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Debunking the Myth: Dietary Fat vs. Carbohydrates in Obesity Development

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Abstract: ***Fats in the diet have long been regarded as a leading factor contributing to obesity, and as a result, low-fat dietary recommendations were made widely available. However, newer research suggests that the development of obesity may be influenced more by refined carbohydrates and lack of exercise than they are affected by dietary fat alone. This review critically assesses the scientific evidence available comparing the effectiveness of low-fat vs. low-carbohydrate dietary approaches, takes into consideration the metabolic pathways that apply to energy expenditure and storage, reviews the effects of processed foods and added sugars on the process of lipogenesis, and determines how the development of Metabolic Syndrome and insulin resistance occurs. The results of this evaluation point out that excessive consumption of refined carbohydrates, particularly in conjunction with sedentary behaviour, are more likely to impact obesity development than the effects of dietary fat alone via enhanced de novo lipogenesis, altered insulin signaling, and altered metabolic homeostasis. As a result, the change in this paradigm will affect the nutritional recommendations and guidelines provided by health professionals, as well as public health interventions regarding obesity control and prevention.***

Keywords: Obesity, Lipogenesis, Carbohydrates, Dietary Fat, Insulin Resistance, Metabolic Syndrome, Physical Activity, De Novo Lipogenesis

1. Introduction

The World Health Organization (2021) estimates that the rate of global obesity is expected to increase nearly threefold by 1975, making obesity one of the most urgent challenges facing health care systems in the twenty-first century. Historically, the primary focus of obesity prevention and treatment has been on decreasing dietary fat consumption because fats have more calories than carbohydrates or protein (9 kcal/g compared to 4 kcal/g), making it more likely to contribute to excess body weight (Hall & Guo, 2017). For over 30 years, health organisations around the world have therefore published guidelines recommending a low-fat dietary pattern.

The dramatic increase in rates of overweight and obesity, which some researchers attribute to low-fat dietary recommendations, has led to a re-examination of the relative contributions of macronutrient composition and the role that other mechanisms play in the aetiology of obesity. Specifically, new evidence that indicates refined carbohydrate consumption, especially when coupled with low levels of physical activity, has been identified as being a greater contributor to obesity than originally understood (e.g., Ebbeling, *et al.,* 2018; Ludwig & Ebbeling, 2018).

This review will evaluate the scientific literature on the relative contributions of dietary fat and carbohydrate intake to obesity with respect to the following issues:

1) The relative effectiveness of lower-fat and lower-carbohydrate diets for weight management;
2) The metabolic pathways through which energy is accumulated and expended, including de novo lipogenesis;
3) The effects of processed foods and refined sugars on lipogenesis and metabolic health;
4) The mechanisms by which insulin resistance and metabolic syndrome are linked to dietary patterns and levels of physical activity.

This review will synthesize the current understanding of these topics to provide an overall perspective of the ways that macronutrient intake, physical activity, and obesity interact. Understanding these interactions will enable the development of evidence-based dietary recommendations, clinical practice guidelines, and population health interventions designed to confront the global obesity epidemic.

2. Comparison of Low-Fat vs. Low-Carbohydrate Diets

2.1 Historical Context of Dietary Recommendations

The dietary guidelines stating that it is important to restrict the intake of fats came primarily from epidemiologic research done between the 1950's and the 1970's on the relationship between dietary fat consumption levels and cardiovascular disease risk (Keys *et al.,* 1986). These findings contributed to the conclusion that the percentage of calories consumed as fat should not exceed 30%, and that the maximum amount of saturated fat should be less than 10% (USDA, 1980). Although this was considered a very strong recommendation for many years, there has been very little evidence to prove that limiting the amount of dietary fat consumed has led to a decrease in body weight (Tobias *et al.,* 2015).

2.2 Randomized Controlled Trials Comparing Low-Fat vs. Low-Carbohydrate Approaches

Historically, large-scale, randomized controlled trial (RCT) research studies have recently compared these two different dietary approaches to weight control and metabolic health; however, it's important to note that the number of studies in this area has increased significantly in the past few years.

2.2.1 Short-term Studies (≤6 months)

Most of the current research in this area is focused on RCT's which take 1 to 6 month(s) to complete.

The meta-analyses indicate that short term low carbohydrate diet studies have typically produced greater weight loss than short term low fat diet studies (Sackner Bernstein, *et al.,* 2015; Mansoor *et al.,* 2016). A recent RCT study performed by Bazzano *et al.* (2014) found that, on average, the participants who followed the low carbohydrate diet experienced a much larger weight loss than those on the low fat diet (-3.5 kg) over a 12-month period, even though they had the same calorically restricted diet. In addition to weight loss, many (but not all) low carbohydrate diet studies show a greater decrease in triglycerides, an increase in HDL cholesterol and improved glycemic control when compared to low fat diet studies (Gjuladin Hellon, 2019).

2.2.2 Long-term Studies (>12 months)

Long-term studies (more than twelve months in duration), such as Johnston *et al.'s* (2014) examination of low-carbohydrate diets in clinical settings have shown a reduced advantage of low-carbohydrate diets when compared to other forms of dieting over the course of time. In addition to Johnston *et al.'s* (2014) findings, there are still several long-term clinical trials that have shown an advantage for low-carbohydrate diets as compared to traditional dieting methods. Shai et al. (2008) conducted the DIRECT Study and found that the Mediterranean Diet was just as effective as Low-Carbohydrate Diets in producing greater weight loss than that of the Traditional Low-Fat Diet over a two-year time period. Gardner *et al.* (2018) also participated in a long-term clinical study (the DIETFITS study) using participants that had Insulin Resistance, and these participants experienced significantly greater weight loss on Low-Carbohydrate Diets compared to Low Fat Diets.

2.3 Impact on Body Composition and Energy Expenditure

Not only does changing one's diet lead to weight loss, but the way in which someone does this may result in changes in body composition and/or energy expenditure as well. As noted by Ebbeling *et al.,* (2018), those following a low-carb diet post-weight loss likely expend about 200 - 280 more calories daily compared to individuals on a high-carb diet during weight maintenance, suggesting that restricting carbs may enhance metabolism. The current literature also shows that low carb diets produce more reductions in body fat with relative maintenance of lean body mass as opposed to high carb diets (Volek *et al.,*2010).

2.4 Differential Effects Based on Individual Factors

A critical factor influencing the efficacy of dietary interventions is the high level of variability between individuals in response to these interventions, with multiple factors contributing to an individual's capacity to respond to a dietary intervention. Some of the individual differences influencing the degree of success of a dietary intervention include insulin sensitivity, genetic variants (specifically those involved in carbohydrate and fat metabolism), gut microbiome composition, and baseline metabolic health (Gardner *et al.,* 2018; Hjorth *et al.,* 2018). Therefore, the best approaches for maximising the success of dietary interventions will involve developing personalised recommendations rather than using broad macronutrient guidelines.

3. Role of Metabolic Pathways in Energy Storage and Expenditure

3.1 De Novo Lipogenesis: Converting Carbohydrates to Fat

De novo Lipogenesis (DNL) is an essential metabolic pathway through which excess carbohydrates are converted to fatty acids and subsequently stored as triglycerides in adipose tissue in the liver (Sanders & Griffin, 2016). Historically considered a relatively small component in the development of fat accumulation in humans, recent research has indicated that under conditions of excess carbohydrates (e.g., consuming a diet high in refined carbohydrates or sugars), DNL can make a significant contribution to the deposition of fat (Schwarz *et al.,* 2015).

DNL is regulated by a series of important enzymes, including Acetyl-CoA Carboxylase (ACC) and Fatty Acid Synthase (FAS), which are upregulated by insulin and carbohydrates through a variety of transcription factors, including Sterol Regulatory Element-Binding Protein-1c (SREBP-1c) and Carbohydrate-Responsive Element-Binding Protein (ChREBP) (Herman *et al.,* 2012). The way high-carbohydrate diets cause an increase in fatty acid production via insulin-induced stimulation of DNL is one of the main ways that such diets lead to the development of fat accumulation.

3.2 Beta-Oxidation: Mobilizing Fat for Energy

The process of beta-oxidation (i.e., the breakdown of fatty acids into forms the body can use for energy in the mitochondria) plays an essential role in fat breakdown and mobilization/usage (Houten & Wanders 2010). Furthermore, beta-oxidation has been shown to increase when undertaken whilst participating in an increased level of physical activity (Bergouignan *et al.* 2011), as increased beta-oxidation activity occurs through the upregulation of genes associated with fatty acid transport into and through the mitochondria and thus enables stored fat to be used for energy during this period.

However, lipolysis and beta-oxidation are greatly reduced with the presence of high levels of insulin in the body (usually the consequence of consuming a high-carbohydrate diet), resulting in an inability for adipose tissue to release fat, thus preventing beta-oxidation and, consequently, the breakdown of the body's fat stores for energy (Stralfors & Honnor 1989). In this way, a reduction in carbohydrate intake would allow for increased beta-oxidation due to lower insulin levels, increasing lipolysis and allowing for the use of fatty acids for energy (Volek *et al.* 2009).

3.3 Carbohydrate-Insulin Model of Obesity

According to the carbohydrate-insulin model, the main cause of obesity is not due solely to excess calories, but rather due to the impact of food choices (specifically those high in refined carbs) on hormone levels and the body's metabolism (Ludwig & Ebbeling, 2018). As such, it proposes that high carb diets will lead to an excess amount of insulin being secreted which pushes calories into fat storage, limits the amount of energy available for the active metabolizing tissues in the body, and creates a "cycle of dysfunction" promoting an increase in food intake by creating feelings of hunger and an increased desire to eat.

There is a significant amount of evidence which supports the carbohydrate-insulin model including:

The association of increased glycemic load (a measure of the carbohydrate content in a food) with increased body mass in longitudinal cohort studies (Mozaffarian *et al,* 2011)

The protective effects of restricting carbohydrates during periods of weight stabilization on total energy expenditure (Ebbeling *et al,* 2018)

The association between the amount of insulin secreted and subsequent weight gain (Chaput *et al,* 2014).

Critics of the carbohydrate-insulin model contend that this hypothesis greatly oversimplifies the complex pathophysiology of obesity and that energy balance remains the primary driver of changes in body mass (Hall *et al,* 2017). Current controversies regarding the mechanism by which diet composition affects energy balance and how the two influence body mass regulation suggest a need for continued research into the area.

3.4 Role of Physical Activity in Metabolic Regulation

There are many pathways through which physical exercise impacts the energy storage and usage of one's body. Regular physical activity increases the insulin sensitivity (the body's ability to use insulin effectively), the rate at which new mitochondria (the cells' powerhouse) are being formed, the amount of fatty acids that can be oxidized (used for energy), and metabolic flexibility, which means one's body's ability to switch between using fat or carbohydrate for energy based on what is available (Goodpaster & Sparks, 2017).
On the other hand, when someone does not engage in physical exercise, all these pathways are adversely affected. Physical inactivity causes insulin resistance (the inability to use insulin effectively), decreased functioning of mitochondria, and impairment of the metabolism of fatty acids (Bergouignan *et al.,* 2011). The combination of these metabolic effects of sedentary behavior plus the adverse metabolic effects of poor dietary quality creates the perfect environment for the development and progression of obesity.

4. Impact of Processed Food and Sugar on Lipogenesis

4.1 Refined Carbohydrates and Lipogenesis

The increase in glucose and insulin levels following eating refined carbohydrates (due to the fast absorption rates) were significantly higher than those seen with unrefined whole grain carbs and, therefore, an increased level of insulin produced in response to the eating of refined carbs occurred. As stated by Stanhope *et al.* (2009), this increased insulin level activates DNL by stimulating SREBP-1c and ChREBP, which, as a result, stimulates the production of fatty acids and triglycerides.

In experimental studies conducted on humans, when people replaced the same number of calories they eat per day from refined carbs and sugars instead with complex carbohydrates, their DNL levels significantly increased. The research done by Schwarz *et al.* (2015) found that the overconsumption of simple sugars for just one week tripled levels of hepatic DNL and caused an excessive amount of fat accumulation in the liver. Likewise, Luukkonen *et al.* (2018) conducted similarly designed research and concluded that a high-carbohydrate diet with an equal number of total caloric calories than a high-fat diet led to both increased amounts of fat in the liver and increased levels of hepatic DNL.

4.2 Fructose: A Unique Metabolic Challenge

Due to having different hepatic metabolism from Glucose (Tappy & Lê 2010), Fructose, which is a sugar (added sugar) such as Sucrose and High Fructose Corn Syrup, carries special metabolic challenges. While Glucose has regulatory checkpoints associated with Glycolysis, Fructose has no such checkpoints when it is taken up by the liver and metabolised. Through the unregulated uptake and metabolism of Fructose, acetyl-CoA (major component of DNL) is produced along with increased expression of lipogenic genes through the activation of ChREBP (Herman *et al.,* 2012).

Investigations into the clinical readership have confirmed that Fructose intake enhances DNL while also favouring higher concentrations of fat accumulation within the liver compared with an equal intake of Glucose (Stanhope *et al.,* 2009). In addition to these effects of Fructose on DNL and fatty liver accumulation, there is evidence that Fructose decreases Insulin Sensitivity and preferentially increases Visceral Adiposity compared with other Carbohydrates, very possibly via its impact on both the metabolic processes of the Liver and the inflammatory nature of the Liver (Cox *et al.,* 2012).

4.3 Ultra-Processed Foods: Beyond Macronutrients

Although ultra-processed foods are often composed of macronutrients in an unbalanced way, ultra-processed foods may contribute to the development of obesity through a number of mechanisms:

1) **Hyperpalatability**: Processed foods are usually created by combining various food ingredients (sugar, fat, salt, and flavourings) to create products that may trigger the reward pathways of the brain, thereby encouraging overconsumption (Monteiro *et. al.,* 2018).

2) **Altered satiety signaling:** Ultra-processed foods can alter the body's normal signalling pathway for satiety and hunger by accelerating their rate of digestion (speed of digestion), changing the way hormones are secreted from the gut, and modifying the gut bacteria (Hall *et al.,* 2019).
3) **Food matrix disruption:** The act of food processing can disrupt the natural food matrix and, therefore, it may affect the metabolic effects of nutrients that exist within the food matrix (Fardet, 2016).
4) **Environmental contaminants:** Several common substances produced during food processing (e.g. Phthalates, Bisphenols) have been shown to act as Obesogen substances, disrupting the hormonal regulation of metabolism and increasing adipose tissue (Heindel *et, al.,* 2017).

In general, a meta-analysis of all Randomised Controlled Trials involving Ultra-Processed Diets versus diets composed of their unprocessed counterparts (Hall et al., 2019) suggests that Ultra-Processed Diets have been shown to result in excess caloric consumption and weight gain when compared to a diet of unprocessed foods, regardless of macronutrient content, fibre, and energy density. The results of this study further support the conclusion that the act of food processing may contribute to the development of obesity in addition to the effects of the macronutrient composition of the foods consumed.

4.4 Dietary Patterns and Lipogenesis

Dietary Patterns, rather than the individual components of a diet, have a more pronounced effect on the Lipogenic process. Mediterranean-style Diets (e.g., High in Plants, Fish, Olive Oil; Low in Refined Carbohydrates) have been shown to have lower hepatic fat accumulation and better metabolic function than Typical Western Diets (Ryan *et al.,* 2013). Low Glycemic Index (GI) Diets (e.g., Low-Glycemic and Low-Carbohydrate) have been found to have lower de novo Lipogenesis (DNL) activity and increased Insulin Sensitivity (Schwarz *et al.,* 2017).

The above evidence demonstrates that we need to consider the overall quality of a person's Diet rather than just how much they consume of a certain macronutrient to understand how Diet affects Lipogenesis and the development of Obesity.

5. Insulin Resistance and Metabolic Syndrome: Mechanisms and Development

5.1 Insulin Resistance: Definitions and Measurement

Insulin resistance (IR) is defined as an abnormal biological response to normally circulating Insulin as measured by hours 0-12 of an IVGTT and/or an OGTT, where a normal biological response would be the maintenance of glucose homeostasis (Reaven; 2004). There are many different methods available to assess IR; however, the gold standard for assessing IR is through hyperinsulinemic-euglycemic clamps which measure insulin's tissue response (DeFronzo *et al.,* 1979).

In addition to using a gold standard to assess the severity of IR, it is also important to note that insulin resistance may develop within tissues at varying rates; thus, hepatic, muscular and adipose insulin resistance may each have very different metabolic effects (Samuel & Shulman 2016).

5.2 Mechanisms Linking Refined Carbohydrates and Insulin Resistance

Consumption of refined carbohydrates contributes to the development of insulin resistance through several dated mechanisms:

1) **Lipotoxicity:** When consuming a large number of refined carbohydrates, individuals will have an increase in the amount of carbohydrates being converted to fat (referred to as "de novo lipogenesis"), resulting in very high levels of saturated fatty acids (chiefly palmitate) stored in tissues that shouldn't regularly store fat like the liver and muscles. The presence of these fatty acids produces an insulin-resistant state by activating protein kinase C (PKC) via diacylglycerol accumulation within these cells (Samuel & Shulman, 2016).
2) **Inflammation:** Diets high in glycemic indexes lead to an increase in the production of free radicals (reactive oxygen species), the accumulation of advanced glycation end products (AGEs), and the production of pro-inflammatory cytokines, all of which disrupt normal insulin signaling (Esposito *et al.,* 2010).
3) **Hyperinsulinemia:** Prolonged exposure to elevated levels of insulin is associated with the development of insulin resistance through receptor downregulation and the alteration of both pre- and post-receptor signaling pathways, leading to the increased removal of insulin from circulation (Shanik et al., 2008).
4) **Changes in Gut Microbiota:** The consumption of refined carbohydrates alters the composition and function of the gut microbiome, most likely leading to an insulin-resistant state from subsequently reduced short-chain fatty acid (SCFA) production, increased lipopolysaccharide (LPS) absorption, and altered bile acid metabolism (Sonnenburg & Bäckhed, 2016).

5.3 Physical Inactivity and Insulin Resistance

Many different physical, biological, chemical, and cognitive factors lead to insulin resistance. Physical inactivity due to a sedentary lifestyle has unique characteristics that contribute directly to the development of insulin resistance via the following mechanisms:

1) **Reduced GLUT4 expression:** A decrease in the amount of GLUT4 in skeletal muscle (Richter & Hargreaves, 2013) because a lack of physical activity will cause the amount of GLUT4 in skeletal muscle to decrease, ultimately causing an impaired transfer of glucose from the vascular system into skeletal muscle during insulin-stimulated glucose uptake.
2) **Impaired mitochondrial function:** The reduction of mitochondrial function and mitochondrial content due to a decrease in mitochondrial oxidative metabolism caused by a lack of physical activity (Booth *et al.,* 2012) leads to incomplete metabolic oxidation of fatty acids which then leads to the accumulation of lipid metabolites that can interfere with the function of insulin.
3) **Reduced AMP-activated protein kinase (AMPK) activity:** A decrease in the activity of AMPK (Ruderman

et al., 2013) represents a further mechanism whereby a reduction in the activation of AMPK through a lack of exercise causes lower levels of stimulation of insulin.

4) **Altered myokine production:** A decrease in myokines released from skeletal muscle (Pedersen & Febbraio, 2012) caused by a lack of exercise diminishes the release of myokines, which, through the use of the AMPK pathway, increases insulin sensitivity and contributes to metabolic health.

The combined effect of diet and physical activity appear to synergistically affect insulin sensitivity, not merely through additive effects. For example, a single bout of exercise will improve insulin sensitivity in relation to a period of overfeeding (Walhin *et al.,* 2013), demonstrating the strong impact physical activity has on metabolic health.

5.4 Metabolic Syndrome: The Culmination of Metabolic Dysfunction

The metabolic syndrome (MetS) is defined as a combination of medical conditions including excessive abdominal fat (visceral adiposity), hypertension, altered fat levels (dyslipidemia), and disordered glucose metabolism (impaired glucose tolerance). These conditions increase an individual's risk of cardiovascular disease and type 2 diabetes (T2D) (Alberti *et al.,* 2009). While different diagnostic definitions exist, there is agreement among the definitions that the primary contributing factor to the development of the MetS is insulin resistance.

There are three phases in the process leading to the development of MetS:

1) **Initial Phase:** Excess energy intake (especially from refined carbohydrates) combined with a lack of physical activity result in visceral fat accumulation and the development of hepatic insulin resistance.
2) **Progressive Phase:** Insulin resistance that develops in the liver promotes increased gluconeogenesis and the development of dyslipidemia. As these metabolic changes occur, an increase in insulin levels (hyperinsulinemia) occurs, resulting in sodium retention, sympathetic nervous system activation, and increased proliferation of the vascular smooth muscle cells.
3) **Advanced Phase:** The development of pancreatic Beta-cell dysfunction occurs, resulting in the eventual loss of glucose tolerance and the eventual development of T2D (Cornier *et al.,* 2008).

The progression from the initial to the advanced phase not only illustrates how interconnected the various components of MetS are but also illustrates how central insulin resistance is in the development of the MetS.

6. Clinical and Public Health Implications

6.1 Dietary Recommendations: Beyond Low-Fat Approaches

This evidence supports the idea that dietary recommendations to reduce fat intake, while a useful component of a strategy for obesity prevention and treatment, is inadequate by itself. The most effective strategies might include:

1) **Carbohydrate quality emphasis:** A focus on carbohydrate quality rather than simply reducing fat (Ludwig, *et al.,* 2018) may improve insulin sensitivity through improved metabolism of glucose.
2) **Personalized approaches:** Personalized dietary approaches that take into account individual characteristics, such as insulin sensitivity, genetics, and preferred food choices (Hjorth, *et al.,* 2018).
3) **Food-based guidelines:** When developing food-based dietary guidelines, the focus should be on recommending whole, unprocessed foods rather than telling people what ratios of macronutrients to consume (Mozaffarian, 2016).
4) **Consideration of timing:** Chrononutrition should be considered, because the timing of meals affects how we metabolically respond to identical meals (Garaulet & Gómez-Abellán, 2014).

6.2 Physical Activity: An Essential Component

The significant metabolic advantages of engaging in physical activity emphasize that it is vital for the prevention and treatment of obesity. For example:

1) **Activity Guidelines:** Currently, the minimum recommendation for physical activity is 150 minutes per week of moderate-intensity physical activity; however, higher volumes of physical activity create even greater metabolic benefits (Piercy *et al.,* 2018).
2) **Resistance Training:** Resistance training provides distinct metabolic advantages over and above the benefits of aerobic exercise for properties such as insulin sensitivity and glycaemic control (Shiroma *et al.,* 2017).
3) **Sedentary Behaviour Reduction:** While structured exercise (e.g., scheduled gym memberships) is beneficial, breaking up prolonged periods of sitting with short physical activity breaks also helps improve the same metabolic indicators (Dempsey *et al.,* 2016).
4) **Activity Promotion Strategies:** Promoting environments/policies/technological advancements that allow for the development of active lifestyles may continue to be more effective than trying to make changes at the individual level through behaviour modification alone (Sallis *et al.,* 2016).

6.3 Food Environment and Policy Considerations

Effective solutions to obesity will ultimately include the following:

1) **Food reformulation:** Policymakers may help decrease public health concerns related to the carbohydrate quality of processed foods by creating or supporting public policies that require or encourage the food industry to reformulate its products to contain less sugar (Scott *et al.,* 2017).
2) **Economic Incentives:** Subsidizing fruits, vegetables, and whole grains as well as taxing sugary beverages can help improve the diet of lower socioeconomic class individuals, through increased access to healthy, high quality food (Mozaffarian *et al.,* 2018).
3) **Food Labelling:** Consumers who understand and can easily interpret front-of-package food labelling systems will be in a better position to identify and avoid foods that contain high amounts of refined carbohydrates and added sugars (Khandpur *et al.,* 2018).

4) **Built Environment:** Designing communities that facilitate an active lifestyle (e.g., Walkable Communities, Accessible Recreation Facilities, and Safe Options for Active Transportation) and are conducive to enabling individuals and families to live an active lifestyle (Sallis *et al.,* 2016).

7. Conclusions and Future Directions

The current manuscript draws attention to diet-related fat restriction being wrongly viewed as the primary nutritional approach for combating and preventing obesity. Rather, evidence suggests that carbohydrates—specifically, highly refined carbohydrates, in combination with being sedentary—have a greater impact on the progression of obesity via their contribution to lipogenesis, insulin signalling and metabolic regulation.

The following are the main takeaways / key conclusions of this review article:

1) Low carbohydrate diets generally provide more short-term weight loss than low fat diets, therefore offering greater benefits to individuals who suffer from insulin resistance.
2) An important mechanism by which excess carbohydrates (especially from refined sources) result in fat accumulation is via de novo lipogenesis.
3) Inactivity has a negative, additive effect on the adverse metabolic effects of a poor diet because inactivity decreases fat oxidation and creates insulin resistance.
4) Additional mechanisms, in addition to their macronutrient composition, exist by which ultra-processed foods contribute to obesity.
5) A combined approach that evaluates both dietary quality (including an emphasis on carbohydrate quality) and activity levels is needed for preventing and treating obesity effectively.

Future research should focus on:

1) Improving the Phenotyping of Individuals to Help Predict Dietary Responses and Hence Promote Personalised Nutrition.
2) Longer Duration Studies to Assess Sustainability and Health Impacts of Various Types of Dietary Patterns onHealth Beyond Weight Alone.
3) Understanding the Inter-relationship of Dietary Composition, Physical Activity and Gut Microbiome in regard to the Development of Obesity.
4) Evaluating Policy Level Intervention Related to Food Environments and Physical Activity Access.
5) Formulating and Evaluating Practical Clinical Diagnostic Tools to Evaluate Insulin Sensitivity and Metabolic Health to Directly Assist in Formulating Personalised Interventions.

Based upon combining the information from Nutrition Science, Metabolic Processes and Public Health, a 'Deeper Appreciation' for the Complexities of Pathogenic Processes associated with Obesity, and Therefore, More Effective Strategies for Addressing the Global Obesity Epidemic Will Follow.

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