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NUTRITION AND OBESITY (S MCCLAVE AND E OMER, SECTION EDITORS)

Processed Foods – Getting Back to The Basics

Osman Mohamed Elfadil[1] · **Jalpan Patel**[1] · **Ishani Patel**[1] · **Matthew W. Ewy**[2] · **Ryan T. Hurt**[1,2,3] ·
Manpreet S. Mundi[1]

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Abstract

Purpose of Review Real-world data suggested that more than half of daily energy intake is coming from processed and ultra-processed foods in most western countries. This high consumption of processed foods is of concern, given laboratory and epidemiological studies' findings that prove overwhelming harms of processed foods on human health.

Recent Findings Data demonstrate that consumption of processed foods is increasing with more reports linking ultra-processed foods to various medical conditions; namely, obesity, metabolic syndrome, atherosclerotic cardiovascular diseases, and certain types of cancer. Scientific community's understanding of the mechanisms and substances by which processed foods are affecting human health is expanding. Holistic approach to the current critical situation is advisable and requires collaborative public health strategies.

Summary The current review describes recent classification of processed foods and highlights the pertinent findings in the relationship between processed foods and health. It also outlines key clinical data relevant to the topic.

Keywords Processed food · Ultra-processed foods · Additives · Foods

Introduction

When agriculture and animal husbandry began to expand, preserving food became imperative to prevent spoilage and survive in the time of shortage [1]. Processing of food utilized novel techniques to preserve food and was perhaps the first technology to be successful enough to bring about urbanization in the industrial sector. More recently, between 2010 and 2014, food manufacturers and other professional organizations have implemented broader conceptualization for food processing to include processes involved in any change made in food before consumption [2••]. In this context, it is important to recognize that every food consumed by humans is essentially processed in some ways by one of several common processes such as hydrolyzation, hydrogenation, or extrusion; therefore, differentiating potentially beneficial processes from those potentially harmful is necessary [2••]. Moreover, other poorly defined terms have been commonly used to describe food processing such as heavily processed or junk food. This paucity in definitions led to emergence of specific classifications of processed food.

A popular classification that has been universally used in scientific literature is NOVA food classification [2••, 3]. NOVA classification allocates food processing into four groups:

Group (A): Unprocessed or minimally processed foods (MPFs) – Foods in this group typically consist of edible parts of plants, fungi and animals after separating them from nature without any process; however, minor preservation processes such as drying, crushing, pasteurization, refrigeration, or roasting may be used [2••].
Group (B): Processed culinary ingredients (PCIs) – These are ingredients derived from group (A) like butter

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✉ Manpreet S. Mundi
mundi.manpreet@mayo.edu

[1] Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA

[2] Division of Internal Medicine, Mayo Clinic, Rochester, MN, USA

[3] Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA

or sugar, or from nature like salt. Typically, they may not be consumed alone but along foods from group (A) [2••].

Group (C): Processed foods (PFs) – These are foods made by mixing substances from previous two groups together for purpose of durability. Examples for processed foods are cheese, breads, canned fish, fruits in syrup, and bottled vegetables. They can be consumed on their own or most favorably used in combination with other foods [2••].

Group (D): Ultra-processed foods (UPFs) – Foods in this group are industrial formulations prepared mostly or entirely from salt, oil, fats, and/or sugar combined with other substances such as hydrogenated oils, soya protein, maltodextrin, modified sugar and starches [2••, 4•]. Examples of foods in this group are sodas, sweet or savory packaged snacks, canned drinks, desserts, meat balls, nuggets and other meat products, soup and noodles, and frozen ready-to-eat meals among others [2••, 4•, 5]. Additives may also be used including dyes, color stabilizers, artificial sweeteners, emulsifiers, humectants, flavor enhancers as well as several other processing aids for bulking, de-foaming, blazing, or carbonating agents [4•, 6]. The main purpose of additives in UPFs is to augment the sensory qualities and to minimize or mask unwanted taste of the final product. UPFs aim to take over food and consumer market by producing attractive, ready-to-eat, convenient, palatable, and highly profitable food products that displace other food groups [2••]. UPFs typically have higher added sugars content than PFs [4•].

The current review describes processed foods in relation to human health and focus on concerns related to increasing consumption of UPFs world-wide.

Consumption of Ultra-Processed Foods

Energy intake from UPFs and Added sugars

The consumption of ultra-processed food has substantially increased across the globe [9, 10•]. Sales data from North and South America, Europe, and New Zealand estimated that UPFs deliver quarter to two-thirds of daily energy intake to the population of these counteries [9]. In a cross-sectional study [4•], half of average daily energy intake of Americans was derived from consumption of UPFs.

Additionally, more than 80% of the study population exceeded recommended daily limit of added sugar energy intake with close to 90% of added sugar intake coming from UPFs. Added sugars defined as any sugar added to foods or drinks that is not naturally available in unsweetened dietary items [7] and include white, cane, brown, or granulated sugar, as well as dextrose, honey, maple syrup, and pancake syrups [8]. Frequently consumed added-sugar-containing UPFs include soft drinks, fruit drinks, cakes, cookies, pies, breads, and desserts [4•].

Production and Marketing of UPFs

UPFs typically contain higher amounts of saturated fat, added sugars, and salt compared to other less processed foods and lack essential micronutrients, dietary fibers, and proteins [4•, 6]. However, they tend to be much cheaper to produce with production cost estimated to be around $ 0.5/100 kcal, while unprocessed foods cost in average 150% of UPFs cost for every 100 kcal [11]. In addition to high energy density and low production cost of UPFs, commercial advertisements and marketing strategies probably play major role in UPFs popularity [12, 13]. Notably, communities living in low socio-economic areas may be more exposed to UPFs advertisements. [14].

Impact of Processed Foods on Human Health

Key Issues and Concerns

Increasing consumption of unhealthy UPFs, especially in western countries, over other types of foods has always been a topic of a research interest to nutrition community [15, 16], particularly in relation to effects on human health [10•, 17]. Several recently published studies, systemic reviews, and meta-analyses have noted a relationship between increasing consumption of UPFs and obesity [18], atherosclerotic cardiovascular diseases and dyslipidemia [19–21], cardiovascular mortality [22, 23], renal diseases [24], metabolic disorders and non-alcoholic fatty liver disease [25], and cancer [5, 26••, 27, 28].

Additionally, increasing consumption of UPFs among children is of special concern. For instance, in a cross-sectional observational study, da Rocha et al. [29] described wide availability of UPFs for children under 3 years and suggested food legislation to regulate marketing of UPFs. Another survey [30] analyzed dietary data from 960 preschoolers concluded that consumption of UPFs in children may be associated with diets promoting non-communicable diseases. Moreno-Galarraga et al. [31] reported direct relationship between high consumption of UPFs and wheezing respiratory diseases in children. Notably, maternal consumption of UPFs was reportedly found to have negative effects on pregnancy and newborns. [32–35].

Due to these health concerns and growing evidence of risks associated with UPFs, addressing high and increasing consumption of UPFs world-wide needs a public health strategy involving governmental and non-governmental sectors of concern, and certainly more than clinical and dietetic approaches alone. Adams and colleagues [36] reviewed key public health interventions that may be required to minimize health implications of the prevalent high consumption of UPFs and suggested that such interventions should be structural and aim to provide access to affordable MPFs. Moreover, they emphasized that efforts should focus mainly on consumption rather than certain nutrients or behaviors.

Clinical Data on Cardiovascular Health and Incidence of Diabetes

In the era of NOVA food classification, researchers were able to investigate the impact of food processing on health, particularly UPFs and cardiovascular health. In addition to the growing evidence discussed earlier that suggested UPFs may have long-term effects of human health, other reviews and ecological studies described potential harmful metabolic changes with higher consumption of UPFs [9]. For instance, development of significant dyslipidemia with UPF-rich dietary pattern was reportedly noted in children and adult cohorts [9, 19, 37]. Moreover, altered glycemic and satiety control have been described in relation to consumption of UPFs [9]. These metabolic and biological implications of processed foods are probably leading to the adverse effects on heart health and are certainly attributed to UPFs nutrients' composition. Studies from North and South America have noted higher content of saturated fats and added sugars as well as low content of fibers, proteins, micronutrients, and fibers in most of UPFs consumed by studied populations [38–40].

Clinical data from various parts of the world and among different cohorts constantly characterized significant cardiovascular risks in relation to high consumption of UPFs [9, 22, 23]. In a prospective cohort study, Srour et al. [9] noted 10.8% increase in cardiovascular risk with high consumption of UPF diet including overall cardiovascular risk, and risk of coronary heart and cerebrovascular diseases. Additionally, Mendonça et al. 41 described positive relation between consumption of UPFs and hypertension in middle age adults. This concern has further been raised recently by Scaranni and colleagues [42] as they noted direct relation between the amount of UPFs consumed and risk of hypertension in a cohort included more than 8500 adults. Similarly, metabolic syndrome was linked to consumption of UPFs leading to higher cardiovascular risks in adolescents and adults in several clinical investigative works [25, 43, 44].

Additionally, excessive consumption of UPFs can increase the risk of type II diabetes mellitus (T2D) by around 40% [45]. In contrast, minimally processed foods and plant-based diet can decrease fasting blood glucose levels and may reduce risk of development of T2D by around 19% [45]. Furthermore, in a large prospective observational study of more than 100,000 subjects who were predominantly women [46]$^{(p2)}$, risk of development of T2D was proportional to consumption of UPFs. Similar conclusions were reached by another study [47] as consumption of UPFs was associated with risk for development of T2D in diabetes free population after adjustment for anthropometric, socioeconomic, and lifestyle variables.

All of these outlined findings support concerns of increased cardiovascular diseases and T2D risk with higher consumption of UPFs; however, larger prospective epidemiological studies are needed to further characterize these associations and strategically plan for meaningful interdisciplinary interventions [11].

Processed Meat and Risk of Cancer

Red meats include meat of veal, beef, horse, mutton, pork, goat and lamb whereas processed meats are products of processing of any red meats and typically include salted, cured, or smoked meats [48]. Consumption of red meat is increasing especially in wealthy western countries [49]; however, effects of high meat intake on human health remain controversial [50]. In literature, increased consumption of processed red meat has reportedly been linked to development of cancer especially colorectal malignancies [27, 28, 51, 52]. The International Agency for Research on Cancer (IARC), based on available scientific evidence, has determined that red meat is probably carcinogenic to humans (group 2A) and processed meat is carcinogenic to humans (group 1) [48]. Certain potential carcinogenic substances typically occurring during red meat processing are probably playing a major role in carcinogenicity of processed meats namely, N-nitroso-compounds (NOCs), heterocyclic aromatic amines (HAAs), and polycyclic aromatic hydrocarbons (PAHs) [53].

The exact mechanisms by which red processed meats may cause carcinogenicity remains unclear however, several theories have been discussed in the literature. Possible mechanisms may include the effect of excessive NOCs load causing DNA adducts and lipid peroxidation in intestinal epithelium [54]. Other mechanisms are thought to be either related to activation of pro-malignant cascades resulting from pro-inflammatory responses to potentially carcinogenic substances or related to epithelium proliferative stimulation by metabolites or haem [54]. As well, red meat derived metabolite, glycan, could be responsible for inflammation and subsequent cancer progression [55]. Furthermore, it was suggested that non-human sialic acid N-Glycolylneuraminic acid (Neu5Gc) from processed meat may incorporate into human tissues and interact with inflammation provoking antibodies leading to carcinogenicity [56].

Interestingly, other carcinogenic substances may naturally present or contaminate raw or under-cooked meat such as dioxin-like polychlorinated biphenyls, and polychlorinated dibenzo-p-dioxins and dibenzofurans, polybrominated diphenyl ethers, and hexachlorobenzene which might increase the chance of cancers even after consuming unprocessed meat [48]. Another important consideration is that certain cooking procedures could augment already present carcinogens contaminating raw meat [48].

Published clinical data on association between red processed meat and cancer examined former theories among others. Colo-rectal cancer remained the most studied type of cancer in relation to red processed meat [57]. In a critical review of meta-analyses, Lippi et al. [57] recognized well-established evidence for direct association between processed meat and colorectal cancer. They also described significant association between processed meat and gastric, esophageal, and bladder cancers. In addition to gastrointestinal tract cancers, Inoue-Choi et al. 58 and Boldo et al. [59] reported an association between processed meat and postmenopausal breast cancer. Bouvard et al. 53 explored a connection between red meat and prostate and pancreatic cancers as well [53].

Food Processing Mechanisms and Health Related Considerations

Maillard reaction products

In this section, we recognize and discuss an important concept that is essential to understand direct and indirect implications of food processing on health. That is the Millard reaction, a term that – in fact – refers to group of non-enzymatic processes that take place during food processing mainly involving amino acids and sugars and typically resulting in the brown color and various flavors to the food [60]. The reaction was described by and named after the french physicist and chemist Maillard, LC. It is essential to recognize any alteration of animal and plant cells' properties and availability of micronutrients with exposure to heat and chemicals during food processing [54]. Additionally, food processing may also result in neo-formed substances which may have negative effect on health, particularly cardiovascular health [9]. Maillard reaction is typically observed during processes that expose foods to high temperature. [60].

Any product that may occur because of Maillard reaction is referred to as Maillard reaction product (MRP). Based on certain properties, some MRPs can be beneficial including antioxidative, anti-allergenic, bactericidal, and anti-browning products [61]. More importantly and concerning, other MRPs can have potential to cause serious health harm by acting as pro-oxidatives or carcinogenics [60, 62]. An important example of a harmful MRP is the carcinogenic [63] heterocyclic amine (HCA) and heterocyclic aromatic amines (HAA), which can result from processing of food, especially meat, by boiling, frying, roasting, or grilling [60, 62, 64]. While tens of HAAs and HCAs are known and linked to food processing, different types of meat and processes may lead to variable types and amounts of HCAs/HAAs; with charcoal grilled chicken and duck meats likely containing highest amount of HCAs/HAAs and roasted chicken and beef contain lowest amount of HCAs/HAAs [60, 64].

Acrylamides are another important potentially carcinogenic [65] MRP that can be produced during food processing [62]. In addition to carcinogenicity, results from the National Health and Nutrition Examination Survey (NHANES) suggested that acrylamides were associated with higher incidents of cardiovascular diseases [66]. Fortunately, asparaginase which can be found in potatoes and cereals or formed during carbon dioxide extrusion of foods, can counteract or reduce the effect of acrylamides. Asparaginase can be generated in labs and is widely used in food processing for its beneficial anti-acrylamide properties [60, 67].

Additives used in food processing

Additives are frequently used in food processing to add color or flavor as well as to modify texture and stability. Additives can also be used to add value to cost of processed food. More than 2500 chemicals are used as additives in food industry, in addition to more than 10 thousand substances that may be found in food supply systems and unintentionally be added to foods [68]. The World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) are responsible agencies to evaluated impact of food additives on human health world-wide [69]. In the United States (US), Food and Drug Agency (FDA) regulates the usage of additives in food processing and assesses their safety [70]. These agencies as well as the scientific community have frequently raised concerns about safety of certain additives; however, this remains an ongoing scientific and regulatory effort leading to frequent changes in the additives used in food processing. Therefore, additives are continuously examined in animal-based experiments. For example, glutamates initiated atherosclerosis in rats by increasing oxidative stress through lipid peroxidation [71] and linked to obesity and metabolic syndrome [72], sulfates caused heart damage in rats [73], emulsifiers like carboxymethylcellulose and polysorbate-80 have expressed probable part in encouraging inflammation and metabolic syndrome in mice [74]. Carrageenan, a frequently used food additive as a thickener, was found to likely cause glucose intolerance by inhibiting insulin signaling and disturbing insulin pathways leading to insulin resistance [75]. Given that the risk of metabolic syndrome with UPFs is multifactorial, it is believed that many food additives are playing a role in metabolic complications with high consumption of UPFs. Interestingly, non-nutritive sweeteners like neotame, aspartame, stevia, saccharin, and sucralose commonly used to lower calorie content in diet and as additive in many processed foods, are possibly causing microbiotal dysbiosis promoting insulin resistance and causing other serious metabolic changes [76].

As discussed, the list of additives used in food processing is huge and expanding. It is probably impossible to discuss all their potential effects on human health. However, available clinical, epidemiological, and laboratory data remain concerning about consumption of many additives. These health concerns are replicated in children population as well [77]. This review aims to highlight major substances and health related concerns. In the following sections, we will outline some of the key chemicals used in food processing.

Bisphenol A

Bisphenol A (BPA) is frequently used chemical in food packaging industry. It is primarily used as food contact material and thermal stabilizer. These food contact materials are often used in manufacturing storage containers with a direct contact with food; for example, kitchenware, coating of jar caps, and inner surface of cans to prevent direct exposure of food to metals [78]. Thus, exposure to BPA is thought to be very wide world-wide [79]. The exposure may increase with BPA leakage into cans' content after being heated during sterilization of cans or food preparation [78]. BPA can enter the human body through various ways including respiratory tract, skin, and gastrointestinal tract [80].

Biologically and in relation to human health, BPA has been known as endocrine disturbing chemical (EDC) for close to a century. It was first described to have estrogenic activity in 1930s [81]. For further characterization of BPA as an EDC, BPA is a nuclear estrogen receptor agonist and thyroid hormone receptor antagonist [81]. These biological properties of BPA can explain its association with certain disorders such as polycystic ovarian syndrome (PCOS), infertility in both genders, and precocious puberty [78]. Moreover, BPA can cause several changes on ovaries including cystic endometrial hyperplasia, endometriosis, and ovarian cysts in addition to risk of ovarian cancer [82]. This carcinogenicity of BPA is not limited only to ovarian cancer, but consumption of BPA involves significant risk of breast cancer. In fact, animal-based models as well as in vivo studies on human cells have proven this association [82].

Phytoestrogens

Phytoestrogens are natural substances that can be found in larger quantities in legumes, especially soy, and in lesser amount in vegetable, fruits, and cereals. They belong to polyphenols because of the phenolic groups in their structure. Phytoestrogens are further classified into coumestans, isoflavones, and lignans based on chemical structure. In human diet, phytoestrogens consumed are mostly isoflavones and lignans [83, 84].

Phytoestrogens reportedly have many beneficial effects on human health. Moderate consumption of soy, which is rich in phytoestrogens, was linked to fewer incidents of cardiac diseases and help in managing menopausal symptoms. On the other hand, while phytoestrogens are similar in chemical structure to 17-β-estradiol, they do not seem to cause side-effects including breast or endometrial cancers [83, 84]. Moreover, phytoestrogens were found to probably be protective from colorectal neo-proliferative growths as well as hormone-sensitive tumors [83]. Due to these benefits, soy products containing significant amounts dietary phytoestrogens are frequently used in food industry [84]. Consumption of dietary phytoestrogens varies widely between communities, with Chinese and Japanese remaining the largest consumers of soy and subsequently phytoestrogens [85].

Although the consumption of processed and fast food has increased significantly, the impact of UPFs on dietary phytoestrogens remains unclear. To further study these effects, it is essential to quantify phytoestrogens in human body directly or indirectly. The process can be challenging and may correlate to urinary and serum levels of enterodiol and enterolactone. Another possible marker could be urinary enterolignan concentration reflecting lignan intake [86]. Available evidence suggests that UPFs may reduce bioavailability of lignans by several mechanisms including lowering lignans dietary intake and/or lowering conversion of lignans to enterolignans. Changes in gut microbiota with high consumption of UPFs can also lead to reduce absorption of lignans from intestine [86].

Conclusion

Processed food consumption is increasing world-wide. Data are consistent in attributing this increasing prevalence to current marketing strategies. Increasing consumption of ultra-processed foods in all communities and age-groups remain a concern. However, low-income areas seem to be more affected.

In relation to human health, we recognized the overwhelming evidence of harm associated with consumption of ultra-processed foods. Furthermore, we recognize that ongoing research efforts to investigate MRPs and food additives in relation to human health are necessary to address concerns in the time of rapidly growing food industry due to advancements in technology and massive production plans.

While efforts are exerted to regulate food industry in developed countries, concerns regarding significant increases in prevalence of obesity, cardiovascular diseases, and cancer with modern lifestyle and unhealthy dietary habits require more than epidemiological or clinical investigations. A comprehensive public health interdisciplinary strategy is needed to meaningfully design and implement interventions that can help reverse the current "processed food pandemic".

Declarations

Conflicts of Interest Ryan T. Hurt is a consultant for Nestle. Manpreet S. Mundi has research grants from Realfood blends, Nestle, and Fresenius Kabi and is on advisory board for Baxter. Osman Mohamed Elfadil, Jalpan Patel, and Ishani Patel have no relevant conflict of interest to report.

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