1 Nutrition and health or nutrients and health?

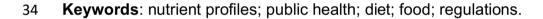
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21 Abstract

22 Diet is an important contributor to human health and public health bodies are issuing guidelines aimed at favouring healthy food choices. Aim of our paper is to discuss the 23 aspects underlying the concept of nutrient profiles, i.e. defining levels of energy, some 24 25 macronutrients, or salt which should not be exceeded in individual foods, according to the available evidence, to help understanding to what extent such approach may actually be 26 useful for improving nutrition and quality of life of European consumers. We list several 27 pitfalls and oversimplifications of the current approaches to nutrient profiling and of the 28 29 dichotomic classification of foods into 'healthy' and 'unhealthy' products. In view of the 30 current "Facilitating healthier food choices – establishing nutrient profiles" EU initiative, we 31 believe that further debate among all stakeholders is warranted and must consider all the limitations outlined in this paper. 32

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36 Introduction

The importance of diet in the maintenance of human health is supported by a large body of evidence: according to the latest results from the ongoing Global Burden of Disease Study, one in five deaths in the world, mainly from cardiovascular diseases and cancers, can be attributed to an unhealthy diet (The Global Burden of Disease Diet Collaborators 2019). This is why prevention of diet-related non-communicable diseases has become one of the main global objectives of health policies, aimed at creating healthy environments and empowering people to choose healthy foods.

44 Among them, the Farm-to-Fork Strategy is one of the key pillars of the European Green Deal (Purnhagen et al. 2021; The European Commission 2020), aiming also at 45 developing a fair, healthy, and environmentally-friendly food system, in turn boosting the 46 47 transition to a more sustainable food system. This transition would be difficult to achieve without a shift in people's diets, considering the current double burden of 48 malnutrition/overnutrition - with a growing rate of overweight and obesity - and 49 50 undernutrition, with million people still suffering from stunting and ~20% of food being wasted (FUSIONS 2016; National Academies of Sciences 2020). 51

52 In this context, the European Commission highlights the role that food processors, food service operators, and retailers can play in contributing to improve consumers' dietary 53 choices via ameliorating the nutritional characteristics of the food they produce or sell. 54 Therefore, the European Commission will seek: i) commitments from food companies and 55 56 organizations to take concrete actions on health and sustainability of their products, and ii) 57 opportunities to facilitate the shift to healthier diets and stimulate product reformulation. This set of strategies includes the setting up of a system of nutrient profiles, to restrict the 58 59 promotion of foods high in fat, sugar, and salt, and in perspective to become the reference 60 for nutritional information to the general population, which should be achieved by Q4 2022.

In fact, the development of a nutrient profile model as a common tool for use or adaption by Member States across Europe (on a voluntary basis and taking into account national conditions and peculiarities) has since been identified as a key activity in the European Food and Nutrition Action Plan 2015–2020, for the purposes of restricting the marketing to children of foods with possible unfavourable nutritional effects (WHO Regional Office for Europe 2014).

67 Whether such strategy can effectively impact not only on consumers' choices, but 68 also, above all, on their health, is still a matter of debate and should probably undergo a 69 thorough evaluation process. Interestingly, in 2008 the definition of nutrient profiles has been 70 addressed by the experts of the European Food Safety Authority (EFSA), who critically 71 evaluated the theoretical bases of the nutrient profile system, concluding that this approach 72 has a number of inherent weaknesses, which need to be carefully considered (EFSA Panel 73 on Dietetic Products 2008). The whole proposed system must in any case take in adequate 74 consideration the large body of evidence which has emerged in recent years about the impact of nutrition, including both nutrient intake and food consumption, on human health, 75 without neglecting aspects related to consumer science and public health. 76

Aim of this paper is to discuss the aspects underlying the concept of nutrient profiles (i.e. defining levels of some macronutrient, energy, or salt which should not be exceeded in individual foods) (Drewnowski, Amanquah, and Gavin-Smith 2021), according to the available evidence, to help understanding to what extent such approach may actually be useful for improving nutrition and quality of life of European consumers.

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83 The framework: Positive vs. Negative Nutrition

The role of evidence-based information in the communication of food and health information to the consumer has been recognised by all international organisations which

have taken a position on this issue. Even the European Commission Regulation 1924/2006
(The European Parliament 2006), promoting nutrient profiles as a criterion to regulate the
use of nutrition or health claims for food products, clarifies that principles underlying nutrient
profiles should consider scientific evidence relative to the relationship between diet, nutrition
and health as well as dietary recommendations and public health considerations.

Such evidence is rapidly evolving, and new concepts to be used as framework of new
recommendations are emerging in recent years.

Traditionally, nutrition sciences have focused on the health risks associated with the consumption of excessive amounts of energy (leading, especially if combined with a sedentary lifestyle, to overweight and its sequalae such as type 2 diabetes), of fats (particularly saturated fats that increase plasma cholesterol levels and, hence, the risk of cardiovascular diseases), and of sodium, the high intake of which may lead to increased blood pressure and eventually to an increased risk of stroke and other cardiovascular disorders (The Global Burden of Disease Diet Collaborators 2019).

100 The scientific literature on nutrition and health of the last decade, on the other hand, strongly supports a different approach based on the priority of promoting the consumption 101 of favourable nutrients such as vitamins, minerals, and fibre (The Food and Agriculture 102 103 Organization of the United Nations 2007 (updated 2018)) and to recommend the consumption of specific food groups, such as fruit and vegetables (Yip, Chan, and Fielding 104 2019), wholegrain (Zhang et al. 2018), legumes (Viguiliouk et al. 2019), and nuts (de Souza 105 et al. 2020), which have been associated with protective and beneficial effects on human 106 health if included in appropriate dietary patterns, rather than limiting nutrient consumption 107 with possible adverse effects. 108

109 This is very relevant, because nutrient profiles and, as a consequence, some of the 110 most popular labelling systems proposed to provide additional nutritional information on the

front-of-pack of food products, are, conversely, based on setting limits aimed at reducingthe intake of such untoward nutrients.

High consumption of many of the aforementioned salubrious foods is typical of the 113 Mediterranean diet (Martini and Bes-Restrollo 2020), which is a plant-based dietary pattern 114 characterized by high amounts of fruit and vegetables, cereal-based foods (consumed 115 preferably as wholegrain), with moderate amount of animal foods, and olive oil as the 116 preferred source of fats (Russo et al. 2021; Visioli et al. 2018). The Mediterranean diet has 117 118 been shown to exert the strongest beneficial effect on anthropometric parameters and cardiometabolic risk factors (Esposito et al. 2015; Dinu et al. 2020) and has been associated 119 with a reduced risk of overall mortality and of developing several chronic diseases (Bonaccio 120 121 et al. 2018; Soltani et al. 2019; Dinu et al. 2021).

These beneficial effects can be attributed to the set of foods that is consumed in adequate amounts - in terms of serving size and frequency of consumption - in this diet and, in turn, to their manifold components such as fibre, vitamins and minerals, but also to a plethora of bioactive compounds like (poly)phenols, that positively act through several mechanisms, including protection from low-grade inflammation (Calder et al. 2017) and modulation of the gut microbiota (Shortt et al. 2018), further explaining the health benefits of the Mediterranean diet (Wang et al. 2021).

The relationship between a nutrition more focussed on foods to be consumed, rather than on foods/nutrients to be avoided (for sake of simplicity: "positive nutrition") and the Mediterranean diet needs to be discussed in detail. It is, in fact, worth underscoring how the Mediterranean diet, largely considered by the scientific community as the reference dietary model because of its manifold actions (Godos et al. 2017), is a specific example of the prevalence of "positive" (more cereals, more fruit and vegetables, more fish, etc.) on "negative" messages (less meat, less whole milk and dairy products), none of which

concerns individual nutrients (Bach-Faig et al. 2011). Many of the studies assessing the 136 specific contribution of the various dietary components to the association between the 137 favourable health effects of the Mediterranean pattern (generally assessed by scoring 138 systems) (Eleftheriou et al. 2018) have confirmed this hypothesis and concluded that the 139 final protective effect is determined above all by the consumption of vegetables, fruit, 140 legumes, nuts, sources of fibre (Mente et al. 2009). The PREDIMED study, a randomized 141 and controlled primary prevention study conducted in a Spanish cohort and comparing the 142 effect on cardiovascular mortality of a low-fat diet (control arm) with diets supplemented with 143 either extra virgin olive oil or nuts (intervention arms), found that, in both intervention arms, 144 145 cardiovascular events over time were significantly reduced as compared to the control arm 146 (Estruch et al. 2018). In short, even if the control diet was characterized by a food pattern 147 with a lower lipid content, which would imply (according to standard systems that penalize the fat content of foods) a more favourable nutritional profiling than those included in the two 148 intervention diets, cardiovascular mortality decreased significantly more in the latter than in 149 150 the former (Estruch et al. 2018). These data strongly support the view that the nutritional 151 characteristics of diet rather than compliance with nutrient profiles dictate their overall health effects. 152

The increasing evidence about the importance of consuming adequate amounts of "positive foods" is mirrored by the growing debate about the real effect, on human health, of reducing individual specific nutrients, namely salt, total and/or saturated fats, or sugars, which are included in the nutrient profiling systems, of which they actually represent the theoretical basis.

The role of salt, for example, is undergoing an, as yet not completed, process of critical revision based on the available literature performed by leading and independent groups of experts (see as an example O'Donnell et al. 2020). A recent Cochrane review

161 (Graudal, Hubeck-Graudal, and Jurgens 2020) also showed that the reduction of sodium consumption to low or very low intakes is effective in reducing blood pressure in 162 hypertensive subjects, but not in healthy (normotensive) subjects. According to the cited 163 164 ongoing revision, moreover, the reduction of blood pressure among hypertensive patients, was not associated with significant effect on cardiovascular events or on all-cause 165 mortality. Thus, based on current debate, it appears to be quite complex to set shared 166 limits for sodium intake for the overall population; the ongoing randomized clinical trials 167 may, in the near future, help clarify this issue. 168

The role of saturated fats on health, and particularly cardiovascular risk, needs in a 169 170 similar way to be reconsidered based on the conclusions of various groups of experts (see as an example Astrup et al. 2020). According to at least three metanalyses (Siri-Tarino et 171 172 al. 2010; de Souza et al. 2015; Zhu, Bo, and Liu 2019), increasing intakes of saturated fatty 173 acids are not associated with an increased risk of cardiovascular effects and/or all-cause mortality. Based on these observations, the authors formally asked for a reassessment of 174 current restrictive policies suggested by guidelines, which "are not aligned with the current 175 176 evidence base" and may potentially lead to unfavourable consequences (Astrup et al. 2020). In this case, the specific recommendation is to distinguish the different sources of saturated 177 178 fats by, e.g. differentiating milk and dairy products from other foods. This will be cumbersome in the current nutrient profiling systems. 179

The limitation of added sugar consumption to less than 10% of total calories (or even 5%, according to a more restrictive version), on the other hand, was formalized in 2015 in a WHO document, which contains the textual statement that such recommendation is based on low or very low to moderate quality evidence from studies specifically referring to the cariogenic risk related to these intakes of sugars (in the absence of proper oral hygiene or adequate fluorination) (WHO 2015). Thus, as with sodium, it appears difficult, based on the inconclusive available evidence, to identify and to set shared limits for sugar intake valid for
 the whole population.

In light of this ongoing scientific debate, the description of the food by means of a nutritional profile defined on the basis of arbitrary cut-off levels for nutrients appears even weaker. Moreover, it is worth observing that one nutrient can be critical, or even noxious, for specific groups of population, but not for others, and that there is large inter-individual variability in response to nutrient intakes and dietary patterns due to several factor such as metabolism, genetic characteristics, and microbiota (Zeevi et al. 2015; Ramos-Lopez et al. 2021).

In this context, the emerging concept that "one size does *not* fit all" has led to the development of new disciplines such as personalized nutrition, that uses information on groups with shared characteristics or on individuals, respectively, to develop targeted nutritional advice for the dietary management of specific vulnerable groups, such as people with specific diseases, or pregnant, or older adults, but also for the development of more effective tailored interventions for improving public health at individual level (Ramos-Lopez et al. 2021).

Last but not least, our knowledge of the physiological and health effects of a food 202 item cannot ignore its actual levels of consumption. While it is true that the intake of 203 excessive amounts of sugar, fat, and salt can contribute to cardiovascular risk and, more 204 generally, to poor health, it is also true that these amounts should be defined not only in 205 206 terms of concentrations of the nutrients in the individual food (as nutrient profiles usually 207 do), but also on the basis of the size of the unit of consumption (portion) and on the consequent absolute amount consumed in a day or in even longer time frames. One notable 208 209 example is dark chocolate, which is rich in saturated fats and sugars and has a high energy 210 density. However, it is consumed in small amounts (smaller than the 100 g proposed by

211 most nutrient profiling systems), and it can contribute, according to accumulated literature, to the intake of specific (poly)phenolic compounds, i.e. flavanols with potentially interesting 212 favourable health effects (Khawaja, Gaziano, and Djousse 2011; Visioli et al. 2009). Indeed, 213 214 such consumption would be penalized by a nutrient profiling system defining limits of specific nutrients, especially sugars and fat which cannot be exceeded per 100 g of food products. 215 216 In a similar way, a moderate cheese intake, which is not associated with untoward health effect according to recent metanalysis, would be strongly discouraged by a classical profiling 217 system due to the usually high content in salt and saturated fats in these foods (Chen, 2017). 218

In such complex and rapidly evolving context, both education and dissemination of correct information on nutrition and health, rather than simple but possibly inaccurate system of classification based on food profiling, are crucial to help people make informed choices in relation to the food they consume, to build adequate food patterns, and to understand the contribution or importance of each food to the energy and nutrient content of a diet (Schwingshackl, Schunemann, and Meerpohl 2020; Hemrich 2020).

At first, food labels can be used as a (in)formation tool, as long as they include all the necessary characteristics and are able to transmit proper data to the consumer. On the other hand, both institutional and regulatory documents reaffirm the centrality of education to allow the general population to make healthy food choices and consume each food product as part of an overall healthy diet, in terms of both caloric intake, macro- and micromicronutrients, as opposed to a system of nutrient profiling of the single product (U.S. Department of Agriculture and U.S. Department of Health and Human Services 2020).

232 Nutrient profiling in the food regulation

233 It may be useful, with regard to such issues, to reconsider the context and the needs234 which promoted the birth and the definition of nutritional profiles.

The issue of nutrient profiling was first proposed by Regulation (EC) 1924/2006, to establish the conditions of use of nutrition or health claims for foods or food categories, by classifying them on the basis of predefined threshold levels of specific nutrients (essentially salt, total and/or saturated fat, sugar) (Flynn 2012). The stated aim was (and still is) to avoid that nutrition or health claims can mask the overall nutritional status of a food product, possibly misleading consumers looking for healthy options.

However, several profiling systems have been developed worldwide, by both governments and other organizations, with a variety of applications, such as to define criteria for regulating/self-regulating not only marketing but also advertising to children or to promote innovation and the reformulation of food products to make them healthier. Algorithm based profile models have been proposed in Australia, Ireland, New Zealand, Norway, Sweden, the United Kingdom and the United States.

In the European region, the UK and its Food Standards Agency (FSA) has been the 247 regulatory body most active in this area. The first nutritional profile was the UK Coronary 248 Prevention Group Banding Scheme (Rayner, Scarborough, and Stockley 2004), which was 249 followed by the Swedish Green Keyhole scheme, launched in 1989 (Larsson, Lissner, and 250 Wilhelmsen 1999). In 2005, the first FSA conclusions were published (Rayner et al. 2005): 251 a system based on scores was developed where scores are assigned on the grounds of the 252 253 nutritional content of a food item or a beverage. Worth noting, nutrients are assessed on a per 100 g basis to define and limit the multifaceted issue of recommended portion size. 254

Other systems have been proposed over the years. Noteworthy examples include the American Heart Association Diet and Lifestyle Recommendations (American Heart Association Nutrition Committee et al. 2006); Canada's food guide (Katamay et al. 2007; Health Canada 2019); Tripartite (Scarborough et al. 2007); The Center for Science in the Public Interest's Guidelines (U.S. Department of Agriculture and U.S. Department of Health

and Human Services 2020); The EFSA Scientific Opinion published in 2008 (EFSA Panel
on Dietetic Products 2008); and FoodProfile (Visioli et al. 2007).

Some guidelines, e.g. the American and Canadian ones, do not employ algorithms to classify individual food items and, rather, provide general advice on how to optimize the overall diet. A tripartite classification (preferably, middle road, exceptionally) was generated, based on the nutritional quality of products and indicating favourable and less favourable choices within the separate subgroups (Quinio et al. 2007).

The general approach of nutrient profiling was critically evaluated in 2008 by experts convened by the EFSA (The EFSA Panel on Dietetic Products 2008) who mainly found "an inherent difficulty in seeking to apply to individual food products nutrient intake recommendations that are established for the overall diet". These conclusions appear to be still valid today, even in the light of both the scientific literature published on this topic in the subsequent years and the nutritional guidelines defined by scientific, governmental, and international organizations.

The main criticism is the fact that the human diet is composed of multiple food items, with different characteristics and composition. Therefore, it does not appear necessary (and might be perhaps counterproductive) that each food is intrinsically "balanced" in its nutrient composition, which is at the heart of the nutrient profile system. On the contrary, there is a need to focus on the combination of the various foods that compose the dietary pattern, which is the one that needs to be overall balanced.

In addition to this, two major considerations should be made: the first is that many foods, e.g. olive oil are usually consumed in small quantities due to their composition and a profiling system could wrongly (and uselessly) penalize them; the second consideration is that we must always take into account the impact on the consumer's psychology and behaviour of actions that could reasonably seem healthy, such as the product reformulation

with decrease of fat, salt and sugar. Multiple evidences in the literature show that perceptions about healthiness or "fatteningness" of foods may bias estimations of caloric content (Carels, Harper, and Konrad 2006), with subsequent overconsumption (Cleeren et al. 2016). Consumers translate health claims as incentives to purchase (and this is well known by marketing managers) and increases consumption.

Moreover, the offer of so-called healthy references, lightened or in some way fortified or modified in terms of nutritional composition, has been constantly growing in the last 20 or 30 years, but it would not seem to have been actually useful in the fight against obesity, which indeed is constantly increasing, despite the increase in sales of light products or products with other nutrition claims or with health claims.

295 Another point raised by the EFSA experts concerns the differences in patterns of food 296 consumption among the various European countries, also determined by different traditions 297 and food culture, that make it difficult to define common principles of nutritional evaluation. Therefore, the critical dietary habits, on which the profile system should necessarily be 298 based to impact the overall diet, would be different from country to country. The effects of 299 adopting a unique profiling system throughout the European Union could, therefore, be 300 positive in some countries and negative in others. Likewise, a system which - on average -301 302 may appear to work well at the population level may work poorly at the individual level: the aforementioned concept of "one size fits all", on which the idea of nutrient profiling is based 303 304 is unlikely to be efficacious because it does not consider the metabolic interindividual differences. 305

Finally, due to great differences among the various food categories, it would be probably necessary to adopt specific profiling systems for each individual category, to avoid an approximate system. For instance, the same sodium limit could not be adopted for cheeses or foods based on processed meats and products based on vegetables and

310 derivatives. Such an approach would create a very complex system, which would also be difficult to implement and authenticate. Moreover, as mentioned above, policies aimed at 311 penalizing foods with marked fat and sugar content, for example through front-of-pack 312 warning labelling schemes, and/or limiting the possibility of accessing nutritional claims, etc. 313 conflict with the previously discussed evolution of the scientific literature. A large body of 314 recent research suggests that dietary policies focusing on the promotion of dietary 315 components for which current intake is less than optimal might have a greater effect than 316 317 those targeted on sugar and fat, highlighting the need for comprehensive food system interventions (The Global Burden of Disease Diet Collaborators 2019). Nutrient profiles 318 319 favour lower consumptions of foods with purported unhealthy compositional characteristics 320 which is supposed to drive consumption of other ones with more favourable features. This 321 strategy will, however, be much less effective than the direct promotion of foods with better nutritional composition. 322

Nutrient profiles of individual food products, additionally, are not in line with Reference Intakes - which have been defined for energy, macronutrients, vitamins and minerals - on which the regulation of the use of information on the nutritional and health effects of foods to the consumer is based (EFSA Panel on Dietetic Products 2008, 2009). The expression of the energy, macro and micronutrient levels in relation to the relevant reference values defined for the general population allows comparing the nutritional values of different foods and can help convey the relative meaning of any individual product in the context of diet.

Finally, an approach that includes the use of nutrient profiles would be detrimental for some specific foods, for which reformulation aimed at reaching the thresholds defined for the same profiles would not be possible, which therefore could be perceived as "unhealthy" even though they can play an important and positive nutritional role.

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335 Conclusions

According to the most recent scientific evidence any classification of foods into 336 'healthy' and 'unhealthy' products is a venturesome oversimplification of the complex 337 relationship between diet and health. In fact, this approach fails to consider that healthiness 338 is determined not only by the nutrient composition of a product, but also by the quantity 339 340 consumed and the contribution of the product to the total diet. The importance of all these aspects is widely supported by the most recent scientific literature and the most preeminent 341 342 food-based guidelines, highlighting the synergistic role of nutrients and foods consumed in various combinations over time (namely, dietary patterns) in affecting human health (Dietary 343 344 Guidelines for Americans, 2020-2025).

The approaches involving the definition of nutrient profiles have merits, namely the intention to trigger both attention and choices of consumers on healthier diet and lifestyle; however, actual health benefits related to the possibility to distinguish overall 'healthy' from 'unhealthy' products are, at present, based on uncertain science.

In view of the current "Facilitating healthier food choices – establishing nutrient profiles" EU initiative, we believe that further debate among all stakeholders is warranted and must consider all the limitations outlined in this paper.

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- 353 Acknowledgments
- 354 None

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356 Disclosure of Interest

AP and FM are the Chairman and Head of Research, respectively, of NFI - Nutrition
 Foundation of Italy, a non-profit organization partially supported by Italian and non-Italian

359 Food Companies. FV, AG, and DM declare no conflict of interest associated with this

360 publication.

- 361
- 362 Funding
- 363 None
- 364
- 365 References
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