different sizes of yellow dot corresponds to density of ascertained cases, the larger the dot indicates the higher level of contagion. [75]

Ponzo et al. (2020) observed an inverse correlation between the AMD and the risk of infection and consumption of cereals. Interestingly, the higher consumption of cereals resulted in lower odds of infection. Since there was no distinction between the types of consumed cereals (whole or refined), the observed protective effects are associated with the overall cereal intakes, not only the whole portion. Apparently, total grain consumption (even with a lesser extent of whole grains) displays an immunomodulatory activity by modulating the gut microbiota. In addition to cereal grains, other components of the Mediterranean Diet such as fruits, vegetables, nuts, olive oil, and even red wine are rich in antioxidants, which are famous for their anti-inflammatory and anti-viral activities. Consequently, the immunostimulatory impacts of the Mediterranean Diet are due to the synergies between all components in the overall diet and not only one single group. However, it is noteworthy to emphasize that a hypothetical direct relationship between infection rate and the AMD, which showed the opposite gradients, is not definite. Apart from differences in dietary patterns, there might be many confounding factors involved, such as cultural and societal norms, various healthcare systems, and governmental responses to the pandemic, as it is admitted by the authors as well. [67], [72]

In addition to dietary changes, other food-related behavioral changes have been observed during the COVID-19 pandemic. According to reports, Italians overspent 17 % more on packaged products from 17 February to 15 March 2020 than the previous four weeks, while

compared to the same weeks in 2019, it was increased by 19%. [74], [76] This phenomenon might be due to an immediate reaction of consumers to the pandemic situation by increasing their food stocks. Mainly, food items that have been purchased were those known as emergency products with a longer shelf-life, such as flour, frozen vegetables, and canned meat. Moreover, compared to pre-Covid times, approximately 80 % of participants in studies reported more sensitivity to food waste. [73] Considering the total closure of the Hotel, Restaurant, Catering (Ho.Re.Ca) channel, modern distribution such as online shopping increased correspondingly by 81 % in the last week of February and 97 % in the second week of March. [76]

4. Conclusion

Nowadays, most dietary guidelines only recommend the consumption of whole grains, consequently, the exclusion of all refined ones. However, the Mediterranean diet suggests preferring whole grains but not exclusively their consumption.

The Mediterranean diet is not a single dietary pattern but rather a framework that originated from the olive-growing regions of the Mediterranean basin, each country adopts the framework based on its own unique culture, tradition, and socio-economic status of its population. In this sense, a greater focus is on the lifestyle rather than the eating habit itself, since the origin of the word ‘diet’ is the Greek concept of ‘diaita’ which means lifestyle and cultural practices.

In the complex context of the dietary pattern, the interactions of different food groups and the level of physical activity both play significant complementary roles in nutrition research. Those studies that aim to change a single food group (such as grains) without considering the synergic interactions with other groups and the overall lifestyle, can barely be conducted blindly and the results are mainly confounded. Therefore, the choice of foods that are replaced (e.g., refined grains) can be as important as those that are added.

Even though the mechanisms by which whole grains can be health-promoting are not yet completely understood, a greater consumption of them accompanied by maintaining a healthy lifestyle lower the risk of chronic diseases to a greater extent. However, many barriers prevent consumers from increasing their consumption, including unclear labeling and inconsistent definition of whole-grain products, undesirable taste, and higher cost. Undoubtedly, only recommending people to consume foods with less than ideal sensory qualities or higher costs

is unrealistic and impractical. Unless first they can afford those products and they learn to appreciate them. For this purpose, some policies are prerequisites such as:

- Setting clear labeling for whole-grain products which are credible and easily recognizable by consumers
- Attempts in changing the taste preference of consumers gradually through increasing their awareness and repeated exposure
- Increasing availability, affordability, and palatability through technological improvement to recipes of whole-grain products

Besides, both refined- and whole-grain products may be calorically dense due to added fats and sugars to reinforce their palatability. As one of the basic concepts of dietary behaviors, energy intake and expenditure should be equal to maintain the body's energy balance.

However, one drastic influence of the COVID-19 pandemic is increasing motivation to eat. When accompanied by a sedentary lifestyle due to home confinement, it can cause energy imbalance which is the major risk factor for many chronic diseases. Grains at the base of the dietary pyramid have a twofold role during the pandemic. They are the essential providers of a wide range of bioactive compounds with a longer shelf-life. Whereas their overconsumption through a constant carbohydrate craving, as an anti-depressant mean, during quarantine has a destructive impact on energy balance. Therefore, in the current stress-overeating situation, the primary goal should be restricting calories intake due to reduced physical activity during isolation.

References

[1] "Whole grain definition by HEALTHGRAIN consortium," 2013. [Online]. Available: https://healthgrain.org/whole-grain/#toggle-id-3.

[2] Food and Agriculture Organisation of the United Nations, "FAO Cereal Supply and Demand Brief," 2021. [Online]. Available: https://www.fao.org/worldfoodsituation/csdb/en/.

[3] M. Klerks, M. Bernal, S. Roman, S. Bodenstab, A. Gil, and L. Sanchez-Siles, "Infant Cereals: Current Status, Challenges, and Future Opportunities for Whole Grains," *Nutrients*, vol. 11, no. 2, p. 473, Feb. 2019, doi: 10.3390/nu11020473.

[4] A. Fardet, "New hypotheses for the health-protective mechanisms of whole-grain cereals: What is beyond fibre?," *Nutr. Res. Rev.*, vol. 23, no. 1, pp. 65–134, 2010, doi: 10.1017/S0954422410000041.

[5] K. K. Adom and R. H. Liu, "Antioxidant Activity of Grains," *J. Agric. Food Chem.*, vol. 50, no. 21, pp. 6182–6187, Oct. 2002, doi: 10.1021/jf0205099.

[6] A. Gani, W. SM, and M. FA, "Whole-Grain Cereal Bioactive Compounds and Their Health Benefits: A Review," *J. Food Process. Technol.*, vol. 03, no. 03, 2012, doi: 10.4172/2157-7110.1000146.

[7] A. Fardet, "New Approaches to Studying the Potential Health Benefits of Cereals: From Reductionism to Holism," *Cereal Foods World*, vol. 59, no. 5, pp. 224–229, Sep. 2014, doi: 10.1094/CFW-59-5-0224.

[8] E. M. Barrett, M. J. Batterham, S. Ray, and E. J. Beck, "Whole grain, bran and cereal fibre consumption and CVD: a systematic review," *Br. J. Nutr.*, vol. 121, no. 8, pp. 914–937, Apr. 2019, doi: 10.1017/S000711451900031X.

[9] J. W. Van Der Kamp, K. Poutanen, C. J. Seal, and D. P. Richardson, "The HEALTHGRAIN definition of 'whole grain,'" *Food Nutr. Res.*, vol. 58, 2014, doi: 10.3402/fnr.v58.22100.

[10] European Commission, "whole grain, Health Promotion and Disease Prevention Knowledge Gateway." https://knowledge4policy.ec.europa.eu/health-promotion-knowledge-gateway/whole-grain_en#recommended (accessed Nov.

22, 2021).

[11] A. B. Ross *et al.*, “Perspective: A Definition for Whole-Grain Food Products—Recommendations from the Healthgrain Forum,” *Adv. Nutr.*, vol. 8, no. 4, pp. 525–531, 2017, doi: 10.3945/an.116.014001.

[12] R. Korczak and J. L. Slavin, “Definitions, regulations, and new frontiers for dietary fiber and whole grains,” *Nutr. Rev.*, vol. 78, pp. 6–12, 2020, doi: 10.1093/NUTRIT/NUZ061.

[13] S. Sette *et al.*, “Intakes of whole grain in an Italian sample of children, adolescents and adults,” *Eur. J. Nutr.*, vol. 56, no. 2, pp. 521–533, Mar. 2017, doi: 10.1007/s00394-015-1097-5.

[14] K. B. Miller, “Review of whole grain and dietary fiber recommendations and intake levels in different countries,” *Nutr. Rev.*, vol. 78, no. Supplement_1, pp. 29–36, Aug. 2020, doi: 10.1093/nutrit/nuz052.

[15] I. Tetens, “Substituting whole grain for refined grain: what is needed to strengthen the scientific evidence for health outcomes?,” *Am. J. Clin. Nutr.*, vol. 105, no. 3, pp. 545–546, Mar. 2017, doi: 10.3945/ajcn.117.152496.

[16] European Food Safety Authority, “Scientific Opinion on the substantiation of health claims related to niacin.,” *EFSA J.*, vol. 8, no. 1924, p. 7(9):1224, 2009, doi: 10.2903/j.efsa.2010.1766.Available.

[17] C. J. Seal and I. A. Brownlee, “Whole-grain foods and chronic disease: Evidence from epidemiological and intervention studies,” *Proc. Nutr. Soc.*, vol. 74, no. 3, pp. 313–319, 2015, doi: 10.1017/S0029665115002104.

[18] FDA, “Draft Guidance for Industry and FDA Staff: Whole Grain Label Statements.” https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-and-fda-staff-whole-grain-label-statements%0Ahttps://www.fda.gov/Food/GuidanceRegulation/ucm059088.htm (accessed Nov. 14, 2021).

[19] “Letter to the FDA on a whole grain food definition,” 2014. [Online]. Available: https://wholegrainscouncil.org/sites/default/files/atoms/files/WGCtoFDAJan2014.pdf.

[20] FDA, “Health claim notification for whole grain foods,” 1999. https://www.fda.gov/food/food-labeling-nutrition/health-claim-notification-whole-grain-foods (accessed Nov. 14, 2021).

[21] J. M. Jones, C. G. García, and H. J. Braun, “Perspective: Whole and Refined Grains and Health - Evidence Supporting ‘make Half Your Grains Whole,’” *Adv. Nutr.*, vol. 11, no. 3, pp. 492–506, 2020, doi: 10.1093/advances/nmz114.

[22] Jones, “Whole Grains--Issues and Deliberations from the Whole Grain Task Force,” *Cereal Foods World*, vol. 53, no. 5, pp. 260–264, 2008, doi: 10.1094/CFW-53-5-0260.

[23] C. W. Thane, A. R. Jones, A. M. Stephen, C. J. Seal, and S. A. Jebb, “Whole-grain intake of British young people aged 4–18 years,” *Br. J. Nutr.*, vol. 94, no. 5, pp. 825–831, Nov. 2005, doi: 10.1079/BJN20051557.

[24] M. G. Ferruzzi *et al.*, “Developing a Standard Definition of Whole-Grain Foods for Dietary Recommendations: Summary Report of a Multidisciplinary Expert Roundtable Discussion,” *Adv. Nutr.*, vol. 5, no. 2, pp. 164–176, Mar. 2014, doi: 10.3945/an.113.005223.

[25] Whole Grain Initiative, “Global Whole Grain Food Definition (Version Nov. 2020),” 2020. https://www.wholegraininitiative.org/publications (accessed Jan. 17, 2022).

[26] D. J. Jenkins *et al.*, “Wholemeal versus wholegrain breads: proportion of whole or cracked grain and the glycaemic response.,” *BMJ*, vol. 297, no. 6654, pp. 958–60, Oct. 1988, doi: 10.1136/bmj.297.6654.958.

[27] M. Kristensen *et al.*, “Wholegrain vs. refined wheat bread and pasta. Effect on postprandial glycemia, appetite, and subsequent ad libitum energy intake in young healthy adults,” *Appetite*, vol. 54, no. 1, pp. 163–169, Feb. 2010, doi: 10.1016/j.appet.2009.10.003.

[28] W. Frølich, P. Åman, and I. Tetens, “Whole grain foods and health – a Scandinavian perspective,” *Food Nutr. Res.*, vol. 57, no. 1, p. 18503, Jan. 2013, doi: 10.3402/fnr.v57i0.18503.

[29] G. A. Gaesser, “Perspective: Refined Grains and Health: Genuine Risk, or Guilt

by Association?," *Adv. Nutr.*, vol. 10, no. 3, pp. 361–371, May 2019, doi: 10.1093/advances/nmy104.

[30] K. R. Kissock, E. P. Neale, and E. J. Beck, "Whole Grain Food Definition Effects on Determining Associations of Whole Grain Intake and Body Weight Changes: A Systematic Review," *Adv. Nutr.*, vol. 12, no. 3, pp. 693–707, 2021, doi: 10.1093/advances/nmaa122.

[31] A. Ampatzoglou *et al.*, "Increased Whole Grain Consumption Does Not Affect Blood Biochemistry, Body Composition, or Gut Microbiology in Healthy, Low-Habitual Whole Grain Consumers," *J. Nutr.*, vol. 145, no. 2, pp. 215–221, Feb. 2015, doi: 10.3945/jn.114.202176.

[32] S. H. Hosseini, Y. Papanikolaou, N. Islam, P. Rashmi, A. Shamloo, and H. Vatanparast, "Consumption Patterns of Grain-Based Foods among Adults in Canada: Evidence from Canadian Community Health Survey—Nutrition 2015," *Nutrients*, vol. 11, no. 4, p. 784, Apr. 2019, doi: 10.3390/nu11040784.

[33] D. Aune *et al.*, "Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies," *BMJ*, vol. 353, p. i2716, Jun. 2016, doi: 10.1136/bmj.i2716.

[34] O. Sadeghi, A. Hassanzadeh-Keshteli, H. Afshar, A. Esmaillzadeh, and P. Adibi, "The association of whole and refined grains consumption with psychological disorders among Iranian adults," *Eur. J. Nutr.*, vol. 58, no. 1, pp. 211–225, 2019, doi: 10.1007/s00394-017-1585-x.

[35] D. Wu, Y. Guan, S. Lv, H. Wang, and J. Li, "No Evidence of Increased Risk of Stroke with Consumption of Refined Grains: A Meta-analysis of Prospective Cohort Studies," *J. Stroke Cerebrovasc. Dis.*, vol. 24, no. 12, pp. 2738–2746, 2015, doi: 10.1016/j.jstrokecerebrovasdis.2015.08.004.

[36] K. Pol, R. Christensen, E. M. Bartels, A. Raben, I. Tetens, and M. Kristensen, "Whole grain and body weight changes in apparently healthy adults: a systematic review and meta-analysis of randomized controlled studies," *Am. J. Clin. Nutr.*, vol. 98, no. 4, pp. 872–884, Oct. 2013, doi:

10.3945/ajcn.113.064659.

[37] H. Khosravi-Boroujeni *et al.*, “White Rice Consumption and CVD Risk Factors among Iranian Population,” *J. Heal. Popul. Nutr.*, vol. 31, no. 2, pp. 252–261, Sep. 2013, doi: 10.3329/jhpn.v31i2.16390.

[38] L. Schwingshackl *et al.*, “Food groups and risk of colorectal cancer,” *Int. J. Cancer*, vol. 142, no. 9, pp. 1748–1758, May 2018, doi: 10.1002/ijc.31198.

[39] P. G. Williams, “Evaluation of the evidence between consumption of refined grains and health outcomes,” *Nutr. Rev.*, vol. 70, no. 2, pp. 80–99, Feb. 2012, doi: 10.1111/j.1753-4887.2011.00452.x.

[40] H. I. Katcher *et al.*, “The effects of a whole grain–enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome,” *Am. J. Clin. Nutr.*, vol. 87, no. 1, pp. 79–90, Jan. 2008, doi: 10.1093/ajcn/87.1.79.

[41] H. Hauner *et al.*, “Evidence-Based Guideline of the German Nutrition Society: Carbohydrate Intake and Prevention of Nutrition-Related Diseases,” *Ann. Nutr. Metab.*, vol. 60, no. s1, pp. 1–58, 2012, doi: 10.1159/000335326.

[42] N. M. McKeown, L. M. Troy, P. F. Jacques, U. Hoffmann, C. J. O’Donnell, and C. S. Fox, “Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study,” *Am. J. Clin. Nutr.*, vol. 92, no. 5, pp. 1165–1171, Nov. 2010, doi: 10.3945/ajcn.2009.29106.

[43] L. A. Bazzano, Y. Song, V. Bubes, C. K. Good, J. E. Manson, and S. Liu, “Dietary Intake of Whole and Refined Grain Breakfast Cereals and Weight Gain in Men,” *Obes. Res.*, vol. 13, no. 11, pp. 1952–1960, Nov. 2005, doi: 10.1038/oby.2005.240.

[44] C. J. Seal, C. M. Courtin, K. Venema, and J. de Vries, “Health benefits of whole grain: effects on dietary carbohydrate quality, the gut microbiome, and consequences of processing,” *Compr. Rev. Food Sci. Food Saf.*, vol. 20, no. 3, pp. 2742–2768, 2021, doi: 10.1111/1541-4337.12728.

[45] L. Tebben, Y. Shen, and Y. Li, “Improvers and functional ingredients in whole

wheat bread: A review of their effects on dough properties and bread quality," *Trends Food Sci. Technol.*, vol. 81, no. August, pp. 10–24, Nov. 2018, doi: 10.1016/j.tifs.2018.08.015.

[46] S. Raffan and N. G. Halford, "Acrylamide in food: Progress in and prospects for genetic and agronomic solutions," *Ann. Appl. Biol.*, vol. 175, no. 3, pp. 259–281, Nov. 2019, doi: 10.1111/aab.12536.

[47] S. Rousseau, C. Kyomugasho, M. Celus, M. E. G. Hendrickx, and T. Grauwet, "Barriers impairing mineral bioaccessibility and bioavailability in plant-based foods and the perspectives for food processing," *Crit. Rev. Food Sci. Nutr.*, vol. 60, no. 5, pp. 826–843, Mar. 2020, doi: 10.1080/10408398.2018.1552243.

[48] J. L. Slavin, "Whole grains, refined grains and fortified refined grains: What's the difference?," *Asia Pac. J. Clin. Nutr.*, vol. 9, no. SUPPL., 2000, doi: 10.1046/j.1440-6047.2000.00171.x.

[49] R. Bortolus *et al.*, "Prevention of congenital malformations and other adverse pregnancy outcomes with 4.0 mg of folic acid: community-based randomized clinical trial in Italy and the Netherlands," *BMC Pregnancy Childbirth*, vol. 14, no. 1, p. 166, Dec. 2014, doi: 10.1186/1471-2393-14-166.

[50] M. Fischer, M. Stronati, and M. Lanari, "Mediterranean diet, folic acid, and neural tube defects," *Ital. J. Pediatr.*, vol. 43, no. 1, p. 74, Dec. 2017, doi: 10.1186/s13052-017-0391-7.

[51] G. Cormick *et al.*, "Impact of flour fortification with calcium on calcium intake: a simulation study in seven countries," *Ann. N. Y. Acad. Sci.*, vol. 1493, no. 1, pp. 59–74, Jun. 2021, doi: 10.1111/nyas.14550.

[52] Y. Papanikolaou *et al.*, "Do Refined Grains Have a Place in a Healthy Dietary Pattern: Perspectives from an Expert Panel Consensus Meeting," *Curr. Dev. Nutr.*, vol. 4, no. 10, pp. 1–16, Oct. 2020, doi: 10.1093/cdn/nzaa125.

[53] Y. Papanikolaou and V. L. I. Fulgoni, "The Role of Fortified and Enriched Refined Grains in the US Dietary Pattern: A NHANES 2009–2016 Modeling Analysis to Examine Nutrient Adequacy," *Front. Nutr.*, vol. 8, no. September, pp. 1–12, Sep. 2021, doi: 10.3389/fnut.2021.655464.

[54] A. Bach-Faig *et al.*, “Mediterranean diet pyramid today. Science and cultural updates,” *Public Health Nutr.*, vol. 14, no. 12A, pp. 2274–2284, 2011, doi: 10.1017/S1368980011002515.

[55] A. D’Alessandro and G. De Pergola, “Mediterranean diet pyramid: A proposal for italian people,” *Nutrients*, vol. 6, no. 10, pp. 4302–4316, 2014, doi: 10.3390/nu6104302.

[56] S. Dernini and E. M. Berry, “Mediterranean Diet: From a Healthy Diet to a Sustainable Dietary Pattern,” *Front. Nutr.*, vol. 2, no. May, pp. 1–7, 2015, doi: 10.3389/fnut.2015.00015.

[57] A. D’Alessandro, L. Lampignano, and G. De Pergola, “Mediterranean diet pyramid: A proposal for Italian people. a systematic review of prospective studies to derive serving sizes,” *Nutrients*, vol. 11, no. 6, 2019, doi: 10.3390/nu11061296.

[58] P. Catzeddu, “Sourdough Breads,” in *Flour and Breads and their Fortification in Health and Disease Prevention*, Elsevier, 2011, pp. 37–46.

[59] F. Scazzina, D. Del Rio, N. Pellegrini, and F. Brighenti, “Sourdough bread: Starch digestibility and postprandial glycemic response,” *J. Cereal Sci.*, vol. 49, no. 3, pp. 419–421, May 2009, doi: 10.1016/j.jcs.2008.12.008.

[60] G. Albagli, I. do M. Schwartz, P. F. F. Amaral, T. F. Ferreira, and P. V. Finotelli, “How dried sourdough starter can enable and spread the use of sourdough bread,” *LWT*, vol. 149, no. June, p. 111888, Sep. 2021, doi: 10.1016/j.lwt.2021.111888.

[61] L. Serra-Majem *et al.*, “Updating the mediterranean diet pyramid towards sustainability: Focus on environmental concerns,” *Int. J. Environ. Res. Public Health*, vol. 17, no. 23, pp. 1–20, 2020, doi: 10.3390/ijerph17238758.

[62] A. Drewnowski and N. Darmon, “Food Choices and Diet Costs : an Economic Analysis,” *J. Nutr.*, pp. 900–904, 2005.

[63] N. Darmon and A. Drewnowski, “Does social class predict diet quality?,” *Am. J. Clin. Nutr.*, vol. 87, no. 5, pp. 1107–1117, May 2008, doi: 10.1093/ajcn/87.5.1107.

[64] M. Bonaccio, L. Iacoviello, and G. De Gaetano, “The Mediterranean diet: The reasons for a success,” *Thromb. Res.*, vol. 129, no. 3, pp. 401–404, 2012, doi: 10.1016/j.thromres.2011.10.018.

[65] S. Kuznesof, I. A. Brownlee, C. Moore, D. P. Richardson, S. A. Jebb, and C. J. Seal, “WHOLEheart study participant acceptance of wholegrain foods,” *Appetite*, vol. 59, no. 1, pp. 187–193, Aug. 2012, doi: 10.1016/j.appet.2012.04.014.

[66] J. Haro-Vicente, M. Bernal-Cava, A. Lopez-Fernandez, G. Ros-Berruezo, S. Bodenstab, and L. Sanchez-Siles, “Sensory Acceptability of Infant Cereals with Whole Grain in Infants and Young Children,” *Nutrients*, vol. 9, no. 1, p. 65, Jan. 2017, doi: 10.3390/nu9010065.

[67] V. Ponzo *et al.*, “Mediterranean Diet and SARS-COV-2 Infection: Is There Any Association? A Proof-of-Concept Study,” *Nutrients*, vol. 13, no. 5, p. 1721, May 2021, doi: 10.3390/nu13051721.

[68] Our World in Data, “Mortality Risk of COVID-19.” https://ourworldindata.org/mortality-risk-covid (accessed Dec. 26, 2021).

[69] R. Zupo *et al.*, “Preliminary Trajectories in Dietary Behaviors during the COVID-19 Pandemic: A Public Health Call to Action to Face Obesity,” *Int. J. Environ. Res. Public Health*, vol. 17, no. 19, p. 7073, Sep. 2020, doi: 10.3390/ijerph17197073.

[70] E. Romeo-Arroyo, M. Mora, and L. Vázquez-Araújo, “Consumer behavior in confinement times: Food choice and cooking attitudes in Spain,” *Int. J. Gastron. Food Sci.*, vol. 21, no. June, p. 100226, Oct. 2020, doi: 10.1016/j.ijgfs.2020.100226.

[71] M. Bonaccio *et al.*, “Changes in ultra-processed food consumption during the first Italian lockdown following the COVID-19 pandemic and major correlates: Results from two population-based cohorts,” *Public Health Nutr.*, vol. 24, no. 12, pp. 3905–3915, Aug. 2021, doi: 10.1017/S1368980021000999.

[72] M. Prete *et al.*, “Changes in Lifestyle and Dietary Habits during COVID-19 Lockdown in Italy: Results of an Online Survey,” *Nutrients*, vol. 13, no. 6, p.

1923, Jun. 2021, doi: 10.3390/nu13061923.

[73] F. Grant, M. L. Scalvedi, U. Scognamiglio, A. Turrini, and L. Rossi, “Eating Habits during the COVID-19 Lockdown in Italy: The Nutritional and Lifestyle Side Effects of the Pandemic,” *Nutrients*, vol. 13, no. 7, p. 2279, Jun. 2021, doi: 10.3390/nu13072279.

[74] L. Izzo *et al.*, “An Italian survey on dietary habits and changes during the COVID-19 lockdown,” *Nutrients*, vol. 13, no. 4, p. 1197, Apr. 2021, doi: 10.3390/nu13041197.

[75] S. Lolli, Y.-C. Chen, S.-H. Wang, and G. Vivone, “Impact of meteorological conditions and air pollution on COVID-19 pandemic transmission in Italy,” *Sci. Rep.*, vol. 10, no. 1, p. 16213, Dec. 2020, doi: 10.1038/s41598-020-73197-8.

[76] R. M. Fanelli, “Changes in the Food-Related Behaviour of Italian Consumers during the COVID-19 Pandemic,” *Foods*, vol. 10, no. 1, p. 169, Jan. 2021, doi: 10.3390/foods10010169.