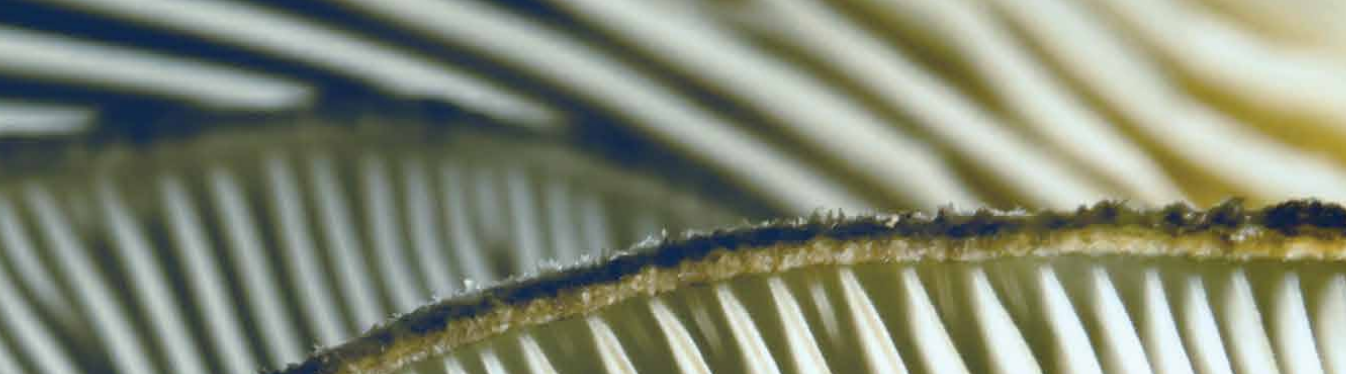




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Global Perspective on the Relationship Between Dietary Habits and Health

*Edited by Akkinapally Venketeshwer Rao
and Leticia Rao*



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and Leticia Rao*

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Aims and Scope of the Series

The significance of food is undeniable, especially in light of the impending challenge facing humanity: ensuring there will be enough food to meet the basic needs of a population expected to reach approximately 10 billion by 2050. These food-related challenges align with some of the United Nations' sustainable development goals, with a target to achieve them by 2030. One thing is certain: food should be not only nourishing and safe but also tailored to the diverse needs of individuals throughout their lifetimes, all while meeting consumers' sensory expectations. Understanding the diverse chemical composition of food, often referred to as biodiversity, and how these components can contribute to human health by considering factors like bioaccessibility, bioavailability, and bioactivity at the organ level, is crucial for grasping and promoting a healthy diet. Thanks to the continuous evolution of analytical methods and interdisciplinary research, significant strides have been made in the field of food science and nutrition.

Meet the Series Editor



Maria Rosário Bronze has been working in Analytical Chemistry since 1986. Her Ph.D. in 1999 contributed to the study of food products using capillary electrophoresis. The main goal of her research since 1999 has been focused on Analytical Chemistry applied mainly to the analysis of foods and by-products of food industry. She conducted research in collaboration with national and international research groups, at iBET and ITQB Technology Division. From 2017 until 2021 she was head of Food & Health Division at iBET and head of the Food Functionality and Bioactives Laboratory. MR Bronze has been an Associate Professor at the Pharmacy Faculty of Lisbon University and head of the Structural Analysis Laboratory since 2012. As a researcher, MR Bronze is a Senior Scientific Advisor at Food & Health Division at iBET and Head of Food Functionality and Bioactives Laboratory at the same Institute, Collaborator at iMED and Researcher at ITQB NOVA. Her current research is focused on quality and beneficial health effects of food components. Gas and liquid chromatography associated with mass spectrometry are used by MR Bronze in the characterization of samples. Sensory evaluation is also an important area of her research. The main food products studied by her are olive tree products (olive, olive oil, leaves), cereals such as maize, legumes (faba bean, pea, chickpea, lentils) fruits (apple, grapes, opuntia ficus), fruit juices and wine, among others. More recently her interests have also involved biodiversity, bioaccessibility, and bioavailability studies on food products and their components, mainly phytochemicals as phenolic compounds, using different analytical tools such as mass spectrometry. As a senior scientific advisor at Food & Health Division at iBET she is involved in different areas: (i) isolation, characterization and formulation of bioactive and functional compounds or extracts from natural sources and wastes from food and other related industries; (ii) pre-clinical assays to provide support to understand health claims related with the beneficial effects of food nutrients/bioactive components; (iii) establishment of analytical methodologies including mass spectrometry state-of-the-art to fully characterize different matrices, from food products, natural extracts or biological fluids (Food Functionality and Bioactives Laboratory).

Meet the Volume Editors



Dr. Akkinapally Venketeshwer Rao, a Professor Emeritus in the Department of Nutritional Sciences at the University of Toronto's Faculty of Medicine, has established a significant focus on diet and health. His research has focused on the role of oxidative stress and antioxidant phytochemicals in the causation and prevention of chronic diseases, with particular emphasis on the role of carotenoids and polyphenols. His research interest also includes the role of prebiotics and probiotics in human health. He has published extensively in peer-reviewed journals, as well as several books and book chapters. He has also presented talks at national and international conferences. He has a distinguished academic career spanning over 58 years. The international media often seek him to express his opinions about nutrition and health.



Dr. Leticia Rao is a Professor Emeritus at the University of Toronto, Ontario, former Director of the Calcium Research Laboratory, Department of Medicine, University of Toronto, and former staff scientist at St. Michael's Hospital, Toronto, Ontario. Her expertise lies in bone cell biology, with a focus on preventing osteoporosis through laboratory studies of bone cells and the evaluation of basic and clinical research on drugs, nutritional supplements, and phytonutrients, including carotenoids and polyphenols, in postmenopausal women. Her research has been presented at national and international conferences and symposia and has been published extensively in peer-reviewed scientific journals. She co-authored *The Bone-Building* book. She edited eight books on nutrition and health for IntechOpen. Several international organizations invited her to present her research.

Contents

Preface	XV
Section 1	
Eating Habits and Health	1
Chapter 1	3
Introductory Chapter: Global Perspective of the Relationship between Dietary Habits and Health <i>by Akkinapally Venketeshwer Rao and Leticia Rao</i>	
Chapter 2	7
A Review of Food Consumption and Food Security Challenges in South Africa <i>by Rudzani Nengovhela, Lesetja Jacob Ledwaba and Jan Johannes Hlongwane</i>	
Section 2	
Factors Influencing Food Quality and Health	23
Chapter 3	25
Compressed Modernization and Nutrition Transition: Implications for Diet Quality and Disease Prevalence in Southeast Asia <i>by Helda Khusun</i>	
Chapter 4	41
Sociocultural Factors Impacting Contemporary Appearance among Young Adults: Disordered Eating and Health <i>by Sanja Stanić, Doris Žuro and Maria Antoana Čolaković</i>	
Chapter 5	59
The Role of Ultra-Processed Foods in Inflammation and Aging <i>by Pelin Baltacı and Nezihe Şengün</i>	
Section 3	
Diet Quality, Disease Prevention and Management	81
Chapter 6	83
Exploring the Interplay of Vitamin A, Retinoids and the Microbiota-Immune System Axis in Urinary Bladder Cancer Prevention and Treatment <i>by Larisa Tratnjek, Aleksandar Janev, Tadeja Kuret and Daša Zupančič</i>	

Chapter 7	113
Trends in Health Inequalities by Household Income in Japan in the 2010s: Estimates from the National Health and Nutrition Survey Reports <i>by Daisuke Machida</i>	
Chapter 8	127
Use of Different Dietary Indexes for Predicting the Quality of Diet and Risk of Chronic Disease <i>by Mehran Rahimlou and Fatemeh Maleki Sedgi</i>	

Preface

In addition to genetic and hereditary traits, lifestyle factors are now recognized as having a significant effect on our health. Among the lifestyle factors, diet is considered to play a crucial role in managing both physical and mental health, as well as reducing the risks of diseases. Several factors, including cultural and religious beliefs, economic stability, and technological development, influence dietary intakes and patterns worldwide. It is now well-documented that the type of food consumed is closely related to patterns of human health.

Non-communicable diseases predominate in the developing parts of the world. In contrast, in the countries where the diet is mainly meat-based, chronic diseases such as cancer, cardiovascular diseases, diabetes, and obesity are the main health issues. Research has shown that consuming diets that are mainly plant-based has a significantly lower incidence of chronic diseases compared to the consumption of meat-based diets. This observation led to the initiation of research on the reasons why plant-based foods are beneficial. Plants contain essential nutrients, such as vitamins and minerals, as well as other biologically active phytonutrients, including water-soluble polyphenols and fat-soluble carotenoids. They also contain dietary fiber and health-friendly unsaturated lipids as opposed to the meat-based diets. To better understand the reason for their beneficial effects. New research is being undertaken to investigate the mechanisms of action of phytonutrients, including their antioxidant properties and their ability to enhance the immune system, among other examples. It is hoped that the information provided in the book will contribute to the development of up-to-date dietary guidelines that will not only improve health but also enhance the overall quality of life.

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Section 1

Eating Habits and Health

Introductory Chapter: Global Perspective of the Relationship between Dietary Habits and Health

Akkinapally Venketeshwer Rao and Leticia Rao

1. Introduction

Over the past few decades, our understanding of issues that influence our health has undergone significant change. At one time, it was believed that genetics and inheritance were the main factors that influenced our health and diseases. Although genetics is still recognized as an important factor, now there is convincing evidence to suggest that lifestyle factors have equal or even greater influence on our health [1]. Among the lifestyle factors, diet is considered as playing an important role in managing physical and mental health as well as risks for other diseases. Dietary habits and patterns vary considerably around the globe, depending upon economic stability, technological development, cultural and religious beliefs, and food security, as some of the factors that contribute to the types of food populations eat around the globe. Individually and in synergy with other factors, diets play an important role in health outcomes [2–4]. Epidemiologic studies have documented very convincing evidence that supports the findings that not only do the types of diets differ around the globe, but patterns of diseases also vary considerably [5, 6]. Whereas, in the developing countries of the world, non-communicable diseases predominate, in the technologically developed countries, the main cause of death is related predominantly to chronic diseases such as cardiovascular diseases, cancer, diabetes, and obesity [5]. Further research into the nature of the diets showed that those populations whose diet was predominantly plant-based had relatively lower incidences of chronic diseases compared to those that consumed meat-based and super-processed foods [7–9]. This led global health organizations of various countries to draft dietary recommendations to increase the consumption of plant-based diets [10]. Active research is currently being undertaken to understand why diet, and in particular consuming a plant-based diet, are beneficial for lowering the risk of chronic diseases and mortality and improving the quality of life. One of the findings is that plants, in addition to contributing essential nutrients such as good lipids that are low in saturated fats, proteins, and high fiber carbohydrates, also contain several biologically active compounds such as carotenoids and polyphenols. By acting through several mechanisms such as prevention of oxidative damage of lipids, protein, DNA, and other component of the body, which otherwise will lead to increased risk of diseases, providing support for the immune system to fight damaging toxicants in the body, and other still to be discovered mechanisms, they are beneficial to our health and significantly lower the risk of chronic diseases.

2. Conclusion

In summary, the dietary habits and human health disorders vary considerably around the globe. An important relationship has also been documented showing that the types of diet consumed are related significantly to the types of diseases that are encountered among the global populations. Research has shown that several factors including culture, availability of food, and monetary status are all responsible for the type of foods that are consumed by global populations.

By fully understanding these relationships and identifying the reasons as to why some dietary patterns may be beneficial to lower the risk of some human diseases and other do not, we can gain important information that can be used to formulate dietary recommendations that complement existing recommendations and at the same time they can be more effective in the prevention of human diseases and improve the quality of life. This can be accomplished mainly by continuing to undertake research in the future.

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A Review of Food Consumption and Food Security Challenges in South Africa

*Rudzani Nengovhela, Lesetja Jacob Ledwaba
and Jan Johannes Hlongwane*

Abstract

Food security in South Africa remains a significant challenge, especially in rural areas where access to food is limited. Despite 80% of households having sufficient food access in 2021, 21% still faced severe food insecurity, requiring targeted interventions. The issue is exacerbated by high poverty, unemployment, the lingering effects of COVID-19, rising living costs, and global economic shocks. Health problems, such as malnutrition, obesity, and noncommunicable diseases like diabetes and hypertension, are linked to poor dietary patterns stemming from food insecurity. South Africa also faces 45% food wastage from the value chain. The country experiences a triple burden of malnutrition, with undernutrition, micronutrient deficiencies, and obesity being prevalent. Unhealthy food consumption, driven by income inequality and unemployment, further worsens the situation as many households opt for cheap, calorie-dense foods. To address food insecurity, sustainable practices like climate-smart agriculture, supporting small-scale farmers, reducing food wastage, and improving market access are crucial. Community-based solutions, such as school gardens and food redistribution programmes, can enhance food access, reduce wastage, and promote sustainable food security. International partnerships and strategic government policies will be key to realizing a food-secure nation.

Keywords: food security challenges, food consumption patterns, socioeconomic factors, sustainable agriculture, South Africa

1. Introduction

The food security challenge in South Africa has significantly impacted many households, with some struggling to maintain a healthy diet and ensure adequate access to food [1]. This issue is particularly severe in rural areas, where large family groups frequently face hunger and even starvation. Statistics South Africa [2] noted that in approximately 179 million households recorded in South Africa in 2021, nearly 80% (14.2 million) were reported to have sufficient access to food. In contrast, 15% (2.6 million) indicated inadequate access, while 6% (1.1 million) reported severely insufficient access to food. These figures highlight significant progress in ensuring

food security for the majority of households; however, the persistent levels of food inadequacy and severe insufficiency among 21% of households are concerning. This disparity underscores the urgent need for targeted policies and interventions to address food insecurity, particularly among vulnerable populations.

South Africa faces significant health and nutrition challenges, including malnutrition, obesity, and high rates of noncommunicable diseases like diabetes and hypertension [2]. Mbhatsani et al. [3] noted that food insecurity, along with obesity and hypertension, continues to be a significant public health challenge linked to nutrition in South Africa. Undernutrition remains prevalent in rural areas, particularly among children, due to limited access to healthy food [4]. At the same time, urban areas are seeing a rise in unhealthy diets and lifestyle-related health issues [5].

According to Statistics South Africa [2], South Africa is confronted with a range of pressing challenges, including high poverty and unemployment rates, an energy crisis, rising energy tariffs, increasing interest rates, and a growing cost of living driven by soaring food and fuel prices. In addition, employment is a key factor in maintaining a household's food security, as approximately 19.0% of households without an employed member experienced hunger, compared to only 7.9% of households with at least one employed member. Although the nation remains food secure at a macro level, these factors have severely undermined access to food for many, likely contributing to a rise in food insecurity and hunger among individuals and households [2].

For decades, South Africa has struggled with poverty, inequality, and unemployment, challenges that directly impact food security [6]. High poverty levels, limited economic growth, and unemployment leave many households unable to afford adequate and nutritious food [7]. Inequality further exacerbates disparities in access to resources. In contrast, inadequate social protection systems and poor access to essential services, such as healthcare, water, and sanitation, undermine efforts to achieve food security [8]. Additionally, global economic shocks have intensified these challenges, particularly affecting vulnerable populations and worsening hunger and malnutrition across the country.

The World Health Organization (WHO) [9] noted that maintaining a healthy diet is crucial for overall well-being and proper nutrition, helping to prevent chronic noncommunicable diseases like heart disease, diabetes, and cancer. The World Health Organization further indicated that a balanced diet includes a variety of foods while limiting salt, sugar, and harmful fats, such as saturated and industrially produced trans fats, to support long-term health.

The COVID-19 pandemic significantly impacted South Africa, not only straining the healthcare system but also exacerbating food insecurity across the country [10]. Lockdowns, job losses, and disruptions in supply chains left many households struggling to access nutritious food, particularly in low-income communities [11]. The economic downturn further widened existing inequalities, making it difficult for vulnerable populations to afford necessities [12]. School closures also affected children who relied on school feeding programmes for daily meals [13]. The crisis highlighted the need for sustainable food systems and social support programmes to ensure long-term food security, especially during future health and economic crises.

2. Patterns of food consumption in South Africa

According to Ronquest-Ross et al. [14], South Africa's food consumption patterns have shifted dramatically over the past decades towards a more Western-oriented

diet, a trend expected to continue, with studies linking these changes to rising obesity and other noncommunicable diseases. The rise in obesity and overweight is primarily driven by urbanization and the nutrition transition, which involves shifting from traditional diets to a Westernized diet high in animal protein, saturated fat, and sugar, while also being linked to lower energy expenditure [15]. In addition, Ronquest-Ross and Sigge [16] also found that dietary patterns have shifted towards increased consumption of sugar-sweetened beverages, processed and packaged foods, animal-source foods, and added caloric sweeteners, while vegetable intake has declined, raising public health concerns. One possible reason for this shift could be the growing availability and affordability of processed foods compared to fresh vegetables.

According to Frank et al. [17], low-income adults in South Africa consume inadequate protective dietary components, while ultra-processed food (UPF) intake remains high, with higher UPF consumers ingesting more nutrients associated with an increased risk of chronic diseases. One possible reason for this trend could be the affordability and accessibility of ultra-processed foods compared to healthier options. Kearney [18] also indicated that food consumption is influenced by the availability, accessibility, and selection of food options. Many low-income adults in South Africa may prioritize cheaper, calorie-dense foods over nutrient-rich alternatives due to financial constraints, limited availability of fresh produce, and time constraints that make convenience foods more appealing [19, 20]. Additionally, marketing strategies and urbanization may contribute to the widespread consumption of ultra-processed foods.

3. Public health issues in South Africa

In South Africa, food and nutrition security is a constitutional right and a key strategic priority for the government. To uphold this, various policies, strategies, and programmes have been designed and implemented to ensure access to sufficient and nutritious food for all [21]. However, malnutrition continues to be a major global issue, particularly in relation to food security, with far-reaching consequences such as undernutrition, micronutrient deficiencies, and obesity, affecting millions of people worldwide [9].

Food security remains a critical public health issue in South Africa, with many households lacking consistent access to sufficient and nutritious food [22]. Despite the country's agricultural capacity and various government interventions, poverty, unemployment, and rising food prices contribute to widespread food insecurity [23]. As a result, many South Africans, particularly in low-income communities, face malnutrition in the form of undernutrition and micronutrient deficiencies. At the same time, the country is experiencing a rise in diet-related noncommunicable diseases, such as obesity and diabetes, due to the increasing consumption of processed and unhealthy foods [15]. Addressing food insecurity requires not only improving food availability but also ensuring affordability and promoting healthier dietary choices.

According to Bloom Financial Services [24], South Africa faces a significant burden of public health issues, with diseases such as tuberculosis (TB), HIV/AIDS, and diabetes ranking among the leading causes of death. TB remains the country's top health concern, exacerbated by high HIV prevalence, while diabetes affects millions, contributing to severe complications like organ damage [9]. Cardiovascular diseases, strokes, hypertension, and respiratory infections like influenza and pneumonia also pose major health threats, particularly among vulnerable populations [24]. Efforts to

combat these diseases include government-led initiatives, healthcare programmes, and access to chronic medication; however, socioeconomic factors, limited healthcare infrastructure, and lifestyle-related risks continue to hinder progress [25]. Strengthening public health interventions, improving healthcare accessibility, and promoting preventive measures are essential to reducing the impact of these illnesses and improving overall health outcomes in South Africa.

4. Nutritional gaps and health impacts

Simelane [26] reported that over the past 30 years, South Africa has experienced a nutritional transition marked by the triple burden of malnutrition, where households face undernutrition, hidden hunger, and overweight or obesity due to diets lacking essential nutrients. Govender et al. [27] also noted that both undernutrition and overnutrition are prevalent in South Africa. While children experience stunting and excessive weight gain, obesity is particularly common among adults, especially women. Diets, particularly in African rural communities, often lack diversity [27]. The lack of dietary diversity in African rural communities may be due to limited access to diverse foods, economic constraints, and traditional eating habits. Seasonal availability, climate change, and insufficient nutrition education also contribute to this issue.

The World Health Organization [28] noted that a nutritious diet supports the prevention of malnutrition in all its forms and reduces the risk of noncommunicable diseases (NCDs) such as diabetes, heart disease, stroke, and cancer. Key factors contributing to malnutrition include food and nutrition insecurity, poverty, deficiencies in vitamins or minerals, excess weight, obesity, and associated diet-related noncommunicable diseases and unhealthy lifestyle choices [27, 29].

5. Sustainable practices for improved food security

Sustainable practices to improve food security in South Africa include promoting climate-smart agriculture, which utilizes drought-resistant crops and efficient water management to ensure stable food production despite climate challenges. Supporting small-scale farmers is also crucial, as providing training, resources, and market access can help boost food production and income in rural areas [30]. Additionally, reducing food waste across the entire food supply chain, from production to consumption, can significantly increase food availability [31]. Diversifying crops and diets encourages a broader range of nutrient-rich foods, improving both food security and nutritional health [32].

Moreover, improving access to markets is essential for empowering farmers by enhancing infrastructure that connects them with local and regional markets [33]. Community-based initiatives, such as local food banks, cooperatives, and community gardens, can strengthen self-sufficiency and resilience. Lastly, supportive policies and investments are needed to back sustainable agricultural practices, rural development, and social safety nets for vulnerable populations. Together, these approaches can contribute to a more resilient and secure food system in South Africa. Each household should be encouraged to have a backyard garden to enhance food security, providing access to fresh produce and diverse food options. This will help ensure a balanced diet, promoting better health and nutrition for families.

6. Socioeconomic factors influencing food security

Food security of various countries can be influenced by both internal and external factors, and these factors determine a country's access to food, affordability levels, quality of food consumed and the safety aspects of the food. From a national perspective, Aromolaran et al. [34] looked at the determinants of poverty in South Africa, which is one aspect of food security. The study recognizes the pivotal role that government expenditure on education and artificial intelligence play, which are key variables in the modern economy. Aromolaran et al. [34] reported a positive relationship between food consumption and investment in both education and artificial intelligence.

Most households in South Africa are unable to meet most of the elements of a food-secured home because of poor socioeconomic status [35, 36]. Weaker socioeconomic indicators make households vulnerable to food insecurity because they may not be able to access, afford, or even make a choice for quality. Undoubtedly, income is among the key determinants of food security in South Africa. Hence, a positive relationship between food preference and income was reported by Wekeza and Sibanda [37], and this outcome aligned with Daneshi-Maskooni et al. [38], who reported an inverse relationship between low-income households and the purchase and consumption of healthy food among cancer patients.

Additionally, research findings by Oduniyi and Tekana [39], Mthethwa and Wale [40] and Mazenda et al. [41] confirm the existence of a positive relationship between income and food security. Even though other research findings revealed the opposite, a negative relationship between salary and food security was reported in Limpopo province of South Africa [42]. The above reviewed studies lead to a series of questions about the possibility of reducing the poverty level in South Africa considering that the country is characterized by high levels of income inequality and alarming levels of absolute poverty [43, 44].

Food security in most cases is positively associated with better employment rates of a country. Though, in South Africa the status of food security seems to be influenced by findings that reveal a 45.5% unemployment among youth aged between 15 and 34 years and a general unemployment rate of 32.9% [45]. A research study conducted recently by Gwacela et al. [42] highlights the pivotal role that employment has on food security, where a positive relation was reported between employed households who do not own gardens and food security. With employment being expected to play an essential role in curbing poverty, its contribution was lessened by the effects of covid-19 on the economy and the economy that was struggling to generate enough employment even before the pandemic [46].

Food security is also determined by the availability of and access to nutritious food, a criterion that South Africa struggles to meet successfully. A study by Frank et al. [17] advocated for aligning the food systems in South Africa and making healthy options achievable to all. This is after their study revealed that 7% of 2521 respondents met the World Health Organization recommended intake of 400 g in a day. Frank et al. [17] further note the importance of developing policies that will discourage the consumption of ultra-processed products to add to the current policy that discourages high-sugar drinks. The latter policy has seen the emergence of sugar-free and less sugar products being brought into the South African markets.

The presence of backyard gardening is one of the interventions that could contribute positively to household food security in South Africa through the provision of nutritious products such as fruit and vegetables. This was affirmed by Aphane and

Muchopa [47] who reported that backyard gardening contributed 67% towards food security in urban settings. The importance of practicing backyard gardening was also highlighted by David and Grobler [48], indicating the impact of high prices on access to nutritious products that can be produced by households.

Additionally, Gwacela et al. [42] reported about the influence that access to land has on household food security, which is one of the aspects that needs to be addressed if South Africa is to curb food insecurity. Land in South Africa is surrounded by issues of being underutilized and not fairly distributed among its citizens and as a result, food security in South Africa and the African continent at large may not be met [49].

7. Poverty, health expenditure and inflation

Figure 1 illustrates the relationship between health expenditure per capita, poverty, and inflation in South Africa from 2015 to 2023. The graph was created using publicly available secondary data from the World Bank Open Data and analyzed in Excel. The figure shows that the poverty line in South Africa increased from 2015 to 2016, with a more significant rise observed between 2022 and 2023. In contrast, health expenditure per capita decreased between 2015 and 2016, followed by steady growth from 2016 to 2018 and a significant decline from 2018 to 2021, based on World Bank data. The graph also shows inflation on a scale from 0 to 8, highlighting a period of decline from 2016 to 2020 and an increase from 2020 to 2023. Between 2017 and 2020, health expenditure and inflation displayed a unidirectional relationship. The period from 2020 to 2022 saw a rising trend between inflation and poverty, which could be attributed to the impacts of COVID-19 and other factors. In summary, health costs per capita and poverty line in South Africa have been within the same ranges between 2016 and 2019, with deviation noted from 2019 to 2021, while poverty remained low and declining during the same periods. According to the World Bank [50] and Valodia [51], it is reported that South Africa is experiencing a high level of unemployment rate (33.5%) and a consumption Gini coefficient of 0.67. While food security is every country's problem, the importance of considering factors such as health care expenditure, gross domestic product, cost of living and poverty line in a country cannot be over-emphasized [52, 53], as these factors may make low-income household and individual not to meet the food security standards. As households

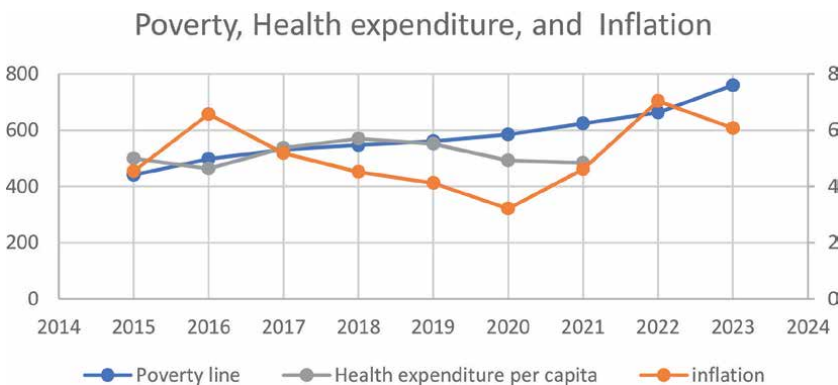


Figure 1. Poverty, health expenditure and inflation data from 2015 to 2023. Source: World Bank [50].

will be forced to make trade-offs between healthy food and medical bills and further exacerbate the malnutrition and related health issues [52]. Lastly, maintaining food security within communities is essential in managing chronic diseases that strain the final system of the health sector because countries cannot strive to increase access to comprehensive health services without increasing their share of health expenditure in gross domestic product [54] and this is what the South African government tries to achieve in introducing the National Health Care Insurance.

8. Policy and governance for food security

As quoted by Greer-Love [55] and in alliance with the constitution of South Africa under sections 26 and 27 of 1996, every citizen of the country has the right to adequate food, water and social security. However, according to an emphasis made at the Food Summit in Rome in 1996 food security will exist when everyone at all times has physical, social and economic access to sufficient, safe and nutritious food that meets the dietary needs [56]. To support this move by the South African government, food security was prioritized from the financial year 2010/2011 to date [57, 58]. Besides the commitment for a food-secure nation, the country seems to be capable of living up to the commitment at national level and having a sizeable number of households who are not food secured.

To ensure that food security issues are addressed, the South African government introduced strategies such as Integrated Food Security Strategy (IFSS) in 2002 [59]. According to Pereira and Drimie [60] this approach focused on one aspect of food security, which is food availability and could not address areas such as nutrition and safety. Additionally, the shortcoming of focusing on one section, which prioritized the involvement of mainly state participation, resulted in its failure to deliver on its mandate [59]. Additionally, the sustainability of this approach was at stake because it did not train people to provide for themselves but made food available through welfare payments, feeding schemes and food packages, and these approaches can only be useful for particular time period and to a certain group of people, for example, if you are not in school and do not meet some of its requirements, it may not cater for you [61].

To improve on the failure of the Integrated Food Security Strategy, Food and Nutrition was introduced in 2013 to still respond to food security problems [60]. Unfortunately, this policy intervention followed the top-down approach which led to limited consultation with other stakeholders and responding to government views only. This exclusion of other stakeholders in policy decisions is also identified by Mazenda [62], who emphasizes that food security requires the governance of the sphere because governance can be dependent on factors such as globalization, multi-national dominance of companies as well as struggling public institutions which are drivers of food security [63]. In response to the challenges surrounding the two policies the National Development Plan 2030, which seeks to improve food access, was launched by the South African movement. This policy intervention strives to foster food security social engagement among various stakeholders and the government which allows for a multi-sectoral approach in response to food security issues.

The government of South Africa have also established a number of food security programmes which were geared at fighting poverty and food insecurity which, including Land Redistribution for Agricultural Development (LRAD), Poverty Relief Programme (PRP), Unemployment Insurance Fund (UIF), Food Parcel Scheme (FPS), National

School Nutrition Programme (NSNP), Agricultural Starter Pack Programme (ASPP) and Comprehensive Agricultural Support Programme (CASP) among others. Shushu et al. [44] did a study on the impact of these food security projects on 533 farmers and revealed that farmers ranked Land Redistribution for Agricultural Development (LRAD) and Poverty Relief and Land Restitution programmes high compared to the others.

9. Agricultural production and food supply chains

International and local markets are vital for production and distribution of food, and they may have either a positive or negative impact on security worldwide [64]. Production and supply shocks caused by factors such as climate change, natural disasters, political instability and civil wars can negatively affect the distribution systems of food value chains and lead to high levels of food insecurity among nations [65, 66]. A concrete analysis of the effects of these factors on food security is dependent on concerted efforts among various stakeholders.

South Africa, like many other countries, is reliant on its internal and external supply for food security and is exposed to various risks that can disrupt the food supply at any time; according to Masipa [67], the country has limited access to technology that can accurately predict and manage the challenges. In South Africa, the occurrence of extreme weather such as drought and flood has become common because of the growing climate change [46, 68]. Additionally, research revealed that the country has experienced disasters such as tornadoes, flash floods, strong winds, sudden cold spells, infested water, COVID-19, civil war, break out of diseases such as avian flu, foot and mouth and armyworm [69].

Research was done on the impact of war between Russia and Ukraine on food security, considering that the two countries contribute immensely to food provision in the world [46, 70]. The two countries are considered to be among the global breadwinners, producing and exporting grains, minerals, fertilizers and energy. Research further agrees that the Russia and Ukraine war affected the supply of food, fuel, and fertilizer prices and thus raising global poverty and food insecurity [71]. As a result, rising interest rates, inflation, fuel and food prices were witnessed in South Africa, leaving households with no option but to reduce the purchase of preferred food items. Moreover, Mazenda et al. [41] and Mbhenyane and Tambe [46] indicated that the expected lasting effects of the war remain the disruption of the food chain supply, poor access to nutritious food items and prevalence of food insecurity among poor households.

These unfortunate events have affected the supply and distribution of food from both external and internal sources. Currently, the price of eggs in South Africa which used to be the cheapest source of protein, is struggling to adjust to its average prices before the avian flu outbreak, and additionally, the price of cooking oil and other essential products have not returned to their averages even after Covid-19 have passed [69, 72, 73]. Moreover, businesses are still battling the effects of both covid restrictions and load-reduction which lead to high levels of retrenchments. All these aspects make the food security status of poor households who spend most of their income on food worse.

10. Community-based solutions for food security

According to Oelofse et al. [74], a staggering amount of food (45%) in South Africa goes to waste due to inefficiencies within value chains, and this calls for an

intervention to safeguard some of the food. Some food that is still of good quality can be collected and redistributed to regions that experience deficit and even be processed to prolong their shelf life. The problem can also be addressed by improving food distribution in areas where products are not available.

There is also a need to promote already existing food security programmes which the government have created such as Food Security Capacity Building Programme, Special Programme for Food Security, and Fortune 40 incubation programmes, which are aimed at reducing poverty and improving food security status of households. Most households in South Africa come from rural settings with sufficient land to practice backyard gardens, and the practice is useful in ensuring access and availability of nutritious food. Hence, there is a need to improve household food security through training and skills development geared towards improving household participation in food production.

Communities in South Africa are also practising food gardens in schools which are aimed at improving the provision of healthy food and imparting farming knowledge to the younger generation [42]. The EduPlant School Gardening and Nutrition Programme establishes school-linked food security projects that focus on schools, learners and the community at large. This programme aligns well with school feeding schemes in South Africa and has the potential to increase the availability of healthy food in schools.

11. Conclusions

Food security remains a critical challenge in South Africa, influenced by multiple socioeconomic, environmental, and policy-related factors. Despite progress in ensuring access to food for the majority of households, a significant portion of the population continues to experience food inadequacy, exacerbated by poverty, unemployment, and economic instability. The disparities in food security are particularly evident between urban and rural areas, with rural communities facing higher risks of malnutrition due to limited access to nutritious food.

The transition towards Western dietary patterns, characterized by increased consumption of ultra-processed foods, has contributed to rising obesity rates and diet-related noncommunicable diseases. At the same time, undernutrition and hidden hunger persist, particularly among children in impoverished areas. These dual burdens of malnutrition necessitate comprehensive strategies that promote dietary diversity, nutrition education, and access to affordable, healthy food options.

Sustainable agricultural practices, including climate-smart farming, crop diversification, and reducing food waste, offer viable solutions to improving food security. Supporting small-scale farmers, enhancing market access, and promoting backyard gardening can contribute to self-sufficiency and resilience at the household level. However, systemic challenges such as land distribution inequalities and limited technological advancements in agriculture must be addressed to achieve long-term food security.

Government interventions, including food security policies and social protection programmes, have made strides in alleviating hunger and malnutrition. However, past initiatives have faced challenges related to implementation, sustainability, and inclusivity. The integration of multi-sectoral approaches, stakeholder collaboration, and investment in food systems governance will be crucial in enhancing the effectiveness of future policies.

Global economic disruptions, climate change, and geopolitical conflicts continue to impact South Africa's food security landscape. The COVID-19 pandemic and the war in Ukraine have exposed vulnerabilities in the country's food supply chains, leading to increased food prices and reduced access to essential commodities. These challenges highlight the need for resilience-building measures, including diversified food imports, improved storage infrastructure, and strategic economic policies.

In conclusion, ensuring food security in South Africa requires a multi-faceted approach that addresses economic, social, and environmental determinants. Policymakers must prioritize sustainable food systems, equitable resource distribution, and employment opportunities to mitigate hunger and malnutrition. Strengthening food security governance through evidence-based policymaking, inclusive stakeholder engagement, and community-driven initiatives will be key to building a food-secure future for all South Africans.

Conflict of interest

The authors declare no conflict of interest.

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Section 2

Factors Influencing Food Quality and Health

Compressed Modernization and Nutrition Transition: Implications for Diet Quality and Disease Prevalence in Southeast Asia

Helda Khusun

Abstract

The rapid economic, social, and cultural transformations occurring in Southeast Asia—referred to as compressed modernization—have significantly reshaped dietary patterns in the region. This phenomenon has accelerated the nutrition transition, shifting traditional diets rich in whole foods toward energy-dense, ultra-processed food consumption. Urbanization, economic growth, and globalization have collectively altered food environments, increasing the availability of and preference for fast food, processed products, and sugar-sweetened beverages. These dietary changes have contributed to declining diet quality, as reflected in various diet quality indices, and have resulted in rising obesity rates and an increasing burden of diet-related non-communicable diseases (NCDs), such as cardiovascular disease and type 2 diabetes. Additionally, compressed modernization has exacerbated socioeconomic disparities in diet quality, with lower-income groups disproportionately affected by the affordability and accessibility of unhealthy food options. The co-occurrence of undernutrition and overnutrition in the region, known as the double burden of malnutrition, further complicates public health efforts. In response, various policy interventions have been implemented, including food labeling regulations, nutrition education programs, and taxation on sugar-sweetened beverages; though their effectiveness varies across different countries. Emerging food technologies, sustainable dietary initiatives, and cultural preservation efforts offer potential solutions to counteract the adverse effects of compressed modernization on diet quality. Future research should focus on the long-term impacts of nutrition transition, the effectiveness of policy interventions, and the development of strategies to improve food security and public health outcomes in the region.

Keywords: compressed modernization, nutrition transition, diet quality, food environment, obesity, non-communicable diseases (NCD), Southeast Asia

1. Introduction

The prevalence of obesity in Southeast Asia has increased significantly over the past decades, becoming a major public health concern. Recent studies indicate that

obesity rates in the region have risen sharply, with some countries reporting prevalence levels as high as 40% [1, 2]. The proportion of overweight adults has surged by 38% compared to the 1990s, now affecting 40.9% of the population [3]. In Malaysia, nearly 50% of the population is overweight or obese, while Indonesia has recorded a 28% obesity rate among adults, reflecting a marked increase over the past two decades [3, 4]. Rising obesity rates have led to an increased burden of non-communicable diseases (NCDs), such as cardiovascular disease, diabetes, and hypertension, straining healthcare systems that remain underprepared for managing chronic illnesses [5–8].

Childhood obesity is also rising, particularly in urban areas where access to processed foods and physical inactivity contribute to weight gain [9, 10]. The World Health Organization (WHO) reports that the proportion of overweight and obese adolescents aged 5–19 has increased from 4% in 1975 to over 18% in recent years [2]. This shift is exacerbated by the double burden of malnutrition, where undernutrition and obesity coexist within the same populations, particularly in low- and middle-income countries (LMICs) undergoing rapid economic changes [3, 11–13]. These patterns highlight the need to examine the structural drivers of dietary change and obesity, particularly the role of nutrition transition and compressed modernization [14, 15]. These shifts are not solely personal choices but are shaped by food system transformations, evolving social norms, and global trade policies [16–19].

Obesity in Southeast Asia is strongly linked to nutrition transition, a process driven by urbanization, economic growth, and globalization [6, 13, 16, 20, 21]. Historically, Southeast Asian diets were high in whole grains, vegetables, and plant-based proteins, but are increasingly being replaced by Westernized diets rich in processed foods, refined sugars, and saturated fats [21–24]. The rise of multinational food corporations has made calorie-dense, nutrient-poor diets more available, particularly among younger populations [16]. These changes are particularly evident in urban settings, where access to fast food and convenience foods have expanded significantly [20, 21, 23–25]. The expansion of food delivery services and supermarket chains has reinforced unhealthy dietary habits, increasing the consumption of high-calorie, low-nutrient foods [26, 27]. Moreover, in countries such as Malaysia, Vietnam, and Indonesia, rapid economic expansion has led to increased consumption of processed foods and a decline in traditional diets [22, 23, 28]. However, in some settings higher-income groups have access to healthier food options, while lower-income populations relied on cheaper, highly processed foods, contributing to both obesity and micronutrient deficiencies [29, 30].

The impact of nutrition transition on diet is reflected in declining scores on dietary measuring diet quality [31, 32]. Poor diet quality has led to higher obesity rates and a rising burden of NCDs, such as cardiovascular diseases and diabetes [33]. Improving diet quality requires interventions that go beyond caloric sufficiency, but also on nutrient adequacy [34].

When urbanization, economic development and societal changes occur within a short time frame, the phenomenon is known by compressed modernization [14]. This process accelerated nutrition transition. This chapter examines compressed modernization and nutrition transition in Southeast Asia, and analyzing their effects on diet quality. This study situates diet quality within broader economic and social transformations, providing a comprehensive analysis of shifting food systems, dietary patterns, and public health outcomes. By synthesizing empirical research and policy insights, this chapter highlights key challenges and policy recommendations to improve diet quality and reduce obesity in Southeast Asia.

2. Compressed modernization and nutrition transition

As mentioned previously, compressed modernization refers to the phenomenon in which developing countries undergo rapid and simultaneous economic, political, social, and cultural transformations within a short timeframe, leading to significant societal changes [14]. Unlike conventional modernization, which took place over centuries, compressed modernization accelerates these transitions, creating dynamic and often disruptive shifts in economic and social conditions. Drivers of compressed modernization include urbanization, economic growth, globalization, women's workforce participation, technological advancement, and food system transformation. **Table 1** explains the interrelationship of compressed modernization, nutrition transition, diet quality, and health outcomes in Southeast Asia.

Southeast Asia exemplifies this model, as nations, such as Vietnam, Indonesia, and Malaysia, have experienced rapid urbanization and globalization, transforming their economies and traditional ways of life in just a few decades. The expansion of foreign direct investment (FDI), technological advancements, and integration into global markets have further intensified these transitions, producing significant societal changes. This accelerated process has had significant consequences for public health, particularly in dietary behavior and nutrition [15–18].

The drivers of compressed modernization—urbanization, economic growth, and globalization—have collectively reshaped food environments, leading to widespread dietary changes. Rapid urbanization has contributed to increasing migration to cities, where food environments offer greater access to processed and convenience foods [20, 23, 26, 35, 38]. Economic growth has enabled greater purchasing power, making high-calorie, energy-dense foods more accessible and preferred for convenience [29, 30]. The interaction among these factors has resulted in a shift away from traditional diets, which were largely plant-based, toward diets high in fats, sugars, and ultra-processed foods [23]. Moreover, technological advancements, such as online food delivery services, have expanded access to fast food, reinforcing modern dietary habits [49].

Moreover, globalization has facilitated the expansion of multinational food corporations, reinforcing the proliferation of Western dietary patterns across the region [16, 56]. Multinational food corporations have significantly influenced dietary patterns by introducing Western-style fast foods and processed products into local markets [40]. Research indicates that multinational corporations' entry into Southeast Asian food markets has led to a decline in traditional diets, with consumers opting for heavily marketed processed foods [42, 43]. Furthermore, the expansion of global food supply chains has disrupted local agricultural systems, as imported foods become more accessible and affordable than locally sourced produce [16, 40, 57].

The shift in dietary patterns has resulted in a significant nutrition transition. Nutrition transition was described as a movement away from traditional, high-fiber diets toward energy-dense diets, and a shift that is often accompanied by an epidemiologic transition [6]. As the burden of disease moves from infectious illnesses to non-communicable diseases (NCDs), such as obesity, diabetes, and cardiovascular disorders, public health challenges intensify [6, 8]. In Southeast Asia, this transition is particularly evident in urban centers, where the consumption of processed foods, sugary beverages, and fast foods has become increasingly prevalent [35]. The phenomenon has also contributed to the dual burden of malnutrition, where

Drivers of compressed modernization	Nutrition transition features	Changes in diet quality	Associated health outcomes	Affected populations	Supporting references
Urbanization	Increased access to fast food outlets and supermarkets	Decline in consumption of traditional foods; increase in ultra-processed foods	Rising obesity, type 2 diabetes, and cardiovascular diseases	Urban adults and adolescents	[20, 23–26, 35–38]
Economic growth	Higher disposable income and dietary westernization	Increased intake of sugar, fats, and animal-based foods	Elevated metabolic syndrome risk	Middle-income and high-income urban households	[22, 29, 30, 39–41]
Globalization	Expansion of multinational food corporations; aggressive marketing	Greater consumption of processed snacks and sugary beverages	Double burden of malnutrition (coexisting undernutrition and overnutrition)	Children, low-income families	[16, 42–44]
Women's workforce participation	Reduced time for meal preparation	Shift from home-cooked meals to convenience and ready-to-eat foods	Lower dietary diversity, increased fast food reliance	Working women, school-aged children	[45–48]
Technological advancement	Online food delivery and digital food environments	Frequent dining out, irregular meal patterns	Poor adherence to dietary guidelines	Youth, urban workers	[49–52]
Food system transformation	Decline in local agriculture and traditional food systems	Dependence on global food supply chains, limited access to fresh food	Nutrient deficiencies (iron, calcium, and vitamin A/C); poor HEI/DQI-I/AHEI scores	Low-income urban and rural communities	[16, 17, 27, 40, 53–57]

Table 1.
Impact of compressed modernization and nutrition transition on diet quality and health outcomes in Southeast Asia.

undernutrition coexists with obesity, especially among lower-income populations, exacerbating health disparities [58].

Comparisons with other rapidly modernizing regions, such as Latin America and East Asia, highlight both similarities and differences in nutrition transition. Like these regions, Southeast Asia has seen an increase in fast food consumption, sugar-sweetened beverages, and processed foods [57]. As food environments evolve, dietary behaviors in Southeast Asia continue to shift, reinforcing patterns of overnutrition and poor diet quality. Traditional diets that once emphasized whole grains, fresh vegetables, and lean proteins are increasingly replaced by ultra-processed foods high in sugar, fat, and sodium [57, 59]. However, Japan and South Korea have managed

to integrate traditional dietary elements into modern food environments, maintaining higher diet quality despite modernization [60–62]. This trend mirrors changes observed in Latin America, where processed food consumption has led to increased obesity rates [63, 64].

However, while Latin America has regulatory policies to address these issues, Southeast Asia struggles with policy enforcement and food industry regulation [65]. Latin America has implemented regulatory policies, such as front-of-package labeling and soda taxes, to mitigate unhealthy diets—measures that remain largely absent in Southeast Asia [63]. Without targeted policy interventions, the trajectory of nutrition transition in Southeast Asia will likely exacerbate diet-related diseases, placing even greater pressure on healthcare systems and public health infrastructure.

3. Modernization, socioeconomic changes, and the impact on food consumption patterns

Modernization has changed employment patterns, income levels, urban living conditions, and women's workforce participation in Southeast Asia. As economies transition from agrarian to industrial and service-based sectors, job structures and labor markets evolve, leading to higher household incomes and improved access to goods and services [59]. Along with the economic transition, rural populations migrate to cities seeking better economic opportunities. This movement fosters social mobility and economic growth but also results in profound lifestyle changes [17, 18]. While these transformations contribute to economic prosperity, they also create challenges in maintaining dietary quality and health outcomes [20, 21]. As incomes rise, traditional dietary staples rich in fiber and micronutrients are increasingly replaced with energy-dense foods high in fat, sugar, and sodium, contributing to the rising burden of non-communicable diseases (NCDs) such as obesity and diabetes [6, 13].

With higher disposable incomes and time constraints due to employment commitments, urban households are increasingly relying on ready-to-eat meals, packaged foods, and dining out instead of traditional home-cooked meals [39, 50]. The demand for Western-style diets has increased as economic development allows for more discretionary spending on food items that were previously unaffordable [54]. The widespread presence of supermarkets and fast-food chains has further facilitated this transition, making industrially processed foods more accessible and appealing [27, 37, 66]. The urbanization has also played a key role in transforming food environments. In contrast to rural settings where fresh and locally sourced foods are more prevalent, urban areas expose populations to a greater variety of processed and imported food products, leading to changes in dietary habits [52].

At the same time, the increasing participation of women in the workforce, driven by globalization and industrialization, has altered traditional household structures. As women take on formal employment roles, household dynamics shift, affecting food preparation practices and meal choices [67]. This led to profound shifts in food consumption patterns, with greater reliance on convenience foods [52]. Dual-income households, in particular, are more likely to purchase processed and ready-made meals, as they require less time for preparation [67]. Studies indicate that working women tend to prioritize convenience over nutritional value when selecting meals, further accelerating the transition to diets high in ultra-processed foods [68]. This shift reflects broader socioeconomic changes in household decision-making and

nutritional intake, where the pursuit of convenience often comes at the cost of diet quality and long-term health outcomes.

The impact of modernization on food consumption is particularly evident in the widening socioeconomic disparities in diet quality and nutrition. Wealthier individuals typically have access to a broader selection of food options, including fresh and nutrient-dense foods, while lower-income households often resort to inexpensive, calorie-dense processed foods due to financial constraints [39, 41]. This economic divide has led to an increase in diet-related health inequalities, where obesity and micronutrient deficiencies coexist within the same communities [8, 11]. Urbanization has further exacerbated these disparities, as the cost of living in cities continues to rise, limiting the affordability of fresh and healthy food options for low-income populations [69, 70].

Rural populations experience distinct nutritional challenges compared to their urban counterparts. While access to traditional food sources is generally better in rural areas, economic limitations and reduced integration into commercial food markets hinder dietary diversity [70–72]. However, the penetration of global food supply chains has increasingly exposed rural populations to processed foods, leading to dietary shifts similar to those seen in urban areas [73]. Unlike urban populations, rural communities may still maintain aspects of their traditional diets, but as modernization continues, the prevalence of processed foods is expected to rise [59]. The increasing accessibility of low-cost processed foods in both urban and rural settings continues to shape dietary habits, contributing to the widespread low diet quality and affecting the burden of diet-related diseases.

4. Compressed modernization and its effects on diet quality

The rapid modernization and the resulting ongoing nutrition transition, characterized by a move from traditional, plant-based diets to high-calorie, processed food consumption, has resulted in declining diet quality across various demographic and socioeconomic groups [31]. Diet quality in Southeast Asia has been assessed using various indices, including the Healthy Eating Index (HEI) and Diet Quality Index-International (DQI-I). Studies using these measures indicate a consistent decline in diet quality, particularly in urban areas [74]. The HEI, which evaluates adherence to dietary guidelines, has shown lower scores across Southeast Asian countries due to increased consumption of sugar, refined grains, and saturated fats, while the intake of whole grains, fruits, and vegetables has decreased [75–77]. Similarly, the DQI-I, which measures dietary diversity, adequacy, moderation, and balance, indicates that many Southeast Asian populations are failing to meet recommended dietary standards [32, 78–80].

Urbanization, lifestyle changes, and the expansion of fast-food industries have significantly influenced overall diet quality scores groups [31, 76], including in Southeast Asian countries [21, 57]. Studies confirm that urban populations exhibit lower diet quality scores due to a higher intake of unhealthy fats, refined sugars, and processed foods, while traditional diets are becoming less common [35, 38]. The demands of urban work schedules and time constraints have also contributed to reduced home cooking, as individuals opt for convenient meal options that prioritize speed over nutritional value [52]. The increasing dependence on food delivery services and pre-packaged meals further reduces adherence to balanced, home-prepared diets, accelerating the decline in diet quality across urban communities.

The decline in diet quality has led to widespread nutritional deficiencies and imbalances among different population groups in Southeast Asia, leading to deficiencies in essential [81–83]. These deficiencies contribute to a range of public health concerns, including stunted growth in children, osteoporosis in adults, and weakened immune function across various age groups. On the other hand, the relationship between the decline of traditional diets in Southeast Asia and rising rates of obesity, metabolic syndrome, and diet-related chronic diseases is well-documented [57, 84].

In conclusion, compressed modernization has led to a significant decline in diet quality in Southeast Asia, driven by increasing reliance on processed foods, changing urban lifestyles, and socioeconomic disparities in food access. As a result, obesity, metabolic syndrome, and other chronic diseases are becoming increasingly prevalent, emphasizing the urgent need for public health interventions and policies aimed at promoting healthier food environments. Addressing these challenges requires multisectoral efforts, including nutrition education, policy regulations on processed foods, and strategies to improve access to fresh and nutrient-dense foods, ensuring long-term improvements in diet quality and public health outcomes in Southeast Asia.

5. Future trends in nutrition transition, and public health implications

The compressed modernization and rapid nutrition transition occurring in Southeast Asia pose significant public health implications, particularly concerning obesity, type 2 diabetes, and cardiovascular diseases. Studies have shown that countries like Malaysia and Indonesia are witnessing alarming increases in obesity prevalence, leading to a corresponding rise in type 2 diabetes and cardiovascular diseases [21–23].

With the continuously unresolved undernutrition problems, Southeast Asian faced the double burden of malnutrition various forms, where significant segments of the population experience both undernutrition and overnutrition concurrently [85]. This dual challenge reflects structural inequalities in food accessibility and dietary habits among different socioeconomic groups [21]. For instance, while urban populations may struggle with obesity and diet-related chronic diseases, rural communities often face food insecurity and micronutrient deficiencies. The long-term health consequences of this double burden are manifold, potentially leading to increased healthcare costs, decreased productivity, and prolonged cycles of poverty as health systems become strained due to rising non-communicable diseases (NCDs) [11, 81]. Addressing the double burden is essential for promoting equitable health outcomes and ensuring that populations from all backgrounds have access to nutritious food.

In response to the adverse effects of nutrition transition, several policy interventions and public health strategies have been implemented in Southeast Asia. These strategies include the enforcement of food labeling regulations, the promotion of healthy eating campaigns, and the enhancement of food security measures [4, 86, 87]. For instance, Malaysia's National Plan of Action for Nutrition has focused on reducing obesity prevalence through public awareness programs and promoting healthful diets [73]. Additionally, initiatives, such as nutrition education in schools, aim to encourage healthier eating behaviors [88]. Moreover, Southeast Asian governments are increasingly recognizing the importance of multisectoral approaches to tackle malnutrition comprehensively, emphasizing collaboration across the health, agriculture, and education sectors [87]. Furthermore, it is also important to collaborative efforts with local communities to develop culturally sensitive dietary guidelines to promote traditional

food practices alongside modern nutritional advice [89, 90]. These interventions aim not only to address the challenges of overnutrition but also to ensure that vulnerable populations have access to the nutrients necessary for healthy development. Initiatives promoting the incorporation of indigenous crops and traditional cooking methods into modern dietary frameworks to support healthful eating and preserve cultural identity is crucial in combating the adverse effects of nutrition transition.

Future research is important to prevent the adverse consequences of compressed modernization and the subsequent negative impacts on diet quality in Southeast Asia. More studies are required to elucidate the mechanisms by which urbanization influences dietary patterns and health outcomes, particularly among vulnerable populations. Qualitative research exploring the lived experiences of individuals and families in navigating food choices and their perceptions of nutrition can enhance our understanding of behavior change and social determinants of health. Additionally, longitudinal studies examining the effects of food policy interventions will be critical in assessing the effectiveness of implemented strategies aimed at improving diet quality and health outcomes. Investigating how emerging food technologies can be integrated into existing food systems, while respecting cultural contexts and dietary needs, will provide valuable insights for future food policy development. Finally, interdisciplinary approaches combining nutrition, public health, agriculture, and environmental studies will be essential in fostering sustainable and health-promoting food systems.

6. Conclusion

The phenomenon of compressed modernization has significantly influenced the nutrition transition in Southeast Asia, accelerating shifts toward Westernized dietary patterns characterized by high consumption of processed and ultra-processed foods. The drivers of this transition—urbanization, economic growth, and globalization—have contributed to changes in food environments, making unhealthy dietary choices more accessible and prevalent. As a result, diet quality has deteriorated, with a growing reliance on energy-dense, nutrient-poor foods, leading to increased obesity rates and a higher prevalence of diet-related NCDs. The expansion of multinational food corporations and global supply chains has further exacerbated these trends, reinforcing unhealthy eating behaviors and diminishing traditional food consumption.

The consequences of compressed modernization extend beyond diet quality, manifesting in significant public health challenges, including the double burden of malnutrition. While obesity and NCDs rise among urban populations, undernutrition persists in many rural and low-income communities, widening health disparities across socioeconomic groups. Policy interventions have been introduced to mitigate these adverse effects, including food labeling regulations, taxation on unhealthy food products, and public health campaigns promoting traditional diets and locally sourced foods. However, the effectiveness of these measures remains inconsistent, highlighting the need for comprehensive, multisectoral approaches that integrate food security, nutrition education, and regulatory oversight.

Looking ahead, the future trajectory of nutrition transition in Southeast Asia will be shaped by advancements in food technologies, sustainable dietary practices, and cultural preservation efforts. Strengthening local food systems, promoting indigenous food production, and implementing targeted public health policies will be critical in reversing declining diet quality and improving nutritional outcomes. Future research should focus on longitudinal studies that assess the long-term impacts

of dietary shifts, evaluate policy effectiveness, and explore innovative strategies to foster resilient and health-promoting food environments in the region. Addressing the complexities of compressed modernization requires a holistic approach that considers economic, social, and cultural dimensions to ensure sustainable improvements in public health and dietary quality.

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Sociocultural Factors Impacting Contemporary Appearance among Young Adults: Disordered Eating and Health

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Abstract

In the contemporary appearance culture, young people increasingly recognize the social benefits of a “good” appearance and a body shaped by contemporary beauty ideals. Dissatisfaction with the body and physical appearance can be a trigger for the development of disordered eating. Although multiple factors cause disordered eating behaviors, this chapter focuses on sociocultural influences: peer groups, family, and media. The chapter presents the results of a survey conducted among students at the University of Split, Croatia (N = 200). The research question was related to assessing the influence of sociocultural risk factors on body dissatisfaction and, consequently, disordered eating behavior. The results confirm that the media, family, and peers play a significant role in shaping body perception and eating behavior. Students who are more often exposed to idealized bodies in the media show a higher degree of body dissatisfaction and are more prone to disordered eating. While media influence was the strongest predictor of weight control behaviors, family and peer influences also played significant roles, particularly in emotional eating patterns. Research on this issue in Croatia is rare. The contribution of this research lies in the results achieved and the knowledge that can provide a starting point for future research.

Keywords: body dissatisfaction, disordered eating, research, students, Croatia

1. Introduction

Reflecting cultural, social, and economic circumstances, physical appearance has been important in a person's life since the earliest beginnings of human history. In contrast to the continued significance of appearance, beauty ideals have changed over time. Consistent with current beauty ideals, a “good” appearance contributes to a person's self-esteem. It plays an important role in achieving an individual's social contacts and interactions. The concept of physical beauty and attractiveness has always been an evaluative factor more for women than for men.

The plump female body has been valued in earlier history. For example, the Venus of Willendorf figure represented the ideal female body of that time. In ancient

Greece, as well as in the period of the Renaissance, a beautiful female body was characterized by wide hips, a full belly, and voluptuous breasts. Although the ideal of a woman's physical appearance has changed throughout history, significant changes have been recorded in the 1920s. Women's emancipation was reflected in women's fashion and clothing, promoting androgynous body appearance. In the 1960s, under the influence of the fashion industry and the popular model Twiggy, the thin appearance was massively accepted among women. A thin female body will remain the ideal of beauty nowadays. Originally characteristic of developed Western countries, despite cultural and civilizational differences, the ideal of thinness has become global. Breaking down cultural, ethnic, and class barriers, women have accepted a slim body shape in all parts of the world and all social classes.

The body shaped by contemporary standards of beauty plays an important role in an individual's life. Physical attractiveness provides numerous advantages in private and social life. Research has confirmed the stereotype that "what is beautiful is good." "Not only are physically attractive persons assumed to possess more socially desirable personalities than those of lesser attractiveness, but it is presumed that their lives will be happier and more successful [1]."

The study confirmed the "beauty premium" phenomenon. Attractive appearance appears to be a mediator in the work environment, which brings employees advantages and rewards [2]. Physically attractive employees have more self-confidence, while employers consider physically attractive workers more capable [3]. Beauty is important not only in the business world but also in the academic environment. Research has shown that the appearance of female students matters. Less attractive female students received lower grades in traditional classrooms. The importance of appearance was also confirmed by the correlation with online classes, where female students with above-average appearance received lower grades than those in traditional classrooms [4]. The stereotype of negative judgment of unattractive people has been recorded in adults and children [5].

The benefits of a beautiful and thin appearance strongly encourage individuals to shape their bodies to achieve the social ideal. Contemporary appearance culture is a "powerful structure that encourages individuals to think of health and appearance as primarily a personal choice and to work towards constant improvement [6]." In contemporary appearance culture, a new individual emerges who is informed about desirable body proportions and recognizes the social importance of appearance.

2. Body image, body dissatisfaction, and disordered eating behaviors

A body image is a multidimensional construct involving biological, psychological, and external cultural and social factors. In earlier history, the body was considered an individual's intimate sphere, hidden behind layers of clothing. Social norms forbade the display of the body. In contemporary society, the body is exposed to the gaze of others. This change is reflected in the interpretation of body image as the image of one's body that we form in our minds [7] to the visuals that others have of someone based on that person's appearance [8].

Due to the discrepancy between the actual body and the socially promoted ideal, a person can develop body dissatisfaction. Negative body evaluation can lead to feelings of inferiority, suffering from tension, depression, and social isolation. Although it is a matter of individual thinking and emotions, body dissatisfaction is caused by external factors. To manage body image, people can use a variety of acceptable but also extreme and unhealthy weight control behaviors. Restrictive diets, skipping

meals, eliminating foods from the diet, excessive exercise, and obsession with calorie counting and weighing are ways that can damage health and develop eating disorders.

Many people manage their bodies by changing their eating behaviors, but they do not develop an eating disorder. Therefore, it is important, especially in the case of designing research, to conceptually distinguish disordered eating (DE) and eating disorders (ED). According to Pereira and Alvarenga [9], the key difference is that eating disorders, unlike disordered eating, are diagnosed, severe, and long-lasting, accompanied by medical complications and psychological states and problems in interactions. On the other hand, the eating behaviors and psychological distress in individuals with disordered eating may be remarkably similar. However, they do not meet the frequency, duration, and level of psychological impairment thresholds necessary for a diagnosable eating disorder.

Disordered eating is much more common in the population than eating disorders. In appearance culture, individuals often do not perceive their disordered eating behaviors as wrong or unhealthy but rather see them as a means of achieving a goal that is socially valued and desirable. Therefore, many people with disordered eating patterns do not seek professional help, which is the reason for the high gray numbers.

3. Most common eating disorders and health consequences

Eating disorders are defined as behavioral and psychological disorders. The American Psychiatric Association (APA) [10, 11] defines them as severe and persistent disturbances in eating behaviors and associated distressing thoughts and emotions. Eating disorders can be a severe condition affecting the physical, psychological, and social function of the individual. Types of Eating disorders include anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED), avoidant restrictive food intake disorder (ARFID), other specified feeding and eating disorders, pica, and rumination disorder. Taken together, EDs affect up to 5% of the population, which most often develop in adolescence and young adulthood. Several, especially anorexia nervosa and bulimia nervosa, are more common in women but can occur at any age and affect any gender.

Academy for Eating Disorders (AED) [12] maintains that eating disorders can cause serious consequences for health, productivity, and relationships and can affect every organ system in the body, and for some people, these illnesses are fatal. The most common consequences of eating disorders affect the cardiovascular system, gastrointestinal system, neurological function, endocrine system, and other aspects of health.

Mortality rates for eating disorders vary. Most studies suggest that anorexia nervosa has the highest mortality rate. A meta-analysis by Sullivan [13] found a mortality rate of 5.9% for anorexia nervosa regardless of cause. A study by Crow et al. [14] found that mortality rates were 4.0% for anorexia and 3.9% for bulimia. The study also found a high suicide rate in bulimia nervosa.

The elevated mortality risks for bulimia nervosa and EDNOS were similar to those for anorexia nervosa. Auger et al. [15] confirm that anorexia nervosa has the highest mortality rate of any psychiatric condition, causing the death of about 5% of people within 4 years of receiving a diagnosis. Death causes include starvation, substance abuse, and suicide. According to the Eating Disorder Hope (EDH) [16], 5–10% of people with anorexia nervosa die within 10 years of contracting the condition, with 18–20% of people struggling with the disorder dying within 20 years of first presenting with anorexia nervosa.

4. Media, peer groups, and family environment as risk factors

Psychological factors cannot fully explain eating disorders and their strong increase in recent decades. A comprehensive explanation requires that we also consider the influence of sociocultural factors. Thompson et al. [17] developed a tripartite system based on the influence of the media, peers, and family as factors that can influence body image, body dissatisfaction, and the development of disordered eating behaviors. The influence of the media, peers, and family is indirect and occurs through the internalization of socially accepted appearance standards and appearance comparison. Through the processes of internalization and comparison, a person can feel body dissatisfaction and develop disordered weight control behaviors.

Using visual content to promote unrealistic body appearances, the media are an important promotor of contemporary appearance culture. Media send the message that the body is a measure of happiness, success, and one's value. Duncan [18] distinguishes two mechanisms by which magazines influence women's attitudes towards their bodies. The first is the "Efficiency Initiative," which appeals to women to commit to making a change. The second mechanism is "Feeling Good Means Looking Good," which emphasizes the importance of health but places an emphasis on appearance.

Numerous studies confirmed the influence of traditional media. Content analysis of women's magazines between 1970 and 1990 showed a change in the female body, which became androgynous [19]. It has been confirmed that negative body attitudes increase after exposure to visual content depicting thin female bodies. This effect is more potent in girls under 19, indicating greater sensitivity at this age [20]. The media influence young people's self-perception, body dissatisfaction, body weight concerns, and consequently inappropriate weight control behaviors [21]. The correlation between developed media literacy and low levels of body dissatisfaction has been confirmed. Authors advocate for media literacy and activism to encourage change in the widespread body dissatisfaction [22].

Research confirmed the influence of "new media." Correlational studies consistently show that social media usage, such as Facebook, is associated with body image concerns, while longitudinal studies suggest that this association may strengthen over time [23]. A recent study by Gao [24] highlights the importance of photo filters on social media in reinforcing unrealistic beauty standards. Digitally manipulated and not real photographs can lead to body dissatisfaction and the development or worsening of disordered eating habits. This research also warned about the growing power of influencers who frequently present idealized looks and lifestyles, encouraging social comparison. Studies also show that the impact of social media platform algorithms is crucial to viewers. When a person reacts to a post, social media platforms display similar posts, tags, comments, etc. These amplified photos usually depict influencers that fit societal beauty standards and are sometimes advocating for eating disorders and weight loss. These continuous algorithms boost various posts and comments that focus on appearance, indirectly promoting disordered eating.

Peer groups, as a risk factor in the sociocultural model, can encourage positive and healthy behaviors in their members as well as negative and unhealthy behaviors. Physical appearance is important for teenagers and youth, and many consider it part of their identity. Studies show that peers can influence body image and the tendency to compare themselves with others, thus developing unhealthy eating habits. Al-Sheyab et al. [25] confirmed the connection between peer pressure and disordered eating behavior in adolescents. The results showed that disordered eating behavior is strongly influenced by interaction with peers, which included talking with

peers about appearance, exercising together, and comparing physical appearance and proportions with each other. Matera et al. [26] determined that the influence of peer attributes and talking with friends about appearance while teasing peers about appearance directly impacted the level of dissatisfaction. A study by Meyer and Gast [27] showed a strong correlation between peer influence and disordered eating behavior. It was also shown that peer influence is present in both sexes.

Some studies have examined the comparative influence of media and peers on the development of body dissatisfaction. A study of Chinese students by Shen et al. [28] confirmed the specific influence of media and peers. Peers directly and significantly influence body image, while a direct influence was not found in the media. The authors concluded that media attention and peer impact further increased the negative evaluation of college students' figures through the chained indirect effect of appearance comparison and internalization of the thin ideal.

Along with the media and peers, family is the third factor in the tripartite model of sociocultural influences. Like peer influence, family members can play a positive role in shaping children's eating habits. However, a lack of family support can foster feelings of body dissatisfaction in both girls and boys [29]. The mother-daughter relationship is often highlighted. Mothers who have or have had eating disorders are more concerned about their children's weight, and their children are more likely to report emotional eating [30]. Parenting styles can also affect eating disorders in adolescents. Authoritarian, neglectful, and authoritative parenting styles each appears to have a distinct influence on whether an adolescent is at greater risk of developing an eating disorder or not [31].

The family is not considered the only or primary mechanism for initiating and developing eating disorders in children [32]. However, some family characteristics may be a risk for the development of problematic eating behaviors in childhood and adolescence. According to Patel et al. [33], risk factors and mechanisms for the transmission of eating disorders from parent to child are genetic factors, parental eating psychopathology, parental preoccupation with food and body image, poor role of parents as role models in transmitting healthy eating habits, and disturbed relationships in the family. Del Casale et al. [34] conducted a literature analysis on family risk factors in AN, pointing out the complexity of family influence and a broad spectrum of risks: increased food intake in the family, perfectionism, higher parental demands, emotional reactivity, family taboos regarding nudity and sexuality, low familial involvement, negative affectivity, family discord, dependence, negative family history for ED (as a predictor of poor outcome), family history of depression, positive family history for psychiatric disorders, affective disorders in family members, alcohol and drug abuse, having a sibling with AN, and relational trauma. Some other risk factors identified may relate to the role of the mother during childhood especially, and are as follows: lack of maternal caresses, dysfunctional interaction during feeding, attachment insecurity, dependence, and maternal diet [31].

5. Disordered eating behaviors in Croatia: Assessments and research results

In Croatia, 65% of adults were overweight in 2019. That was the highest rate among EU countries [35]. Obesity is also common among children in Croatia. At the age of 8 to 8.9, 35% of children are overweight or obese. These data place Croatia in fifth place among countries in the European Region [36]. The problem of overweight

and obesity is perceived as a concern in Croatia, and regular measurements and monitoring are carried out. Although there may not be an obvious connection between obesity and disordered eating behaviors, the prevalence of overweight and obesity in the population may be a risk factor for the development of disordered eating behaviors. For example, binge eating disorder and night eating syndrome are two forms of disordered eating associated with overweight and obesity [37].

Data on overweight and obesity in Croatia could be of concern regarding the epidemiology of eating disorders. However, despite being a serious and escalating problem in Croatia, eating disorders are an under-recognized public health problem and have not received adequate scientific attention, especially in the social sciences.

On the other hand, as previous research shows, disordered eating behaviors in Croatia are an escalating problem that affects more and more young people. Pokrajac-Bulian et al. [38] found that 35.6% of girls are dissatisfied with their body weight, while Sambol and Cikač [39] estimate that around 40% of boys and 50% of girls aged 15 are dissatisfied with their body weight. According to them, 35,000 to 45,000 people suffer from eating disorders. Livazović and Mudrinić [40] noted an increase in the number of respondents who want to lose weight, to 65.5%. Girls were more dissatisfied with their bodies than boys, 48.6% of whom wanted a thinner body. This study established a correlation between dissatisfaction with body appearance and eating disorders, while the influence of peers was not confirmed.

The studies clearly show an increase in body dissatisfaction and disordered eating behaviors. However, precise epidemiological data on the number of people suffering from eating disorders in Croatia do not exist. The Tesa Psychological Center [41] provides a worrying estimate that around 90,000 people are suffering from eating disorders, most of them are female persons aged 12 to 30. It is worrying as well that the age limit for children suffering from these disorders has dropped from 12 to 8 years in the last few years [42]. In such circumstances, it is encouraging that the Committee for Health and Social Policy of the Croatian Parliament [43] held a thematic session dedicated to eating disorders. It was emphasized that these disorders are a public health problem in Croatia. It was pointed out that there is a need for greater support for associations that aid sufferers and their families, stronger institutional action, health administration, as well as public awareness.

The motives for the research that will be presented further in this chapter are multiple but can be reduced to the (1) underestimation of the seriousness of eating disorders and their institutional and scientific neglect in Croatia. Eating disorders have long-term and multiple consequences for a person, endangering their health and the achievement of life goals and negatively affecting their interactions in social groups, especially disrupting family relationships. People who suffer from these disorders are often stigmatized and left to their own devices and beyond the possibility of systematic health and other assistance. The second motive is (2), as stated above, the modest available data in Croatia. At the same time, we witness the escalation of the number of people with disordered eating behaviors and eating disorders, with a lowering of the age limit for the disease.

6. Investigating the influence of sociocultural factors on disordered eating among students

Understanding the complex interplay between sociocultural influences and disordered eating behaviors is essential for addressing body dissatisfaction and the

emergence of unhealthy eating patterns. This study examines how external pressures from media, family, and peers shape individuals' perceptions of their bodies and influence their eating behaviors. By investigating these sociocultural dimensions, the research aims to provide deeper insight into the mechanisms that drive unhealthy dietary habits and weight control strategies. As societal concerns regarding body image and its psychological consequences continue to grow, understanding the influence of sociocultural factors on disordered eating is increasingly relevant. This study is structured around three key research questions:

- How do family interactions and discussions regarding body image contribute to the development of disordered eating patterns?
- What role do peer interactions play in shaping body dissatisfaction and eating behaviors?
- To what extent do idealized body representations in the media influence body dissatisfaction and subsequent disordered eating behaviors?

Guided by these inquiries, the study operates on the fundamental hypothesis that sociocultural factors play a significant role in fostering body dissatisfaction and, in turn, contribute to the development of disordered eating behaviors.

6.1 Measurement instrument and statistical analysis

A structured online questionnaire was designed to collect data on sociocultural influences on body image and disordered eating among students at the University of Split, Croatia. The questionnaire consisted of multiple sections, each targeting different aspects of the respondents' experiences with media, family, and peer influences. The first section gathered sociodemographic data, including age, gender, and socioeconomic status. The subsequent sections assessed participants' exposure to media influence, experiences of peer pressure, and the role of family interactions in shaping attitudes towards body image and disordered eating. Specific measures targeted weight control behaviors and emotional eating patterns. The statements used in that section of the questionnaire, which assessed the dependent variable through participant agreement with specific claims, were adapted from *The Minnesota Eating Behavior Survey: A Brief Measure of Disordered Eating Attitudes and Behaviors*.¹

The collected data were analyzed using SPSS statistical software, employing both descriptive and inferential statistical methods. To examine the underlying structure of the dependent variables, a principal component analysis (PCA) with varimax rotation was conducted, confirming two key factors: *Weight Control and Body Dissatisfaction* and *Emotional Eating and Extreme Measures*. The adequacy of the factor model was confirmed through Kaiser-Meyer-Olkin (KMO) measure (0.82) and Bartlett's test of sphericity ($p < 0.001$). For hypothesis testing, multiple linear regression analyses were performed to determine the predictive power of media influence, peer influence, and family influence on the two dependent variables. The models were evaluated using R^2 values, standardized regression coefficients (Beta), t-statistics, and significance levels (p-values). The significance threshold was set at $p < 0.05$.

¹ For the purposes of this research, statements that corresponded to the objectives of the research were selected from the aforementioned questionnaire.

	n	%		n	%
Sex			Number of brothers/sisters		
male	72	36.0	zero	17	8.5
Female	128	64.0	one	83	41.5
Age			two	60	30.0
18–23	154	77	three or more	40	20.0
24–29	40	20	Household income		
30 and more	6	3	≤ 1.499,00 €	12	6.0
Residence			1.501,00–2.999,00 €	91	45.5
Big city	132	66.0	3.000,00–4.999,00 €	72	36.0
Small city	43	21.5	≥ 5.000,00 €	25	12.5
Countryside	16	8.0			
Island	9	4.5			

Table 1.
Sociodemographic characteristics of the sample.

6.2 Sampling and sample characteristics

A non-probability sampling method was used to recruit participants for this study. The data were collected through an online questionnaire created using Google Forms, which was distributed via social media platforms. The survey was open for responses from August 01, 2024, to August 30, 2024. Students from the University of Split were invited to take part in a survey examining the sociocultural factors influencing body image and disordered eating behavior. The final sample consisted of 200 participants, representing a diverse group in terms of gender, age, household income, and place of residence.

Table 1 presents the sociodemographic characteristics of the sample. Most of the respondents were female (64%), with male participants accounting for 36%. Most participants were between 18 and 23 years old (77%), with smaller proportions in the 24–29 age group (20%) and those aged 30 and above (3%). Regarding residential background, most respondents lived in big cities (66%), followed by small cities (21.5%), countryside (8%), and islands (4.5%). Family structure data indicated that 41.5% of participants had one sibling, while 30% had two siblings, and 20% had three or more siblings. A small proportion of respondents (8.5%) reported having no siblings. Household income levels varied across the sample, with 6% reporting an income of ≤1499.00 €, 45.5% between 1501.00 € and 2999.00 €, 36% between 3000.00 € and 4999.00 €, and 12.5% reporting an income of ≥5000.00 €.

7. Results and discussion

7.1 Attitudes towards eating habits, emotional reactions to food, and body weight

The analysis of participants' responses to statements regarding their eating habits, emotional relationship with food, and concerns about body weight (see **Table 2**)

Claims	Strongly disagree		Disagree		Neutral		Agree		Strongly agree	
	f	%	f	%	f	%	f	%	f	%
1. I often diet to control my weight.	48	24.0	71	35.5	23	11.5	29	14.5	29	14.5
2. I eat when I'm upset about things.	13	6.5	54	27.0	22	11.0	74	37.0	37	18.5
3. I have thought about throwing up (vomiting) to lose weight.	114	57.0	37	18.5	17	8.5	29	14.5	3	1.5
4. The shape of my body is fine.	27	13.5	39	19.5	59	29.5	58	29.0	17	8.5
5. I think a lot about dieting (or losing weight).	52	26.0	53	26.5	17	8.5	46	23.0	32	16.0
6. I feel terribly guilty if I overeat.	35	17.5	49	24.5	16	8.0	59	29.5	41	20.5
7. My weight is very important to me.	38	19.0	40	20.0	36	18.0	47	23.5	39	19.5
8. I'm always wishing that I were thinner.	48	24.0	46	23.0	22	11.0	42	21.0	42	21.0
9. I think a lot about overeating (eating a really large amount of food).	76	38.0	74	37.0	23	11.5	19	9.5	8	4.0
10. I often weigh myself to see if I am gaining weight.	64	32.0	58	29.0	16	8.0	27	13.5	35	17.5

ⁱ. Claims are used from *The Minnesota Eating Behaviour Survey: A Brief Measure of Disordered Eating Attitudes and Behaviour*.

Table 2.
Distribution of responses on eating behaviors and body image concernsⁱ.

revolved around insightful patterns in their attitudes and behaviors. The findings suggest a complex interplay between cognitive, emotional, and behavioral factors influencing eating behaviors. A significant proportion of students indicated a strong preoccupation with weight control, as nearly half (48%) reported frequent dieting to regulate their weight. Additionally, 29% of participants stated that they often weigh themselves to monitor any weight gain. These behaviors reflect the prominence of weight management concerns in their daily lives. Emotional responses to food were also evident, with 37% of respondents admitting to eating in response to emotional distress, such as feeling upset. This finding aligns with research on emotional eating, where food is used as a coping mechanism for negative emotions. Furthermore, 29.5% of participants reported experiencing intense guilt after overeating, highlighting the emotional burden associated with eating behaviors. Concerns about body image were also prevalent among them. More than half (59.5%) expressed frequent thoughts about dieting or losing weight, while 42% wished they were thinner. These findings indicate that body dissatisfaction is a significant issue within the sample. Of particular concern is the presence of extreme weight control behaviors among a subset of students; 14.5% acknowledged having considered vomiting as a weight loss strategy, signaling an alarming risk for disordered eating patterns. While this percentage is lower than that of more common weight control methods, it nonetheless emphasizes the need for awareness and interventions targeting unhealthy eating behaviors. Overall, these findings illustrate the pervasiveness of weight-related concerns, emotional responses to eating, and body dissatisfaction among participants.

7.2 The influence of family, peers, and media on body image and eating behaviors

For many individuals, body image perceptions do not develop in isolation but are shaped by interactions within their social environment. Family members, peers, and media act as powerful forces that influence self-perception and dietary behaviors, sometimes in subtle ways, other times more explicitly. In our study, the *role of family* in shaping body image is particularly evident in the findings. Nearly half of the participants recounted instances where their parents or other family members commented on their weight. While some remarks were framed as health-related advice, others were perceived as judgmental, leaving a lasting impact on self-esteem. In addition, 39.5% of respondents recalled being directly compared to other family members, reinforcing beauty expectations within the household. Encouragement to lose weight was also a common theme, with a third of participants reporting pressure from their family to alter their eating habits. Beyond family, *peers* serve as another critical influence on body image concerns. Among the respondents, 32.5% reported that discussions about dieting, weight loss, or exercise frequently occurred in their social circle.

More than a quarter admitted feeling pressure to conform to peer-defined beauty standards. The effects of these interactions may not always be overt but can manifest in the form of social comparisons, influencing one's motivation to engage in restrictive eating behaviors or excessive exercise. The *media's impact* was particularly pronounced, with nearly 50% of participants actively following content related to dieting and weight loss. Exposure to these idealized representations of body image had tangible consequences: 32.5% of participants reported feelings of dissatisfaction with their bodies due to media content, while 24.5% altered their eating habits in response to media portrayals of beauty norms. Furthermore, 29.5% felt direct pressure to modify their appearance in ways that aligned with the unrealistic ideals promoted in digital and traditional media (see **Table 3**).

Claims	Strongly disagree		Disagree		Neutral		Agree		Strongly agree	
	f	%	f	%	f	%	f	%	f	%
1. My parents or other family members have commented on my body weight.	27	13.5	39	19.5	10	5.0	67	33.5	57	28.5
2. My parents or other family members have negatively commented on my eating habits.	32	16.0	58	29.0	19	9.5	55	27.5	36	18.0
3. My parents or other family members have encouraged or pressured me to lose weight.	62	31.0	62	31.0	8	4.0	46	23.0	22	11.0
4. My parents have compared my appearance to that of others.	56	28.0	52	26.0	13	6.5	53	26.5	26	13.0
5. My peers have negatively commented on my body weight or appearance.	56	29.5	72	36.0	17	8.5	44	22.0	8	4.0
6. My peers talk about dieting, losing weight, or exercising.	35	17.5	46	23.0	13	6.5	81	40.5	25	12.5
7. My peers have encouraged me to follow specific diets.	87	43.5	73	36.5	13	6.5	20	10.0	7	3.5
8. I feel pressure from my peers to adhere to beauty standards.	68	34.0	59	29.5	24	12.0	38	19.0	11	5.5
9. I follow media content related to health, dieting, and weight loss.	44	22.0	61	30.5	17	8.5	62	31.0	16	8.0
10. The media content I follow promotes feelings of dissatisfaction with my body.	54	27.0	67	33.5	13	6.5	43	21.5	23	11.5
11. I have changed my eating habits or started a diet because of the media content I have followed.	57	28.5	70	35.0	24	12.0	35	17.5	14	7.0
12. I have felt pressure to change my appearance to better align with the ideal portrayed in the media.	54	27.0	47	23.5	15	7.5	55	27.5	29	14.5

Table 3.
Distribution of responses on family, peer, and media influences on body image and eating behaviors.

These findings suggest that body dissatisfaction and disordered eating behaviors are shaped by a complex interplay of influences. The family environment establishes early attitudes towards weight and diet, peers reinforce societal expectations through direct and indirect social pressure, and media provide a continuous stream of unattainable beauty ideals. Addressing these factors requires a multifaceted approach that goes beyond individual responsibility and considers the broader sociocultural context that informs these attitudes and behaviors.

7.3 Sociocultural predictors of disordered eating behaviors

To structure the dependent variables, a factor analysis was conducted using principal component analysis (PCA) with varimax rotation. The results identified two primary factors (meaningful constructs) which explained 71.03% of the total variance, indicating a strong structure for further regression analysis:

- Factor 1: *Weight control and body dissatisfaction* (“I often diet to control my weight,” “I frequently think about dieting or losing weight,” “I feel extremely guilty if I overeat,” “My weight is very important to me,” “I always wish I were thinner”).
- Factor 2: *Emotional eating and extreme weight control measures* (“I eat when I am upset or stressed,” “I have thought about vomiting to lose weight,” “I often think about overeating,” “I frequently weigh myself to check my weight”).

To better understand the predictors of disordered eating behaviors, the independent variables from **Table 2** were grouped into three key sociocultural influences: family influence (claims 1–4), peer influence (claims 5–8), and media influence (claims 9–12). Before grouping, internal consistency and correlation analyses were conducted to confirm that the selected variables were conceptually and statistically related. The Cronbach’s alpha values for each predictor category were above the acceptable threshold ($\alpha > 0.70$), indicating good reliability. Additionally, inter-item correlations showed moderate to strong associations within each factor, supporting their conceptual coherence.

A multiple linear regression analysis was conducted to examine the predictive power of family influence, peer influence, and media influence on the two dependent variables: Weight Control and Body Dissatisfaction and Emotional Eating and Extreme Weight Control Measures.

The results demonstrated that media influence was the most significant predictor of weight control and body dissatisfaction ($\beta = 0.41$, $p < 0.001$), strongly supporting H1. This suggests that individuals frequently exposed to idealized body representations through media are more likely to experience dissatisfaction with their body image and engage in weight control behaviors. Family influence ($\beta = 0.29$, $p < 0.01$) and peer influence ($\beta = 0.22$, $p < 0.05$) were also significant predictors indicating that family discussions about weight and peer interactions contribute to body dissatisfaction and dieting behaviors.

For emotional eating and extreme weight control measures, the strongest predictor was family influence ($\beta = 0.36$, $p < 0.001$). This finding suggests that family attitudes towards food and weight exert a strong influence on emotional eating behaviors, potentially fostering stress-related eating habits. Peer influence ($\beta = 0.28$, $p < 0.01$) was the second most significant factor, highlighting the role of social

Predictor variable	Weight control and body dissatisfaction (β)	p-value	Emotional eating and extreme weight control (β)	p-value
Family influence	0.29	0.01	0.36	0.001
Peer influence	0.22	0.05	0.28	0.01
Media influence	0.41	0.001	0.19	0.05

Table 4.
Regression analysis of predictors of disordered eating behaviors.

interactions in developing unhealthy eating patterns. Media influence ($\beta = 0.19$, $p < 0.05$), though weaker than family and peer influences, still played a notable role in extreme weight control measures, suggesting that exposure to media messages about dieting and weight loss may contribute to restrictive eating behaviors.

These results provide a clear indication that sociocultural factors play a crucial role in shaping eating behaviors. While media exposure has the strongest impact on body dissatisfaction and dieting behaviors, family and peer influences are particularly important in explaining emotional eating and extreme weight control behaviors. The interplay of these factors highlights the need for interventions that address media literacy, promote positive family discussions around food and body image, and foster supportive peer environments to mitigate the development of disordered eating behaviors (Table 4).

8. Conclusion

The comprehensive overview of research results in this chapter provides compelling evidence of the significant role of sociocultural factors in shaping disordered eating behaviors among students and youth in general. The findings confirm that exposure to idealized body images in the media strongly predicts body dissatisfaction and weight control behaviors, while family influence emerges as the strongest predictor of emotional eating behaviors. Additionally, peer influence plays a significant but more nuanced role, primarily affecting emotional responses related to eating rather than directly contributing to weight control efforts. In our study, approximately every second student reported concerns related to body dissatisfaction, weight control, or disordered eating behaviors, underscoring the widespread impact of societal pressures on their eating habits. Among the sociocultural influences examined, media had the strongest effect on weight control behaviors. However, family influence was more prominent in shaping emotional eating tendencies, suggesting that parental attitudes and discussions around weight and food can reinforce stress-related eating behaviors.

Understanding the impact of media, family, and peer influences on students' eating behaviors is crucial for developing effective prevention and intervention strategies. This study underscores the importance of addressing sociocultural pressures at multiple levels—media literacy, family communication, and peer support—to promote healthier relationships with food and body image. By fostering a more supportive and informed social environment, we can contribute to reducing the prevalence of disordered eating behaviors and improving overall well-being among students.

While this study provides important insights, certain limitations should be acknowledged. The sample consists exclusively of university students from Split, Croatia, limiting the generalizability of findings to other student populations or young adults in different sociocultural contexts. Additionally, the study relies on self-reported data, which may be subject to social desirability bias. Future research should consider expanding the study to include a more diverse and representative sample across different regions and educational institutions, incorporating qualitative methodologies (e.g., interviews, focus groups) to provide deeper insights into students' experiences and coping strategies related to sociocultural pressures, and examining protective factors that may help buffer against body dissatisfaction and disordered eating behaviors, such as self-esteem, body acceptance, and resilience-building strategies.

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The Role of Ultra-Processed Foods in Inflammation and Aging

Pelin Baltacı and Nezihe Şengün

Abstract

Processed foods are foods that undergo physical, chemical, or biological processes to enhance durability, extend shelf life, improve taste and texture, alter nutritional content, or facilitate consumption. While traditional processed foods are preserved and packaged through methods such as canning or salting, ultra-processed foods (UPFs) are industrially produced formulations that are ready-to-eat or ready-to-heat and typically contain little or no whole food ingredients. Recent evidence suggests that the adverse health effects of UPFs may not only be due to the nutrients they provide but also to non-nutritive components and their impact on gut health. Diets rich in UPFs are associated with cellular changes leading to oxidative stress, which in turn contributes to inflammation and aging processes. In this context, reducing the consumption of UPFs, limiting refined carbohydrates, and modifying meal timing and frequency are recommended for improving health.

Keywords: ultra-processed foods, NOVA classification, diet quality, low-grade inflammation, aging

1. Introduction

Food processing (any procedure that alters the natural state of food) is fundamental to food preparation. Basic processing techniques have been around for thousands of years and involve removing inedible parts of foods, cooking, and chopping. Most foods are processed in some way before consumption. Processing methods such as bottling, canning, or using food additives help extend shelf life, improve safety [1], and reduce food waste [2]. These methods have ensured food security for millions of people worldwide. However, some processing techniques can also be harmful to food safety and health [3].

The NOVA food classification system, which defines and categorizes ultra-processed foods (UPFs), is the most widely applied system in scientific literature [4]. The NOVA system is used to classify foods based on their level of processing. A practical way to identify an ultra-processed product is to check if the ingredient list contains at least one characteristic feature of the NOVA ultra-processed food group, that is, food components that are rarely or never used in kitchens (e.g., high fructose corn syrup, hydrogenated or interesterified fats, hydrolyzed proteins) or classes of food additives designed to make the final product tastier or more appealing (e.g., flavorings, flavor enhancers, colorants, emulsifiers, emulsifying salts, sweeteners, thickeners,

anti-foaming agents, volume enhancers, carbonation agents, foaming agents, gelling agents, and glazing agents) [5].

The nutritional profile of a diet that includes the consumption of UPFs is associated with the development of cellular changes that lead to oxidative stress. A chronic prooxidative state creates an environment that affects the proliferation, apoptosis, and signaling pathways of immune cells. Similarly, reduced transcription factor NRF2 due to increased production of reactive oxygen species (ROS) leads to changes in immune function and responses to infections [6].

Inflammation is a key component of innate immunity [7]. Aging is associated with complex changes and disruptions in the immune system and its inflammatory components [8, 9]. A diet rich in UPFs typically contains high amounts of sugar, salt, saturated fats, and trans fatty acids, which can directly promote the development of chronic inflammation. The relationship between high intake of these nutrients and their potential modulation of inflammation has been studied separately, but the results obtained so far are mixed [10].

The health effects of the components that make up the UPF categorization need to be investigated, and the metabolic roles of food processing in health regulation should be understood. Environmental sustainability should also be considered in UPF studies. Since UPFs generally have higher energy density than nutrient density, recommendations to limit UPF consumption are unlikely to pose additional risks or harm but may offer nutritional benefits. Emphasizing nutrient-dense, healthy foods and dietary patterns will continue to be a key strategy for promoting overall health, healthy aging, and preventing chronic diseases. This comprehensive review examines studies related to UPF consumption, exploring its relationship with inflammation, dietary profile, and aging.

2. General information

2.1 Ultra-processed foods

Food, which is essential for life, refers to the process of combining nutrients and components necessary for the growth, maintenance, and repair of body tissues, as well as regulating vital bodily processes. Today, food processing has become widespread as a result of technological advancements and innovative approaches. The processing stages include various methods such as cutting, chopping, cooking, cooling, freezing, salting, canning, drying, pasteurization, fermentation, and packaging, with rigorous and precise techniques used in all processing activities [11].

Processed foods are those that undergo physical, chemical, or biological processes to enhance durability, extend shelf life, improve taste and texture, alter nutritional content, or facilitate consumption. Processed products are subjected to preservation and packaging methods to increase their shelf life. Additionally, processing techniques are applied to eliminate or deactivate harmful microorganisms in foods, ensuring food safety. The growing food processing and packaging technology has reduced material waste during production and enhanced the global portability of products. Various processing techniques can be used to meet consumer preferences for different tastes, textures, and presentations. Nutrients can also be added to processed foods to enhance their nutritional value. Developing classification systems that categorize foods and their processing levels has become crucial for standardizing research on processed foods [12]. The United States Department of Agriculture defines processed

food as “any raw material subjected to a series of unit operations (cleaning, cutting, grinding, heating, cooling, packaging, etc.) that alters its natural state” [13].

Various techniques have been developed for processing food. One of the most commonly used methods for food preservation since the establishment of settled societies has been sun drying. Later, techniques such as salting, pickling, and smoking were used. After the Industrial Revolution, the demand for products such as vegetable oils, animal fats, sugars, flour, and salt grew, leading to increased production and the technological development of industrial processing methods. Over time, these innovations ensured the microbiological safety of foods, made consumption easier, and improved their storage and practicality. Mechanical and physical techniques (e.g., roller milling, pressure processing, and extrusion) as well as chemical techniques (e.g., hydrogenation and hydroxylation) have been developed through the use of artificial flavors, preservatives, and other additives [14]. Foods are processed at different levels to extend shelf life and prevent spoilage, but many foods are industrially processed at advanced levels and consumed with their original structures and characteristics significantly altered [15].

Unlike traditionally preserved processed foods, such as those preserved by canning or salting, ultra-processed foods (UPFs) are industrially produced ready-to-eat or ready-to-heat formulations that contain little or no whole food and are typically supplemented with food additives [16].

Ultra-processed food and beverage products (ultra-processed foods—UPF) typically contain ingredients that are not used or rarely used in kitchens, such as hydrogenated or interesterified fats, hydrolyzed proteins, soy protein isolate, maltodextrin, invert sugar, and high-fructose corn syrup. They also include food additives such as colorants, color stabilizers, flavorings, flavor enhancers, sweeteners, thickeners, volume enhancers, anti-caking agents, anti-foaming agents, anti-clumping agents, glazing agents, emulsifiers, preservatives, and humectants [17]. Most of these products contain little or no whole food. Since these products are properly packaged and ready to be consumed immediately, they require little to no preparation in the kitchen [18].

2.2 NOVA classification

NOVA is a system that classifies foods not based on their nutrient content, but according to the nature, extent, and purpose of the industrial processes they undergo. In this classification, foods are assigned to one of four groups:

- *Group 1* includes unprocessed or minimally processed foods, meaning edible parts of plants or animals that are taken directly from nature or have undergone minimal processing or preservation. Examples of foods in Group 1 include dried apricots, blueberries, fruit salads, eggs, raw nuts, plain yogurt, and plain potatoes.
- *Group 2* contains processed culinary ingredients, such as salt, sugar, oil, or starch, which are derived from Group 1 foods.
- *Group 3* includes processed foods that are produced by combining Group 1 and Group 2 foods, such as canned vegetables or freshly baked bread.
- *Group 4* consists of ultra-processed foods (UPFs), which are “mostly designed for industrial use, containing little or no whole food and typically created through a range of industrial techniques and processes” [5, 19].

A study evaluates the nutritional composition of foods in the traditional Mediterranean diet pyramid according to NOVA groups and pyramid levels found the following:

- Foods in NOVA Group 1, such as olives, legumes, nuts, fruits, and vegetables, were richer in protein content than foods in NOVA Group 4.
- NOVA Group 3 foods, such as fish, dairy products, fruits, and vegetables, were also richer in protein than those in NOVA Group 4.
- Dairy products in NOVA Group 1 had lower protein content compared to their counterparts in NOVA Group 4.
- Foods in NOVA Group 1, such as olives, legumes, nuts, and unrefined grains, had lower total and saturated fat content compared to their NOVA Group 4 counterparts.
- Dairy products in NOVA Group 1 had lower total fat content compared to those in NOVA Group 4.
- Fruits and vegetables in NOVA Group 1 had lower sugar content compared to those in NOVA Group 4.
- Foods in NOVA Group 1, such as unrefined grains, fruits, vegetables, dairy, olives, legumes, and nuts, contained less salt compared to their NOVA Group 4 equivalents [20].

Examples of foods in each NOVA group are provided in **Table 1** below [5].

Despite the widespread use of the NOVA classification, its robustness and functionality remain largely unexplored. While assignments for some foods are more consistent than others, overall consistency between evaluators was low, even when content information was available. These results suggest that the current NOVA criteria do not allow for consistent and functional food assignments [21].

Increasing quintiles of the NOVA-UPF score have been linearly associated with a higher risk of BMI gain [22]. It is thought that the NOVA classification is not widely known in society, and there is a lack of information regarding the classification of all foods considered harmful to health as UPFs, despite the fact that NOVA classifies foods based on their level of processing [23].

2.3 Diet quality in ultra-processed foods

Food processing can significantly affect the nutritional quality of the diet. There is a wide range of processing, from minimal processing (e.g., frozen vegetables, dried fruits without additives, pasteurized milk) to ultra-processing (e.g., soft drinks, fast food, industrial breads, hot dog sandwiches) [5]. Processing can have significant health impacts by altering the nutritional, physical, and chemical properties of foods. Additionally, different types of processing can influence long-term dietary behaviors, satiety signals, and food reward systems [16].

Ultra-processed foods (UPFs) are typically produced using cheap, industrially sourced dietary energy and nutrients along with additives. These foods are energy-dense

NOVA group	Food examples
Group 1: Unprocessed/ minimally processed foods	Fresh, frozen, or dried fruits and leafy/root vegetables; fruit and vegetable juices; rice (brown or white), corn, wheat; beans, lentils, chickpeas; starchy roots and tubers (potatoes, sweet potatoes); fresh or dried mushrooms; red meat, poultry, fish, and seafood (fresh, chilled, or frozen; whole or in fillets and other cuts); eggs; fresh or pasteurized milk; fresh or pasteurized fruit or vegetable juices (no added sugar, sweeteners, or flavors); semolina, flakes, or flour from corn, wheat, or oats; oilseeds (no added sugar or salt); herbs and spices used in cooking (e.g., oregano, basil, mint, pepper, clove, and cinnamon, whole or powdered, fresh or dried); fresh or pasteurized plain yogurt; tea, coffee, and drinking water. This group also includes products made from two or more of these ingredients (e.g., dried mixed fruits, pasta made from flour, or semolina and water) and foods like wheat or corn flour enriched with vitamins and minerals to replace nutrients lost during processing.
Group 2: Processed culinary ingredients	Plant oils (e.g., from seeds, nuts, or fruits, especially olives); butter; sugar or molasses obtained from beets or sugar cane; honey from hives and syrup from maple trees; starches extracted from corn and other plants; rock salt, sea salt, and table salt; vegetable oils containing antioxidants; salted butter, etc.
Group 3: Processed foods	Canned, bottled, or pickled vegetables and legumes; salted or sweetened nuts and seeds; salted, dried, smoked, or cured meats and fish; canned fish (with or without preservatives); fruit in syrup (with or without added antioxidants); freshly made, unpackaged bread and cheese.
Group 4: Ultra- processed foods (UPFs)	Carbonated, sugary beverages; sweet or salty packaged snacks; chocolates, candies (confectioneries); ice cream; mass-produced packaged bread and cakes; margarines and other spreadable products; biscuits, pastries, cakes, and cake mixes; breakfast cereals, cornflakes, and energy bars; energy drinks; milk drinks, fruit yogurts, and fruit beverages; cocoa drinks; ready-made sauces; infant formulas; follow-on milks; meal replacement powders and drinks.

Table 1.
Examples of foods according to the NOVA classification.

and rich in unhealthy fats, refined carbohydrates, free sugars, and salt, but they are deficient in protein, dietary fiber, and micronutrients. UPFs have a long shelf life, are always and easily available, and are highly tasty and appealing [24]. As a result, the consumption of UPFs has become widespread, replacing foods that should be part of a healthy diet, such as those containing fiber, complex carbohydrates, and healthy fats. These foods generally contain high energy, free sugars, and saturated fats [25].

Food processing can affect not only the nutritional content of foods but also their physical structure and chemical properties. For example, it has been noted that polysaccharides such as pectin can change during the processing process, and these changes can have significant effects on the texture, rheological, and nutritional properties of products [26]. The high contents of fats, salt, sugar, and artificial sweeteners in UPFs cause them to be excessively flavorful, which can deactivate satiety signals [27]. UPFs are typically more hypercaloric and less satiating, which can lead to excessive energy intake [28].

Carbohydrates form the primary energy source in the diet, but their health effects are still debated. Recent epidemiological research has shown that an increase in carbohydrate consumption may raise the risk of obesity and mortality. On the other hand, some populations with traditional diets, such as the Okinawans, despite having carbohydrate-rich and protein-poor diets, live long and have healthy lives [29]. It has also been found that UPFs have a high glycemic index, which can lead to weight gain, inflammation, oxidative stress, and endothelial dysfunction [30].

It has been reported that UPF consumption is associated with allergic symptoms; however, it is not yet clear whether this is due to the nutrient components they contain or their allergen load [31]. Additionally, UPF consumption reduces the intake of bioactive compounds such as polyphenols and other phytochemicals. Fresh foods are richer sources of polyphenols, while UPFs are deficient in such bioactive compounds [32]. Data shows that an increase in UPF consumption negatively impacts the nutritional quality of the diet, and the excessive consumption of such foods can have adverse effects on health [33]. It is well known that dietary fiber plays an important role in health, and fiber from plant sources is generally more beneficial [34]. Moreover, the increase in UPF consumption is associated with a reduction in animal food consumption [35]. The functional components in ultra-processed foods also change during processing. These foods are typically lacking in antioxidants and other beneficial components. For example, oxidized sterols (DOxS) found in UPFs can have negative effects on health [36].

Finally, there is a strong relationship between increased UPF consumption and higher body weight, obesity, elevated fasting glucose, metabolic syndrome, cholesterol levels, and the risk of hypertension. These findings suggest that excessive consumption of UPFs can have serious negative effects on health [37, 38].

3. Inflammation

The immune system consists of two systems: the innate and the adaptive, both of which are equally important. The innate immune system consists of components such as macrophages, dendritic cells, and mast cells. Its primary function is to detect bacteria, viruses, and foreign bodies in the organism and activate the adaptive immune system and complement cascades. The adaptive immune system, on the other hand, is highly specific and develops throughout our life. It is composed of T and B lymphocytes, and the activation of the adaptive immune system involves pattern recognition receptors, such as Toll-like receptors, and cytokine induction [39]. Inflammation is a key component of innate immunity. In general, inflammation is a response characterized by increased blood flow, capillary dilation, leukocyte (white blood cell) infiltration, and the localized production of various chemical mediators in response to cellular damage [7]. In particular, cytokines are small proteins produced by various cells, including T and B lymphocytes. Cytokines can be pro-inflammatory (promoting inflammation) or anti-inflammatory (suppressing inflammation) and can trigger the release of other cytokines. Cytokines play an important role in chronic inflammation caused by oxidative stress [39]. Specifically, high-circulating levels of acute-phase proteins, C-reactive protein (CRP), tumor necrosis factor alpha (TNF- α), and interleukins (IL-1 β , IL-6, and IL-17), along with increased infiltration of immune cells such as macrophages and T lymphocytes into insulin-dependent tissues, are characteristic of inflammation [40].

Inflammation can manifest as acute or chronic (high-grade or low-grade). Acute inflammation is short-lived, and its effects diminish within a few days when damage/infection/irritation is repaired or eliminated. It generally involves innate immune system cells. In contrast, chronic low-grade inflammation is long-lasting and can create a damaging process with mild but persistent induction of inflammation. In response to such induction (e.g., metabolic stressors), tissue-resident cells and localized leukocytes become activated. As a result, pro-inflammatory mediators are secreted, leading to the accumulation/infiltration of pro-inflammatory leukocytes [41]. Therefore,

inflammation, which plays a central role in the body's homeostasis, can create both beneficial and harmful conditions for health. Although it is a fundamental component of immune surveillance and host defense, chronic low-grade inflammation is a pathological feature of many chronic conditions such as metabolic syndrome (MetS), non-alcoholic fatty liver disease (NAFLD), type 2 diabetes (T2DM), and cardiovascular diseases (CVD) [42]. Due to the relationship between metabolic imbalance and inflammation, the existing chronic low-grade inflammation can also be described as metainflammation [43].

Adipose tissue inflammation begins with hypoxia and mechanical stress resulting from hypertrophy and hyperplasia, leading adipocytes to secrete pro-inflammatory cytokines and adipokines. This inflammation shifts the metabolic balance in adipocytes from glycolysis to lipolysis, increasing free fatty acid levels and triggering cellular metaflammatory pathways. Gut inflammation is associated with dysbiosis, which impairs the microbiome-gut system's adaptability. This condition can negatively affect epithelial barrier function and immune function, leading to the passage of bacterial endotoxins from the gut into systemic circulation, potentially spreading low-grade inflammation to other organs. The liver is exposed to these gut-derived products, which can cause liver inflammation in metabolic syndrome. Additionally, metabolic stressors activate hepatocytes, leading to the release of inflammatory molecules, thus activating local inflammatory responses [44]. Low-grade inflammation plays an important role in the development of cardiovascular diseases as it is linked to atherosclerosis progression. Moreover, it can promote the progression of various types of cancer by stimulating cell proliferation, reducing apoptosis, enhancing angiogenesis, and supporting metastasis [45, 46].

Several risk factors trigger low-level inflammatory responses. Factors such as aging, mitochondrial dysfunction, and free radical accumulation lead to increased levels of inflammatory molecules. Obesity is associated with the secretion of pro-inflammatory molecules from adipose tissue, acting as an endocrine organ. Diets containing saturated fats, trans fats, and refined sugars, particularly in individuals with diabetes or those who are overweight, show inflammation-enhancing effects. Smoking triggers inflammation by reducing anti-inflammatory molecules. Low sex hormones suppress the production of pro-inflammatory markers. Additionally, stress and sleep disorders increase inflammatory cytokine secretion, raising the risk of chronic inflammation [47].

3.1 Diet and low-grade inflammation relationship

Among the environmental and lifestyle factors that can trigger or intensify inflammation, increasing scientific evidence supports the role of diet. Potential food compounds that can affect both acute and chronic inflammatory processes include macronutrients, micronutrients, bioactive molecules such as polyphenols, and certain food components [48]. In general, plant-based dietary patterns characterized by a high intake of vegetables, fruits, and whole grains, moderate consumption of legumes and fish, and low consumption of red meat are associated with higher anti-inflammatory potential. These include various traditional healthy diets, such as the Mediterranean diet, which is typically based on minimally processed or unprocessed foods [49, 50]. Unhealthy fat sources, ultra-processed foods with added sugars, and a sedentary lifestyle make individuals more susceptible to overweight and obesity. While lipids are an integral component of the organism, excessive and abnormal lipid accumulation that exceeds the storage capacity of lipid droplets leads to the

release of harmful lipid species by disrupting the intracellular composition of fatty acids, causing a pathological condition known as lipotoxicity. This condition leads to endoplasmic reticulum stress, mitochondrial dysfunction, inflammatory responses, and cell death [51].

Dietary fatty acids can affect inflammatory processes through their effects on body weight, fat mass, and membrane composition and function. Within cells, fatty acids derived from membranes and their derivatives can modulate inflammation as modulators of NF- κ B and PPAR- α/γ transcription factor pathways, and also serve as precursors to eicosanoids and docosanoid oxidation products produced by the action of epoxxygenases, lipoxygenases, and cyclooxygenases [7]. Many studies have shown that saturated fatty acids (SFAs) activate adipose tissue inflammation through Toll-like receptor 4 (TLR4). TLR4 is a receptor that binds bacterial lipopolysaccharides (LPS) and plays a key role in the innate immune response as a pattern recognition receptor [52]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)-derived resolvins and protectins stand out as molecules that actively improve a pro-inflammatory condition [53].

Advanced glycation end products (AGEs) are the result of non-enzymatic post-translational reactions between reducing carbonyl groups and protein-amino groups, nucleic acids, or aminophospholipids [54]. In recent years, the increase in processed foods, sugar, and fat consumption has also increased exposure to AGEs. Several factors affect the formation of AGEs, including food composition, temperature, and cooking methods. The AGE content of high-heat processed meat products, such as roasting and oven frying, is higher than that of carbohydrates subjected to long cooking times. Glycation of cellular proteins negatively impacts cell and tissue functions, molecular aging, and chronic disease development. In addition to endogenous formation, AGEs also form during the thermal processing of foods, which significantly increases the amount of AGE (dAGE) that individuals are exposed to through their diet. Food-derived AGEs are part of a heterogeneous group of chemically stable molecules derived from the Maillard reaction; some of these play a role in improving flavors, aromas, and browning, while others are thought to be involved in negative health effects (e.g., chronic inflammation, degenerative diseases, aging, insulin resistance) [55].

Dietary sugars primarily consist of hexoses, such as glucose, fructose, sucrose, and high fructose corn syrup (HFCS). These sugars are typically absorbed in the intestines as fructose and glucose. Over the past 30 years, the consumption of high-sugar beverages and processed foods has significantly increased [56]. High intracellular glucose concentrations first lead to an increase in anabolic rates, and the increased intermediary metabolites of oxidative metabolism cause substrate concentrations to reach enzymatic saturation. Approximately 95% of oxygen entering the mitochondria is used in oxidative processes (acetyl-CoA oxidation), primarily in the Krebs cycle. The remaining 5% reacts spontaneously with water molecules to form hydrogen peroxide (H_2O_2) and other reactive species ($OH\cdot$, $O_2\cdot-$), which are collectively known as reactive oxygen species (ROS) [57]. The accumulation of reactive oxygen species (ROS) within cells leads to the oxidation of macromolecules, damage to cellular organelles, and irreversible injury. Chronic cellular damage and subsequent cell death cause cellular waste accumulation, which triggers leukocyte infiltration and the activation of pro-inflammatory mechanisms [58]. Excessive sugar consumption has been shown to lead to metabolic disorders and trigger an increase in inflammatory mediators and certain pro-inflammatory cytokines in various tissues, causing insulin resistance and low-grade chronic inflammation [59].

The gut microbiota is increasingly recognized as a metabolic organ that plays a crucial role in nutrition, immune regulation, and the maintenance of homeostasis through its functions in systemic inflammation. Low fiber intake leads to disturbances in the gastrointestinal microbiota [60]. *Bifidobacteria* and some *Clostridia* subgroups (*Roseburia* and *Eubacterium rectale*) show a significant decrease with low or limited fiber intake [61]. High consumption of simple carbohydrates promotes the growth of lactic acid bacteria in *Clostridium* cluster IV, particularly *Faecalibacterium* species. According to Vega-Magaña and colleagues, the *Firmicutes* phylum is significantly increased in Western diets, while the *Bacteroidetes* phylum decreases. The loss or reduction of *Bacteroides* species, influenced by the substrates of an ultra-processed diet, can lead to dysbiosis and the loss of specific microbial niches in the gut, contributing to the observed differences in microbial phylogenies. The increase in *Firmicutes* and the decrease in *Bacteroidetes* lead to irregularities in the production of short-chain fatty acids. The reduction in *Faecalibacterium*, *Roseburia*, and *Eubacterium* species significantly decreases butyrate production, while increasing the proportion of harmful microorganisms that produce lipopolysaccharides (LPS), ROS, and pro-inflammatory cytokines [62]. Evidence over the last decade has highlighted gut dysbiosis as an etiological factor for metabolic diseases, considering its regulatory role in fat accumulation and energy expenditure.

The Western diet is a modern dietary model characterized by high intakes of packaged foods, refined grains, red meat, processed meats, sugary drinks, candies, sweets, fried foods, traditionally raised animal products, high-fat dairy products, and high-fructose products. It is believed that changes in dietary habits, particularly the lack of fiber, contribute to the increasing prevalence of chronic inflammatory diseases such as inflammatory bowel disease, metabolic syndrome, and cancer [63]. In a study, researchers observed a rapid decrease in the number of gut bacteria when mice were switched from standard grain-based rodent food to a high-fat, low-fiber Western-style diet. Mice fed the Western-style diet were less able to clear the pathogen *Citrobacter rodentium* from the colon. Furthermore, these mice became more prone to developing chronic infections upon re-infection with the pathogen. This study concluded that a Western-style diet reduced the number of gut bacteria and potentially influenced the immune system's preparedness and response to pathogenic bacteria by promoting the spread of the microbiota to the gut [64].

In the postprandial state, the human body is exposed to high concentrations of a mixture of macronutrients, endocrine signals, gut-derived factors, and others, each with distinct plasma peak concentrations. Many of the factors contributing to the postprandial response affect metabolism, inflammation, and health [65]. Different dietary habits and macronutrients are associated with the activation of the innate immune system, which can trigger low-grade systemic inflammation and contribute to the development of many diseases. A high-fat diet, a high-carbohydrate diet, or their combination lead to postprandial inflammatory responses as well as the production of reactive oxygen species (ROS) [66]. Another study found that a diet characterized by high caloric intake and high amounts of sweets, refined grains, red and processed meats, snacks, and sugary beverages was associated with increased pro-inflammatory potential and higher levels of CRP and IL-6 [67]. Since many chronic diseases ultimately result from diet-induced inflammation, a logical way to minimize the impact of these inflammatory conditions is to follow anti-inflammatory diets. Excessive energy intake and sustained obesity lead to systemic inflammation, while moderate calorie restriction (CR) without nutritional deficiencies demonstrates strong anti-inflammatory effects [68].

4. Effects of UPF on inflammation

A diet rich in UPF typically contains high amounts of sugar, salt, saturated fats, and trans fatty acids, which can directly promote the development of chronic inflammation. When separately evaluated, the high intake of these nutrients and their possible relationships with inflammation modulation, the results obtained so far are mixed. UPF is typically high in simple sugars, which are either sucrose or high-fructose syrup, and are foods with a high glycemic index/load, meaning they rapidly and significantly raise blood glucose levels. This postprandial increase in blood sugar leads to an increase in insulin levels, which in turn promotes a pro-inflammatory condition [10]. Although these mechanisms seem to play an important role in the promotion of diet and low-grade inflammation, no clear result has been obtained in intervention studies. In the TOSCA.IT study, a relationship was found between the consumption of added sugars exceeding 10% of daily energy intake and an increase in C-reactive protein (CRP) levels in adults with diabetes [69].

The nutritional profile of a diet containing UPF consumption is associated with the development of cellular changes that lead to oxidative stress. A chronic pro-oxidative state leads to an environment that affects immune cell proliferation, apoptosis, and signaling pathways. Similarly, the decrease in the transcription factor NRF2 due to increased production of reactive oxygen species (ROS) leads to changes in immune function and responses to infections [6].

In a study, those who consumed high amounts of UPF foods were found to produce higher levels of reactive oxygen species (ROS) compared to those who consumed low amounts. Consequently, levels of xanthine oxidase, tumor necrosis factor α (TNF α), interleukin (IL)-6, IL-15, and leptin were found to be significantly higher in individuals with higher UPF intake. Furthermore, it was found that participants with metabolic syndrome (MetS) who had high UPF consumption exhibited more pro-oxidant and inflammatory profiles compared to those with low UPF consumption, despite showing similar biochemical blood profiles [70]. UPF consumption has been shown to be associated with an increase in IL-6 concentrations [71]. The relationship between low-quality nutrition and pro-inflammatory markers resulting from UPF consumption has been reported to have significant harmful effects observable even from adolescence [72]. It has been reported that high UPF intake is related to changes in basal metabolic rate (BMR) through alterations in high-sensitivity C-reactive protein (hs-CRP), plasminogen activator-1 (PAI-1), monocyte chemoattractant protein (MCP-1), and interleukin-1 beta (IL-1 β) production [73].

The gut microbiome plays a critical role in a range of physiological processes such as metabolic functions like nutrient absorption, energy production, and vitamin synthesis; and immune system regulation, neurotransmitter production, and modulation of the inflammatory response. The gut microbiome is predominantly composed of phyla such as Firmicutes, Bacteroidetes, Actinobacteria, Verrucomicrobia, Proteobacteria, and Euryarchaeota [74]. Firmicutes is the most abundant phylum in clinically healthy adults, followed by Bacteroidetes and Actinobacteria [75]. Previous research has highlighted the vital link between dietary fiber intake and gut microbiome composition. High-fiber consumption has been shown to increase beneficial bacteria like *Bifidobacteria* and *Faecalibacterium*, and these bacteria enhance the production of short-chain fatty acids (SCFAs), which are crucial for gut health [76]. Metagenomic studies have shown that UPF consumption is associated with dysbiosis, manifested as a reduction in microbial diversity, disruption of the balance between beneficial and harmful bacteria, increased intestinal permeability, and inflammation [77]. Diets

rich in UPFs are believed to affect the gut microbiome through several mechanisms, including reduced bacterial diversity, increased expression of bacterial virulence genes, and an increase in the abundance of invasive or adhesive bacterial strains. These changes can lead to reduced production of SCFAs, increased bacterial invasion of the intestinal epithelium, degradation of the mucus barrier, and increased gastrointestinal epithelial permeability. As a result, cytokine or chemokine production and immune cell recruitment can lead to the disruption of immune cell homeostasis and inflammation, resulting in reduced levels of anti-inflammatory cytokines and increased levels of pro-inflammatory cytokines and chemokines [78]. A study that assessed differences in gut microbiome composition among university students based on dietary fiber intake, UPF consumption, gender, body mass index (BMI), and socioeconomic status (SES) analyzed 82 stool samples. The study found that dietary fiber intake strongly influenced gut microbiome composition. Low fiber intake was associated with higher prevalence of *Parabacteroides* and *Muribaculaceae*. *Prevotella* was more common in individuals with low UPF intake, while *Phascolarctobacterium* was more prevalent in those with high UPF intake. Women consumed more UPF, and this was correlated with different gut microbiome profiles [79].

Diet is closely linked to the gastrointestinal (GI) system and has strong effects on intestinal immune homeostasis. Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the GI system [80]. Reducing UPF consumption is thought to be a dietary strategy that could minimize symptoms and inflammation in individuals living with IBD [81]. The positive relationship between UPF consumption and CRP levels in women is believed to arise through the presence of obesity [82]. In this context, studies on the triggers of inflammation remain uncertain. A consistent and significant relationship has been reported between UPF consumption and the risk of various cancers, including colorectal, breast, and pancreatic cancers [83].

Another mechanism that could explain the effects of UPF consumption on biology or metabolism is related to the endocrine-disrupting chemicals commonly found in UPF product packaging, such as bisphenol A (BPA) [16]. While the exact mechanisms of BPA are not yet fully understood, some evidence suggests that BPA increases insulin resistance, oxidative stress, inflammation, and adipogenesis (the formation of fat cells), which in turn increases the risk of diabetes, general and abdominal obesity, and cardiovascular diseases such as hypertension [84].

Late-eating habits have been reported to be associated with poor metabolic health through poor diet quality. A study examined the relationship between eating time and UPF consumption. The data from the Italian Nutrition and Health Survey (INHES) conducted between 2010 and 2013 were analyzed, involving 8688 Italian participants (aged 19 and above). In the study, participants were classified as early or late eaters based on the median timing of breakfast, lunch, and dinner for the population. According to the study, in multivariate regression models, late eaters were found to have lower consumption of minimally processed foods, higher UPF intake, and reduced adherence to the Mediterranean diet [85].

5. The relationship between ultra-processed foods and aging

Aging is associated with complex changes and irregularities, including the immune system and its inflammatory components. The aging of the immune system, known as immunosenescence, is proposed to result from chronic exhaustion caused by continuous antigenic overload. Aging is accompanied by a low-grade, chronic

inflammatory state, which is clearly demonstrated by the 2–4 times increase in serum levels of several inflammatory mediators in elderly individuals [8, 9].

Most elderly individuals develop a condition known as inflammaging, which is characterized by high levels of blood inflammatory markers and increased sensitivity to chronic morbidity, disability, frailty, and early death. Potential mechanisms of inflammaging include genetic susceptibility, central obesity, increased intestinal permeability, changes in microbiota composition, cellular aging, NLRP3 inflammasome activation, oxidative stress caused by dysfunctional mitochondria, immune cell dysregulation, and chronic infections [86].

Healthy diets are inversely related to biological aging. However, the nutritional content of food is only one aspect of its overall health potential, and more attention is now being paid to non-nutritional food characteristics, such as food processing. Cross-sectional analyses were conducted on 22,495 participants registered in the Moli-sani Study (2005–2010, Italy). Food intake was assessed using a 188-item food frequency questionnaire, with UPF defined according to the Nova classification. The ratio of UPF (g/day) to total food consumption (g/day) was calculated, and diet quality was evaluated using the Mediterranean Diet Score (MDS; ranging from 0 to 9). The results showed that a diet rich in UPF was associated with accelerated biological aging in a large sample of Italian adults, linked to the poor nutritional composition of highly processed foods. This suggested that biological aging may be negatively impacted by the non-nutritional properties of food [87].

A study aimed to examine the relationship between UPF consumption and biological aging, and to evaluate how much of this relationship could be explained by overall diet quality. This cross-sectional study evaluated data from 16,055 participants aged 20–79 years (51% female, average age 46 ± 0.3 years) from the 2003–2010 National Health and Nutrition Examination Survey (NHANES). The amount of UPF in the diet was measured using the Nova system, and diet quality was assessed using the American Heart Association 2020 and the Healthy Eating Index 2015. Biological aging was evaluated using the PhenoAge algorithm. The study found that each 10% increase in the energy intake from UPF led to a biological aging of 0.21 (95% CI 0.16–0.26) years according to PhenoAge. Participants in the highest quartile of UPF intake (68–100%) were 0.86 (95% CI 0.55, 1.16) years biologically older compared to those in the lowest quartile ($\leq 39\%$) (P for trend ≤ 0.001). Adherence to a healthy diet moderately weakened the relationship between UPF and PhenoAge (adjusted $\beta = 0.14$ per 10% increase in UPF). Adults with higher UPF consumption tended to be biologically older. This relationship is partly independent of diet quality, suggesting that food processing may contribute to the acceleration of biological aging [88].

Thermal processing of foods leads to the formation of various new compounds, including advanced glycation end-products (AGEs), among others. AGEs result from non-enzymatic glycation reactions between reducing sugars and the free amino groups of proteins, peptides, or amino acids. Due to their potential harmful effects, digestive AGEs are also called glycotoxins [89]. Some culinary techniques, such as UPFs and dry cooking methods, are major sources of advanced glycation end-products (AGEs) in the diet. The potential mechanisms underlying the effects of AGEs include high oxidative stress and neuroinflammation, which are key pathophysiological mechanisms underlying neurodegeneration and mental disorders. Reducing the intake of AGEs in the diet is expected to improve neurological and mental health outcomes [90]. It is suggested that the accumulation of AGEs accelerates the multisystem functional decline associated with aging and, therefore, contributes to the aging phenotype [91].

Age-related pathologies are also linked to oxidative stress, inflammation, and cellular aging, and these conditions can affect telomere length (TL) [92]. However, there is limited research examining the effects of UPF consumption on TL. Studies have found that sugary beverages (SSBs), alcohol consumption, processed meats, and other sugar-rich foods high in saturated fatty acids (SFAs) are associated with shorter telomeres [93–96].

Adherence to a Mediterranean diet has been reported to have positive effects on telomere length, with fruit and vegetable consumption being positively associated with TL. However, inconsistent results were found regarding processed meats, grains, and sugar consumption [97]. Men, younger individuals, and those who are overweight/obese tend to consume higher levels of UPFs compared to older individuals [98]. According to one study, telomere length (TL) was measured in 886 participants aged 57–91 years at baseline using real-time qPCR from saliva samples, and UPF consumption was collected using a validated 136-item food frequency questionnaire (FFQ) and classified according to the NOVA system. The study found that participants with the highest UPF consumption were nearly twice as likely to have shorter telomeres compared to those with the lowest consumption. Results indicated that higher UPF intake (>3 servings/day) was associated with a higher risk of shorter telomeres in an elderly Spanish population [99].

High intake of saturated fats and trans fats, commonly found in ultra-processed foods (UPFs), has been shown to negatively affect cognitive function and telomere length. On the other hand, other dietary fats such as omega-3 polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) are associated with better cognitive performance and reduced telomere attrition. There are conflicting results regarding omega-6 polyunsaturated fatty acid intake and its effects on cognitive function. Dietary fats can affect telomere length and cognition through oxidative stress, inflammation, and insulin resistance [100].

In another study investigating the relationship between the consumption of ultra-processed foods (UPFs) and leukocyte telomere length (LTL), data from a total of 64,690 participants were used. LTL was measured using Q-PCR with natural logarithmic transformation and Z-score normalization. Dietary data were collected through a 24-hour recall survey from 2009 to 2010. UPFs were classified according to the Nova food classification system. The study found that compared to participants consuming ≤ 3.5 servings of UPFs daily, those consuming 3.5 to <6, 6 to ≤ 8 , and > 8 servings per day had a reduction in LTL of 0.025 (95% CI: -0.047 , -0.004), 0.034 (95% CI: -0.055 , -0.012), and 0.038 (95% CI: -0.062 , -0.015), respectively (P for trend = 0.001). High UPF consumption was found to be associated with shorter LTL. This relationship indicates that ready-to-eat foods, animal products, artificial sugars, and beverages have negative effects on LTL, while breakfast cereals and vegetarian alternatives show positive effects on LTL [101].

6. Conclusions

Fresh and processed food products are rich in bioactive molecules, including polysaccharides, vitamins, carotenoids, peptides, antioxidants, phenolics, phytosterols, and novel lipids. Bioactive molecules in foods have the potential to prevent various diseases (e.g., metabolic syndrome, cardiovascular diseases, cancer). Ultra-processed foods (UPFs) are associated with poor diet quality and negative health outcomes. High consumption of UPFs has been shown to be linked to non-communicable

diseases, overweight, and obesity. It is predicted that increasing UPF consumption in younger populations could have a significant impact on the risk of unhealthy aging in the long term, posing a serious risk factor. In this context, it is suggested that restricting UPFs and refined carbohydrates, as well as modifying meal timing and frequency, could be beneficial. There is a growing need for nutrition recommendations to reduce UPF consumption. There is considerable evidence supporting the use of UPFs as a scientific concept to evaluate the “healthiness” of foods within dietary patterns and to assist in the development of dietary guidelines and nutrition policy actions. Research should investigate the health effects of the components that constitute UPF categorization, understand their metabolic roles in regulating food processing health impacts, and consider environmental sustainability in UPF studies. Since UPFs generally have higher energy density than nutrient density, limiting UPF consumption is unlikely to cause any additional risks or harm. On the contrary, it is believed to provide more nutritional benefits. Emphasizing nutrient-dense healthy foods and dietary patterns will remain a key strategy for promoting overall health, supporting healthy aging, and preventing chronic diseases.

Conflict of interest

The authors declare no conflict of interest.

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Section 3

Diet Quality, Disease
Prevention and Management

Exploring the Interplay of Vitamin A, Retinoids and the Microbiota-Immune System Axis in Urinary Bladder Cancer Prevention and Treatment

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Abstract

Vitamin A is a crucial nutrient that must be obtained from the diet. Its bioactive metabolites have been identified as having a broad spectrum of effects on the development, proliferation, differentiation and apoptosis of cells, as well as metabolism, microbiota and the immune system in vertebrate organisms. Through epidemiological studies, it has been observed that a diet rich in vitamin A potentially reduces the risk of developing urinary bladder cancer. Additionally, vitamin A and its derivatives, retinoids, have been identified as potential therapeutic agents in bladder cancer treatment, as they can regulate cell differentiation, growth and apoptosis through retinoid signaling pathways, which play a significant role in bladder cancer development and progression. However, further research is necessary to understand their mechanisms of action and improve their effectiveness in clinical settings. Bladder cancer patients often have reduced serum vitamin A levels and an imbalance of gut microbiota, which can impact retinoid effectiveness. Recent evidence suggests that retinoids can influence the relationship between host cells and the gut microbiota, while the microbiota itself can influence retinoid metabolism. In addition, retinoids have shown various effects on immune cells, suggesting a possible role in regulating the immune response in cancer. The aim of this chapter is to investigate the role of vitamin A and retinoids in the prevention and treatment of bladder cancer, including their involvement in the microbiota-immune system axis.

Keywords: urinary bladder cancer, vitamin A, retinoids, retinoid signaling, cancer prevention, cancer treatment, gut microbiota, immune system

1. Introduction

Bladder cancer is a prevalent disease, ranking as the fifth most common cancer in the European Union and the ninth most common worldwide [1, 2]. It has a high recurrence rate and current treatments show low efficiency, which is why it is necessary to monitor patients in the long term even after treatment. As bladder cancer represents a major social and financial burden for society and individuals [3, 4], more effective treatments are urgently needed. Several risk factors have been identified as contributors to the development of bladder cancer, including smoking, exposure to certain chemicals, medications, radiation and chronic bladder *Schistosoma* infection [5]. Despite extensive research, effective preventive measures remain elusive. Therefore, it is crucial to delve deeper into the modifiable risk factors associated with bladder cancer in order to develop effective preventive strategies.

The first link between vitamin A and cancer incidence was established by rodent experiments in the 1920s and 1930s, showing that vitamin A deficiency increased the incidence of spontaneous and carcinogen-induced tumors [6–8]. Subsequent animal studies in 1970s and 1980s demonstrated the efficacy of natural and synthetic analogs of vitamin A (retinoids) as inhibitors of urinary bladder carcinogenesis in rodents [9–22]. In 1979, a retrospective study of dietary habits and bladder cancer showed an association between increased risk of bladder cancer and low vitamin A intake, supporting the findings in animal studies [23]. Since then, numerous epidemiological, preclinical and clinical studies have been conducted to further investigate the role of vitamin A and retinoids in bladder cancer chemoprevention and/or therapy. Meta-analyses of epidemiological studies show that vitamin A plays an important role in the prevention of bladder cancer. Higher levels of vitamin A in the diet and thus in the blood plasma of individuals are associated with a lower risk of developing bladder cancer [24–27]. As a fat-soluble vitamin that cannot be synthesized by the human body, vitamin A must be obtained from the dietary sources [28]. Consequently, the influence of vitamin A intake on the risk of developing bladder cancer holds significant public health implications.

Natural and synthetic retinoids have been extensively studied due to their role in the regulation of a wide range of biological processes. These include normal embryogenesis and development, vision, immune function, maintenance of differentiated epithelial tissues, cell proliferation and apoptosis [29]. The potential of retinoids in cancer treatment and chemoprevention is significant especially due to their vital involvement in the regulation of cell differentiation, proliferation and apoptosis. Retinoids have been identified as valuable agents in the pursuit of combating cancer, as evidenced by their high receptor-binding affinities and gene regulation capabilities [30]. In fact, retinoids have already been successfully used in clinical settings to treat certain types of cancer, such as acute promyelocytic leukemia in adults and neuroblastoma in children [31–33]. However, while preclinical studies have shown promising results for the use of retinoids in treating bladder cancer, it has been difficult to translate these findings into effective clinical treatments. New, innovative approaches for retinoid application and new synthetic retinoids have emerged [33–35], which could significantly improve the efficacy of retinoids for chemoprevention and treatment of bladder cancer.

An essential aspect of retinoid efficacy in treating bladder cancer is the gut microbiota. Recent studies have illuminated the influence of gut microbiota on vitamin A metabolism, revealing how specific microbial populations impact the biosynthesis and regulation of retinoic acid (RA), the bioactive form of vitamin A [36–41].

Concurrently, vitamin A has been shown to shape the composition and functionality of gut microbiota [42–44]. Depending on the composition of the gut microbiota, vitamin A-induced signaling can trigger immune responses that either support protective immunity or drive pathogenic outcomes [45–49].

In the context of bladder cancer, emerging evidence suggests that changes in vitamin A levels and gut microbiota composition correlate with disease progression [50]. By examining the bidirectional relationship between vitamin A and gut microbiota, this chapter aims to provide insights into their interconnected roles in maintaining immune homeostasis and the potential implications for bladder cancer prevention and treatment.

The chapter concludes by exploring the potential role of retinoids, especially all-trans-retinoic acid (ATRA), in modulating immune responses within the bladder tumor microenvironment. Given the significant impact of immune cells on tumor development, progression and response to therapy, retinoids may provide therapeutic benefits by modulating immune cell differentiation, particularly in counteracting the immunosuppressive effects of tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs) [51–54].

2. Human requirements, sources, absorption and metabolism of vitamin A

Vitamin A is an essential nutrient for humans, as the body cannot synthesize it *de novo* and must be obtained from food or supplementation. Two primary forms of vitamin A can be found in food: preformed vitamin A (primarily in the form of retinyl esters and retinol) and provitamin A carotenoids. Preformed vitamin A can be obtained from animal-based foods such as offal, meat, dairy products, eggs and fish. In contrast, provitamin A carotenoids are found in plant-based foods, including carrots, tomato, pumpkin, dark green leafy vegetables, red peppers, citruses, mangos and melons (**Figure 1**). Among the provitamin A carotenoids, β -carotene is the most abundant in the diet [55]. Preformed vitamin A is efficiently absorbed in the gastrointestinal tract, with an absorption rate of 70–90%. In contrast, the absorption of provitamin A carotenoids is much more variable, ranging from 5 to 65%, depending on dietary composition, genetic traits and environmental factors [56].

Dietary retinol is absorbed directly into enterocytes from the intestinal lumen, while dietary retinyl esters must first undergo enzymatic hydrolysis in the lumen to form retinol before uptake. Provitamin A carotenoids, such as β -carotene, are taken up *via* the scavenger receptor class B type I (SR-B1). Inside enterocytes, β -carotene is either converted to retinal by β -carotene monooxygenase 1 (BCMO1) and subsequently to retinol or incorporated intact into chylomicrons. Retinol binds to cellular retinol-binding protein 2 (CRBP2) and is esterified into retinyl ester by lecithin retinol acyltransferase (LRAT). Retinyl esters are packaged into chylomicrons for transport to liver stellate cells *via* the lymphatic system, where they are stored. When needed, these esters are mobilized, converted back to retinol in hepatocytes and released into circulation (**Figure 1**) [55, 57].

In circulation, retinol is transported to extrahepatic tissues bound to retinol-binding protein 4 (RBP4). At target tissues, the retinol-RBP4 complexes enter cells through a transmembrane receptor, stimulated by retinoic acid 6 (STRA6), which facilitates the influx of retinol while RBP4 remains extracellular (**Figure 1**) [58]. STRA6 is predominantly expressed in cells at blood–tissue barriers, such as Sertoli cells in the testis, choroid plexus cells in the brain and retinal pigment epithelium

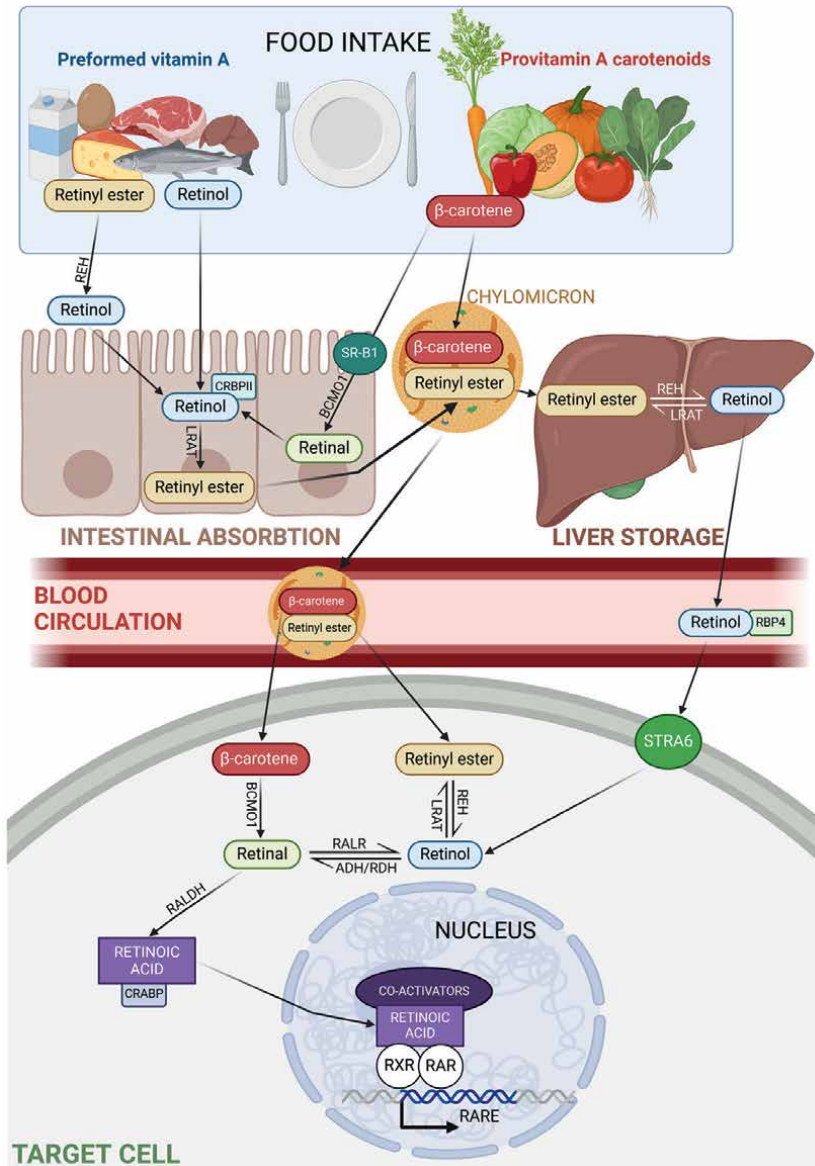


Figure 1.

Absorption, transport and storage of vitamin A in the intestine and redistribution to target cells. Vitamin A is obtained from the diet in the form of retinol and retinyl esters (from animal sources) and as provitamin A carotenoids (from vegetables and fruits). Intestinal enzymes are required for several processes leading to re-esterification of retinol to retinyl ester by lecithin retinol acyltransferase (LRAT) in enterocytes prior to incorporation into chylomicrons for lymphatic transport. Additionally, β-carotene can be included intact within chylomicrons. In the liver, vitamin A is stored as retinyl esters, which are hydrolyzed by retinyl ester hydrolase (REH) and released as retinol in response to the body's needs, maintaining a stable concentration of retinol in plasma bound to retinol-binding protein 4 (RBP4). Within target cells, retinol undergoes local conversion to retinoic acid (RA) through sequential oxidative steps involving alcohol dehydrogenase (ADH) and retinol dehydrogenase (RDH), followed by retinaldehyde dehydrogenases (RALDH). RA then enters the nucleus to bind to retinoic acid receptors, including retinoic acid receptor (RAR) and retinoid X receptor (RXR), to modulate gene transcription. BCOM1: β-carotene monooxygenase 1; CRABP: cellular retinoic acid-binding protein; CRBP2: cellular retinol-binding protein 2; RALR: retinal reductase; RARE: RA response element; SR-B1: scavenger receptor class B type 1; STRA6: receptors stimulated by retinoic acid 6. Figure was created using BioRender.

cells [59]. It is also expressed in the urothelium of the urinary bladder [60]. In tissues with low STRA6 expression, like fat and lung, retinol-RBP4 delivery does not rely on STRA6 [61].

Once inside target cells, retinol can be esterified by LRAT for storage or oxidized into its most active metabolite, RA, through a two-step enzymatic process. The first step, a reversible oxidation of retinol to retinal, is catalyzed by alcohol dehydrogenases (ADHs) and retinol dehydrogenases (RDHs). The second step, an irreversible oxidation of retinal to RA, is mediated by retinaldehyde dehydrogenases (RALDHs) [62]. RA has multiple isomeric forms, including all-trans RA (ATRA) or tretinoin (the most common form), 9-cis-RA (alitretinoin), 13-cis-RA (isotretinoin) and 9-13-dicis-RA, which are all found in various human organs [63]. RA binds to cellular RA-binding proteins (CRABPs) or fatty acid-binding proteins (FABPs). These proteins control the availability of ligands and determine the physiological response of cells and tissues to vitamin A (**Figure 1**) [64]. They transport RA to the nucleus for receptor binding and gene regulation (described further in Chapter 4). In the cell, excess RA undergoes degradation by cytochrome P450 enzymes (CYP26A1, CYP26B1 or CYP26C1) [65].

The biological value of compounds with vitamin A activity is expressed in retinol equivalents (RE) to account for the lower absorption efficiency of provitamin A carotenoids and their conversion to retinol. According to the Scientific Committee for Food (SCF) for the European population [66], 1 µg RE corresponds to 1 µg retinol, 6 µg β-carotene or 12 µg of other provitamin A carotenoids (e.g., α-carotene or β-cryptoxanthin). Vitamin A requirements can be fulfilled with any combination of preformed vitamin A and provitamin A carotenoids that collectively provide an equivalent amount of vitamin A, expressed in µg RE per day. The European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA) [66] has established daily population reference intakes for vitamin A as follows: 750 µg for adult men, 650 µg for adult women, 250 to 750 µg for infants and children (depending on age) and 700 µg for pregnant women to accommodate the needs of the fetus and maternal tissue growth [66].

Vitamin A status is most accurately assessed by measuring total retinol stored in the body, primarily as free retinol or as storage form of retinyl esters or by evaluating liver vitamin A concentrations [67]. However, serum or plasma retinol levels can also indicate deficiency: a concentration of 200 µg/mL (0.70 µmol/L) or less signifies moderate vitamin A deficiency, while levels of 100 µg/mL (0.35 µmol/L) or less indicate severe deficiency [68]. The most specific clinical manifestation of vitamin A deficiency is xerophthalmia, characterized by ocular signs and symptoms, such as night blindness [69].

3. Urinary bladder cancer and the impact of vitamin A on bladder cancer risk

In 2020, 600,000 new cases of bladder cancer were registered, which corresponds to around 3% of all cancer cases worldwide [1, 70]. Due to the aging and growing population, it is expected that the number of new cases of bladder cancer and the deaths caused by it will increase in the future. Most newly diagnosed cases of bladder cancer occur in people over the age of 60, which will ultimately lead to an increasing burden on the healthcare system and society as a whole [1].

The bladder is a hollow organ with a thick muscular wall. Its function is to collect urine and store it until it is emptied. The inner surface of the bladder lumen is covered by a specialized, multilayered transitional epithelium, the urothelium, which forms the blood-urine barrier. This barrier prevents toxic substances from the urine re-entering the blood [71, 72]. The urothelium and the underlying connective tissue, the so-called lamina propria, together form the mucosa. The bladder wall also consists of smooth muscle, which allows urine to be expelled from the bladder during urination and a serosa, a loose connective tissue that covers the outer surface of the bladder [73–75].

In most cases, bladder carcinoma originates from the urothelium, where morphologically recognizable atypia of the urothelial cells occurs first. It is a heterogeneous disease with a wide spectrum of pathological conditions with different clinical outcomes [76]. Depending on the extent of invasion into the bladder wall, bladder cancer is divided into a group of non-invasive and invasive cancers, which can also be classified according to the TNM clinicopathological classification, which evaluates the extent of the tumor at the local (T – tumor), regional (N – nodes, lymph nodes) and systemic level (M – metastases) [77]. Non-invasive cancers include papillary urothelial carcinoma – stage Ta cancers, which grow into the bladder lumen and are more likely to recur, spread and progress. Another non-invasive cancer is superficial urothelial carcinoma *in situ* (CIS, stage Tis), which is confined to the mucosal tissue. Invasive forms include tumors that invade the lamina propria (T1) or the muscularis mucosa (T2) and tumors that invade through the muscularis mucosa of the bladder into the serosa (T3) or adjacent organs (T4) [78]. For therapeutic purposes, Tis, Ta and T1 tumors are collectively classified as non-muscle invasive bladder carcinomas, which account for 75% of all bladder carcinomas, while T2, T3 and T4 are collectively classified as muscle invasive carcinomas [79].

The most common method for diagnosing and treating bladder cancer is cystoscopy, during which the urologist examines the urethral mucosa and the bladder and removes any visible tumors by means of a transurethral resection. Samples of the cancerous tissue are taken for histopathology. Depending on the risk of cancer progression, patients with non-muscle-invasive cancer may be treated with cytostatic drugs (mitomycin C, epirubicin) or immunotherapy with a suspension of tubercle bacillus Calmette Guérin (BCG) injected into the bladder lumen [80]. The recurrence rate of non-muscle invasive bladder cancer is high (50–70%) and requires systematic surveillance of patients for several decades after initial treatment [81]. However, progression of non-invasive cancer is rare (10–15%) and the 5-year survival rate is high (90%) [82]. For muscle-invasive bladder cancer, the gold standard treatment is radical cystectomy with regional lymph node dissection and systemic chemotherapy when necessary and appropriate [83]. In men, the prostate, seminal vesicles and distal ureters are surgically removed in addition to the bladder. In women, the entire urethra and part of the vagina, uterus and distal ureters are surgically removed [83]. Despite the invasive nature of the procedure, muscle-invasive bladder cancer is associated with a high metastatic rate and a 5-year survival rate of less than 50% [82, 83].

Several epidemiological studies from the last century have shown that a diet rich in vitamin A reduces the risk of bladder cancer, but the results have been inconsistent [84]. However, in 2014, Tang and colleagues conducted a meta-analysis that included 25 studies examining the quantitative impact of vitamin A on the risk of developing this cancer. This meta-analysis revealed that increased dietary vitamin A intake and higher blood retinol levels are associated with a lower risk of bladder cancer [24]. These findings further corroborated significantly reduced serum levels of retinol

documented in patients with bladder cancer compared to controls [85]. In support of these findings, a more recent study in 2019 by Fradj and colleagues [86] also concluded that bladder cancer patients had significantly lower levels of plasma vitamin A compared to the control group and higher plasma levels of vitamin A were associated with a lower occurrence of urothelial bladder cancer. It was also demonstrated that vitamins A and D interact antagonistically with each other and with tobacco to modulate bladder cancer risk [85]. The authors suggest that these interactions should be considered in the prevention of bladder cancer. In general, diet is one of the modifiable risk factors and could therefore contribute to the prevention of bladder cancer [26, 87]. Although vitamin A is present in various foods, people often do not consume enough of it, mainly due to malnutrition and selective diets [88]. It is of utmost importance to educate people that adequate intake of vitamin A can contribute to the prevention and also to a more effective treatment of bladder cancer.

4. Retinoids induce intracellular signaling and transcription activation

Retinol is biochemically composed of three major units: the cyclic end group (cyclic ring), the polar end and a polyene chain linking the 2 units. This structure makes retinol poorly soluble in water but soluble in organic solvents and lipids [89]. Modifications to any of these 3 units can result in the production of different synthetic retinoids, each with potentially unique properties and applications [90]. Based on molecular structure, receptor selectivity and considering historical context of their development and introduction into clinical use, retinoids are classified into four generations (**Table 1**) [90–92].

Natural endogenous retinoids such as ATRA, retinol and retinaldehyde are the retinoid derivatives generated from the retinoid-containing diets through the retinoid metabolism pathway (**Figure 1**). These compounds are metabolized intracellularly into active RA (**Figure 1**) [33]. Their clinical use for cancer treatment is limited due to various factors such as poor water solubility, high toxicity, poor drug resistance, low affinity and side effects [33]. They have limited effectiveness because they can undergo isomerization, which can produce variants with different activities. Additionally, they can be broken down by cytochrome P450 enzymes [93]. Synthetic retinoids are more stable and can specifically target different types of retinoic acid receptors, with varying mechanism of action and metabolic processes. Hence, they have lower toxicity, and higher effectiveness compared to natural derivatives (**Table 1**) [33, 94].

Retinoids trigger a series of events (e.g., retinoid signaling pathway) that lead to the transactivation of several target genes. Specifically, cellular retinoid-binding proteins such as CRABP II and fatty acid-binding protein 5 (FABP5) deliver retinoids into the nucleus. In the nucleus, they can activate gene expression by binding to specific nuclear retinoid receptors: RA receptors RAR (α , β and γ) and retinoid (rexinoid) X receptors RXR (α , β and γ) and their numerous isoforms to regulate the expression of target genes (**Figure 1**) [93, 95, 96]. RARs, belonging to the steroid/thyroid hormone nuclear receptor superfamily, operate principally as ligand-inducible transcription factors. RXRs, belonging to the same superfamily, act as imperative heterodimerization partners for RARs but can also self-dimerize or heterodimerize with other nuclear receptors and have therefore the potential to affect the signaling of other pathways [96, 97]. ATRA induces the activation of RARs. 9-*cis* RA has a high affinity for its targets and can activate both RARs and RXRs [98]. On the other hand,

Generation	Chemical structure	Members	Feature/properties
<i>First generation</i>	Naturally occurring, non-aromatic	Retinol Retinaldehyde Retinyl acetate ATRA (tretinoin) 13-cis-RA (isotretinoin) 9-cis-RA (alitretinoin)	Do not act selectively Short biological half-life
<i>Second generation</i>	Synthetic mono-aromatic	Etretinate Acitretin	More lipophilic and greater bioavailability than earlier generation
<i>Third generation</i>	Synthetic poly-aromatic	Adapalene Tazarotene Bexarotene Fenretinide (4-HPR)	More selective receptor binding Better stability than earlier generations
<i>Fourth generation</i>	Synthetic pyranones	Seletinoid G Trifarotene	Most selective receptor targeting Enhanced tolerability due to selective receptor binding

Bold – retinoids used in the clinical studies for bladder cancer treatment.

Table 1.
Generations of retinoids.

13-cis-RA acts as an agonist of RXRs and RARs, but its affinity is lower compared to ATRA and 9-cis-RA [98].

In the classical canonical genomic RA signaling pathway, unliganded RAR-RXR heterodimers bind to DNA with high affinity at RA response elements (RAREs) (**Figure 1**), repressing transcription of downstream genes. Upon RA binding, these receptors undergo conformational changes that activate transcription [99, 100]. In addition to this canonical pathway, RXR serves as a binding partner for nuclear receptors, such as the liver X receptor (LXR) and peroxisome proliferator-activated receptor (PPAR), resulting in the involvement of RA in regulating the pathways of these receptors as well [97]. In tumor biology, RA signaling has been found to exhibit a dualistic nature. For example, after RA is transported to the nucleus by the CRABP, RA binds to dimers of RAR α and RXR (α , β or γ) to induce expression of its downstream target genes, including RAR β . Upon activation, RAR β can regulate its own expression and that of its downstream genes, mainly functioning to inhibit cell growth and induce cell differentiation [101]. Inactivation of RAR β results in tumor proliferation and cancer progression [102]. Alternatively, RA can be bound and transported to the nucleus by other factors such as FABP5. This protein delivers RA to PPAR β/δ which activates pro-survival genes and results in tumor growth [101, 103].

The RA pathway demonstrates a complex and multifaceted functionality, encompassing both epigenetic context-dependent differential gene expression, mediation of apoptotic pathways and immune system regulation [104]. Furthermore, the downstream signaling of RA is shaped by a complex network of factors, including RA availability, cellular binding proteins, nuclear receptor types and abundance and the presence of RAREs [105].

5. The role of retinoids in the treatment of bladder cancer

Retinoid signaling plays a crucial role in regulating multiple aspects of urothelial development, maintenance and regeneration [106, 107]. In bladder cancer cells, the retinoid signaling pathway is disrupted at multiple levels, contributing to the complex pathogenesis of bladder cancer and affecting cell proliferation, differentiation and survival. At the level of receptors and transcription factors, it was shown that RAR β is frequently downregulated, likely due to epigenetic silencing through promoter hypermethylation. Studies have shown significant elevation in the frequency of methylation for RAR β in human bladder cancer, ranging from 15 to 93% [108–112]. Further analysis has revealed that methylation frequencies at the promoter regions of RAR β 2 in both normal and Tis samples from patients with urothelial cell carcinoma positively correlate with the progression of the disease [113]. Furthermore, recurrent RXR α mutations are observed in 5–8% of human bladder cancer patients. These mutations activate PPAR to drive urothelial proliferation [114]. The upregulation of PPAR γ /RXR α transcriptional activity has emerged as a key event in luminal bladder tumors [115]. The activation of PPAR γ /RXR α pathway has been linked to PPARG gains/amplifications resulting in PPAR γ overexpression and to recurrent activating point mutations of RXR α . Furthermore, recurrent mutations of PPAR γ also activate the PPAR γ /RXR α pathway [115].

Next, changes in the expression of enzymes involved in retinoid metabolism, such as RALDHs and LRAT, have been found. It has been reported that ALDH1A1/RALDH1A1 and its putative downstream target gene TUBB3 are overexpressed in bladder cancer. A clinical survival database revealed that TUBB3 expression may be associated with poor prognosis in bladder cancer patients [116]. Additionally, LRAT expression is significantly reduced in human bladder cancer and a strong inverse correlation has been shown between LRAT expression and increasing tumor stage [117].

Furthermore, disruptions in PD-L1/ITGB6/STAT3 signaling axis, regulated by RA-related orphan receptor C (RORC), have been shown to contribute to the pathogenesis of bladder cancer [118]. RORC functions as a DNA-binding transcription factor and was found to be downregulated in tumor tissues from bladder cancer patients [118]. Lower RORC expression was also observed in advanced tumors and those resistant to chemotherapy. Additionally, enhanced expression of RORC suppressed cell proliferation in both *in vivo* and *in vitro* studies [118].

The complexity of the mechanism of retinoid action and the disrupted retinoid signaling occurring at multiple levels make it challenging to predict and optimize the therapeutic outcomes of retinoid treatment. Several retinoids have been tested for bladder cancer treatment in preclinical studies, leading to conflicting results. Natural retinoids such as ATRA, 9-cis-RA, 13-cis-RA and retinyl acetate have been shown to inhibit cell growth, induce apoptosis and inhibit matrix metalloproteinases, which play an important role in the process of degrading the extracellular matrix, essential for tumor growth and invasion [20, 119–121]. A recent study demonstrated that ATRA reduced the aggressiveness of malignant arsenite-transformed malignant human urothelial cells by decreasing cell proliferation and increasing differentiation markers. Mechanistically, the antiproliferative effect of ATRA was attributed to the downregulation of c-myc, a key transcription factor that controls cell proliferation in multiple cancer cells [122]. In animal studies of bladder cancer, both ATRA and 13-cis-RA were found to reduce the number and size, incidence and severity of tumors [12, 16]. Retinyl acetate also showed promise in reducing urothelial atypia and apoptosis in early bladder cancer [60]. Administration of 13-cis-RA, either

simultaneously or with a delayed onset, was found to inhibit urothelial carcinoma and proliferative lesions of the bladder [9, 13–15]. This is important in a clinical setting, as the onset of retinoid administration is likely to be delayed in bladder cancer patients with respect to the earliest preneoplastic changes. However, another study found that 13-cis-RA exhibits no effect on the incidence or severity of bladder cancer *in vivo* [17, 18]. Furthermore, some studies have shown resistance to ATRA and 9-cis-RA [85] in bladder cancer cell lines, most of which do not express RAR β . However, ATRA did have an inhibitory effect on bladder cancer cell lines that express RAR β , indicating that the ATRA effect might be RAR β -dependent [123, 124]. ATRA was also demonstrated to induce dose- and time-dependent proliferation of bladder cancer cells (T24 cell line) with an overexpression of FABP5 in conjunction with the down-expression of CRABP II [125].

Synthetic retinoids, such as N-(4-hydroxyphenyl)-retinamide (4-HPR or fenretinide) and 6-[3-(1-adamantyl)-4-hydroxyphenyl]naphthalene-2-carboxylic acid (CD437, also known as AHPN or Ro 472,077), generally show stronger effects on growth inhibition and apoptosis induction compared to natural retinoids such as ATRA and 9-cis-RA [123, 124]. They were shown to induce expression of different RARs in various bladder cancer cell lines and differentially alter the expression of apoptosis-associated genes, such as p53, GADD45, bcl-2 and casp3 [123, 124]. Synthetic retinoids, such as N-(ethyl)-all-trans-retinamide and N-(2-hydroxyethyl)-all-trans-retinamide, were also found to be less toxic to animals in *in vivo* studies, compared to 13-cis-RA [12]. Fenretinide was shown to increase the expression of E-cadherin and the translocation of β -catenin from the nucleus to the cytoplasm in invasive bladder cancer T24 cells [126]. These proteins are important for cell-to-cell adhesion and the results of this study suggest that fenretinide may partly regulate T24 bladder cancer cell invasion by modulating the expression of E-cadherin [126]. In 2024, Ozgun and co-authors used fenretinide and retinoid GSK-126 together with inhibitors of the methyltransferase *EZH2* (enhancer of zeste homolog 2). *EZH2* is the catalytic subunit of the repressive Polycomb complex 2 and acts as a transcriptional repressor *via* the trimethylation of lysine 27 of histone 3 (H3K27me3). Their results showed that this coordinated targeting strategy increased apoptosis and cell cycle arrest in an orchestrated manner [127]. In an animal model of bladder cancer, fenretinide did not reduce tumor incidence but did affect tumor differentiation and led to changes in nuclear size and DNA ploidy [21]. However, synthetic retinoids do not always exhibit a significant effect. For instance, the synthetic RXR agonist bexarotene (also known as LGD1069 or Ro 26-445, brand name Targretin) had minimal effect on various bladder cancer cells *in vitro* [124]. Etrretinate (ethyl etretinate or Ro 10-9359, brand name Tigason) inhibited urothelial papillary or nodular hyperplasia in a dose-dependent manner in an animal study [19], but it also showed no effect in the same animal model of bladder cancer in another study [22]. On the other hand, bexarotene was shown to increase the incidence and size of tumors in an animal model of bladder cancer [128]. The authors speculated that this effect could be mediated by PPAR γ heterodimer formation [128].

The use of natural (13-cis-RA and ATRA) and synthetic retinoids (fenretinide and etretinate) in clinical studies for bladder cancer treatment has shown varying levels of potential benefits. In a phase I/II study of patients with Ta and T1 tumors, 13-cis-RA treatment was found to be toxic. Due to the lack of positive results, the study was terminated [129]. However, in patients with Ta and T1 tumors, ATRA combined with ketoconazole (a potent inhibitor of RA -catabolizing cytochrome P450s) improved survival time and reduced recurrence rate.

These positive effects were achieved with tolerable and reversible side effects and were attributed to a reduction of mitogenic/angiogenic factors, vascular endothelial growth factor (VEGF) and transforming growth factor α (TGF α), likely through the elimination of malignant cells that produce them [130]. Fenretinide also showed promising results in a phase IIa study, with reduced proliferation and delayed development or reversal of DNA aneuploidy to diploidy [131]. A phase IIb randomized study also found lower levels of insulin-like growth factor-I (IGF-1) [132] in patients with Ta and T1 bladder cancer stage. Research has shown that IGF-1 may play a role in the development and progression of bladder cancer [133]. However, a phase IIb randomized study [134] and a 20-year follow-up [135] demonstrated no significant effect of fenretinide on DNA content, morphology of urothelial cells, recurrence-free survival or outcome in patients with Ta and T1 stage. Similarly, a phase III randomized study with fenretinide and a placebo control in Tis, Ta and T1 patients showed no improvement in time-to-recurrence [136]. However, subgroup analysis revealed that combined treatment with BCG demonstrated a lower risk of recurrence in high-risk patients [136]. The side effects of fenretinide were found to be well tolerated in all studies [131, 134, 136]. Another synthetic retinoid, etretinate, also showed potential for treating bladder cancer, as it prevented the recurrence of cancer in a double-blind, randomized, placebo-controlled study on patients with Ta and T1 stages [137]. It was found to increase the time between tumor recurrences (except for the time to first recurrence) in a separate, prospective, double-blind, placebo-controlled study on Ta and T1 stage patients as an adjuvant treatment after transurethral resection [138]. However, there were significant side effects, particularly at high doses [137] and some patients also experienced cardiac toxicity [138]. Side effects, including symptoms affecting the skin and different mucous membranes, were also a barrier in a randomized, placebo-controlled study on patients treated with etretinate for recurrent non-invasive bladder tumors [139]. Furthermore, the treatment did not have an effect on the recurrence of non-invasive bladder cancer [139]. Recently, Chen and co-authors conducted a meta-analysis on the potential of retinoids in cancer therapy, which included 39 randomized control trials on various cancers including bladder cancer. Although their results show that cancer patients treated with retinoids had a lower recurrence rate and better clinical response compared to the control groups, no significant therapeutic effect was found in bladder cancer [140].

Taken together, the treatment for bladder cancer using retinoids presents two significant obstacles that must be overcome in the clinical setting: toxicity and lack of effectiveness in achieving desired outcomes. Systemic delivery of RA can cause side effects due to its involvement in various biological processes. Large pharmacological doses and long-term treatment with retinoids may produce side effects, primarily affecting the mucocutaneous, skeletal, central nervous system and hepatic and osseous tissues [34, 141]. Retinoid administration is challenging due to the low concentration of retinoids at the tumor site, limited solubility in aqueous solutions, photosensitivity, rapid degradation during digestion and increased catabolism, when administered intravenously [34, 125, 142]. The bioavailability and bioaccessibility are therefore low, reducing retinoids therapeutic efficacy. In addition, retinoid resistance also contributes to the limited successful use of retinoids for chemoprevention and treatment. Various mechanisms are implicated in retinoid resistance, including changes in retinol metabolism (such as regulation of LRAT activity), expression of CRABPs for intracellular transport of retinoids, increased catabolism of RA isomers

by P450s (CYP26), active drug efflux by membrane transporters, downregulated expression of various RAR genes (promoter methylation), altered expression of co-activators or downstream target genes and changes in the activities of other signaling pathways [32].

Strategies for reducing toxicity and enhancing the effectiveness of retinoid treatment include the synthesis of new and more tolerable synthetic retinoid compounds, the development of novel delivery formulations (such as encapsulating retinoids in nanoparticles, micelles or liposomes or binding them to nanoparticles, proteins or polymers) and utilizing retinoids in combination with other differentiation-inducing agents, cytotoxic drugs or drugs that decrease resistance to retinoids [33–35].

6. The gut microbiota influences vitamin A metabolism and vice versa

The gut microbiota is a system of microorganisms, including bacteria, viruses, fungi and other microbes, that reside in the gastrointestinal tract. These microorganisms regulate the immune system and interact with food components by converting them into bioactive compounds that influence systemic metabolism [143, 144].

A growing number of publications have shown strong correlations between the gut microbiota and the biosynthesis of several vitamins [145]. Notably, the gut microbiota plays a crucial role in regulating various aspects of vitamin A metabolism. Studies have shown that *Bacteroidetes*, *Bifidobacterium*, *Clostridium* and *Lactobacillus* directly influence the metabolism of bile acids [36, 37], which are essential for the emulsification and absorption of fat-soluble vitamins, such as vitamin A [146–149]. In addition, gut microbiota influences the production of butyrate [38], a short-chain fatty acid signaling molecule that can modulate the expression of genes involved in the biosynthesis of RA and stimulate the production of RA [39–41]. Furthermore, butyrate acts synergistically with RA to regulate the differentiation and migration of immune cells in the gut [150, 151].

Depending on the composition of the gut microbiota, vitamin A-induced signaling can trigger immune responses that either support protective immunity or drive pathogenic outcomes. The protective role of vitamin A was demonstrated by Grizotte-Lake and colleagues [45]. They showed that *Clostridial* species act as key microbial regulators that inhibit RA synthesis in intestinal epithelial cells of mice *via* *RDH7*, a key gene involved in the conversion of retinol to RA. This in turn led to a reduction in the IL-22 activity, which is essential for colonizing the gut with pathogenic *Salmonella Typhimurium* and triggering intestinal inflammation [45]. Similarly, a recent study by Grace Cao et al. [46], showed that *Faecalibaculum rodentium* decreases RA-producing enzymes ADH1, ALDH1A1 and RDH7, leading to higher proliferation of intestinal epithelial cells. Namely, RA signaling is essential for the survival of certain eosinophil populations, which in turn suppress IFN- γ production by intraepithelial lymphocytes and consequently impede epithelial turnover in the gut [46]. The protective role was also confirmed by Woo et al. [47], who demonstrated that commensal segmented filamentous bacteria and *Bifidobacterium bifidum* are direct sources of RA through the activity of ALDH, as shown in both *in vitro* and *in vivo* experiments. Furthermore, they showed that the increase in luminal RA by segmented filamentous bacteria enhances the defense of intestinal epithelial cells against *Citrobacter rodentium* infection by promoting nitric oxide production *via* activation of nitric oxide synthase 2 [47]. Recent metabolomics analysis has shown that commensal bacteria in the gut of mice can also produce retinoids by converting dietary vitamin A into retinol

and produce active metabolites such as 13-cis-RA and ATRA [48]. In addition, the study was also able to show that *Lactobacillus Intestinalis* isolated from the gut has high ALDH activity and is able to restore ATRA levels in vancomycin-treated mice [48]. Vancomycin targets anaerobic commensals belonging to class Clostridia and Bacteroidia [49].

Conversely, vitamin A also modulates the composition and function of the gut microbiota. A study in vitamin A-deficient mice showed that vitamin A deficiency leads to a reduction in beneficial commensal microbes such as *Clostridium difficile*, *Escherichia coli* and *Lactobacillus*, which in turn shape intestinal tissue immunity by decreasing the differentiation of the proinflammatory Th17 (T helper 17) cells in the lamina propria of small intestine [42]. Another study by Lv et al. [44] showed a decrease in butyrate-producing bacteria such as *Clostridium butyricum* in the gut microbiota of children with persistent diarrhea due to vitamin A deficiency and an increase in opportunistic pathogens such as *Enterococcus faecalis* [44]. On the other hand, *Escherichia coli* and *Clostridium butyricum* predominated in children with sufficient vitamin A [44]. A randomized control study in infants in Bangladesh showed that neonatal vitamin A supplementation led to an increase of *Bifidobacterium* in boys in early infancy (6–15 weeks) and to an increase abundance of *Akkermansia* in girls in late infancy (2 years) [43].

Taken together, vitamin A and gut microbiota play a crucial role in maintaining immune function and gut homeostasis. Vitamin A deficiency and dysbiosis as well as an imbalance in microbial composition, can impair immune function, disrupt the integrity of the intestinal barrier and increase susceptibility to infection and chronic disease [152]. Besides reduced serum vitamin A levels [85, 86] bladder cancer patients also exhibit an imbalance in gut microbiota [50]. A study of the gut microbiota in bladder cancer patients, in comparison to that of healthy individuals in a case-control setting, revealed a significant decrease in the abundance of specific bacteria within the patient population. The number of domain bacteria, *Clostridium cluster XI* and *Prevotella* was significantly lower compared to the healthy group [153]. An *in vitro* study has demonstrated a correlation between urothelial bladder cancer and *Butyricicoccus pullicaecorum*. This butyrate-producing microbe mediated anti-cancer effects on bladder urothelial cells by regulating cell cycle, cell growth, apoptosis and gene expression. The study concluded that to enhance the health of bladder urothelial cells, it may be essential to supplement *B. pullicaecorum*, which can further regulate butyrate-responsive molecular signatures [154]. Understanding the interactions between vitamin A and the gut microbiota can support targeted nutritional and therapeutic strategies to restore microbial balance and improve overall health. Furthermore, maintaining healthy vitamin A levels and a balanced gut microbiota may offer protective benefits against bladder cancer development.

7. Retinoids have a possible role in regulating immune response in bladder cancer

Immune response and immune cells play crucial roles in the development and progression of many types of cancer. In recent years, immunotherapy has gained considerable interest as a promising approach to fight tumors by modulating the tumor microenvironment, which includes different types of immune cells, including immunosuppressive cells that can limit the efficacy of immunotherapy [155]. A

growing body of research has shown that retinoids, particularly ATRA, can regulate the differentiation, polarization and recruitment of immune cells within the complex tumor microenvironment [54].

Cancer cells usually promote the development of immunosuppressive tumor-associated macrophages (TAMs), while they inhibit the function of dendritic cells and thus hinder the formation and maintenance of functional antitumor T cells. Both dendritic cells and TAMs can differentiate from circulating monocytes, but in solid tumors, monocytes preferentially differentiate into immunosuppressive TAMs, which is also the predominant immune cell population in bladder cancer [52]. The presence of immunosuppressive TAMs is associated with an increased number of exhausted CD8⁺ T cells (these cells have a weakened effector function due to prolonged antigenic stimulation), immature natural killer cells and increased expression of immune checkpoints, such as programmed cell death ligand (PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). In addition, immunosuppressive TAMs correlate well with tumor progression, poor prognosis and therapy resistance in bladder cancer patients [156]. Given their central role, TAMs have emerged as a promising target for novel cancer treatment.

In 2002, Liss et al. demonstrated *in vitro* that ATRA can suppress the recruitment and activation of monocytes involved in tumor angiogenesis in squamous cell carcinoma of the head and neck. By reducing the secretion of monocyte chemoattractant protein-1 (MCP-1) and transforming growth factor- β 1 (TGF- β 1), ATRA-treated tumor cells were less able to induce chemotaxis of monocytes from peripheral blood. Reduced TGF- β 1 secretion in ATRA-treated tumor cells also restricted VEGF production and release by TAMs, thereby reducing angiogenesis. These effects of ATRA may result in slower tumor growth and reduced aggressiveness due to decreased tumor vascularity [157]. In another *in vitro* study, Zhou et al. found that ATRA inhibited osteosarcoma metastasis by suppressing IL-13- or IL-4-induced polarization of TAMs into an M2 phenotype, which is anti-inflammatory and contributes to the formation of extracellular matrix. They found that this ATRA-mediated effect was independent of conventional signal transducer and activator of transcription 3/6 (STAT3/6) or transcription factor CCAAT/enhancer binding protein β (C/EBP β) signaling, which normally regulate M2 polarization of macrophages. Instead, quantitative genomic and functional analyses showed that ATRA downregulated IL-13-induced secretion of MMP-12, an elastase secreted by macrophages, which correlated with reduced metastasis [158]. In addition, synthetic retinoid fenretinide (4-HPR) has been shown to inhibit M2 macrophage polarization in both RAW264.7 macrophages and mouse bone marrow-derived macrophages by blocking STAT6 phosphorylation. Using Apc^{Min/+} transgenic mice, an animal model bearing multiple intestinal neoplasia, the authors found that treatment with fenretinide significantly reduced colorectal tumorigenesis *in vivo* by preventing tumor angiogenesis, which was associated with fewer M2-like macrophages in tumor tissue [159]. Overall, these studies highlight the potential of retinoids to exert chemopreventive effects by inhibiting polarization of macrophages toward an M2 phenotype.

Myeloid-derived suppressor cells (MDSCs), another important circulating precursor of immunosuppressive TAMs, have strong immunosuppressive functions and thus protect tumor cells from immune attack and contribute to a poorer cancer prognosis [160]. They can impair T cell function by upregulating immune checkpoints PD-L1 and CTLA-4 and directly promote tumor progression by enhancing angiogenesis, stemness and epithelial–mesenchymal transition [105]. The link between ATRA and

MDSCs was first observed in 2000, when Kuwata and colleagues reported a significant increase in the number of MDSCs in the bone marrow, spleen and peripheral blood of vitamin A-deficient mice. In these mice, spontaneous apoptosis of MDSCs was suppressed and the levels of RAR and RXR, were significantly reduced. These changes were reversed by supplementation with ATRA [161]. Later, Kusmartsev et al. reported that *in vivo* administration of ATRA significantly reduced the number of MDSCs in mice with multiple tumors. Experiments with adoptive transfer showed that ATRA was able to induce the differentiation of MDSCs *in vivo* into mature dendritic cells, macrophages and granulocytes, resulting in an enhanced CD4- and CD8-mediated tumor-specific immune response. In addition, the combination of ATRA with two different types of cancer vaccines significantly prolonged the antitumor effect of the treatment [162]. Mechanistic studies have shown that ATRA significantly increased the phosphorylation of extracellular signal-regulated kinase 1/2 (ERK1/2) in MDSCs, while inhibition of ERK1/2 phosphorylation completely blocked the effect of ATRA on MDSC differentiation, suggesting that ERK1/2 is a downstream target of ATRA [163]. Schröder et al. developed a novel assay using immortalized mouse bone marrow progenitor cells that can be differentiated *in vitro* into MDSCs expressing Arginase-1 and PD-L1, producing reactive oxygen and nitrogen species and suppressing T cell function [164]. Using this model, RNA sequencing and gene expression analyses, the authors found that treatment with ATRA significantly downregulated the expression of genes associated with the Toll-like receptor (TLR) and NF- κ B signaling pathways, suggesting that the effect of ATRA on the differentiation of MDSCs may also be mediated through inhibition of inflammatory pathways [165].

Based on these results, it is plausible to assume that combining ATRA with other therapeutic strategies could lead to better treatment outcomes for cancer. For instance, the efficacy of cancer vaccines is often limited by the presence of MDSCs. The addition of ATRA in this context significantly reduces MDSC populations and increases the efficacy of various vaccines, such as photodynamic therapy-generated cancer vaccines and tumor-exosome-loaded dendritic cells-derived vaccines, as demonstrated in mouse models with squamous cell carcinoma and pancreatic cancer, respectively [166, 167]. In addition to cancer vaccines, ATRA has shown synergistic effects with immune checkpoint inhibitors, as MDSC-mediated upregulation of immune checkpoint molecules is one of the key mechanisms underlying their immunosuppressive function [160]. Lesterhuis and colleagues demonstrated for the first time that co-administration of ATRA with CTLA-4 blockade significantly enhanced therapeutic efficacy and resulted in long-term cure in the majority of mice with AB1-HA mesothelioma [168]. Their findings were subsequently confirmed in a mouse model with multiple tumors (mesothelioma, renal cell carcinoma and fibrosarcoma), in which ATRA was combined with immune checkpoint inhibitors. ATRA was able to rapidly induce an interferon-dominated inflammatory tumor microenvironment with increased CD8⁺ T cell infiltration, significantly improving the efficacy of anti-CTLA4/anti-PD-L1 combination therapy [169]. The synergistic effect of ATRA and immunotherapy was further demonstrated in a randomized phase II clinical trial with patients with advanced melanoma. The addition of ATRA to treatment with ipilimumab (anti-CTLA-4 monoclonal antibody) significantly decreased the frequency of circulating MDSCs compared to ipilimumab monotherapy and improved prognosis. Importantly, the addition of ATRA to standard ipilimumab therapy was safe and well tolerated, as ATRA did not increase the incidence of adverse events [170]. Overall, these results suggest that the combination of ATRA and standard antitumor therapies

is a promising strategy to overcome the immunosuppressive tumor microenvironment and enhance the efficacy of cancer immunotherapies.

Although numerous studies have shown that ATRA can suppress the function of MDSCs and promote their differentiation into functional, mature dendritic cells, some studies have reported contrary results [171, 172]. The relationship between endogenous ATRA levels in the tumor and tumor malignancy is also controversial. While some studies have documented a significant decrease in intratumor ATRA levels during tumorigenesis [173, 174], others have observed the opposite [175, 176]. For example, Devalaraja et al. have shown that the tumor microenvironment in mouse sarcoma models induces tumor cells to produce high levels of ATRA. This increased ATRA promotes the differentiation of monocytes into immunosuppressive TAMs rather than dendritic cells by suppressing the transcription factor IRF4. Genetic or pharmacological inhibition of ATRA production or signaling in the tumor increased the prevalence of monocyte-derived dendritic cells, enhanced T cell-mediated antitumor activity and acted synergistically with immune checkpoint blockade therapies [176]. Furthermore, treatment of dendritic cells derived from healthy blood donors with ATRA inhibited their differentiation and maturation, as well as promoted the differentiation of naïve T cells toward a type 2 helper T cell (Th2) response and the expansion of CD4 + CD25 + Foxp3+ regulatory T cells, which are known for their immunosuppressive properties [171]. These conflicting results may be due to several factors, including the reliance on cell surface markers to assess cellular identity and function, the use of inconsistent or significantly higher than physiologic doses of ATRA, and the influence of additional environmental variables that modulate the effect of ATRA. Taken together, these results suggest that the role of ATRA as an antitumor agent is highly context- and concentration-dependent and varies according to tumor type and microenvironmental conditions [176, 177].

The presence of MDSCs and immunosuppressive TAMs in bladder cancer is well-documented and strongly associated with resistance to standard therapies, including BCG therapy, chemotherapy and immune checkpoint inhibitors [51, 52]. For example, high infiltration of IL-10+ TAMs was associated with poorer overall survival and recurrence-free survival, yet it also correlated with a better chemotherapeutic response in muscle-invasive bladder cancer (MIBC). IL-10+ TAMs with suppressive characteristics contributed to an immunoevasive tumor microenvironment, marked by exhausted CD8+ T cells, immature natural killer cells and increased expression of immune checkpoints [52]. Yang et al. investigated the correlation between peripheral blood MDSCs and tumor stage, finding that the proportion of total MDSCs in bladder cancer patients was significantly higher than in healthy donors. This increase was particularly pronounced in patients with advanced stages (T2–T4) compared to those with early stages (Ta–T1) [178]. A subsequent study by Mu et al. confirmed the significant role of MDSCs in the tumor microenvironment of bladder cancer patients. The authors also observed a stage-associated increase of MDSCs in T3 and T4 versus T1 and T2. When these MDSCs were co-cultured with CD8+ T cells, a significant inhibition of CD8+ T-cell proliferation was shown [179]. Given the emerging evidence that targeting MDSCs with ATRA—either alone or in combination with existing therapies—can boost antitumor immunity and improve clinical outcomes, this approach may also hold promise for bladder cancer patients. However, as the immunomodulatory effects of ATRA vary depending on the tumor type, *in vitro* and *in vivo* studies focusing specifically on the bladder cancer microenvironment are needed.

8. Conclusion

Vitamin A and retinoids show promise for the prevention and treatment of bladder cancer, but further research is needed to overcome current limitations and translate these findings into effective clinical practice. The findings presented in this chapter suggest that further research into the use of retinoids, their interaction with the gut microbiota and their effects on immune responses within the tumor microenvironment holds promise for the development of more effective prevention and treatment strategies for bladder cancer. Given the urgent need for more effective treatments for bladder cancer due to the high recurrence rate and the significant social and financial burden, improving the efficacy of vitamin A in the prevention and treatment of bladder cancer would be an important research endeavor.

Further preclinical studies are needed to understand the detailed molecular mechanisms of retinoid action, its effects in various combinations with chemotherapeutic and immunotherapeutic agents, in combination with microbiota-based interventions and their effects on the immune response in bladder cancer. Randomized clinical trials with larger patient and placebo groups are also needed. By raising the awareness of the importance of a vitamin A-rich diet among the general public, and especially among patients presenting for initial treatment of suspected bladder cancer, we could potentially reduce the risk of disease development and recurrence as well as improve treatment.

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Conflict of interest

The authors declare no conflict of interest.

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Trends in Health Inequalities by Household Income in Japan in the 2010s: Estimates from the National Health and Nutrition Survey Reports

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Abstract

This study aimed to estimate trends in health inequalities by household income in Japan during the 2010s, using data from the National Health and Nutrition Survey reports. Among the food intake, obesity, and lifestyle habits data presented in the 2010, 2011, 2014, and 2018 survey reports, comparable metrics included vegetable intake (g), fruit intake (g), fish intake (g), meat intake (g), obesity rate (%), rate of individuals without exercise habits (%), and smoking rate (%). First, differences between the <2 million yen and ≥ 6 million yen household income groups were calculated for each year. Then, changes in these differences across survey years were analyzed. The 95% confidence intervals for differences between income groups in each year did not include zero for many items across both men and women, indicating consistent health disparities by income. However, the 95% confidence intervals for changes across survey years crossed zero for most items, suggesting that these disparities remained largely unchanged throughout the 2010s. These findings highlight the persistence of health inequalities by household income in Japan and underscore the need for continued policy efforts to address these disparities.

Keywords: health inequalities, dietary disparity, social determinants of health, national health and nutrition survey, Japan

1. Introduction

In recent years, it has become increasingly recognized that social environments, such as income and residential areas, significantly influence human health. These factors, collectively referred to as social determinants of health, contribute to disparities in disease incidence and health outcomes, commonly known as health inequalities [1]. Substantial evidence suggests that economic inequality adversely affects health. For instance, a meta-analysis demonstrated that economic inequality increases

the relative risk of mortality [2], while another review concluded that a causal link exists between income inequality and health [3].

Economic inequality impacts health through mechanisms such as unhealthy behaviors, including poor dietary habits [4]. Higher socioeconomic status is generally associated with greater consumption of whole grains, vegetables, fruits, meats, and seafood. Conversely, lower socioeconomic status is linked to diets rich in refined grains, potatoes, fatty meats, and fried foods [5]. Furthermore, individuals with lower socioeconomic status often experience higher rates of obesity, partly due to the affordability and time efficiency of high-energy, low-nutrient foods [5–7].

Since the 2000s, Japan's economic growth has stagnated relative to other countries [8], raising concerns about heightened health risks among socially disadvantaged populations. In response, policies to address health inequalities have been introduced since the 2010s. For example, the second phase of "Health Japan 21," revised in 2012, identified reducing health disparities as a key objective [9]. Similarly, the Act for Supporting the Self-Reliance of Persons in Need, enacted in 2013 and implemented in 2015, provides life support measures, including food assistance [10, 11]. To assess the effectiveness of these policies, it is crucial to examine trends in health inequalities among the Japanese population during this period.

Previous studies in Japan have analyzed health inequalities by socioeconomic status since 1986, using data from the Comprehensive Survey of Living Conditions [12–16]. One study examining long-term trends from 1986 to 2013 found that health inequalities by income followed a cyclical pattern [12]. This pattern reflects Japan's significant economic fluctuations, including the prolonged stagnation following the collapse of the bubble economy in the 1990s, a partial recovery in the 2000s, and the impacts of the Lehman Shock in 2009 and the Great East Japan Earthquake in 2011. These fluctuations are evident in changes to Japan's unemployment rate [12]. Previous research has also explored how these economic events influenced health and diet, such as dietary changes after the Lehman Shock [17], health outcomes during Japan's "employment ice age" [18], and shifts in health disparities following the bubble economy's collapse [15]. However, the evolution of health inequalities in Japan during the 2010s remains underexplored.

The National Health and Nutrition Survey reports have regularly documented associations between household income and factors such as food intake, obesity, and lifestyle habits since the 2010s [19–22]. These reports have identified income-based disparities in food intake and adherence to dietary guidelines [23, 24]. However, no studies have comprehensively analyzed trends in these disparities over time. Therefore, this study aims to estimate trends in health disparities by household income in Japan during the 2010s, based on data from the National Health and Nutrition Survey reports.

2. Methods

This study used data on food intake, obesity, and lifestyle habits by household income from the 2010, 2011, 2014, and 2018 National Health and Nutrition Survey reports [19–22]. The analysis focused on comparable metrics, including vegetable intake (g), fruit intake (g), fish intake (g), meat intake (g), the proportion of obesity (%), the proportion of individuals without exercise habits (%), and the proportion of smokers (%). Sex-specific estimates were adjusted for age and household size. Notably, only obesity and lifestyle habit data were available for 2010, while only food intake data were available for 2011.

2.1 Analysis procedures

1. Estimation by Year and Income Category

- For each year, estimates and 95% confidence intervals were calculated for the metrics above, stratified by two household income categories: <2 million yen and ≥ 6 million yen.

2. Income-Based Differences

- Differences and their 95% confidence intervals between the two income categories were calculated for each metric and year.

3. Trend Analysis

- The differences in income-based disparities between survey years were computed (2014 minus 2010/2011, and 2018 minus 2010/2011).

2.2 Calculation of confidence intervals and standard errors

The 95% confidence intervals were calculated using the formula:

$$95\%CI = E \pm 1.96SE \quad (1)$$

For food intake in 2014 and 2018, standard errors of the estimates were provided in the National Health and Nutrition Survey reports. For food intake in 2011, since standard errors were not provided, they were estimated using the standard deviation and sample size for each household income group, with the formula:

$$SE_{\text{food intake in 2011}} = \frac{SD}{\sqrt{n}} \quad (2)$$

For obesity and lifestyle habit proportions, standard errors were calculated for all survey years using the formula:

$$SE_{\text{proportion}} = \sqrt{\frac{E(100 - E)}{n}} \quad (3)$$

Standard errors for differences between income groups or survey years were calculated as follows:

$$SE_{\text{difference}} = \sqrt{SE_{\text{group/year}_1}^2 + SE_{\text{group/year}_2}^2} \quad (4)$$

The 95% confidence intervals for these differences were then computed using the same method as above.

2.3 Definitions

In these formulas:

- *E*: Estimates (g or %)

- *CI*: Confidence interval
- *SE*: Standard error
- *SD*: Standard deviation
- *n*: Sample size

Tools.

All figures were generated using Python 3.9.7.

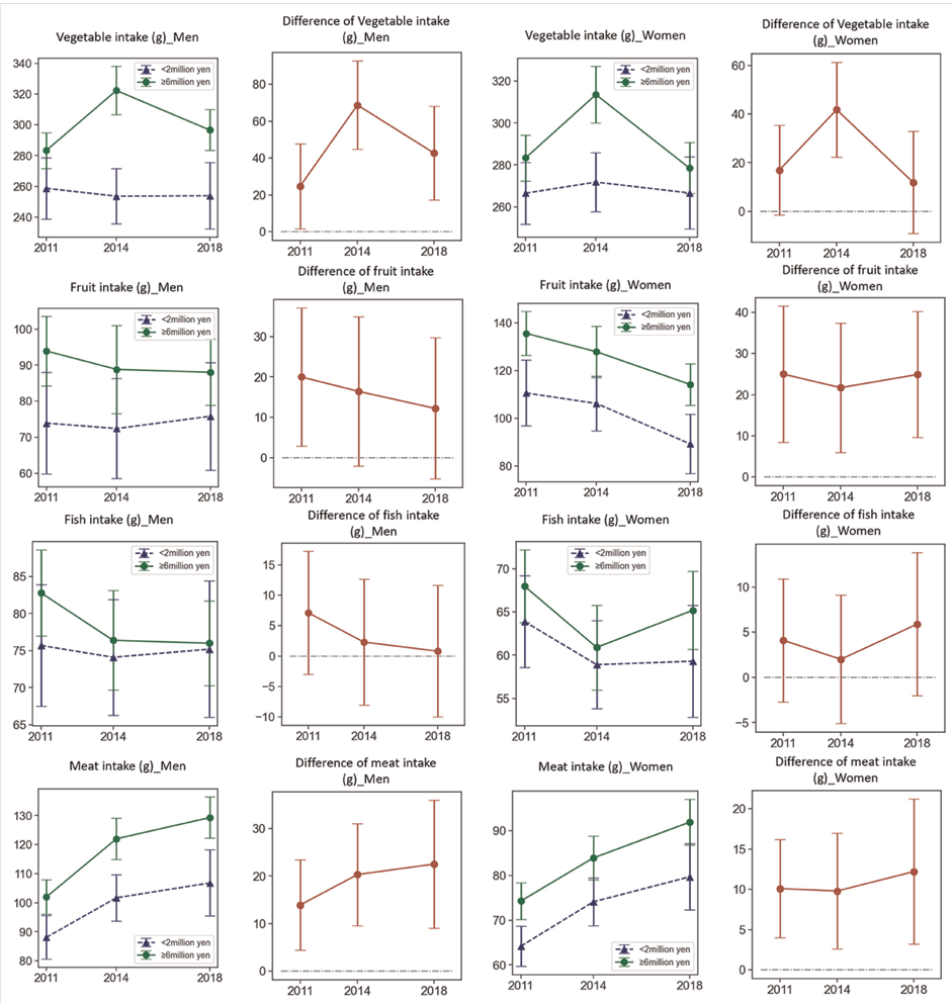


Figure 1. Trends in food intake by household income and differences by household income. The x-axis shows the survey year, and the y-axis shows the estimates (g). ●▲ represent the estimates, and error bars indicate the 95% confidence intervals. The green solid line represents households with an annual household income of 6 million yen or more, while the navy dashed line represents households with an annual household income of less than 2 million yen. The brown solid line represents the differences between income categories. The left side is for men, and the right side is for women. The gray dashed-dotted line indicates 0.

3. Results and discussion

Figures 1 and 2 depict food intake, obesity, and lifestyle habits by household income, along with trends in income-based differences over time. Detailed values for food intake, obesity, and lifestyle habits by household income are presented in Tables A1 and A2, while Table A3 provides values for income-based differences. Across many items for both men and women, the 95% confidence intervals for the differences between the <2 million yen group and the ≥ 6 million yen group did not include zero. These findings align with the results reported in the National Health and Nutrition Survey and the previous study using these data [19–24]. Specifically, for vegetable intake among men, fruit intake among women, meat intake, and smoking prevalence for both genders, the 95% confidence intervals consistently excluded zero across all survey years, indicating persistent health disparities by household income throughout the 2010s.

Figure 3 shows changes over survey years in the differences by household income. Detailed values for these changes are provided in Table A4. For most items, the 95% confidence intervals crossed zero for both men and women, suggesting that health disparities by household income remained relatively stable during the 2010s. A comparison between 2010 or 2011 and 2014 revealed that the disparity in vegetable intake and obesity

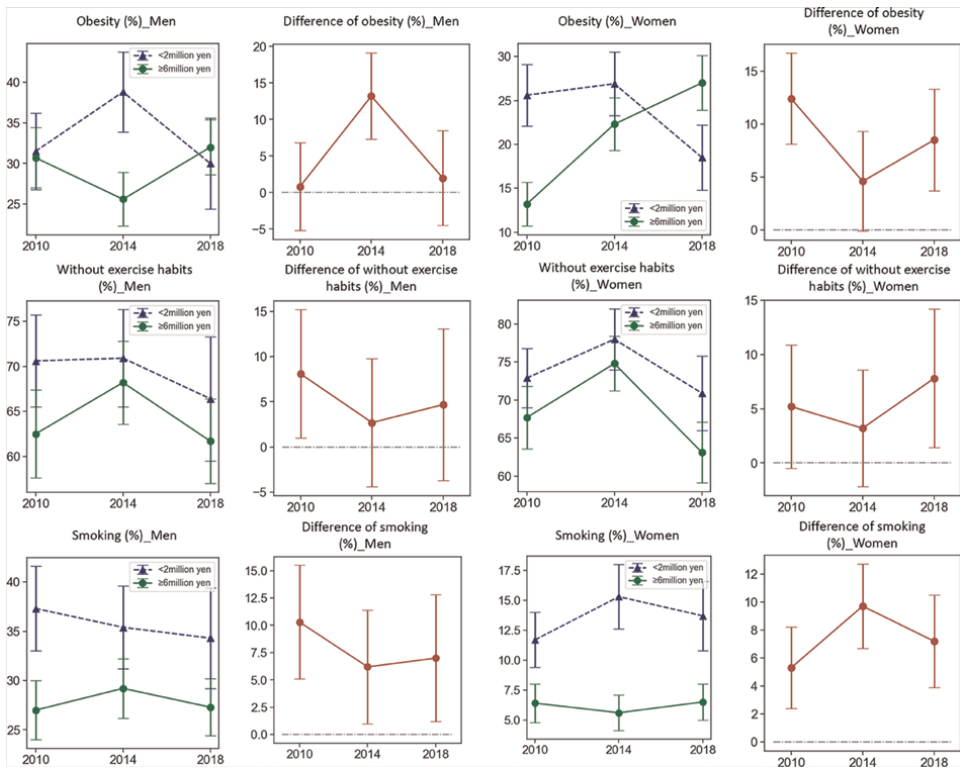


Figure 2. Trends in obesity and lifestyle habits by household income and differences by household income. The x-axis shows the survey year, and the y-axis shows the estimates (%). ●▲ represent the estimates, and error bars indicate the 95% confidence intervals. The green solid line represents households with an annual household income of 6 million yen or more, while the navy dashed line represents households with an annual household income of less than 2 million yen. The brown solid line represents the differences between income categories. The left side is for men, and the right side is for women. The gray dashed-dotted line indicates 0.

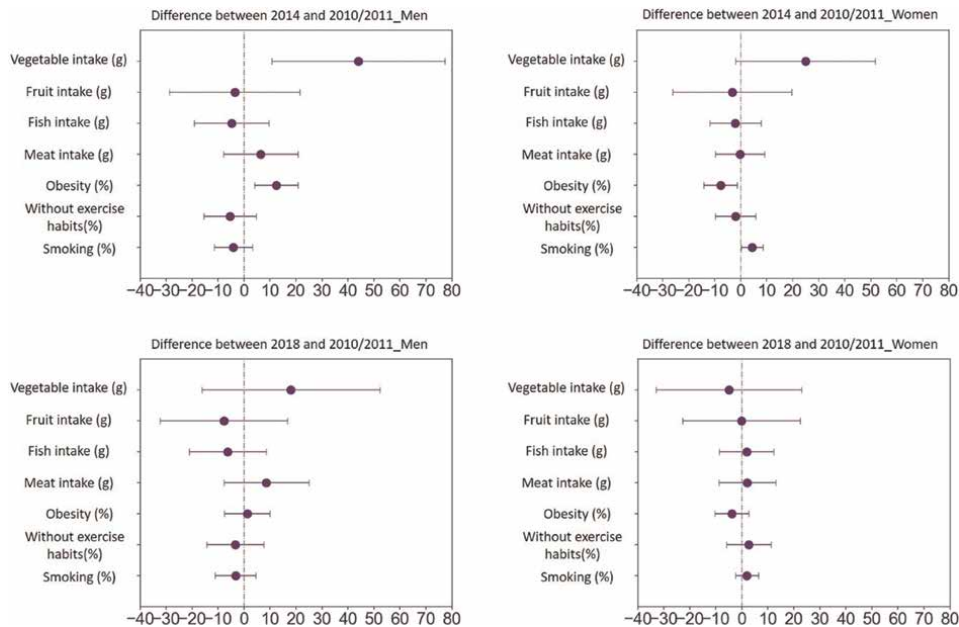


Figure 3. Differences in food intake, obesity, and lifestyle habits by household income and survey year. ● represents the estimates, and error bars indicate the 95% confidence intervals. The left side is for men, and the right side is for women. ● is marked in the negative direction if the difference is shrinking and in the positive direction if it is expanding. The gray dashed-dotted line indicates 0.

rates for men and smoking rates for women had widened, while the disparity in obesity rates for women had narrowed. However, when comparing 2010 or 2011 with 2018, these differences disappeared, implying that no significant changes occurred overall. A study examining trends in health disparities between 1986 and 2013, using self-rated health as an outcome, reported cyclical patterns of expansion and contraction in health disparities [12]. In the present study, the widening disparity observed in 2014 returned to levels seen in 2010 or 2011 by 2018, which may align with this cyclical pattern. However, the period analyzed in this study was too short, and the number of observation points too limited, to confirm this periodicity. Further investigation is required to verify these trends.

This study provides a broad estimation of trends in health disparities by household income in Japan during the 2010s, based on publicly available data from the National Health and Nutrition Survey. Future research should focus on more precise estimations using microdata from the National Health and Nutrition Survey. Additionally, since the mid-2000s, numerous studies have explored the relationship between economic conditions and nutrition or dietary habits in Japan [25]. A meta-analysis of these studies could offer a more comprehensive understanding of long-term trends in health disparities.

4. Conclusion

This study evaluated health disparities based on annual household income in Japan during the 2010s, using data from the National Health and Nutrition Survey. The findings indicate that these disparities remained largely unchanged. While some fluctuations were observed, such as a temporary widening of disparities in 2014, the

overall trends suggest a persistent pattern of health inequality associated with household income.

The persistence of these disparities underscores the need for continued and enhanced policy efforts to address social determinants of health in Japan. Interventions such as improving access to affordable, nutritious food, and promoting equitable health behaviors should be prioritized. Additionally, the cyclical nature of health disparities observed in previous studies, coupled with the limitations of this study's observation period, highlights the importance of longitudinal research to capture long-term trends and periodic fluctuations.

Future research should leverage microdata from the National Health and Nutrition Survey to enable more precise estimations and identify the underlying mechanisms driving these disparities. Meta-analyses of related studies may also provide a broader understanding of how economic conditions impact health outcomes over time. Collaborative efforts between policymakers, researchers, and public health practitioners will be essential to designing and implementing effective strategies to reduce health disparities and promote health equity across all socioeconomic groups.

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Conflict of interest

The author declares no conflict of interest.

A. Appendix

Annual household income (million yen)								
<2					≥6			
	n	Estimates g or %	95%CI lower	95%CI upper	n	Estimates g or %	95%CI lower	95%CI upper
Vegetable intake(g)								
2010	455	256.0			755	293.0		
2011	404	258.7	238.7	278.7	719	283.4	271.8	295.0
2014	423	253.6	235.6	271.6	758	322.3	306.6	338.0
2018	281	253.9	232.3	275.5	821	296.6	283.3	309.9
Fruit intake (g)								
2011	404	73.9	59.8	88.0	719	93.9	84.3	103.5
2014	423	72.4	58.5	86.3	758	88.8	76.6	101.0
2018	281	75.8	60.9	90.7	821	88.0	78.8	97.2

Annual household income (million yen)								
<2			≥6					
Fish intake(g)								
2011	404	75.7	67.5	83.9	719	82.8	77.0	88.6
2014	423	74.1	66.3	81.9	758	76.4	69.7	83.1
2018	281	75.2	66.0	84.4	821	76.0	70.3	81.7
Meat intake(g)								
2011	404	88.1	80.6	95.6	719	102.0	96.1	107.9
2014	423	101.7	93.7	109.7	758	122.0	114.9	129.1
2018	281	106.8	95.4	118.2	821	129.3	122.2	136.4
Obesity (%)								
2010	380	31.5	26.8	36.2	600	30.7	27.0	34.4
2014	383	38.8	33.9	43.7	659	25.6	22.3	28.9
2018	260	30.0	24.4	35.6	732	32.0	28.6	35.4
Without exercise habits (%)								
2010	302	70.6	65.5	75.7	381	62.5	57.6	67.4
2014	267	70.9	65.5	76.3	393	68.2	63.6	72.8
2018	179	66.4	59.5	73.3	407	61.7	57.0	66.4
Smoking (%)								
2010	497	37.3	33.0	41.6	815	27.0	24.0	30.0
2014	499	35.4	31.2	39.6	867	29.2	26.2	32.2
2018	337	34.3	29.2	39.4	925	27.3	24.4	30.2
Vegetable intake data for 2010 were not shown in Figure 1 .								

Table A1.
Changes in food intake, obesity, and lifestyle habits by annual household income (Men).

Annual household income (million yen)								
<2					≥6			
	n	Estimates g or %	95%CI lower	95%CI upper	n	Estimates g or %	95%CI lower	95%CI upper
Vegetable intake(g)								
2010	678	270.0			829	305.0		
2011	621	266.5	251.7	281.3	793	283.4	272.4	294.4
2014	620	271.8	257.7	285.9	842	313.6	300.1	327.1
2018	453	266.6	249.4	283.8	900	278.5	266.3	290.7
Fruit intake (g)								
2011	621	110.6	96.8	124.4	793	135.6	126.4	144.8
2014	620	106.2	94.8	117.6	842	127.9	117.1	138.7
2018	453	89.3	76.8	101.8	900	114.2	105.4	123.0

Annual household income (million yen)								
<2			≥6					
Fish intake(g)								
2011	621	63.9	58.6	69.2	793	68.0	63.8	72.2
2014	620	58.9	53.8	64.0	842	60.9	56.0	65.8
2018	453	59.3	52.8	65.8	900	65.2	60.7	69.7
Meat intake(g)								
2011	621	64.2	59.7	68.7	793	74.3	70.2	78.4
2014	620	74.1	68.8	79.4	842	83.9	79.0	88.8
2018	453	79.7	72.3	87.1	900	91.9	86.8	97.0
Obesity (%)								
2010	587	25.6	22.1	29.1	686	13.2	10.7	15.7
2014	576	26.9	23.3	30.5	750	22.3	19.3	25.3
2018	431	18.5	14.8	22.2	804	27.0	23.9	30.1
Without exercise habits (%)								
2010	492	72.9	69.0	76.8	505	67.7	63.6	71.8
2014	417	78.0	74.0	82.0	546	74.8	71.2	78.4
2018	325	70.9	66.0	75.8	560	63.1	59.1	67.1
Smoking (%)								
2010	719	11.7	9.4	14.0	877	6.4	4.8	8.0
2014	705	15.3	12.6	18.0	935	5.6	4.1	7.1
2018	529	13.7	10.8	16.6	1001	6.5	5.0	8.0
Vegetable intake data for 2010 were not shown in Figure 1 .								

Table A2.
Changes in food intake, obesity, and lifestyle habits by annual household income (Women).

Men				Women		
Difference	95%CI lower	95%CI upper		Difference	95%CI lower	95%CI upper
Vegetable intake(g)						
2010	37.0			35.0		
2011	24.7	1.6	47.8	16.9	−1.5	35.3
2014	68.7	44.8	92.6	41.8	22.3	61.3
2018	42.7	17.4	68.0	11.9	−9.2	33.0
Fruit intake (g)						
2011	20.0	2.9	37.1	25.0	8.5	41.5
2014	16.4	−2.1	34.9	21.7	6.0	37.4
2018	12.2	−5.3	29.7	24.9	9.6	40.2

	Men			Women		
	Difference	95%CI lower	95%CI upper	Difference	95%CI lower	95%CI upper
Fish intake(g)						
2011	7.1	−3.0	17.2	4.1	−2.7	10.9
2014	2.3	−8.0	12.6	2.0	−5.1	9.1
2018	0.8	−10.0	11.6	5.9	−2.0	13.8
Meat intake(g)						
2011	13.9	4.4	23.4	10.1	4.0	16.2
2014	20.3	9.6	31.0	9.8	2.6	17.0
2018	22.5	9.1	35.9	12.2	3.2	21.2
Obesity (%)						
2010	0.8	−5.2	6.8	12.4	8.1	16.7
2014	13.2	7.3	19.1	4.6	−0.1	9.3
2018	2.0	−4.5	8.5	8.5	3.7	13.3
Without exercise habits (%)						
2010	8.1	1.0	15.2	5.2	−0.5	10.9
2014	2.7	−4.4	9.8	3.2	−2.2	8.6
2018	4.7	−3.7	13.1	7.8	1.4	14.2
Smoking (%)						
2010	10.3	5.1	15.5	5.3	2.4	8.2
2014	6.2	1.0	11.4	9.7	6.7	12.7
2018	7.0	1.2	12.8	7.2	3.9	10.5

*Difference: Difference in estimated values between <2 million yen and ≥ 6 million yen.
Vegetable intake data for 2010 were not shown in Figure 1.*

Table A3.

Changes in the differences according to annual household income of food intake, obesity, and lifestyle habits.

	Men			Women		
	DID	95%CI lower	95%CI upper	DID	95%CI lower	95%CI upper
Difference between 2014 and 2010/2011 (2014–2010/2011)						
Vegetable intake(g)	44.0	10.7	77.3	24.9	−2.0	51.8
Fruit intake (g)	−3.6	−28.8	21.6	−3.3	−26.1	19.5
Fruit intake (g)	−4.8	−19.2	9.6	−2.1	−11.9	7.7
Meat intake(g)	6.4	−7.9	20.7	−0.3	−9.8	9.2
Obesity (%)	12.4	4.0	20.8	−7.8	−14.2	−1.4
Without exercise habits (%)	−5.4	−15.4	4.6	−2.0	−9.8	5.8
Smoking (%)		−11.5	3.3	4.4	0.2	8.6

	Men			Women		
	DID	95%CI lower	95%CI upper	DID	95%CI lower	95%CI upper
Difference between 2018 and 2010/2011 (2018–2010/2011)						
Vegetable intake(g)	18.0	–16.3	52.3	–5.0	–33.0	23.0
Fruit intake (g)	–7.8	–32.3	16.7	–0.1	–22.7	22.5
Fruit intake (g)	–6.3	–21.1	8.5	1.8	–8.6	12.2
Meat intake(g)	8.6	–7.8	25.0	2.1	–8.8	13.0
Obesity (%)	1.2	–7.6	10.0	–3.9	–10.4	2.6
Without exercise habits (%)	–3.4	–14.4	7.6	2.6	–5.9	11.1
Smoking (%)	–3.3	–11.1	4.5	1.9	–2.5	6.3
DID: Difference in differences based on annual household income and survey years						

Table A4.
Difference in differences based on annual household income and survey years.

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Use of Different Dietary Indexes for Predicting the Quality of Diet and Risk of Chronic Disease

Mehran Rahimlou and Fatemeh Maleki Sedgi

Abstract

Dietary patterns play a pivotal role in determining overall health and the risk of chronic diseases. In recent years, various dietary indexes have been developed to evaluate diet quality and predict health outcomes. Each index provides unique insights into specific dietary aspects, such as adherence to dietary guidelines, glycemic control, inflammatory potential, acid-base balance, and insulin dynamics. These tools enable researchers and healthcare professionals to better understand the complex relationship between diet and chronic diseases, including cardiovascular disease, type 2 diabetes, obesity, cancer, osteoporosis, and mental health disorders. In conclusion, the integration of dietary indexes into research and practice offers a robust framework for evaluating diet quality and its impact on chronic disease prevention, emphasizing the need for balanced, nutrient-dense, and anti-inflammatory dietary patterns to promote overall health and well-being.

Keywords: dietary patterns, Mediterranean diet score, glycemic index, Alternate Healthy Eating Index, nutrition

1. Introduction

Diet is a complex and multifaceted aspect of human health that is frequently summarized using dietary indexes, designed to simplify dietary analysis [1]. These indexes provide a structured means to assess diet by focusing on levels of nutrient intake or food group consumption patterns associated with healthful eating. Analyzing dietary patterns, rather than examining individual nutrients or food items, offers significant advantages, as it accounts for the way in which foods and nutrients are typically consumed together, often with interrelated effects on health [2].

In nutritional epidemiology, analyzing overall dietary patterns has become a prominent approach, particularly in recent years, to assess diet in a comprehensive way [3, 4]. Dietary indexes represent a methodological tool that facilitates holistic evaluations of diet quality [5]. Unlike empirical methods, such as principal components analysis, cluster analysis, or reduced rank regression, dietary indexes offer the advantage of straightforward interpretability [6]. They provide a summary score

indicating the level of adherence to dietary recommendations or the overall quality of an individual's diet, which can be easily communicated and understood.

This simplification makes dietary indexes particularly useful, not only for health professionals but also for a broader audience, including consumers, non-dietetic health professionals (like nurses), and stakeholders such as policymakers [6]. Policymakers, although often lacking specialized nutrition knowledge, are tasked with making informed decisions about public health initiatives. Providing them with accessible, evidence-based dietary information is critical to shaping effective health policies that meet population needs [6].

Dietary indexes have been widely applied in adult populations, yielding valuable insights into relationships between diet and chronic disease risk factors, as well as mortality or diet quality assessment [5, 7]. Numerous studies have also explored the associations between dietary indexes, diet quality, and health outcomes, illustrating the practical relevance of these tools in identifying diet-related risks and benefits [8, 9]. Most established dietary indexes draw upon principles from the Mediterranean diet or other widely endorsed dietary guidelines, such as the Dietary Guidelines for Americans, which are tailored for adult populations [10–12].

In summary, dietary indexes not only aid in simplifying dietary assessments but also play a pivotal role in advancing public health nutrition by highlighting key dietary patterns linked to chronic disease prevention and overall health.

Given the importance of examining individual dietary intakes and patterns in relation to nutritional recommendations and dietary guidelines, assessing diet quality is essential. Furthermore, the association between dietary indexes and the risk of developing common chronic diseases, such as cardiovascular disease, diabetes, and others, is highly significant in today's societies. The aim of this chapter is to explore the relationship between various dietary indexes in predicting diet quality and the likelihood of chronic disease development.

2. Common dietary indexes and their applications

2.1 Dietary quality indexes

Despite numerous nutritional recommendations and dietary guidelines, non-communicable chronic diseases (NCCDs) continue to prevail in both developed and developing nations [13]. The importance of diet quality and physical activity in slowing the progression of chronic diseases has become increasingly evident. Strong and continually expanding evidence highlights the role of a healthy lifestyle comprising a balanced diet, physical activity, abstaining from alcohol, not smoking, and managing stress effectively as essential for wellness programs and interventions for both primary and secondary prevention of NCCDs [14]. Achieving good health and optimal functionality throughout life is possible but requires a lifestyle approach that includes a nutrient-dense, energy-balanced diet, along with regular physical activity to help regulate body weight and support various physiological functions [15, 16].

Certain dietary patterns worldwide are associated with positive health outcomes. Notable examples of beneficial eating patterns include the Mediterranean-style diet and the DASH (Dietary Approaches to Stop Hypertension) diet, both of which are linked to improved health markers [17, 18]. However, a major public health challenge remains: promoting widespread adoption of these healthful dietary patterns despite

significant societal pressures that drive unhealthy choices and behaviors [15]. There is, therefore, a need for simple, affordable methods to assess and monitor diet quality globally. Dietary Quality Indices (DQIs) have been developed to evaluate overall diet quality and classify individuals based on the degree to which their dietary habits align with “healthy” standards [19]. Now, we will examine several commonly used dietary indexes that are essential for assessing diet quality. These indexes have been widely adopted in nutritional research and public health due to their ability to provide a comprehensive measure of diet quality based on established dietary recommendations. By analyzing dietary patterns through these indexes, researchers and healthcare professionals can gain valuable insights into how well individuals’ diets align with optimal health standards. This review will cover the characteristics, applications, and health implications of each index, highlighting their role in dietary assessment and chronic disease prevention.

2.1.1 Healthy Eating Index (HEI)

The Dietary Guidelines for Americans (DGA) form the foundation of U.S. government nutrition policies and serve as the basis for all federal dietary recommendations. Since their inception in 1980, the Dietary Guidelines for Americans (DGA) have been reviewed and updated every 5 years based on evidence to incorporate the latest advancements in nutrition science. To align with these guidelines, the Healthy Eating Index (HEI) was developed as a tool to evaluate overall diet quality independently of dietary quantity. Updated versions, such as HEI-2010 and HEI-2015, were introduced with each iteration of the DGA to incorporate the latest recommendations [1, 20, 21]. All HEI versions up to HEI-2015 were designed for individuals aged 2 years and older [22]. However, with the release of the 2020–2025 DGA, USDA Dietary Patterns for toddlers were introduced for the first time, prompting the development of a separate index, the HEI-Toddlers-2020, specifically for children aged 12 to 23 months [23].

The HEI-2020, designed for those aged 2 years and older, was also released to align with the 2020–2025 DGA. Importantly, no substantive changes were made between the HEI-2015 and HEI-2020 [22]. This consistency adheres to the HEI’s guiding principles, as modifications without new evidence could be misleading. The naming convention of HEI-2020 reflects its alignment with the latest dietary guidelines. The components and standards remained the same between HEI-2015 and HEI-2020, ensuring continuity and avoiding reliance on extreme calorie levels that are only applicable to specific age or sex groups. Maximum standards for most components, except Sodium, are based on the least restrictive recommendations across 1200 to 2400 calorie levels, with Sodium adhering to a limit of 2300 mg [22]. Minimum standards for components such as total fruits, whole fruits, vegetables, whole grains, dairy, and protein foods are set at zero per 1000 kcal, while others like fatty acids, refined grains, added sugars, saturated fats, and sodium are determined based on intake percentiles from the most recent National Health and Nutrition Examination Survey (NHANES) [24].

Evaluation, a crucial final step in the development of the HEI, ensures the tool reflects dietary guidance accurately. Content validity is examined by comparing key recommendations from the 2020–2025 DGA to the components of the HEI-2020. All recommendations related to diet quality through food choices are represented within the HEI-2020 components [22]. This alignment underscores the HEI’s effectiveness as a measure of total diet quality.

2.1.2 Mediterranean diet score (MDS)

The Mediterranean diet (MedD) first gained global attention for its cardiovascular benefits through the work of Ancel Keys [25]. Since then, research has highlighted its role in reducing overall mortality and the risk of chronic diseases, such as diabetes, certain cancers, and neurodegenerative disorders [26]. The first formal scoring system for the MedD was introduced in 1995 by Trichopoulou and colleagues, commonly referred to as the Trichopoulou Mediterranean diet score (T-MDS) [27]. Initially, this index included a range of food groups, but it underwent several modifications over the years. In 2003, fish was added as a beneficial component, and by 2005, the lipid ratio was adjusted to include polyunsaturated fatty acids (PUFAs) alongside the traditional monounsaturated-to-saturated fat ratio [28, 29].

In addition to the T-MDS, several other MedD scoring systems have been developed. One of the most notable is the Panagiotakos Mediterranean Diet Score (MedDietScore), introduced in 2006 [30]. This index is based on the MedD pyramid and consists of 11 food or food group components, each scored on a 0 to 5 scale, leading to a total score ranging from 0 to 55 [31]. Unlike the T-MDS, the MedDietScore considers potatoes and olive oil as positive contributors, excludes nuts, and treats white meat and poultry as negative factors. Initially designed for monthly food frequency questionnaire (FFQ) data, it was later adapted to weekly intakes for easier application [30].

The Mediterranean-Like Diet Score, introduced in 2011, further adapted the T-MDS by modifying the classification of meat and dairy products [32]. Another widely used tool, the 14-point Mediterranean Diet Adherence Score (MEDAS), was developed for the PREDIMED study as a quick self-assessment of adherence to the MedD [33]. This tool, which can be used with FFQ data or dietary records, has been adapted globally and is recognized for its simplicity and reliability in various research and clinical settings [34, 35].

Over the past 25 years, MedD scoring systems have evolved to reflect the changing dietary habits and lifestyles in Mediterranean regions, particularly among younger populations [31]. Initially designed to evaluate the dietary patterns of Mediterranean adults, these scoring systems are now frequently applied in non-Mediterranean countries with varying levels of adaptation and validation. One of the most commonly used adaptations is the Alternative Mediterranean Diet Scale (aMed), introduced by Fung and colleagues in 2005, which modifies the T-MDS to better suit non-Mediterranean populations [36, 37].

Among the available tools, the MEDAS has gained significant popularity due to its brevity, straightforward questions, and ease of scoring. Its applicability has been validated in clinical settings, including rehabilitation units, where it has been enhanced with visual aids to define portion sizes [38]. While the MEDAS is ideal for rapid screening, other scoring systems with more detailed grading are better suited for intervention studies and clinical monitoring, as they can capture partial adherence to MedD principles.

Despite its widespread use, there is no universally accepted MedD scoring system. This lack of standardization arises from the diverse ways in which the MedD is interpreted and implemented across different populations and regions. Scoring systems vary in their components, measurement scales, statistical cut-offs, and the weight assigned to each dietary element. For example, while some systems use the MUFA-to-SFA ratio as a key indicator, others incorporate specific food items like nuts or olive oil [31].

A major limitation in the existing literature is the inconsistency in validation and reproducibility of MedD scoring systems. As highlighted by a comprehensive review by Zaragoza-Martini and colleagues, many of these tools lack thorough validation, which affects their reliability across different populations [39]. Some experts have suggested that incorporating key nutrients, rather than just food components, could enhance standardization and lead to a more universal MedD scoring system [31]. However, focusing solely on nutrients may overlook critical lifestyle aspects of the MedD, such as meal patterns, social eating behaviors, and physical activity.

To improve the accuracy and applicability of MedD scoring systems, future research should focus on developing a comprehensive approach that combines both nutrient and food-based components. This could include expanding the current MUFA-to-SFA ratio to incorporate fiber and added sugar recommendations, thereby providing a more holistic assessment of dietary quality [31]. Additionally, traditional MedD behaviors, such as consuming the largest meal at lunch, limiting snacking, and engaging in regular physical activity, should be integrated into scoring systems to better capture the essence of the Mediterranean lifestyle [40].

2.1.3 Alternate Healthy Eating Index (AHEI)

The Alternate Healthy Eating Index (AHEI) was developed to enhance the predictive capacity of the original HEI by focusing on food choices and nutrient sources that are more strongly associated with reduced chronic disease risk, particularly cardiovascular disease (CVD) [41–43]. Unlike the original HEI, which showed moderate inverse associations with CVD but no significant impact on cancer risk, the AHEI was specifically designed to better capture dietary patterns linked to improved health outcomes [44, 45].

The AHEI consists of nine components, some of which were adapted from the original HEI, such as fruits and vegetables, though with notable modifications [46]. For instance, potatoes and potato products were excluded from the vegetable category to better reflect healthful vegetable consumption. The scoring system assigns each component a value from 0 to 10, where 10 indicates full adherence to dietary recommendations, and 0 reflects non-adherence [47].

In contrast to the original HEI, which provided equal credit for all types of meat, the AHEI assigns higher scores for consuming fish and poultry over red or processed meats [48]. This adjustment is intended to emphasize the health benefits of replacing red meat with white meat. Additionally, the ratio of polyunsaturated to saturated fats (P:S) is incorporated, highlighting the importance of fat quality over quantity. The AHEI also includes components for cereal fiber and moderate alcohol consumption, reflecting their role in reducing chronic disease risk.

When applied to two large prospective cohort studies, the AHEI demonstrated significantly stronger associations with chronic disease risk compared to the original HEI [44, 45]. Men and women whose diets closely aligned with the AHEI guidelines exhibited a 20% and 11% lower risk of major chronic diseases, respectively. This reduction was primarily driven by a substantial decrease in CVD risk, with men and women in the highest AHEI quintile experiencing a 39% and 28% lower risk of CVD, respectively, compared to those in the lowest quintile.

While the AHEI showed a robust inverse relationship with CVD, its association with cancer risk was less pronounced. This discrepancy may be attributed to the limited knowledge of diet-cancer relationships compared to diet-CVD associations.

Additionally, the AHEI's generalized fruit and vegetable component may dilute the effects of specific types of produce that are more strongly linked to cancer prevention.

2.2 Disease-specific indexes

2.2.1 Glycemic index (GI) and glycemic load (GL)

The relationship between the carbohydrate content of foods and their blood glucose response is more complex than previously understood [49]. Traditional methods that measure available carbohydrates fail to accurately predict postprandial glycemic responses. This gap has driven the development of complementary metrics, including the glycemic index (GI) and glycemic load (GL), to manage glycemic responses effectively.

2.2.1.1 Definition and calculation of GI and GL

The GI measures the impact of a food's carbohydrate content on blood glucose levels compared to pure glucose [50]. It is calculated using the following formula [51]:

$$GI = \left(\text{IAUC food} / \text{IAUC glucose} \right) \times \left(\text{Wt glucose} / \text{Wt available carbohydrate in food} \right) \times 100\% \quad (1)$$

This method standardizes the response to a fixed carbohydrate amount, typically 50 g, regardless of typical portion sizes.

The GL integrates the GI and the quantity of carbohydrate consumed to provide a cumulative measure of glycemic exposure over time [52]. It is calculated as [50]:

$$GL = GI / 100 \times P \times \text{weight of food} \quad (2)$$

where P is the proportion of available carbohydrates in the food. Unlike GI, GL accounts for portion sizes but does not differentiate between meal patterns, such as frequent low-GI meals versus infrequent high-GI meals.

2.2.1.2 International tables of glycemic index and glycemic load values

The fourth edition of the International Tables of Glycemic Index and Glycemic Load Values includes over 4000 items, representing a 60% increase since the 2008 edition [53]. These tables are essential resources for clinicians, dietitians, researchers, food scientists, and consumers. They assist in estimating dietary GI and GL by mapping values to food items in food composition databases, food records, or FFQs [54–56]. The tables also support diabetes educators and policymakers in developing dietary guidelines and therapeutic strategies [53].

2.2.1.3 Patterns in glycemic index and food types

Analysis of the data reveals consistent trends across food groups. Dairy products, legumes, pasta, and fruits generally have low GIs (≤ 55), with consistent results worldwide. Cereals, including whole-grain options, show greater variability due to differences in processing methods [53]. While potatoes and rice are often high-GI foods, low-GI varieties have been developed through research.

2.2.1.4 Glycemic index, glycemic load, and disease risk

Recent studies and meta-analyses underscore the relevance of GI and GL in managing and preventing chronic diseases [57, 58]. High-GI and GL diets are strongly linked to increased risks of type 2 diabetes (T2D), coronary heart disease (CHD), and other conditions, independent of dietary fiber intake.

In type 2 diabetes, quantitative dose-response analyses reveal robust correlations between postprandial glycemic markers (GI and GL) and disease development [57]. Adjusting GL to a common metric (e.g., a 2000 kcal diet) aligns global and local risk models, emphasizing the complementary role of GI and GL in predicting diabetes risk. Studies estimate a 90% increase in diabetes incidence globally, supported by Bradford-Hill criteria confirming probable causality [57, 59].

Regarding coronary heart disease, based on recent studies, strong relative risks (RRs) exceeding 1.20, with lower confidence limits above 1.10, highlight the impact of high-GI and GL diets across global populations [60]. The risks are more pronounced at a global level than within specific regions, reinforcing the significance of GI and GL as markers of carbohydrate food quality in dietary guidelines.

2.2.2 Dietary Inflammatory Index (DII)

Extensive research underscores the pivotal role of diet in managing chronic inflammation [61–63]. In light of this, the Dietary Inflammatory Index (DII) was developed as a tool to classify individuals' diets on a spectrum from strongly anti-inflammatory to strongly pro-inflammatory [62]. First introduced in 2009, the DII was validated using longitudinal data from the Seasonal Variation in Blood Lipids (SEASONS) study, with C-reactive protein (CRP) serving as the primary biomarker [64].

Work on the DII began in 2004, spurred by significant advancements in understanding the relationship between inflammation, health, and diet [65, 66]. The initial version of the DII, released in 2009, was based on a thorough review of 927 peer-reviewed articles published up to 2007 [67]. These studies examined the associations between various dietary factors and six key inflammatory biomarkers: IL-1 β , IL-4, IL-6, IL-10, TNF- α , and CRP. Importantly, dietary factors were not predefined, enabling a broad and unbiased inclusion of data.

Despite being the first dietary index to use empirical evidence linking diet and inflammation an essential factor in the development of many chronic diseases, the initial DII faced limited adoption in the biomedical field [68, 69]. To address its shortcomings, the scoring algorithm underwent refinements. These improvements enhanced the validity of the index by standardizing dietary component intake to global distributions and calculating centered percentiles, thereby avoiding the arbitrariness of raw intake units [62]. This method also reduced the influence of extreme values, improving the distribution of DII scores [64].

The revised DII is a versatile and reliable tool that can be applied to any population with available dietary data. Its value is further amplified by its ability to generate comparable results across diverse populations. For instance, a DII score of -2.0 holds the same significance whether calculated in Ontario, Canada; Peshawar, Pakistan; or Bruges, Belgium [70–73]. Lower scores denote a more anti-inflammatory diet, while higher scores indicate a more pro-inflammatory one [74]. While a comprehensive list of dietary factors is typically obtained from detailed sources such as 24-hour dietary recalls or food records, the DII is flexible enough to work with dietary data from any

source [64]. Additionally, it offers a framework for individuals to set dietary goals aimed at reducing inflammation, potentially lowering the risk of chronic diseases.

The DII has been extensively studied for its associations with various diseases, emphasizing its utility in understanding the relationship between diet and health outcomes. A pro-inflammatory diet, indicated by a higher DII score, has consistently been linked to an elevated risk of non-communicable diseases (NCDs) and increased mortality [75]. Recent data from large Spanish prospective studies, involving 18,566 participants, provide robust evidence that inflammatory mechanisms mediate the relationship between an unhealthy diet and premature death [76]. A meta-analysis incorporating these findings, along with data from 10 previous studies, revealed a 23% higher risk of all-cause mortality for individuals with the most pro-inflammatory diets compared to those with the most anti-inflammatory diets [76].

Inflammation plays a foundational role in various cancer-related mechanisms, such as oxidative and nitrative DNA damage, genetic instability, insulin resistance, and vascular dysfunction [77–81]. Numerous studies, including over 100 publications examining the DII in relation to cancer at different organ sites, have demonstrated a strong positive association between a pro-inflammatory diet and both cancer risk and mortality [82–84]. Meta-analyses conducted by independent research groups further support these findings, underscoring the detrimental impact of inflammatory diets on cancer outcomes.

The DII has also been associated with cardiometabolic diseases, encompassing conditions like insulin resistance, metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), and cardiovascular disease (CVD) [85]. Systematic reviews and meta-analyses have generally found that higher DII scores are associated with increased risks of obesity, CVD, and CVD-related mortality, although the relationship with MetS remains less consistent [86, 87].

Emerging evidence suggests that diet-induced inflammation may influence respiratory health across the lifespan [88, 89]. Anti-inflammatory dietary components appear to have protective effects on respiratory outcomes [90, 91].

Persistent low-grade inflammation is also linked to negative mental health outcomes [92, 93]. For example, a meta-analysis by Wang et al., which included data from four prospective and two cross-sectional studies involving 49,584 subjects, found that individuals with the highest DII scores had a 23% greater risk of depression compared to those with the lowest scores [74]. Additional studies using data from the UK Biobank ($n = 68,879$) observed higher DII scores among individuals with schizophrenia and major depressive disorder, further supporting the link between pro-inflammatory diets and mental health disorders [94].

Inflammation also contributes to the progression of musculoskeletal conditions such as osteoarthritis, osteoporosis, and fractures [95–98]. Findings from the Women's Health Initiative cohort study, involving 161,191 postmenopausal women, revealed that those with the most anti-inflammatory diets experienced the smallest bone mineral density (BMD) loss over 6 years [75]. Stratified analyses indicated greater hip fracture risk but lower total and lower-arm fracture risk among women with higher DII scores [98]. Similarly, data from the Korean National Health and Nutrition Examination Surveys (KNHANES) and studies in postmenopausal Iranian women suggest that a pro-inflammatory diet is a risk factor for lower BMD and increased osteoporosis risk [99, 100].

In the context of male fertility, recent findings suggest that a diet with a higher anti-inflammatory potential may be associated with increased sperm count and

motility, although it does not appear to significantly affect sperm morphology [101]. These results highlight the critical role of diet as a modifiable lifestyle factor that regulates inflammation and can influence the risk of male infertility. Separate research corroborates this, demonstrating that dietary modifications can effectively reduce inflammation and mitigate infertility risks [102, 103].

2.3 Emerging dietary indexes

2.3.1 Potential renal acid load (PRAL)

Chronic non-communicable diseases (CNDs), such as cardiovascular disease, cancer, chronic respiratory diseases, and diabetes, account for approximately 70% of deaths in developing countries, making them a significant public health concern [104]. The role of diet in the progression and prevention of CNDs has been well-documented, with growing attention on the impact of diet on acid-base balance and the health repercussions of metabolic acidosis (MA) [105].

The potential renal acid load (PRAL) concept, introduced by Remer and Manz in 1994, estimates the acid or base released into the circulation based on the nutrient profile of the diet [106]. PRAL is calculated by considering the absorption rates of nutrients, the balance of ions such as calcium, magnesium, and potassium, and the dissociation of phosphate at a pH of 7.4. Foods with a positive PRAL increase acid production in the body, while those with a negative PRAL increase alkalinity. For instance, meats, eggs, cheese, and whole grains have positive PRAL values, whereas fruits and vegetables have negative PRAL values. Milk and fats are considered neutral.

Diet plays a central role in maintaining acid-base balance. Once ingested, dietary components influence metabolic processes that regulate arterial pH through interactions between the lungs, kidneys, and buffer systems [105]. The kidneys eliminate acid-forming byproducts, and PRAL provides a useful measure to assess the net effect of dietary acid and base production. Diets high in protein and phosphorus and low in potassium, calcium, and magnesium are acidogenic and contribute to low-grade metabolic acidosis, which has significant long-term health implications [107].

2.3.1.1 Impact on metabolic and musculoskeletal health

Low-grade metabolic acidosis leads to increased cortisol secretion and reduced muscle mass by promoting proteolysis and inhibiting protein synthesis [108]. This condition is associated with sarcopenia, insulin resistance, and an elevated risk of T2DM and CVD [109]. Studies have shown that diets with a high acid load are linked to reduced muscle reserves and frailty, particularly in elderly populations [110, 111]. For example, Japanese women consuming high-PRAL diets showed a high prevalence of frailty [112].

Metabolic acidosis also affects bone health by activating osteoclasts and inhibiting osteoblast activity, leading to calcium and phosphorus release from bones to buffer hydrogen ions. Over time, this can result in osteodystrophy, osteoporosis, and increased fracture risk [113, 114]. Children consuming high-PRAL diets have been shown to have lower cortical bone density, while postmenopausal women with high-PRAL diets demonstrate increased risks of femoral osteopenia and fractures [115–117].

2.3.1.2 PRAL and hypertension

Metabolic acidosis and diets with high PRAL values contribute to increased blood pressure (BP) through mechanisms such as heightened cortisol secretion, altered renal excretion of calcium and magnesium, and reduced renal citrate excretion [118]. While some studies, such as those by Zhang et al., found a strong association between high PRAL and hypertension, other research yielded inconsistent results [119]. A German study identified a 45% greater risk of developing hypertension in individuals with elevated PRAL values [120].

2.3.1.3 PRAL and insulin resistance

Diets with high PRAL values reduce insulin sensitivity by altering insulin receptor expression and reducing AKT phosphorylation. This contributes to hyperglycemia and insulin resistance (IR), increasing the risk of T2DM [105]. Studies in pregnant women have also linked high PRAL diets to gestational diabetes mellitus (GDM), with associated increases in total cholesterol and LDL cholesterol [121]. Longitudinal studies, such as those by Fagherazzi et al., confirm the association between PRAL and T2DM risk in large cohorts [122].

2.3.1.4 PRAL and kidney health

In response to MA, the kidneys increase urinary excretion of phosphorus, chloride, and sodium while reducing citrate excretion, leading to acidified urine and an increased risk of kidney stones [123]. Several studies have shown that individuals with high PRAL and net endogenous acid production (NEAP) scores have a greater risk of developing renal stones [124, 125].

2.3.1.5 Dietary modifications to reduce acid load

Monitoring acid-base balance through non-invasive methods is crucial for managing the clinical implications of low-grade metabolic acidosis. Dietary changes, such as incorporating more fruits and vegetables and reducing the intake of acidogenic foods, can help reduce PRAL and improve health outcomes [126, 127]. Dairy products, which are neutral in PRAL, can be included to meet protein needs without increasing acid load [128]. Reducing processed foods and beverages containing phosphorus additives, such as soft drinks and industrialized products, can further decrease dietary acid load [129]. The routine consumption of mineral water or bicarbonate-enriched beverages has also been shown to raise urinary pH and promote a better acid-base balance [130]. In conclusion, PRAL serves as an essential tool for evaluating the acidogenic or alkalogenic potential of diets.

2.3.2 Dietary Insulin Index

The Dietary Insulin Index is emerging as a significant dietary factor for understanding the insulinemic potential of various foods based on their macronutrient composition [131]. Unlike other indices, such as the GI and GL, which primarily focus on carbohydrate intake, the Dietary Insulin Index captures the insulin response to both carbohydrates and proteins. It measures the insulin response to specific foods

compared to an equal-energy portion of a reference food, such as glucose or white bread, offering a more nuanced perspective on postprandial insulin and glucose dynamics [132].

2.3.2.1 Dietary Insulin Index and chronic disease risk

Numerous studies have investigated the relationship between Dietary Insulin Index and chronic diseases, particularly T2DM [133]. A high Dietary Insulin Index diet, characterized by refined carbohydrates, certain proteins, and saturated fats, is associated with elevated insulin secretion, increased blood glucose levels, and greater insulin demand. Over time, this persistent demand can strain β -cells, leading to their dysfunction, a critical factor in the progression of T2DM [134].

In addition to T2DM, high Dietary Insulin Index diets are linked to metabolic syndrome, weight gain, and IR [135, 136]. Insulin resistance occurs when insulin secretion is impaired, or insulin fails to effectively promote glucose transport into peripheral tissues. This dysfunction contributes to poor glucose metabolism, hyperglycemia, and the onset of cardiometabolic conditions. Emerging evidence suggests that both dietary insulin load and Dietary Insulin Index act as independent dietary risk factors for IR and related chronic diseases [136].

2.3.2.2 Mechanisms linking Dietary Insulin Index to disease

The metabolic effects of high Dietary Insulin Index diets can exacerbate insulin resistance through several mechanisms:

1. **Fat storage and insulin resistance:** Impaired fat storage due to reduced insulin sensitivity in adipose tissue leads to continuous free fatty acid (FFA) release from triglyceride stores. These FFAs are absorbed by the liver, where they can undergo β -oxidation, re-esterification into triglycerides (TGs), or contribute to gluconeogenesis. This process exacerbates hyperglycemia, increases very-low-density lipoprotein (VLDL) production, and promotes hepatic steatosis [137].
2. **Metabolic shifts:** High Dietary Insulin Index diets stimulate insulin secretion, increasing carbohydrate oxidation while reducing fat oxidation. This metabolic imbalance favors fat storage, particularly in the abdominal region, contributing to obesity and an unhealthy metabolic profile [134].
3. **Oxidative stress and inflammation:** Elevated glucose and lipid levels from high Dietary Insulin Index diets increase energy substrate delivery to metabolic pathways, resulting in the overproduction of reactive oxygen and nitrogen species (RONS). This oxidative stress triggers low-grade chronic inflammation, particularly in visceral adipose tissue [138]. Excess fat accumulation in visceral tissues releases FFAs into the portal circulation, further worsening glucose metabolism and fueling inflammation.
4. **Obesity and inflammation:** Chronic inflammation plays a central role in obesity associated with high Dietary Insulin Index diets. Energy surplus and IR promote fat storage in visceral adipose tissue, which increases inflammation and metabolic dysregulation.

2.3.2.3 Health implications

The implications of high Dietary Insulin Index diets extend beyond T2DM and obesity to broader metabolic health concerns. For instance, the increased fat storage driven by elevated insulin secretion contributes to abdominal obesity, a key risk factor for metabolic syndrome. Additionally, high Dietary Insulin Index diets exacerbate the chronic inflammation and oxidative stress linked to cardiovascular disease, further highlighting their role in poor metabolic health outcomes [134].

3. Conclusion

Dietary indexes serve as invaluable tools for evaluating the quality and composition of diets and their relationship to health outcomes. By providing standardized

Dietary index	Key features	Applications	Health implications
Healthy Eating Index (HEI)	Evaluates overall diet quality based on adherence to the Dietary Guidelines for Americans (DGA).	Used in research, public health initiatives, and policymaking to assess diet quality.	Strong association with reduced risk of cardiovascular disease (CVD); no significant association with cancer risk.
Mediterranean diet score (MDS)	Measures adherence to the Mediterranean diet through food group scoring.	Applied globally to evaluate the dietary patterns in Mediterranean and non-Mediterranean populations.	Associated with reduced mortality, CVD, Type 2 diabetes mellitus (T2DM), neurodegenerative disorders, and certain cancers.
Alternate Healthy Eating Index (AHEI)	Builds on the HEI by emphasizing food choices linked to reduced chronic disease risk.	Evaluates dietary patterns specifically associated with chronic disease prevention.	Stronger predictive capacity for CVD and T2DM compared to HEI; less pronounced association with cancer risk.
Glycemic index (GI) and glycemic load (GL)	GI measures carbohydrate impact on blood glucose; GL accounts for both quality and quantity.	Widely used for managing glycemic responses and assessing carbohydrate quality in diets.	Linked to increased risk of T2DM, coronary heart disease (CHD), and other metabolic disorders.
Dietary Inflammatory Index (DII)	Categorizes diets from anti-inflammatory to pro-inflammatory based on empirical evidence.	Assesses the inflammatory potential of diets in relation to chronic diseases.	Pro-inflammatory diets are associated with increased mortality, cancer risk, CVD, obesity, and musculoskeletal disorders.
Potential renal acid load (PRAL)	Estimates dietary acid or base load based on nutrient composition.	Evaluates acid-base balance in diets and their effects on metabolic and musculoskeletal health.	High-PRAL diets are linked to low-grade metabolic acidosis, sarcopenia, osteoporosis, hypertension, and kidney stones.
Dietary Insulin Index	Measures the insulin response to foods containing both carbohydrates and proteins.	Used to assess dietary impacts on insulin dynamics and metabolic health.	High DII is linked to T2DM, obesity, metabolic syndrome, insulin resistance, chronic inflammation, and CVD.

Table 1.
Summary of common and emerging dietary indexes: features, applications, and health implications.

measures, these indexes enable researchers, clinicians, and policymakers to better understand the complex interactions between dietary patterns and chronic diseases.

Indexes such as the HEI and the MDS highlight the importance of balanced, nutrient-dense diets for reducing the risk of cardiovascular diseases, and overall mortality. The AHEI extends these principles by focusing on food choices more strongly associated with improved health outcomes, particularly in the context of chronic disease prevention.

Similarly, the GI, GL, and Dietary Insulin Index address the metabolic effects of dietary carbohydrates and their influence on blood glucose and insulin dynamics, offering critical insights for managing type 2 diabetes and related conditions. The Dietary Inflammatory Index (DII) emphasizes the role of diet-induced inflammation in chronic diseases such as cancer, cardiovascular disorders, and mental health issues, underscoring the need for anti-inflammatory dietary interventions.

Emerging indexes like PRAL expand the scope of dietary assessment by focusing on the acid-base balance, demonstrating significant implications for bone health, muscle preservation, and metabolic conditions.

Collectively, these dietary indexes illustrate the multifaceted impact of diet on health and disease prevention. Incorporating these tools into research and clinical practice can help guide dietary recommendations and interventions to promote healthier lifestyles, prevent chronic diseases, and improve population health outcomes (**Table 1**).

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*Edited by Akkinapally Venketeshwer Rao
and Leticia Rao*

The relationship between lifestyle habits and health has always been and continues to be an important area of interest to public health professionals. Among the lifestyle factors, diet is considered to play a crucial role in managing physical and mental health, as well as reducing the risk of other diseases. Dietary habits and their patterns vary considerably around the globe, depending upon many factors, including cultural and religious beliefs, economic stability, technological development, and food security. Research has documented a significant relationship between dietary habits and health. Recognising the continued interest in this area, this book is being published in response to the need for more current and up-to-date information globally in this important area of human health. Internationally recognized authors with expertise in their respective fields have contributed to the book. The chapters represent both original research and up-to-date and comprehensive research. This book will serve as a valuable source of reference material for a wide range of interest groups. Additionally, the information in the book will serve as the basis for developing important recommendations on maintaining and managing diets that contribute to better health and improve the quality of life.

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