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Obesity and Nutrition (O Pickett-Blakely, Section Editor)

Beyond the Calories—Is the Problem in the Processing?

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Abstract

Purpose of review The purpose of this review is to describe the trends in dietary patterns and food quality over time along with the possible role of ultra-processed foods in obesity, chronic diseases, and all-cause mortality in the US population.
Recent findings There is a rising obesity epidemic, corresponding chronic diseases, and increases in ultra-processed food consumption. In mice and in vitro trials, emulsifiers, found in processed foods, have been found to alter microbiome compositions, elevate fasting blood glucose, cause hyperphagia, increase weight gain and adiposity, and induce hepatic steatosis. Recent human trials have found ultra-processed foods as a contributor to decreased satiety, increased meal eating rates, worsening biochemical markers, and more weight gain. In contrast, Blue Zone, indigenous South American, and Mediterranean populations with low meat intake, high fiber, and minimally processed foods have far less chronic diseases, obesity rates, and live longer disease-free.
Summary As the USA continues to industrialize, food has become more processed and cheaper and more convenient along with the coexistent rise in obesity prevalence. This review highlights the overall trends in food: mild improvements in dietary quality in higher socioeconomic populations, but no significant increases in whole fruit, vegetables, legumes, or nuts. Consumption of ultra-processed food is associated with weight gain and may contribute to metabolic syndrome and chronic disease. To combat this epidemic, we must create and disseminate detailed recommendations to improve diet quality and overall nutrition.

Introduction

Obesity is defined by the Obesity Medicine Association as a chronic, relapsing, multi-factorial, neurobehavioral disease that promotes adipose tissue dysfunction and abnormal fat mass physical forces that results in adverse metabolic, biochemical, and psychosocial health consequences [1]. In 2015–2016, the Center for Disease Control (CDC) reports an obesity prevalence of 39.8% in the USA [2]. There is substantial data that suggests the role of obesity in a multitude of chronic health diseases effecting every organ system including cardiovascular, pulmonary, neurologic, musculoskeletal, gastrointestinal, psychological, the integument system, and even societal biases [1, 3–6]. This multi-faceted disease process is thought to have many contributing factors: genetics, epigenetic modification, environmental, neurobehavior, immunity, metabolism, hormonal milieu, and medications, along with changes in dietary quality and quantity with related microbiome imbalances [1, 6]. There is a rising clinical concern for difficulty in weight loss and prevention of weight regain, beyond simple calories in and calories out. Current clinical questions are what contributed to this epidemic? What has changed over time in the type of food consumed and whether the components of processed foods are playing a role? Does the food source of calories matter or are all calories created equal? This review will describe the data on the trends in dietary patterns and quality as it correlates to the rise in obesity, the role of ultra-processed foods and fiber in health, and practical solutions to improve overall health outcomes.

Pathophysiology of obesity

The pathophysiology of obesity comprises complex hormonal signaling from the stomach, small and large intestines, pancreas, and fat cells to the hypothalamus of the brain which determine appetite stimulation vs. satiation and increased or decreased energy expenditure. There are two known pathways, orexigenic and anorexigenic, within the arcuate nucleus of the hypothalamus with first-order neurons stimulated by peripheral signals which then relay downstream signaling to second-order neurons and beyond. The only orexigenic, appetite-stimulating, hormone is ghrelin which is released from the fundus of the stomach in response to fasting and decreases with eating. Ghrelin stimulates the orexigenic pathway via first-order neurons, agouti-related peptide (AgRP) and neuropeptide Y (NPY), to stimulate appetite and decrease energy expenditure. The anorexigenic, appetite-suppressing, peripheral signals include the following: CCK, GLP-1, OXM, PYY, PP, insulin, amylin, leptin, adiponectin, amino acids, fatty acids, and glucose which act via the first-order peptides of proopiomelanocortin (POMC) and cocaine-and-amphetamine-regulated transcript (CART) to signal satiety and energy expenditure [7]. However, hunger and satiation are not quite that simple with multiple known and likely many unknown contributors to variations. For example, several studies have shown ghrelin to be lower in people with obesity (vs. lean) along with a less-significant decline in ghrelin after meals in patients with obesity (vs. lean), which is thought to be a driving force for over consumptions [7, 8]. Also, ghrelin may take longer to decline with consumption of a processed vs. unprocessed meal, which may account for greater food intake and therefore weight gain. Additionally, high leptin levels have been found in patients with obesity, in which there is thought to be leptin resistance and therefore a

sustained appetite. As described in the obesity definition, this disease process is quite complex, and there remains many unknowns. We will discuss additional hypotheses below.

Trends in obesity, dietary patterns, and food quality

There have been several studies to understand the trends in obesity in relation to sex, race, age, socioeconomic status, dietary patterns, and quality of food over time. It is essential to study the trends in types of food consumed to determine the major contributors to the obesity epidemic and chronic disease states. The National Health and Nutrition Examination Survey (NHANES) has been utilized to explain these very trends with several different models. Flegal et al. compared NHANES obesity prevalence data from 2005–2006, 2007–2008, 2009–2010, 2011–2012 to 2013–2014, adjusting for age, sex, race, smoking history, education level, and classifications of general obesity (BMI ≥ 30 kg/m^2) versus class 3 obesity (BMI ≥ 40 kg/m^2) [9]. Findings included a significant trend towards increasing obesity and class 3 obesity prevalence in women, but not in men [9]. This data supports the CDC findings of increasing rates of obesity and underscores the significance in women.

To study the changes in foods consumed in correlation to changes in weight, Mozaffarian et al. studied three cohorts of healthy volunteers prospectively throughout the USA from 1986 to 2006 and from 1991 to 2003 [10]. The average weight gain in all cohorts over 20 years was 16.8 lbs. Weight gain was positively associated with increasing servings of processed foods such as potato chips, potatoes, sugar sweetened beverages, sweets and desserts, refined grains, red meats, and processed meats. Conversely, there was an inverse association of weight gain with increasing consumption of minimally processed or whole foods such as vegetables, whole grains, fruits, nuts, and yogurt. Ultra-processed or processed foods are defined by Monteiro et al. as foods that have undergone several processing techniques and additives to create durable, cheap, convenient foods with minimal whole food quality; while unprocessed or minimally processed foods are considered whole foods in their natural state with minimal alterations [11]. This data suggests that as hypothesized, increased consumption of processed foods and red meats is associated with a greater weight gain than minimally processed foods, whole grains, fruits, and vegetables.

Focusing on dietary patterns, Rehm et al. compared NHANES data from 1999 to 2012, accounting for differences based on age, sex, race, education level, and income level [12]. The American Heart Association (AHA) diet score, a scoring system based on the AHA 2020 Strategic Impact Goals, was used. Briefly, the AHA score totals adherence with dietary recommendations such as consumption of fruits and vegetables, whole grains, fiber rich, fish, limited saturated fat and cholesterol, minimizing beverages with added sugars, and moderate alcohol intake. AHA diet scores were estimated as follows: poor diet (score < 20 or < 40% adherence), intermediate diet (score between 20 and 39.9 or between 40 and 79.9% adherence), and ideal diet (score > 40 or > 80% adherence) [12]. Findings suggest an overall improvement in primary and secondary AHA scores from 2003–2004 to 2011–2012 from 19 to 21.1%, which translates to moving from poor diet to intermediate diet, albeit a low intermediate score and a very small absolute change. The small changes in AHA

diet score improvements were driven by decreased sweetened beverages and increased whole grains, nuts, seeds, and legumes. However, there were no significant changes in intake of fruits, vegetables, processed meat, saturated fat, or sodium with mild increases in fish and shellfish. There were smaller overall improvements noted in those with lower incomes and less education while there were larger improvements noted in adults with higher incomes [12]. This data suggests that while there were small improvements in diet quality, this was primarily seen in more affluent and white adults. Overall, diets remain low in minimally processed whole foods in all subgroups over this time period in addition to known increases in obesity prevalence.

To assess dietary quality trends as they relate to chronic disease, Wang et al. studied NHANES data from 1999 to 2010 with the Alternate Healthy Eating Index 2010 (AHEI-2010), a score ranging from 0 (least healthy) to 120 (most healthy) [13]. This survey reviewed the combination of foods and the association with chronic disease over time. There was an increase in the AHEI score, which corresponded to a reduction in sugar sweetened beverages, sodium, and trans-fat intake; however, the overall scores of vegetables, fruits, whole grains, nuts, and legumes remained low. The AHEI-2010 score increased from 1999 to 2009–2010 with a potential trend towards higher quality diets. When SES was accounted for, the dietary quality was consistently higher in high SES groups compared with low SES groups [13], echoing the results found by Rehm et al. that the small improvements found are in higher SES groups, and poor diet qualities remain in lower SES groups.

These studies are representative of the body of evidence compiled over the last 20 years in the correlations of dietary trends and obesity. The literature reveals that over the last decade, there has been a linear increase in obesity with only small incremental improvements in dietary quality in higher SES groups, with increases in servings of processed foods. Additionally, there has not been a significant increase in the quantity of unprocessed food consumption (fruits, vegetables, legumes, nuts, beans), and instead an increase in processed foods. While correlations do not represent causation, changes in dietary patterns certainly represent a plausible contributor to the increased prevalence of obesity.

Importance of fiber

While diet quality in higher SES groups may trend towards improvement, dietary fiber intake remains insufficient in the US population overall. This finding may be explained in part by diets higher in processed foods rather than whole foods. The recommended daily fiber intake is 14 g/1000 calories or approximately 25 g for women and 38 g for men [14]. However, the average daily fiber consumption according to the National Health and Nutrition Examination Survey 2009–2010 (NHANES 2009–10) is just 17 g per day on average with men consuming far more fiber than women [15]. Further, black adults (non-Hispanic) in NHANES 2009–2010 consumed significantly less fiber than non-Hispanic white, Hispanic, or other race/ethnicity groups. Other predictors of low fiber intake included lower family income.

A high fiber diet has been found to have links to prevention of precancerous lesions and cancer, cardiovascular diseases and mortality, all-cause mortality,

type 2 diabetes, and Crohn's disease [16]. There are several proposed mechanisms of these benefits including reducing inflammation, improving the gut microbiome diversity and function, improved energy utilization of calories, alteration of the immune system, and increased consumption of micronutrients and bioactive food components (phytonutrients, e.g., polyphenols) that have been connected to human health [16–20].

Additionally, a diet high in fiber accelerates intestinal transit time, as fiber is a bulk-forming agent, which promotes regular bowel movements [21, 22]. Such improvements in gut health reduce constipation, hemorrhoids, and diverticulitis and may reduce colon cancer risk [23, 24]. While low fiber intake is associated with higher rates of colorectal cancer, diabetes, and heart disease [25], emerging research suggests that a high fiber diet also supports gut health as measured by microbiome diversity, a generally accepted marker of a "healthier" microbiome with the caveat that we currently cannot define what a healthy microbiome is [22, 25–28]. Gut microbiome diversity has been linked to efficient nutrient and energy utilization, production of beneficial short-chain fatty acids (SCFAs), and many other roles [22, 26, 29]. SCFAs are produced during microbial metabolism of fiber and are crucial for maintenance of colonocytes and have been shown to have systemic effects including prevention of carcinogenesis and inflammation and even cross the blood-brain barrier [22, 30–32].

Effects of additives in processed foods on health

When reviewing dietary trends, there has been a clear increase in the availability and consumption of processed foods with additives over time along with the increase in the obesity epidemic. The landmark EAT-Lancet Report explains that the rise of obesity and chronic diseases may be explained by several factors: changes in farming practices; increased processing of foods with additives; and large rates of animal production, consumption, and waste; among several other worldwide consumption factors [33••]. Over the last 20 years, there has been a dramatic increase in the number of additives available and the ubiquity of their presence in most food products [34]. These processed foods as described above are cheaper and shelf-stable and thus more available, convenient in our fast-paced lives, and highly palatable, all of which has added to their rise in popularity [34, 35••]. Processed foods are typically high in calories, salt, sugar, and fat and are thought to stimulate over eating [35••]. There have been several trials to understand how the body metabolizes these additives and the effects on overall health. The most commonly studied emulsifiers, which are types of additives used to improve texture, shelf life, flavor, etc., include carboxymethylcellulose (CMC) and polysorbate-80 (P-80) [34]. Several in vitro and mouse-model studies have found that both CMC and P80 contribute to the inflammatory cascade by several mechanisms: decreasing mucin thickness and production, increased tight junction permeability thereby allowing bacterial translocation to trigger inflammatory responses, alterations in the microbiome diversity—all implicated in increased fat mass, hyperphagia, increased blood glucose, and insulin resistance [4, 36•, 37–40]. While there are several limitations to these trials being mostly in mice and in vitro models, these metabolic syndromes are diagnosed routinely in patients with high processed food consumption and obesity in the clinical setting.

It is notoriously difficult to study nutrition in humans in a controlled clinical trial due to differences in baseline characteristics, inability to ensure diet adherence, difficulty in collecting the exact amount and type of diet consumed, inability to control for physical activity, poor recall, and countless other factors. However, Hall et al. were able to complete a 28-day inpatient trial with 20 patients in a cross-over design to assess unprocessed and processed diets matched for calories and macronutrients [35••]. The purpose of the study was to determine whether ultra-processed foods effected energy intake vs. minimally processed foods. Hall et al. used the definition of ultra-processed foods by Steele et al.: formulations mostly of cheap sources of dietary energy and nutrients plus additives, using a series of processes and containing minimal whole foods [35••, 41], while minimal processing (unprocessed) of foods does not add any new substance to the whole foods, such as fruits or vegetables [42]. During this trial, there was a significant increase in energy intake and meal eating rate on the ultra-processed compared with the unprocessed diet. Clinically, this finding is often noted in patient encounters in their lack of prolonged satiation with processed foods and the sensation of an inability to consume only small portions of ultra-processed food products, such as eating an entire bag of chips in one sitting and feeling hungry shortly after. Hall et al. reported corresponding weight loss on the unprocessed diet and weight gain on the ultra-processed diet. Physiologically, PYY, an appetite-suppressing hormone, was noted to be increased on the unprocessed diet while ghrelin, an appetite stimulant hormone, decreased [35••]. Therefore, an unprocessed diet signals greater satiation than an ultra-processed diet, which corresponds to decreased energy intake and less weight gain or even weight loss. Additionally, biochemically, the unprocessed diet group had reduced adiponectin, total cholesterol, CRP, total T3, fasting glucose, and insulin, and increased free T4 and free fatty acids. These findings corroborate prior research showing improvement and even resolution of metabolic comorbidities with an unprocessed diet. Thus, it appears that despite matched calorie and macronutrient content, there is an additional factor in the ultra-processed diet that may lead to unfavorable biochemical markers and hormonal imbalance associated with a higher BMI.

The research literature on obesity has tracked with the prevalence of obesity, increasing to what seems to be a recent plateau (Fig. 1). Around the time of the increase in research on obesity, research literature begins to appear on food additives and processed food (Fig. 1); however, this literature has not seen the exponential growth of obesity research. While there appears to be a more recent increase in the study of food additives and processed food, there is much that remains unknown, and this area deserves more attention.

Human population studies

Although, as previously mentioned, it is difficult to study nutrition in human populations, there are five populations that consistently live over

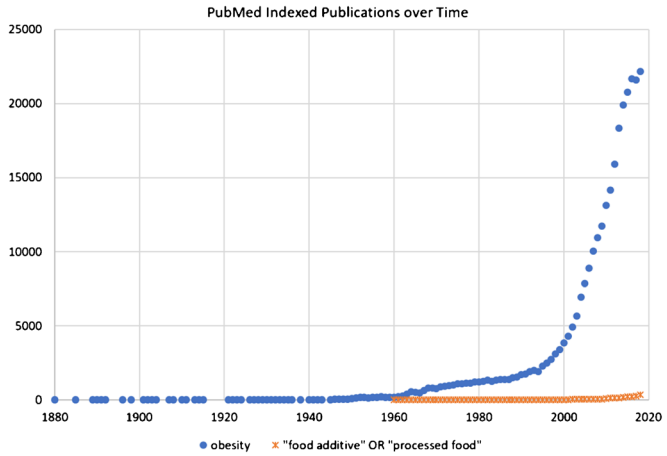

Fig. 1. Time trends in publication on obesity versus food additives and processed food.

the age 100 without chronic disease: the so-called Blue Zones, whose lifestyles and dietary habits have sparked great interest [43]. The five Blue Zones are the following: Loma Linda, CA; Nicoya, Costa Rica; Sardinia, Italy; Ikaria, Greece; and Okinawa, Japan. Research has found 9 commonalities: (1) moving naturally throughout the day, (2) stress management, (3) daily purpose, (4) eating until 80% full, (5) eating mostly plant-based proteins including beans (meat up to 5 times per month), (6) moderate daily drinking with friends, (7) belonging to a faith-based community, (8) family bonds and relationships, and (9) belonging to social circles committed to healthy behaviors (part of the culture) [43]. These populations were found to live a decade longer and have less cancer, heart disease, dementia, and obesity than the typical US population [43, 44]. Loma Linda, CA, is home to a large community of Seventh Day Adventists, the vegetarian Blue Zone. The Adventist 2 Study evaluated American and Canadian Seventh Day Adventists from 2002 to 2009 to assess for an association with a vegetarian diet with reduced mortality [44]. The risk of mortality was reduced by 12% in vegetarians compared with that in non-vegetarians with greater reductions seen in men than in women. Additionally, there were lower rates of associated cardiovascular mortality, endocrine complications, hypertension, and metabolic syndrome in vegetarians.

The Mediterranean diet is not dissimilar from the Blue Zones, emphasizing whole foods and mostly plants. The PREDIMED Study of the health benefits of the Mediterranean diet revealed evidence of protection against cardiovascular disease [45]. Additionally, Kaplan et al. studied coronary risk factors of the indigenous Tsimane population of Bolivia with direct visualization by CT, which correlated with coronary artery calcium (CAC) [46]. This population has low rates of hypertension and arterial stiffness presumably due to their pre-industrialized lifestyles with hunting, gathering, physical activity, and high unprocessed carbohydrate and fiber intake—similar to the Blue Zones. No CAC was observed in 85% of the participants and only 3% had markedly elevated scores. Of those ages 80–90, only 8% had moderately elevated CAC scores. The vascular age of the Tsimane population at age 80 corresponded to an American in their fifties. All of the above populations share several of the 9

principles of the Blue Zone populations, most of which have been neglected in the fast-paced US lifestyle and likely contributed to our obesity epidemic.

Practical clinical recommendations

When counseling for weight loss for improved nutrition and metabolic syndromes clinically, there are many factors to consider with socioeconomic status, access to fresh food, transportation, and work schedules being crucial. There are a few simple approaches to meet patients at their point in the commitment stage. Begin with each patient completing a 2-week food journal of their typical diet. Then, make small changes such as counseling on reducing then eliminating sodas and sugar sweetened beverages and increasing daily water intake. Encourage decreasing the frequency of fast food consumption with the ultimate goal of avoidance. Then, slowly change one meal per day for the next month by substituting several healthier options within the guidelines of their personal preferences and limitations of their lifestyles, for example, a daily salad for lunch with various added vegetables, beans, nuts, fruits. Then, find solutions together of improved food preparation such as baking rather than frying, substituting healthy versions of unhealthy foods such as quinoa or cauliflower rice rather than white rice, and choosing better options when dining out. Provide specific hand-outs, recipes, and brands of foods to purchase, so they do not feel lost once they try to implement this plan. Follow-up often, weekly to bi-weekly in the first 6 months, utilizing phone check ins or virtual visits. Then, demonstrate objective results of improvements with labs, vitals, and pictures/measurements such as weight, waist-to-hip ratio measurements, body fat percentage (bio-impedance testing is now readily available). Re-evaluate changes that have been successful and their feelings frequently to help with necessary changes, especially early in the process. Continue to reinforce and encourage small steps as the new tastes and habit formation occurs. Reassure that over time these improved dietary choices become easier and unhealthy cravings lessen. But, also remind them to allow some pleasurable treats as well and to never punish themselves or feel guilty for enjoying it. A special food upon occasion and in small amounts may be the key to success, as they will not feel deprived or that it is a forbidden fruit.

Conclusions

The epidemic of obesity correlates directly with the pervasiveness of chronic diseases. Rather than simple secondary treatment of diseases with medications alone, we must transition our efforts to food as medicine as well. Many populations around the world have demonstrated that chronic disease with age is not predestined but rather heavily influenced by lifestyle and diet. To decrease all-cause mortality and obesity in the USA, we should avoid or at least limit processed foods and meats and sweetened sugary beverages while increasing our intake of whole vegetables, legumes, nuts, fruits, and water. As diet and lifestyle are the first line of defense in obesity and chronic disease, these dietary recommendations must go along with leading more physically active lifestyles, having meaningful connections with others and having a sense of purpose.

Compliance with Ethical Standards

Conflict of Interest
Janese Laster declares that she has no conflict of interest. Leigh Frame declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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