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Global Trends in Nutrition and Health through the Life Course

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Global Trends in Nutrition and Health through the Life Course

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Preface

The 98th Nestlé Nutrition Institute Workshop, held on the 11th, 14th, and 17th October 2022, was delivered in collaboration with the International Academy of Nutrition Educators and NNEdPro Global Institute for Food, Nutrition and Health.

In this book, we explore various aspects of *Global Trends in Nutrition and Health through the Life Course* in a way that is both informative and thought-provoking. A diverse set of experts from across academic and practice-based disciplines come together as seasoned authors drawing on their own personal experiences, as well as their extensive research, to create a compelling and engaging narrative.

This book contains eight chapters of valuable contribution to the field, and it is sure to spark important conversations among the readers.

Prof. Naglaa Kamal of Cairo University focuses on why interventions in infancy are crucial in addressing the global problem of obesity; Dr. Federica Amati of Imperial College London shares on how the pandemic and economic instability have made it harder to address global malnutrition; Prof. Sumantra Ray of NNEdPro explains why a multiagency approach is needed to tackle malnutrition in all its forms and expounds on double-duty actions; Prof. Martin Kohlmeier of the University of North Carolina highlights the importance of nutrition for optimal functioning of the immune system; Otilia Perichart-Perera, PhD, of the Instituto Nacional de Perinatología, Mexico City, dives into the issue of nutritional supplementation – and the efforts to curb micronutrient deficiencies;

Shane McAuliffe, RD, of the Chris O'Brien Lifehouse, Sydney, argues that nutritional support could keep vulnerable people out of hospital, and help them recover after treatment; Prof. Dhanasekhar Kesavelu, a Pediatric Gastroenterologist at Apollo Children's Hospital and SS Childcare, Chennai, India, shares on his passion for social media a scientific communication tool and how nutrition professionals should approach social media to increase public awareness about nutrition; and Prof. Lauren Ball of the University of Queensland, Australia, Dr. Celia Laur Associate Director at NNEdPro, and James Bradfield, RD, London, delve deeper into the panel discussion topic that focuses on how best we can prepare for the future of nutrition in healthcare delivery.

Additionally, clinical and public health nutritionist Wanja Nyaga and Ebiambu Agwara, a medical doctor with public health and nutrition training, have contributed their expertise and perspectives to the Double Burden of Malnutrition and Nutrition and Immunity chapters, respectively. Members of the NNEdPro Virtual Core have provided insights on the various topics in this book and special thanks are due to Matheus Abrantes as well as the NNI team including Roberta Portes, for operational management of this project.

We enthusiastically recommend this book to anyone who is interested in learning more about advancing science for better nutrition across the life course with a particular focus on the impact of the pandemic and its sequelae on childhood nutrition and subsequent health outcomes.

Prof. Sumantra (Shumone) Ray

NNEdPro Global Institute for Food, Nutrition and Health

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Foreword

The past few years have seen unprecedented times for health and wellness. Across the globe, the pandemic prompted sudden changes in lifestyle that changed the nutrition and diet patterns of families everywhere. For many people, safeguarding immunity and prioritizing wellbeing became the number one concern.

As we open up after the pandemic, what can we do to ensure the optimum health of children? We need to advocate for support that enables families to adopt positive eating habits and food choices. By redefining our practice, we can do even more for our patients and those we care for.

The 98th Nestlé Nutrition Institute Workshop, held on the 11th, 14th, and 17th October 2022, was delivered in collaboration with the International Academy of Nutrition Educators and NNEdPro Global Institute for Food, Nutrition and Health.

On day 1 of the workshop, speakers from all over the world brought fascinating insights on recent developments in nutrition and metabolic health. Prof. Sumantra Ray discussed the connection between nutrition, diet, and malnutrition, and explored why a multiagency approach is needed to tackle malnutrition in all its forms. Prof. Naglaa Kamal looked at why interventions in infancy are crucial to addressing the increasingly global problem of obesity. Wrapping up day 1, Dr. Federica Amati investigated how the pandemic and economic instability have made it harder to address the global malnutrition challenge.

The second day of the workshop gave expert speakers the chance to shed light on the emerging practice patterns in nutrition and healthcare applications. Prof. Martin Kohlmeier examined the link between nutrition and the development of a resilient immune system. Otilia Perichart-Perera, PhD, then took up a discussion on nutrition and immunity, discussing key nutrients and supplementation in women and children. Closing out day 2, Shane McAuliffe, RD, looked at how nutritional support could keep vulnerable people out of hospital, and help them recover after treatment.

Day 3 of the workshop featured an illuminating panel discussion on preparing for the future of nutrition in healthcare delivery. Prof. Sumantra Ray, Celia Laur, PhD, Prof. Dhanasekhar Kesavelu, Dr. Katherine Martyn, and Lauren Ball, PhD, discussed everything from how to ensure equitable access to nutritious food to how nutrition professionals should approach social media.

As always, I hope you find the proceedings of this workshop thought-provoking and insightful. By bringing together nutrition experts from around the world, we can help refine and develop our field, and bring even more benefit to the patients we care for.

Josephine Yuson-Sunga, MD

Global Head of the Nestlé Nutrition Institute, Switzerland

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Double Burden of Malnutrition and Double Duty Actions

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Abstract

The terms diet and nutrition are often used interchangeably, but there are important differences between the two concepts. Diet is not only about what we eat, but the patterns of food consumption – how much or how often we eat certain foods. Dietary patterns determine nutrition, but they are about much more than intake of nutrients. Malnutrition can have severe health consequences when prolonged and takes the form of undernutrition that impacts growth and development, or overnutrition that leads to obesity. The basic principles of a healthy diet are well known, such as breastfeeding which may reduce the risk of obesity and of chronic disease in later life. Certain factors can steer individuals away from a healthy diet: these may be biological, economic, physical, social, or psychological. The pandemic has brought challenges, but the adaptations we have made can also be used in pursuit of a shared goal. To achieve universal access to palatable, affordable, nutritionally replete meals that are easy to prepare is possible, but it requires action by multiple agents combined with increased awareness. The Lancet's double duty actions to address malnutrition represent a useful way to rethink our approach to the challenges of malnutrition, finding new opportunities for action.

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Introduction

Nutrition is defined as the total of the processes referred to as the taking in and the utilization of food substances for growth, repair, and maintenance. It involves ingestion, digestion, absorption, and assimilation. Nutrition science is the study of nutrients in food, how the body uses nutrients, and the relationship between diet, health, and disease [1].

The words nutrition and nutrients cannot be used interchangeably, but they are closely related. Nutrients are stored by the body in various forms and drawn upon when the food intake is not sufficient. Specifically, nutrients are chemical compounds that are needed for growth and metabolism. They must be supplied in the diets as they cannot be synthesized in the body. Macronutrients and micronutrients are two primary categories to describe the nutrient need of animals. Macronutrients are the protein, fat, and carbohydrates that the body needs in large amounts to provide energy for us, as well as maintain the body's structure and systems. Micronutrients, including vitamins and minerals, are only needed in milligram or microgram quantities but are essential for the support of metabolism and maintenance of health [1].

How Are Nutrition, Diet, and Malnutrition Related?

The three are related and each one affects the others. Nutrition can be defined simply as what you eat, which determines what you are, and what you can do. There is an overall fit to the individual, and that determines the capacity of an individual. For diet, it is about the food composition, or food ingredients in the way in which we consume meals, as we eat food, not nutrients. Malnutrition is a serious condition that happens when your diet does not contain the right amount of nutrients, including inadequate intake of one or more nutrients, excessive intake of one or more nutrients, or an imbalance in the intake of nutrients. It presents in three forms, including undernutrition, overnutrition (obesity and diet-related noncommunicable diseases (DR-NCDs) such as heart disease and diabetes), and micronutrient deficiencies.

Principles of a Healthy Diet

A balanced diet is essential for good health and nutrition, which protects you against many chronic noncommunicable diseases (NCDs), such as heart disease, diabetes, and cancer. A healthy diet [2] should follow the five principles below:

1. Start early with breastfeeding, which fosters baby growth and development, reduces later-life metabolic risks, as well as risks of chronic diseases.
2. Choose a wide variety of nutrient-rich foods (diet diversity). The WHO recommends eating a combination of different foods including staple foods such as cereals, legumes such as lentils, vegetables, fruits, and foods from animal sources such as fish, milk, and meat. Eating a variety of whole and fresh foods everyday aids to increasing your chance of acquiring essential nutrients, and avoid a diet high in sugar, fats, and salt which might result in unhealthy weight gain and NCDs.
3. Consume enough amounts of nutritious food and liquids to meet energy needs but not exceed them.
4. Limit those foods that are very energy-dense or processed, such as, pizza, and ice cream.
5. Prepare and store food safely.

All principles should go hand in hand to ensure making a healthy diet [1] from nutrients, quality, quantity, and food safety.

From Food to Health

Food Choices

Food choices [3] refer to how people decide on what to buy and eat and reflect a complex set of factors that vary from person to person as shown below:

- Biological determinants: hunger, appetite, taste;
- Economic determinants: income, cost, and availability of food;
- Physical determinants: access, education, cooking skills;
- Social determinants: culture, religion, family, and peers;
- Psychological determinants: mood, guilt, and stress;
- Other: attitudes, beliefs, and other social constructs.

Food Environment

The food environment encompasses physical, economic, political, and socio-cultural aspects that influence people engaging with the food system and making their decisions about acquiring, preparing, and consuming food. For instance, it can be the distribution of food stores, food service, and the power of food advertising and marketing. If the food environment makes healthy foods less available people will choose foods that are higher in calories and often lower in nutritional value. Therefore, it is significant to create and support a positive and healthy food environment for public health work.

Conceptual Framework to Stepladder from Food to Health

When we think about the big picture from food to health, food environment and dietary choices, food production, and nutrient quality also determine nutritional and health status. The stepladder from food to health [4] covers each important step from food production to health status. At every level, nutritional knowledge and application are significant.

Global Nutrition Transition

This global nutrition transition model [5] was first proposed in 1993 by Barry Popkin and it involves five sequential patterns [6] which have taken place in an evolutionary manner.

Pattern 1 represents the period characterized by hunter-gatherers and the Paleolithic man. In this pattern, people labored intensively for food and ate wild plants and animals high in carbohydrates and fiber but low in fat, resulting in low fertility and low life expectancy.

Pattern 2 is for the period where settlements began, the early monoculture and famine period. In this pattern, cereals played the dominant role in the diet. At this time, there was increased food scarcity with reduced dietary variation causing many people to suffer nutritional deficiencies.

Pattern 3 is of industrialization and receding famine. People in this pattern consumed and increased the number of vegetables, fruits, and animal proteins and decreased starchy staples as compared to the diet in pattern 2. It is worth noting that the mortality rate was reduced. However, the focus on food production and monoculture limited food variety with evidence of different diseases such as stunting and iron deficiency anemia.

Pattern 4 is for the pattern of NCDs with diets high in total fat, cholesterol, sugar, and refined carbohydrates but low in polyunsaturated fatty acids and fiber; people are more likely to suffer obesity and different DR-NCDs such as stroke and diabetes. This period is accompanied by an increasingly sedentary lifestyle.

Pattern 5 is the period of desire for social or behavioral change. We wish to have a more balanced diet and purposeful activity to get to with extended health aging.

Double Nutritional Burden

The double nutritional burden is the coexistence of both undernutrition alongside overweight or obesity which is a major driver of DR-NCDs such as diabetes and stroke. Undernutrition can often be accompanied by micronutrient deficiencies, and equally, those with obesity may also be micronutrient deficient. The double nutritional burden can occur not only in the same populations but also in individuals through the life course at different stages within various countries, cities, and communities who may be experiencing different types of malnutrition. This double burden [7] poses a huge challenge to national policy, health policy, and resource allocation and has led to the WHO concept of double-duty actions to tackle all forms of malnutrition.

2020 Global Nutrition Report – Action on Equity to End Malnutrition

Since 2020, following the COVID-19 pandemic, there has been an increased emphasis on the role of nutrition in health and well-being. Highlighting the fact that nutrition needs to be understood and recognised as an indispensable part of health, food, education, and economic development. Moreover, that inequalities in the global burden of malnutrition which contributes to both under and overnutrition challenges world health systems.

Transforming Food Systems to Deliver Affordable, Healthy Diets for All

The 2020 global nutrition report [8] reveals significant inequalities in nutritional outcomes within countries and populations. This reminds us that now is the time to commit ourselves to eliminate inequalities in nutrition. From the report of the State of Food Security and Nutrition in the World (SOFI 2021) [9], unhealthy diets are the leading cause of most NCDs. Moreover, healthy diets [2] can often be seen costing 60% more than unhealthy ones. In this context, we need to look at the food system more closely to address factors related to the high cost of nutritious food.

Critical Actions to End Malnutrition in All Its Forms

In the 2020 global nutrition report [8], many different statistics relating to overweight, obesity, and stunting coexist in the same populations. In these populations, we need data and data-driven actions. The global nutrition report [8] calls

out to undertake several critical actions to end malnutrition, such as investment, building equitable, resilient, and sustainable food and health systems, and focusing on collaboration between sectors. For example, food production is driven much more by economics and politics, whereas food choices may be driven more by modeling peer behaviors and through health advice. We also need to leverage key moments to revitalize and expand nutrition commitments.

Double Duty Actions

This helps us answer two main questions.

1. What can be done?
2. How should we rethink our approaches to tackle malnutrition in all its forms?

While the double burden of malnutrition may pose a significant public health challenge for nutrition, related sectors, and actors, they also present an important opportunity for integrated action. Addressing the double burden of malnutrition offers an opportunity for alignment and coordination between those charged with addressing nutrition, early nutrition, overweight and obesity, infectious diseases, NCDs, maternal and child illness, and diseases associated with aging. The double burden of malnutrition can be seen as a dual nutrition challenge, or an opportunity for double returns [10]. Programs and policies that aim to address the malnutrition burden through double-duty evidence-based actions are likely to be both successful and cost-effective.

Double-duty actions [11] include interventions, programs, and policies that have the potential to simultaneously reduce the risk of both undernutrition (including wasting, stunting, micronutrient deficiency) and overweight, obesity, or DR-NCDs (including type 2 diabetes, cardiovascular disease, and some forms of cancer) [12].

Some examples that may be included in the policies to ensure access to optimal maternal and antenatal nutrition and care are the protection, promotion, and supporting of breastfeeding [13], including exclusive breastfeeding during the first 6 months, and appropriate complementary feeding in the first 2 years of life; the programs that foster healthy diets [2] in preschools, schools, public institutions, and workplaces; the measures and policies that improve food security and ensure access to healthy foods by all individuals and families; and the initiatives that ensure access to healthy and sustainable diets from appropriate and resilient food systems. However, actions to address different forms of malnutrition are typically managed by separate communities, policies, programs, governance structures, and funding streams.

Example: 10 Double-Duty Actions from the *Lancet*

The *Lancet* Series on the Double Burden of Malnutrition from 2019 [11] showed multiple forms of malnutrition within countries, communities, households, and individuals, which reflected a new nutrition reality that requires successful coping with new strategies, programs, and policies. They examined the causes of this new nutrition reality and designed the ten-double-duty nutrition actions. These actions have been proposed to effectively address malnutrition in all its forms in a more holistic way. It does so by summarizing evidence on common drivers of different forms of malnutrition and documenting examples of unintended harm caused by undernutrition-focused programs on obesity and diet-related-NCDs.

The 10 double-duty actions can be divided into health services, social safety nets, educational settings, agriculture, food system, and food environmental categories.

For health services:

1. Scale up the antenatal care recommendations proposed by the WHO. For example, counseling about healthy eating and keeping physically active during pregnancy to stay healthy
2. Comprehensively implement programs to protect and promote breastfeeding. For example, eliminating the promotion of breastmilk substitutes (infant formula and follow-on formula)
3. Ensure guidance for introducing foods alongside breast-feeding to make mothers aware of the risks of foods, snacks, and beverages high in energy, sugar, fat, and salt. For example, including new training curricula for primary healthcare workers to provide double-duty nutrition counseling
4. Redesign existing child growth monitoring programs. For example, ongoing growth monitoring programs to include the child who is overweight, or weight is becoming a problem, to include referral and appropriate counseling on healthy diets and snacks to address all types of malnutrition
5. Prevent undue harm from energy-dense and micronutrient-fortified foods and ready to use supplements. For example, promoting healthy diets as the default measure to prevent undernutrition

For social safety nets:

6. Design social support and welfare programs to reduce risks from food, snacks, and beverages high in energy, sugar, fat, and salt. For example, to embed healthier eating and behavior opportunities within social support

For educational settings:

7. Redesign school feeding programs and devise new nutritional guidelines for food in and around educational institutions to ensure nutritious food is available instead of foods, snacks, and beverages high in energy, sugar, fat, and salt. For example, involving parents and children in planning meals and snacks in and around schools

For agriculture, food systems, and food environments:

8. Extend the number of agricultural development programs that make nutritious food available, affordable, and appealing. For example, promoting diversity in food production and consumption among poor households living in remote areas with little access to markets
9. Implement new large-scale agricultural and food system policies with a healthy diet as their primary goal. For example, refocusing agriculture toward the production of nutritious food such as fruits, vegetables, nuts, legumes, and whole grains, and making these foods more affordable for all
10. Deliver public policies to improve food environments to tackle all forms of malnutrition. For example, in addition to the actions in 1–9 that aim to improve food environments, it can implement policies such as to monitor and restrict nutrition and health claims on foods, snacks, and beverages high in energy, sugar, fat, and salt

Double Duty in Practice

There are three levels of doing double duty.

The First Level Is Not to Harm

Many important and effective programs are currently being implemented around the world to address the various forms of malnutrition. The first level of doing double duty is to assess and ensure that current initiatives (policies, programs etc.) are not increasing the risk of other forms of malnutrition or NCDs. For example, it is important to ensure that efforts and initiatives to feed young children affected by acute undernutrition also address the long-term risks of becoming overweight and NCDs.

The Second Level Is Retrofit

At this level, the focus of achieving double duty is to look at what actions are already being implemented and ask, “do they or can they have the potential to positively and simultaneously influence other forms of malnutrition?” For ex-

ample, Indian policies of providing school pupils with a free lunch are for targeting undernutrition, while in some extent it also restricts the intake of foods associated with unhealthy diets such as junk foods. Ensuring programs are tailored to reduce the risk of the double burden of malnutrition would reap double returns on initiatives that are already functioning.

The Third Level Is de novo Actions

This level is the most proactive. It involves the development of new actions designed specifically to do double duty. This is based on assessing which of the actions above are potentially the most powerful candidates to be implemented in a particular setting – reflecting the local epidemiology, policy, cultural, environmental, and food contexts. This could include actions focused on existing national priorities, as well as new actions or priority areas.

Conclusion

The type of action, and its effectiveness, will vary between and within countries. Designing for double duty is not an approach of “one size fits all” but a method of crafting nutrition actions that are appropriate to the individual setting. For example, in the global nutrition report [8], India has a higher prevalence of stunting and wasting as compared to Australia; however, Australia has higher incidences of overweight than India. Therefore, the double duty should be designed for different situations to tackle specific nutrition problem. Nutrition is the root of health and all we do, as demonstrated by the United Nations summary of how nutrition is impacted by all the in the Sustainable Development Goals.

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Evolving Trends in Eating Habits of Children

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Abstract

This chapter examines the concept of programming and emphasizes the adverse consequences of both undernutrition and overnutrition in later life. It underscores the intergenerational nature of malnutrition, which begins in utero and persists throughout one's life. It also explores the impact of parental attitudes and family circumstances on infant and childhood nutrition. Early intervention strategies are crucial for optimal development, emphasizing the importance of adequate care for low-birth-weight infants, breastfeeding, immunization, poverty reduction, and avoidance of environmental hazards. In early childhood, promoting adequate complementary feeding, monitoring growth, managing wasting, and providing necessary supplementation play significant roles. However, societal influences, such as poverty and environmental hazards, can obscure the effects of suboptimal nutrition during pregnancy and early postnatal life. The COVID-19 pandemic has further exacerbated malnutrition issues among children, with disruptions to structured school settings, access to nutritious foods, and physical activity. Additionally, food insecurity has increased, with significant impacts on vulnerable populations. Rising global food prices worsen the situation, particularly in low-income countries heavily reliant on cereals for energy intake. In conclusion, addressing malnutrition in school-aged children requires an intergenerational approach with cross-discipline collaboration to tackle underlying determinants such as poverty, maternal health, education, and household food security.

Introduction

Intergenerational Cycle of Malnutrition

Programming is the idea that a stimulus during a critical period in infancy will lead to permanent change in structure or function in later life. McCance and Widdowson [1] discussed the concept of an “ideal plane of nutrition” for different stages of life, and initial studies found that undernutrition during a critical period leads to permanent stunting of growth, whereas undernutrition during a later period only has a temporary effect on growth. Later studies found that both under- and over-nutrition have adverse later consequence.

Infant and child nutrition in utero, but also in infancy and childhood, may affect long-term health. Malnutrition is intergenerational in nature; poor nutrition starts in utero among women with poor nutritional status, and extends throughout the life course, affecting the next generation. In low- and middle-income countries, low-birth-weight babies can be almost 2 to 5 times more likely to experience underweight, stunting, or wasting during childhood [2–5]. This child will grow as a malnourished adolescent, into adulthood, and later a malnourished pregnant woman, and so the intergenerational cycle of malnutrition continues. Also, maternal nutrition (inadequate and excessive) impacts the uterine environment and fetal development, increasing the infant’s risk of obesity and hypertension in later life [6].

Additionally, parental attitudes and family circumstances have a profound influence on infant and childhood feeding and lifestyle practices, so the effects of suboptimal nutrition during pregnancy or early postnatal life may be obscured in later life by the effects of the postnatal environment. Therefore, it can be difficult to determine whether associations, such as those found between infant feeding practices and later obesity, are the result of true programming or the result of common environments and related lifestyle choices.

According to the World Health Organization [7], it is important to act early to ensure the best possible start in life. In infancy, this may include adequate care for low-birth-weight infants, adequate breastfeeding, vitamin A supplementation, adequate immunization, minimized exposure to poverty, minimized vertical transmission of infections, and avoidance of environmental hazards. Evidence has shown a 10% reduced risk of asthma in children exposed to more compared to less breastfeeding duration [8], and a 10% reduction in the prevalence of overweight or obesity in children exposed to longer durations of breastfeeding [9].

In early childhood, early intervention strategies are crucial for optimal development. From a nutritional standpoint, this includes ensuring adequate complementary feeding, monitoring growth, managing wasting, and providing neces-

sary supplementation of iron, vitamin A, iodine, and zinc. Additionally, promoting proper immunization is essential. On the other hand, societal influences play a significant role. Minimizing exposure to poverty and environmental hazards becomes crucial in fostering a healthy upbringing. Maximizing positive caregiver interactions and providing social and cognitive stimulation are also vital components for a child's overall well-being.

Malnutrition in Children before and after the COVID-19 Pandemic

Before the COVID-19 pandemic, global estimates of malnutrition in children under the age of 5 years, published by the UNICEF, WHO, and World Bank Group [10], found that 38.9 million (5.7%) children were affected by overweight, 45.4 million (6.7%) were affected by wasting, and 149.2 million (22%) were affected by stunting. Between the years 2000 and 2020, there had been a decrease in the percentage of stunting from 33.1% to 22%; however, an increase in the percentage of children under 5 years affected by overweight (5.4% to 5.7% for the years 2000 and 2020, respectively).

However, during the pandemic, children spent more time away from structured school settings and isolated from regular mealtimes, access to nutritious foods, and regular physical activity. Research conducted during this time found sharp increases in BMI rates, particularly among those affected by overweight or obesity and younger school-aged children [11]. Children aged 6–11 years experienced the largest increase in their rate of BMI change, with a pandemic rate of change that was 2.50 times as high as the prepandemic rate. Additionally, families and households, who were already predisposed to socio-economic and health inequalities, may have experienced additional disruptions to income, food security, and other social determinants of health. These factors, along with the heightened stress experienced during the pandemic, likely contributed to certain health outcomes and affected the overall health and well-being of children.

Food Insecurity

In recent years, there has been an increase in multiple forms of food insecurity including physical availability and financial access [12]. In the United States, the number of free meal sites increased from 6,254 sites in May 2019 to 31,347 in May 2020. Additionally, child nutrition programs served 1.7 billion meals that may have otherwise not been distributed.

In the United Kingdom, figures released by the Trussell Trust [13] showed that food banks provided more than 2.1 million food parcels to people across the United Kingdom in the past year, with 1.3 million emergency food parcels given out during the April to September 2022 period (higher than ever before for this time period). There were serious financial impacts, with 22% of all households losing income since before the pandemic. The latest findings from the Food Foundation [14] survey conducted in September 2022 found that one in four households with children (25.8%) have experienced food insecurity, affecting an estimated 4 million children in the United Kingdom. This was the highest level of food insecurity since the start of the pandemic. Households with children are more likely to experience food insecurity than households without children (25.8% compared with 16.0%). The pandemic has had a catastrophic impact on the most disadvantaged and vulnerable groups in the United Kingdom, and the issue of household food insecurity is far from resolved.

Exacerbating the problem of food insecurity is the increasing global food prices. Local food prices have surged in response to increasing energy and fertilizer prices, pandemic-induced supply chain disruptions, disruptions resulting from the war in Ukraine, and crop failures resulting from climate change [15]. Wheat prices were up more than 22%, on average, across the Sub-Saharan African, Eastern Europe and Central Asian regions. This has huge implications for food security and health, particularly in developing countries, such as those in Africa and parts of Asia, where cereals contribute as much as 70% of energy intake. The rising food prices have contributed to food insecurity in many low-income countries, which already had increased food insecurity in response to the pandemic, adverse weather events, and numerous conflicts. Numerous risks to agricultural prices remain, including the likelihood of higher-than-expected input prices or energy supply disruptions, further deterioration of the global outlook, adverse weather patterns, and restrictive trade policies.

Conclusion

The current issues of rising food prices, food insecurity, cost of living crisis, and the impact of the COVID-19 pandemic have exacerbated the issues around malnutrition in school-aged children. Therefore, there is a need for an intergenerational approach with cross-discipline collaboration to impact the underlying determinants of malnutrition including poverty, maternal health, education, and household food security.

Conflict of Interest Statement

Federica Amati is affiliated with ZOE, the Personalised Nutrition Company. Sarah Armes has no conflict of interest.

Author Contributions

Federica Amati and Sarah Armes have both made substantial contributions to the conception of the work and have given final approval of the version to be published.

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Nutrition and Immunity

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Abstract

Both the constantly active innate immune system and the later acting humoral defenses depend on adequate supplies of vitamins and trace elements. An array of essential micronutrients, specifically omega-3 polyunsaturated fatty acids (PUFAs), the vitamins A, D and E, as well as iron, copper, zinc, and selenium are of critical importance for protection against many contagious diseases, including viral infections of the upper respiratory tract. Balanced, micronutrient-rich food choices are an important foundation for a strong immune system and resilience against disease. A good vitamin D status appears to play a significant role in the protection against the upper respiratory tract infection COVID-19 caused by SARS-CoV-2, particularly at the time of initial exposure to the virus. The likelihood of infection and mortality risk during the first months of the pandemic was closely linked to skin pigmentation and how far north (latitude) the people lived, pointing to a potential role of sunlight (UV-B) exposure and vitamin D status. The excess risk of people with obesity may be explained at least in part by their typically lower vitamin D concentrations in blood. Habitual use of dietary supplements with moderate amounts of vitamin D was associated with slightly reduced disease risk in some studies.

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Table 1. Greatly simplified elements of the cellular and humoral immune systems

Elements of the innate immune response	Elements of the humoral immune response
Natural killer cells	Macrophage
Cytotoxic T lymphocytes	Dendritic cell
Perforin	Helper T lymphocytes
Granzyme	B lymphocytes
Type 1 interferons	Plasma cells
Interferon gamma	Immunoglobulins G, M, A

Introduction: Innate and Humoral Immune Response

The key elements of human immune response to most infections by viruses and infectious microbes are early acting immunity and the much later acting humoral immunity (Table 1). Let us assume we inhale one of these nasty common cold or influenza viruses which then might infect epithelia in the nasal and upper respiratory passages. Right away, within minutes, our innate immune system springs into action and slows further spread of the infection. Infected cells are broken up and virus replication is blocked [1]. This part of the immune response is already strongly dependent on adequate supplies of the diverse nutrients that play a role in the proliferation and differentiation of various types of immune cells, including natural killer cells and cytotoxic T lymphocytes. These immune cells release generically protective proteins including perforin, granzyme, and lysozyme. These proteins have slightly differing effectiveness against diverse pathogens, but their effectiveness does not depend on prior exposure to these pathogens. This means that the immune system is always ready to act against an infection. Adequate supplies of key nutrients, such as zinc, vitamin A, and vitamin D, maintain the readiness of this first-line immune defense particularly by helping with expression of the genes for their production.

Macrophages and dendritic cells break down and process viruses and microbes that managed to penetrate the first barrier of epithelial cells and overwhelm the innate molecular defenses. These immune cells then present antigenic pathogen fragments to a series of T helper cells and cytotoxic lymphocytes that ultimately induce the production of antibodies specific for antigens from the newly encountered virus. Production of antibodies to newly encountered pathogens is starting only after several days and cannot contribute much to the battle during the first days of an infection. Vaccination prepares and stimulates on the humoral immune response by preparing immune-competent B lymphocytes and plasma cells that produce first mostly immunoglobulin M and then immunoglobulin G. Immune cells of intestinal and other specialized tissues pro-

Table 2. Good food sources of essential nutrients contributing to adequate immune function

Nutrient	Dietary sources
Vitamin A	Milk and cheese, eggs, liver, cold-water ocean fish, fortified cereals, dark orange or green vegetables like carrots, sweet potatoes, pumpkin, squash, kale, spinach, broccoli), red and orange-colored fruit (apricots, peaches, papaya, mango, cantaloupe), tomato
Vitamin D	Fortified foods (some spreads and cereals) liver, eggs, cold-water ocean fish
Copper	Nuts, liver, shellfish, and some vegetables
Selenium	Fish, shellfish, meat, eggs, Brazil nuts
Iron	Meat, liver, beans, nuts, dried fruit (e.g., apricots), whole grains (e.g., brown rice), fortified cereals, dark green leafy vegetables (spinach, kale)
Omega-6 fatty acids	Meat (rich in arachidonic acid), seed-oil, mayonnaise, seeds
Omega-3 fatty acids	Cold-water ocean fish (rich in EPA and DHA)

duce immunoglobulin A. Some pathogens, including parasites, induce the production of immunoglobulin A, while most others do not. Nutrients are important for an effective humoral immune function by supporting the metabolism of the immune cells, by inducing cell proliferation, and by providing the building blocks for the new cells [1].

Essential Nutrients for a Balanced Immune Response

Numerous nutrients are needed for an effective immune response. As already indicated, this is particularly true for the early response that depends on the innate immune system. Vitamins A and D and zinc play crucial roles in the proliferation and differentiation of the various types of immune cells. These three micronutrients, in addition to other functions, mediate targeted expression of specific DNA segments in response to a wide range of mediators. Copper and iron support the metabolism and functions of immune cells. The essential, PUFAs, selenium, and vitamin D will now get further attention. Table 2 lists good food sources of these essential nutrients.

Vitamin A plays essential roles in the normal differentiation of epithelial tissue and immune cell maturation and function. It also plays a crucial role in the maturation of neutrophils leading to impaired phagocytic function when deficient despite the increased number of neutrophils. In addition to this, vitamin A controls maturation of dendritic and CD4 T lymphocytes, while its metabolite retinoic acid is essential for the survival of CD8 cells and proliferation of B lymphocytes [2]. Thus, vitamin A deficiency would lead to impaired barrier func-

tion, altered immune responses, and increased susceptibility to infections. Vitamin A deficiency has been implicated in respiratory infections, measles, and diarrhea, especially in children.

Vitamin D needs to be converted into its active, hormone-like metabolite 1,25-dihydroxyvitamin D₃ in the kidneys and in some peripheral tissues, including immune cells. This active metabolite, combined into a molecular complex consisting of 1,25-dihydroxyvitamin D₃ and retinoic acid attached to a specific protein, the vitamin D receptor, can then attach to one of hundreds of specific receptor-binding elements contained in specific DNA sequences, and thereby regulate the expression of associated genes in response to additional mediators. Vitamin D enhances epithelial cell integrity and induces the synthesis of antimicrobial peptides within these cells and macrophages [3]. In addition to this, it also promotes the differentiation of monocytes to macrophages and promotes antigen processing dendritic cells. Good vitamin D status tends to reduce the risk of upper respiratory tract infections. The vitamin D status of otherwise healthy individuals is strongly influenced by habitual sun exposure and skin pigmentation [4]. Genetic factors also appear to have a significant impact, particularly in carriers of the common GC rs4588 genotype TT associated with lower vitamin D status [5]. Obese individuals tend to have poorer vitamin D status as do people living at high latitude (Canada, UK, Central and Northern Europe).

Both deficiency and excess of iron diminish the function of the immune system. Iron deficiency diminishes production of T lymphocytes and limits natural killer cell activity. On the other hand, evidence suggests that some organisms such as plasmodia and mycobacterium tend to have enhanced activity in the presence of iron above a certain threshold, especially in the tropics. Hence, iron interventions tend to be discouraged particularly in children, immunocompromised patients, and during peak malaria transmission seasons. This is because high free iron concentration favors proliferation of many pathogens [6].

Copper is necessary for iron bioavailability, antioxidant protection, and for supporting the antimicrobial function of neutrophils, monocytes, macrophages, and natural killer cells [7]. It promotes their proliferation and production of IL-2. Poor copper status is associated with decreased lymphocyte proliferation and IL-2 production with an increased risk of bacterial infections, diarrhea, and pneumonia.

Selenium is an essential nutrient that is too often ignored. A particularly rich source are Brazil nuts. A single nut can provide more than enough selenium for a week or two. Deficiency, which is not uncommon, can increase the virulence of several common viruses [8]. Deficiency limits T cell proliferation, lymphocyte toxicity (which is much more desirable than it may sound), and natural killer cell activity [9]. Selenium is also needed for adequate antioxidant enzyme ex-

pression, an important component of an efficient immune response. Finally, deficiency tends to limit the protective effect of vaccines against influenza and potentially other infections [10].

Over the years, PUFAs have been studied with a focus on the impact on the immune system. Omega-6 and omega-3 derived metabolites known as pro-resolving mediators (SPMs) have important immune-regulatory functions. These SPMs can be classified into different families including prostaglandins, leukotrienes, maresins, protectins, and resolvins. In general, the omega-3 derived fatty acids and metabolites tend to be less proinflammatory than the omega-6 metabolites and more supporting resolution of an infection. The synthesis of all these metabolites is enabled by a large portfolio of desaturases, elongases, lipoxygenases, cyclooxygenases, cytochrome P450 monooxygenases, and other highly specific enzymes for many of which the omega-3 and omega-6 precursors compete directly [11]. Hence, in the presence of high omega-3 levels, there is reduced synthesis of omega-6-dependent metabolites, and vice versa. On the other hand, omega-6 PUFAs are needed to sustain a robust immune response. Both omega-3 and omega-6 PUFAs are key materials for building cell membranes in rapidly proliferating immune cells and are precursors for eicosanoid cytokines and chemokines to initiate the inflammatory response to infection and injury. Omega-6 derived metabolites need to be balanced by eicosanoids derived from omega-3 fatty acids, which promote completion of the immune response instead of chronically sustaining inflammation.

Most current food patterns contain much more omega-6 fatty acids than omega-3 fatty acids which tends to promote inflammation and limit the potential for dampening the inflammation and eventual healing. The extreme manifestation of excessive inflammation can be a potentially fatal cytokine storm sustained by high intake of omega-6 fatty acids. This excessive inflammation suppresses the number of CD4, CD8, and T lymphocytes and impairs the ability for CD4 T lymphocytes to produce IFN- γ which are all acquired immune responses [12]. This means that the individuals' ability to deal with the inflammation is hindered. In these situations, a meta-analysis showed that administration of omega-3 fatty acids in combination with other nutrients led to reduced length of intensive care requirement and hospitalization, and improved oxygenation in patients with cytokine storm secondary to Adult Respiratory Distress Syndrome [13]. Examples of these less desirable omega-6 fatty acids are linoleic acid in commonly consumed seed oils and arachidonic acid in meats. The more desirable omega-3 fatty acids are docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) from seafood, and alpha-linolenic acid (ALA) in flax seed and vegetables. ALA needs to be converted into DHA and EPA, which happens less effectively in people with common genetic variants.

As explained just now, the typical symptoms of inflammation, swelling, heat, and pain are mediated more by eicosanoids derived from omega-6 than by eicosanoids from omega-3 fatty acids. Another class of mediators, derived only from omega-3 fatty acids, slows chemo- and cytokine action and eventually restores pro- and anti-inflammatory balance. Since these inflammation-terminating and resolving mediators can only be produced from DHA and EPA, an insufficient supply of these highly unsaturated long-chain fatty acids directly impacts the ability to effectively deal with infections, shorten duration, and avoid excessive tissue and organ damage.

Viral Infections of the Upper Respiratory Tract

Now we are coming back to vitamin D, of which we need at least 400 to 800 IU per day, probably much more for many people, such as those with obesity. Of this, only 100 to 200 IU come from food. Skin exposure to ultraviolet B does the heavy lifting unless we use dietary supplements. For people living in regions at high latitude, there are several months in the year when the sun is low in the sky even at noon and not enough ultraviolet light gets through the atmosphere to generate vitamin D in exposed skin. Of course, the same effect happens when people stay indoors during the day, or if they use extensive coverings or sunscreen.

Numerous clinical trials have been conducted to assess the ability of vitamin D supplementation to prevent infections of the upper respiratory tract as shown in this visual summary. Of course, the effectiveness depends on many factors, such as virus load, prior vitamin D status, individual disposition such as the presence of excess body fat, and more. Nonetheless, taking them all together in a meta-analysis, a modest beneficial effect appears to exist. Thus, a partial solution to the perennial common cold problem may be at hand. This also is probably true more specifically for influenza infections. But what about the current pandemic of COVID-19?

Not very much is known about nutritional factors that might help us to dodge SARS-CoV-2 infections altogether. But we do know with reasonable certainty about several risk factors for poor COVID-19 outcomes. They are mostly nutrition-related factors including excess body fat, diabetes, and hypertension [14]. Older age, dark skin, and male gender may also have some nutrition links. Finally, nutrient deficiencies also appear to contribute, including deficiencies of vitamins A, D, and E, and of omega-3 fatty acids.

Very early in the pandemic, in the spring of 2020, there was a steep gradient of COVID-19-related mortality in US states by degrees of latitude from north to

Table 3. Deaths from COVID-19 during spring 2020 in self-described dark-skinned versus light-skinned population at high versus low latitude (above 39° versus below 39°)

	Deaths of black people	Total black population	Deaths per 100,000	Deaths of white people	Total white population	Deaths per 100,000
All	20,195	51,019,847	39.6	37,386	234,743,614	15.9
Above 39° north	15,460	14,922,146	103.6	32,464	91,919,615	35.3
Below 39° north	4,735	36,097,701	13.1	4,922	142,823,999	3.4

south [14]. Northern states, like North Dakota or Michigan, experienced much higher excess fold mortality than southern states like Texas or Florida. People living in these high latitude northern states are much more likely to be vitamin D deficient in the spring than people living in southern states due to great differences in UV exposure of the skin. Similar differences in COVID mortality by latitude were reported from Europe. Countries in the north reported higher rates of infection and consequently severe outcomes and even death than countries in the south. Further analysis of American data found eight to ten times higher numbers of COVID-19-related deaths in the northern half of the United States compared to the South (Table 3). The regional differences across the states were apparent in both light-skinned and dark-skinned people, though with much higher death rates overall in dark-skinned people. These data led to the hypothesis that more sun exposure and the resulting better vitamin D status might provide some protection against the pandemic infection.

The idea that vitamin D deficiency increases susceptibility to COVID-19 infection may be supported by UK biobank data from people who had their vitamin D levels analyzed in previous years [15]. Vitamin D deficiency was associated with a slightly increased risk of infection, which disappeared after adjustments for ethnicity, obesity, and other variables. There is an argument to be made that ethnicity and obesity are well-documented modifiers of vitamin D status and adjustments may have overcorrected the observations.

Another large-scale contemporary investigation of members in an Israeli healthcare system found a slightly higher risk of infection in those with vitamin D deficiency, here defined as less than 20 ng/mL [16]. Even vitamin D insufficiency was associated with increased risk in this cohort. Many more observational studies have since found similar relationships between deficient vitamin D status and increased COVID-19 risk.

The next question then must be about the causality of the observed association. Response to vitamin D supplementation would strengthen the link. From

a practice perspective, this is probably also the most urgent need to know. Using data from the UK Biobank, investigators found in all properly adjusted models that habitual users of vitamin D supplements had about 30% lower risk of infection than nonusers [17].

Another approach relied on an app that tracked both supplement intakes and COVID infections for extended periods of time [18]. The question was again whether prior use of vitamin D-containing supplements reduces the risk of infection. In the end, almost half a million people in the United Kingdom, United States, and Sweden participated. And again, the data show that vitamin D supplement users were less likely to become infected. The odds ratios indicate a 20–25% lower risk for women and men in the United States and Sweden, and somewhat less in UK participants. In contrast, the use of 400 IU of vitamin D with cod liver oil in a different Norwegian study appeared to be too little to show this kind of benefit [19].

Early on, clinicians wanted to know whether vitamin D supplements improve outcomes after the infection has already taken hold. The answer appears to be that mortality may be reduced with robust supplementation at the very earliest stage. Here, one of the few studies finding such a benefit compared mortality in patients given right away several thousand IU of vitamin D in the form of calcifediol to the outcomes in patients given placebo [20]. The much higher and earlier deaths in patients getting no extra vitamin D are stunning.

Unfortunately, many other clinical trials found no benefit with vitamin D supplementation [21]. As in this example, even large amounts of vitamin D started two weeks or more after detection of the infection did not improve outcomes. It seems simply too late to counteract any impaired and unbalanced immune response.

Conclusion

Avoidance of deficiencies in critical nutrients, generally good nutritional status and balanced metabolism, is the best starting point for a resilient immune system. Infections of the upper respiratory tract may be dealt with best by ensuring good vitamin D and general nutritional status prior to the exposure to infection. Everybody living at high latitudes, such as in north and central Europe or the northern half of the United States or in Canada, should regularly use a moderately dosed vitamin D supplement. Adequate nutrition in combination with vaccination and other protective measures is the best bet to get over respiratory infections without too much damage. This appears to be true for all age groups, from young children to older people, including those with additional risk factors.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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M.K. was responsible for the review design, initial draft, and final revision of the work. E.O.A. contributed to the draft and developed Table 2. E.G.B. contributed to the draft and the development of Table 3.

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Nutrition in Disease Recovery

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Abstract

The topic of nutrition in disease recovery is extremely broad as the impact of nutrition is so great on so many disease processes and outcomes. To take a recent example, the COVID-19 pandemic has shone a light on those in society who are most vulnerable, with many of these groups intersecting with those at highest nutritional risk in our communities.

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Introduction

Nutrition plays a vital role in the development and maintenance of our immune function and response, as well as our susceptibility to and recovery from illness, injury, and infection. This chapter will focus on some of the science and physiology underlying the effects of disease on nutritional status, the effects of nutritional status on disease course, and outcomes.

Nutrition and the Immune System

Micronutrients play important roles, often synergistic, at several stages of the immune response. For example, in the development and maintenance of physical barriers (e.g., skin and mucous membranes), production of antimicrobial

proteins, activity of immune cells and generation of memory, and mediation of inflammatory processes. Micronutrients exert specific functions and some work toward common functions, while others have important effects on one and another. For instance, vitamin C has free radical scavenging activity and can also regenerate vitamin E. Another example is the functioning of selenium and zinc, which both mediate inflammatory responses and reduce viral replication.

Infection increases the metabolic demand for energy yielding substrates (e.g., glucose, amino acids, and fatty acids) to facilitate the production of immune system cells and mediators. These processes also require vitamins and minerals, which act as cofactors in several metabolic reactions. Therefore, an adequate nutritional status contributes to an effective immune response. On the other hand, suboptimal nutritional status might result in blunted responses, as seen in different conditions of macronutrient deficiency. There is a bidirectional relationship between nutrition and infection, whereby poor nutritional status predisposes one to infection and where infection is exacerbated by a poor nutritional status – this can result in a cycle of deficiency, disease, and ultimately poorer outcomes from infection [1].

Case Study – Micronutrient Deficiencies

Vitamin A

Hypovitaminosis A is the leading cause of preventable childhood blindness and increases the risk of death from common childhood illnesses such as diarrhea. Vitamin A deficiency is a major public health problem in low/middle-income countries and is a leading cause of morbidity and mortality in women and children. Its prevalence is striking and is particularly concentrated in areas such as Sub-Saharan Africa and South Asia. Specifically, during vitamin A deficiency, the integrity of the mucosal epithelium (i.e., skin and mucous membrane) is compromised, leading to increased susceptibility to infection via the eyes and respiratory and gastrointestinal tract. Therefore, vitamin A deficiency increases the vulnerability to infectious diseases, including measles and malaria, and diarrheal diseases [2].

There is compelling evidence for the supplementation of vitamin A, including ongoing updates to the Cochrane SR database. Periodic, high-dose supplementation is a proven, low-cost intervention which has been shown to reduce all-cause mortality by 12–24%, as well as leading to significant reductions on the incidence of diarrheal diseases, measles, and preventable blindness [3].

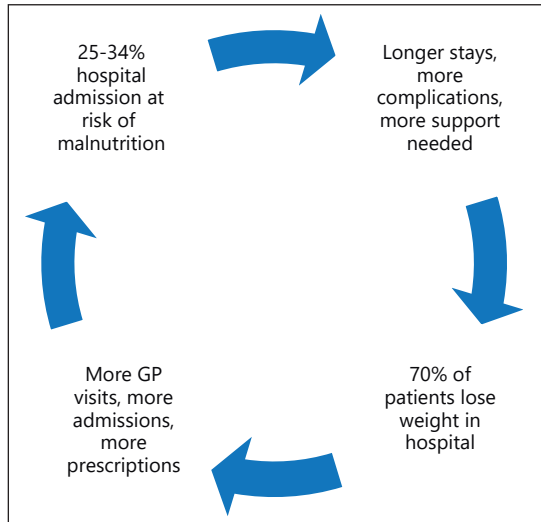


Fig. 1. Adapted from BAPEN Malnutrition Carousel [4]. Adapted from the original with the kind permission of Prof. Marinos Elia, British Association for Parenteral and Enteral Nutrition.

Macronutrients

Malnutrition is a state of nutrition in which an imbalance of energy (deficiency or excess), protein, and other nutrients causes measurable adverse effects on tissue/body form (i.e., body shape, size, and composition), function, and ultimately clinical outcomes. Primarily, optimizing the provision of adequate calories and macronutrients intake will help prevent malnutrition and support immune function. The classical effects of protein-energy malnutrition stem from outcomes observed in malnourished children, including impaired production and function of immune cells and reductions in both innate and adaptive immune responses. From a public health perspective, the prevalence of malnutrition is evident in the community when patients are admitted to secondary care. Malnourished people aged 65 years and over have twice as many hospital admissions compared with nonmalnourished seniors. They also have over 30% longer length of hospitalization and the costs of their admissions are around 2.5 times as much as those for nonmalnourished individuals. Furthermore, this population has more visits to their general practitioners and more prescriptions. Often, patients are discharged from the hospital without adequate nutritional care, which contributes to the cycle of worsened nutritional status, recurrent hospital admissions, and functional decline (Fig. 1) [4].

Acute Illness, Surgery, and Metabolism

Loss of appetite, which often develops during hospitalization, might be either a consequence of an underlying health condition (e.g., pneumonia), medical treatments (e.g., pain medication, chemotherapy), or by social factors, such as depression, social isolation, or advanced age. Both acute and chronic illnesses are associated with loss of appetite and poor nutritional intake, frequently accompanied by a proinflammatory state and loss of lean and adipose tissues. Another scenario is the stress response to surgical procedure, which causes catabolism of energy reserves with release of glucose, free fatty acids, and amino acids. Therefore, these nutrients are diverted from their normal functions, such as maintenance of muscle mass, healing, immune responses, and production of acute phase proteins. In this situation, the nutritional requirements for energy and protein are highly elevated. Other contributing factor is the hormonal imbalance with an increase in glucocorticoid hormones and a decrease in testosterone and other sexual steroids, which may further enhance catabolism and aggravate malnutrition. Additionally, the presence of circulating cytokines (e.g., interleukin 6, tumor necrosis factor- α) influences brain circuitries that control food intake, delayed gastric emptying, and skeletal muscle catabolism. The relationship between acute disease and cachexia is bidirectional, with illness affecting nutritional status and dietary factors influencing the inflammatory response and the course of illness [5].

Nutrition in Disease Recovery – Case Example from a Clinical Trial

The Effect of Early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial (EFFORT) tested the hypothesis that protocol-guided, individualized nutritional support to reach protein and caloric goals reduces the risk of adverse clinical outcomes in medical inpatients at nutritional risk. The nutrition support intervention implemented was based on the following principles: (1) working with hospital kitchens to ensure high-energy high-protein meals and snacks, (2) individualization based on patient preferences, (3) food fortification to increase energy/protein value of meals and snacks, and (4) oral nutritional supplements. The primary outcomes of the trial were the occurrence of adverse clinical outcomes, including all-cause mortality, admission to ICE, readmission to hospital and decline in functional status. The results showed a clear benefit of the individualized nutrition care over standard care. High rates of nutritional risk as assessed by the Nutrition Risk Score resulted in 31% of patients with a score of three, 38% with a score of

four, and 31% with a score of five points or more. Participants that received the intervention achieved significantly higher energy (79% vs. 54% of Estimated Energy Requirement) and protein intakes (76% vs. 55% of Estimated Protein Requirement), equating +290 kcal and +10 g protein per day. Noteworthy, 91% of intervention patients utilized oral nutrition supplementation (ONS) [6].

Enhanced Recovery after Surgery

Enhanced Recovery after Surgery (ERAS) is a multifaceted approach to minimize the stress response associated with and to facilitate the return of function from surgery, which includes preoperative preparation, an emphasis on pre- and postoperative nutrition, and mobilization as key factors in recovery. They were initially developed in colorectal surgery and are now being widely applied in numerous major operations, including ERAS gastric, hepato-pancreato-biliary and genealogical surgeries. Preoperative nutrition intervention includes consumption of solids up to 6 h before procedures, ingestion of clear fluids up to 2 h (with 60–90 min gastric emptying time), and carbohydrate loading the night before and preprocedure. Early oral nutrition is also a key component of ERAS, which demonstrated a significantly lower rate of complications and hospital length of stay. Early oral feeding is also feasible and safe in most patients after surgery and shortens hospital length of stay outside an ERAS program. By a similar logic, in those unsuitable for oral nutrition immediately postsurgery, early enteral nutrition (within 24 h of surgery) is associated with fewer post operative complications and shorter length of stay [7]. A recent systematic review and meta-analysis found that the use of early ONS was associated with reduced infectious complications, pneumonia, ICU admission, and gastrointestinal complications. These data suggest that clinical outcomes are improved with early supplementation, which is a simple, inexpensive, and low-risk intervention for patients [8].

Case Study: Malnutrition Prevalence and the Impact of COVID-19

Mortality from COVID-19 has been highest among older people and those with comorbidities, who are also often most at risk of malnutrition in society (Table 1) [9]. Numerous barriers exist to optimizing nutritional status for those suffering with COVID in the community before ever being admitted to hospital. These challenges exist more widely across multiple patient groups, related to specific illness associated nutrition impact symptoms (Table 2). As well as the

Table 1. COVID-19 fatality rates in high-risk groups [9]

Overall case fatality rate (CFR)	2.3%
70–79 years	8%
80 years and older	14.8%
Cardiovascular disease	10.5%
Diabetes ^a	7.3%
Chronic respiratory disease	6.3%
Hypertension	6.0%
Cancer	5.6%

^aKey observation of effect in poor glycemic control.

Table 2. Side effects of illness impacting on oral intakes

1. Difficulty breathing and requirement for supplemental O₂
2. Loss of appetite, taste, and/or smell
3. Frailty
4. GI disturbances
5. Cognitive disturbances – including low mood

challenges associated with social isolation and difficulties relating to food access, which have always existed, but been brought into the spotlight during the pandemic [10].

Specific to COVID-19, high nutritional risk has been associated with prolonged hospital admissions and pronounced hypermetabolism as documented here by a group in the United States with the use of indirect calorimetry [11]. This has the ability to measure energy expenditure versus what might be expected from predictive equations widely used to calculate nutritional requirements. This demonstrates the significant nutritional demands associated with disease, which is a major driver of increased caloric and protein requirements and poses a risk of nutritional and functional decline when these needs are not met. The NNEdPro COVID-19 Taskforce published a case report during the first wave of the pandemic, documenting the experience of a patient during a prolonged ICU admission with COVID-19 infection [12].

This case study provides further evidence not only of the challenges of accurate assessment of nutritional requirements, but also secondary barriers to achieving nutritional requirements in the critically ill COVID patient. These are contributed to by interruptions to feeding, including the need for proning, tube replacement, and poor GI tolerance of feeding. These factors combined meant that this patient lost a staggering 19 kg over a 52-day admission, or 24% of their initial bodyweight [12]. Accordingly, a focus on nutrition in this patient's rehabilitation should be an important priority. We do now have consensus guide-

lines released in the United Kingdom largely based on many of the first principles [13]. These include the following:

- Screening for malnutrition, which can be carried out using simple screening tools, often used remotely and/or in consultation with the patient themselves.
- Care plans focused on individualized nutrition support, including food-based strategies, oral nutrition support, and referral to a dietitian. Here, the focus will often center around managing specific nutrition impact symptoms and the maintenance and recovery of lean body mass.
- Lastly, an emphasis on continuity of care, which means ensuring that nutrition interventions do not begin and end at the doors of the hospital, but are communicated and followed up through discharge into the community, where the majority of malnutrition exists.

There is compelling evidence that nutritional status is a modifiable risk factor in disease outcomes, and it is highly likely that ensuring adequate nutrition is a fundamental factor in optimizing recovery. To use the example of COVID-19 – this can have a profoundly negative effect on an individual’s nutritional status and plausible that long COVID, as a distinct albeit diverse entity, is also associated with further risk of malnutrition in the longer term.

Crucially, nutritional status can be considered as a modifiable risk factor at both ends of this scale. To promote optimal recovery from illness and build a more resilient population for future health challenges and pandemics, a focus on nutrition increasingly appears to be of paramount importance.

Many guidelines and pathways exist for professionals and members of the public alike, where they can access good, reliable information to improve nutrition-related outcomes.

COVID-19 will be remembered for many reasons and will leave a lasting legacy on healthcare, perhaps a product of this impact could be an increased acknowledgement of the important role of nutrition across the course of disease.

Conflict of Interest Statement

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S.M.: development of presentation material, chapter content, and structure. J.R.B.T.: feedback on proposed manuscript, contributed to content review and modification.

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The Future of Nutrition Care in Health Systems

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Abstract

Leading health systems of the future will embed support for healthy eating as a core component of care. In this chapter, we describe three ways that health systems can act to provide support for healthy eating: (1) being agile in service delivery to adapt to individual's ever-changing support needs, as well as contribute to broader health and food system decision-making; (2) prioritize food as an individual's right to health, and take responsibility for ensuring access to nutritious foods when required; and (3) upholding evidence-informed implementation strategies to underpin evolving healthcare systems. These three interconnected strategies will support the future of nutrition care considering individual and system-level factors.

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Introduction

Food and health care systems have increasingly interconnected and recognized roles in facilitating people to eat well in the pursuit of good health. In the health system, primary care has a key role in disease prevention through providing nutrition care, with increased emphasis on how to enhance practice in a way that is evidence-informed, equitable, and continues to place patients at the center of the care journey. In food systems, strategies are also required to ensure that the food produced is high quality, nutritious, and accessible. Multiple priorities,

changing political landscapes, and social and environmental events, including the COVID-19 pandemic, have made it clear that health and food systems need to be adaptable in order to meet the changing needs of individuals, families, and communities [1].

This chapter describes the areas that we believe should be considered by policymakers when planning for the future of nutrition and healthcare delivery for adults and children. We suggest three ways that health systems can act to provide support for healthy eating: (1) being agile in service delivery to adapt to individual's ever-changing support needs, as well as contribute to broader health and food system decision-making; (2) prioritize food as individual's right to health, and take responsibility for ensuring access to nutritious foods when required; and (3) upholding evidence-informed implementation strategies to underpin changing healthcare systems. These needs were highlighted during a panel discussion held in October 2022, as part of Workshop #98: A collaboration by the Nestle Nutrition Institute and the International Academy of Nutrition Educators (IANE) c/o the NNEdPro Global Institute for Food, Nutrition and Health, entitled: *Global Trends in Nutrition and Health through the Life Course*.

Agile Healthcare Systems

Within an agile healthcare system, the changing needs of individuals need to be considered within the interconnected aspects of a complex system. Leading health systems of the future need to focus on individual needs while maintaining sustainability and equity across populations. Food and healthcare systems are, and should be, strongly interconnected due to the significant role of food in human health. However, food systems have changed significantly as technology and agriculture have advanced. Not only do these changes impact food quality and access, they also impact the healthcare system. The COVID-19 pandemic clearly illustrated the interdependence between health and food systems. For example, disruptions to food supply chains limited access to certain foods and products, which impacted people's health and put additional strain on individuals and on healthcare services [2]. The pandemic also strained business operations in the food industry. The interconnected nature of these systems cannot be ignored and learnings from the COVID-19 pandemic need to be considered in developing more agile, equitable, and sustainable food and healthcare systems that acknowledge their connection and interdependence.

Education has a significant role to play when taking a systems perspective. Shifts in food and agriculture systems impact individuals, leading to the need for increasing knowledge and skills at multiple points within the system. Food is

more than a sum total of its constituent parts, both in terms of the effect on the body as well as its role in people's lives. Education is needed to build capacity throughout food and agriculture systems from those deciding the seeds to plant, to those who decide what food will be available to consumers. All of these factors are impacted by supply chains, which are not necessarily reliable for many reasons, not just economics. Within all of this is the consideration of the cultural importance of food – the role it plays in well-being beyond just health, and the impact our way of eating has on the environment. Throughout this complex ecosystem is the urgent need to consider how our environment and climate change influence our current and future diets, and the impact on the current and future healthcare system [3].

An Individual's Right to Health

The right to health and the right to food are highly connected. While healthcare systems need to be agile to rapidly provide what is needed for the societies that we live in regarding healthy food and quality of care, there are differences in how this looks between countries and populations. Equitable access to health services and to high-quality food is a longstanding issue in many countries. In the past, healthcare actions have not genuinely demonstrated the vast impact of these issues, and this cannot be ignored any longer. Change is needed to find equitable and sustainable approaches to provide long-term access to healthy, high-quality food, regardless of why people do not have access, e.g., socioeconomic, geographical, or a natural disaster.

In recent years, there are many reasons for disruption to food systems which is also disruptive to human health. We now have more people displaced from their homes than ever before and many live in refugee centers, so we must be agile in how we may provide food. The four elements of acute and chronic food and nutrition insecurity must each be considered: (a) physical availability of food; (b) economic and physical access to food; (c) food utilization; and (d) stability of the other dimensions over time [4]. Many responses to food insecurity have focused at the individual level by providing food directly, e.g., food stamps in the United States of America, social prescribing to access food banks in the United Kingdom, and delivery of veggie boxes to rural communities in Australia. However, only focusing on individual access will not address the larger issues of food insecurity, including the role of household income as show in the Canadian annual reports of household food insecurity [5]. Further acknowledgment of the economics and system-level impact on and of food insecurity is needed to make sustainable improvements at the population level.

Evidence-Informed Implementation Strategies

To develop agile food and healthcare systems, evidence-informed implementation strategies at the individual, organizational, and systems levels are needed. At the individual level, behavior change theories can be crucial to support sustained change. For example, the COM-B model articulates how individuals need the *Capability*, *Opportunity*, and *Motivation* to change behavior [6]. For example, for an individual to move toward eating a healthier diet, they need the knowledge and skills (*Capability*) to know what to buy and how to prepare it. Individuals also need the *Opportunity*, such as an income which allows them to buy healthier food, access to food to purchase, and space to prepare the food. *Motivation* is also needed to change their eating patterns. All three elements are needed to encourage behavior change. However, individuals live in systems, and each aspect of the COM-B model is impacted by where people live, the availability of food, the political structure, and other complex and systems level factors.

System-level changes are also essential for equitable access to quality food and healthcare. One strategy for agile systems is to take a learning health system approach. Learning health systems have been defined as systems where “science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience” [7]. Although there are many descriptions of a learning health system approach, a core tenet is the ability to learn from known information and use it to continuously improve care delivery. This approach can be considered in connection with the Quintuple Aim to focus on patient experience, provider experience, cost, population health impact, and health equity [8]. When implementing a learning health systems approach within the current healthcare climate, careful consideration of provider capacity must be considered due to multiple competing priorities, and high rates of burnout. The combinations of change fatigue and burnout mean that implementation of a learning health system needs careful consideration for each aspect of the Quintuple Aim [9].

Preparing for the Next Global Challenge

Food is part of our everyday lives and what we eat is impacted by a complex combination of individual behaviors and system-level factors. To prepare for the future, including the next global challenge, we need to be agile in policy development and service delivery – constantly considering the complex individual and system level factors at play. Food must be prioritized as an individual’s right to health at all times, particularly during times of crisis. Underpinning all of this is

the need for evidence-informed implementation strategies to support individual behavior change and the ever-changing food and health systems. Rigorous research has a role to play in informing how to address the next global challenge; however, a better balance is needed to maintain rigor yet provide a timely response. Technology may have a role to play in achieving this balance, and an overall emphasis on health equity is strongly needed. There are multiple ways to plan for the future of healthcare delivery – overall, it’s about timely consideration and actions to address interconnected individual and system-level needs.

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Author Contributions

C.L., J.B., and L.B. participated in the panel discussion that underpinned this manuscript. C.L., J.B., and L.B. contributed to the initial discussion points, manuscript outline, and drafting. C.L., J.B., and L.B. approved the final version of the manuscript for submission.

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Globesity and Increasing Noncommunicable Diseases

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Abstract

Globesity, a global epidemic characterized by the widespread prevalence of obesity, poses a significant threat to individuals of all ages, ranging from infants to the elderly. This pervasive condition exerts detrimental effects on multiple organ systems within the human body. Consequently, urgent and comprehensive efforts are required to combat this escalating problem. Early intervention during critical developmental stages, such as fetal life and early infancy, holds immense potential for effective intervention with minimal adverse effects. Emphasizing the importance of early nutrition, particularly through breastfeeding support, emerges as a paramount strategy for infant care. In cases where formula feeding is necessary, the utilization of low protein formulas and supplementation with human milk oligosaccharides (HMOs) have demonstrated favorable outcomes. Furthermore, adopting healthy weaning practices, promoting adequate sleep patterns, encouraging regular exercise, and maintaining consistent follow-up throughout an individual's lifespan constitute fundamental pillars in addressing and mitigating obesity. By prioritizing these evidence-based interventions, we can strive to alleviate the detrimental consequences of obesity and promote optimal health outcomes across the entire life cycle.

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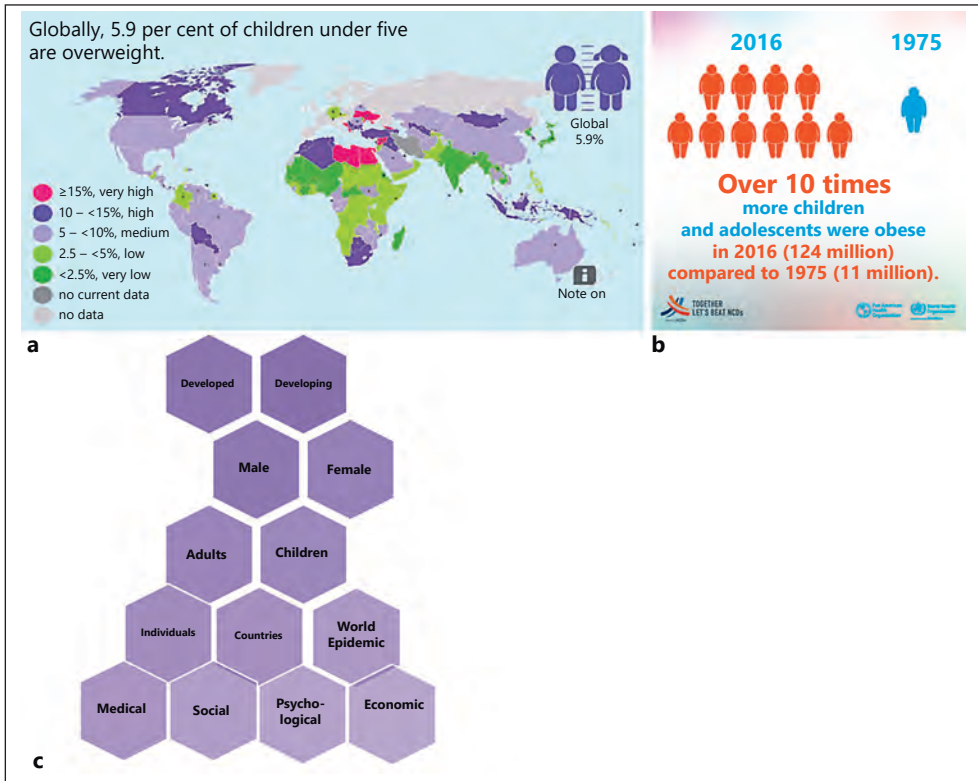


Fig. 1. a Prevalence of overweight in children under five, by country, 2018. Reproduced/ Adapted from WHO [3]. **b** The rising obesity prevalence in children. Reproduced from WHO [4]. **c** The global obesity (Globesity).

Introduction

Globesity is a term which consists of two parts, global and obesity, to imply the global rise of obesity, i.e., the obesity worldwide epidemic. This term was coined by the World Health Organization (WHO) in 2001. Globesity represents the global surge in obesity and signifies the worldwide epidemic of this condition. Presently, the number of individuals affected by obesity is escalating at a rate twice that of those experiencing hunger or malnutrition [1].

Remarkably, for the first time in history, the prevalence of overweight individuals surpasses that of underweight individuals. Globally, adult obesity has become more prevalent than undernutrition, while pediatric obesity has also reached alarming levels, with an estimated incidence of approximately 5.9% among children under the age of five, as reported by UNICEF data in 2019 [1, 2] (Fig. 1a, b).

Contrary to conventional assumptions, the obesity epidemic transcends boundaries, affecting populations in both developed and developing countries, spanning across genders, age groups, and socioeconomic backgrounds (Fig. 1c) [1]. In developing nations, over 115 million people are estimated to be grappling with obesity-related complications (Fig. 1a, b). This pervasive condition imposes substantial medical, social, psychological, and economic burdens on individuals, communities, and nations alike [5].

Obesity and Human Diseases

Obesity and Communicable Diseases: A Bidirectional Relationship

The relationship between obesity and communicable diseases is characterized by mutual influence and interdependence. A striking example of this association was observed during the COVID-19 pandemic, where obesity emerged as a significant risk factor for increased susceptibility to severe disease outcomes and mortality. Studies have revealed that obesity substantially amplified the risk of COVID-19 hospitalization by 3.1 times, while hospitalized patients with obesity faced a 1.4 times higher risk of experiencing severe illness. Moreover, obesity was found to be independently associated with an elevated risk of COVID-19 mortality [6, 7].

Conversely, the COVID-19 pandemic has had detrimental consequences on the globesity epidemic. The implementation of lockdown measures and the resultant shift to remote work and home schooling has led to a notable decrease in physical activity levels among various age groups. This sedentary lifestyle, coupled with changes in dietary patterns and disrupted routines, has contributed to a concerning trend of increased body mass index (BMI) among children. A study conducted by Lange et al., involving 432,302 children, reported a nearly twofold increase in BMI among children aged 2–19 years during the period of lockdown [8]. The same was reported by Hauerslev and her colleagues who requested that global leaders act to change the childhood obesity trajectory [9].

It is evident that the relationship between obesity and communicable diseases is multifaceted and dynamic. The COVID-19 pandemic has served as a poignant reminder of the intricate interplay between these two phenomena, emphasizing the need for comprehensive strategies to address both the global obesity crisis and the prevention and management of communicable diseases.

Obesity and Noncommunicable Diseases

The connection between obesity and noncommunicable diseases (NCDs) is widely recognized and carries substantial implications for individual health and

healthcare systems. Obesity affects almost every organ system in the body, leading to a range of long-term complications and comorbidities [10–14]. Childhood obesity leads to insulin resistance and consequently a diverse array of NCDs including dyslipidemia, metabolic syndrome, prediabetes, diabetes, polycystic ovaries, precocious puberty, and others [15].

Obesity is a major risk factor for numerous chronic conditions, including cardiovascular diseases (such as hypertension, coronary artery disease, and stroke), type 2 diabetes mellitus, certain types of cancer (e.g., breast, colon), musculoskeletal disorders (e.g., osteoarthritis), respiratory problems (e.g., sleep apnea), and mental health disorders (e.g., depression). These conditions not only have a profound impact on individuals' quality of life but also impose a considerable economic burden on healthcare systems, as they require long-term management and treatment [10–14].

Root Causes of Globesity: Unmodifiable and Modifiable Factors

Understanding the root causes of the escalating obesity epidemic is crucial for effective prevention strategies. The etiology of obesity is multifactorial, with certain factors being unmodifiable while others are modifiable [15–17]. Unmodifiable factors include genetic background, ethnicity, and intrauterine influences such as maternal obesity, maternal gestational weight gain, gestational diabetes, and epigenetic factors [15–17]. This gives rise to what is known as the transgenerational cycle of obesity, wherein infants born to obese mothers are more likely to develop obesity due to fetal metabolic programming that begins in early intrauterine life. This programming has implications for later-life obesity, metabolic syndrome, and cardiovascular disease [18]. Furthermore, childhood obesity sets the stage for a vicious cycle that perpetuates into adolescence and adulthood [16].

On the other hand, modifiable factors offer opportunities for intervention and prevention. Dietary habits, lifestyle choices, socioeconomic status, physical activity, and sleep patterns all fall within this domain [16]. Dietary factors including breastfeeding versus formula feeding, consumption of high-energy-dense foods, sweetened beverages, fast food, junk food, and preprepared convenience foods. The influence of food marketing targeted at children is also noteworthy [16]. Insufficient physical activity, sedentary behaviors, reduced exercise levels, excessive academic engagement, and prolonged screen time contribute significantly to the development of obesity [16]. Additionally, sleep problems, including disturbed sleep patterns and obstructive sleep apnea, have emerged as contributors to obesity [16].

Interestingly, emerging evidence suggests a role for the disturbed gastrointestinal (GI) microenvironment and dysbiosis in obesity development [19]. Research is shedding light on the potential transgenerational transmission of dysbiotic bacteria from obese mothers to their infants, emphasizing the impact of dysbiosis on infant obesity. In this context, the question of whether NCDs can be communicable is gaining attention, highlighting the potential implications of dysbiosis in the obesity epidemic [20].

It is important to further investigate these factors and their interplay to inform comprehensive prevention strategies and interventions targeting the multifaceted nature of obesity. By addressing both unmodifiable and modifiable factors, we can strive to break the transgenerational cycle of obesity and curb the rising prevalence of this global health concern.

Globesity Action Plan: A Comprehensive Approach to Prevention

The prevention of globesity requires a multimodal integrated action plan that addresses different levels of prevention: primary, secondary, and tertiary. Primary prevention is of utmost importance as it focuses on preventing obesity and related NCDs, as these conditions are largely preventable [21].

Secondary prevention aims to identify obesity at an early stage and implement interventions to reverse its course, while tertiary prevention aims to manage established obesity and prevent or treat its complications. However, it is worth noting that most current treatment practices primarily aim to control the problem rather than provide a cure [21].

The ultimate goal of the obesity action plan is to achieve and maintain an energy balance throughout an individual's lifespan [21]. Early intervention is crucial as it allows for greater plasticity and reduces the detrimental effects of lifestyle changes. This approach aligns with the life course model of obesity and NCDs, emphasizing the importance of addressing obesity from an early stage and throughout an individual's life (Fig. 2) [23].

The WHO has recognized the problem of globesity as part of the double burden of malnutrition (what) and has highlighted the magnitude of the issue (where), its negative impact on health (who), and the need for an action plan (why act) [24]. Figure 2 shows the WHO infographic of the double burden of malnutrition. However, the global nutrition report released in 2021 indicates that we are off course in meeting the target of halting obesity [25].

To address globesity comprehensively, Arena and colleagues proposed a conceptual model that emphasizes the promotion of healthy lifestyles, education, and interventions [26]. Their model recognizes the influence of various agen-

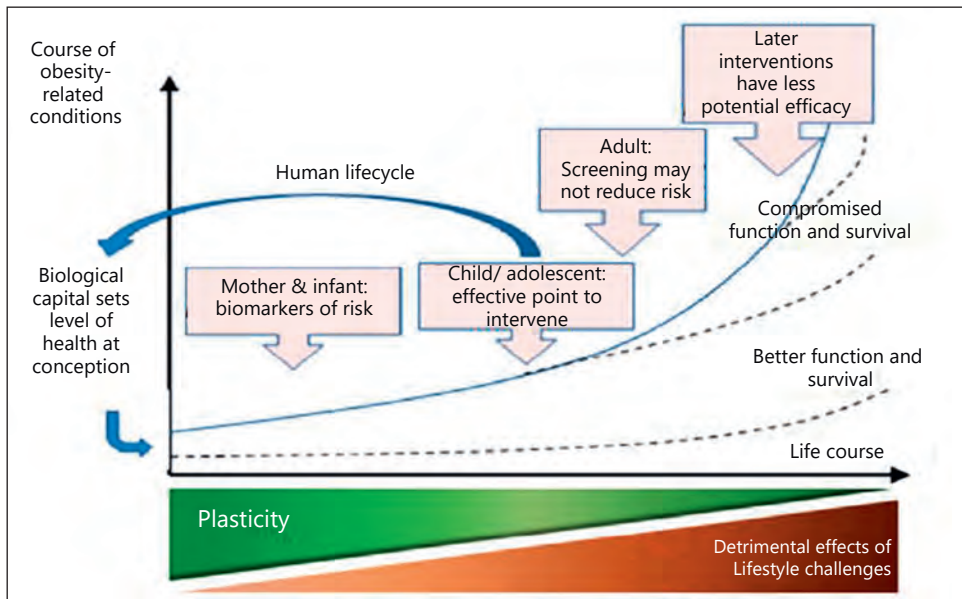


Fig. 2. Life-course model of obesity and other noncommunicable disease risk. Reproduced from Hanson [22].

cies, organizations, and social media platforms at multiple levels, starting from individuals and families, to local, national, and global populations [26].

Focus on Globesity Action Plan in Children

When addressing globesity, particular attention is given to children due to their vulnerability and dependence on their families. Children also have a longer life expectancy, which exposes them to potential complications associated with obesity. Therefore, organizations and societies emphasize the importance of early nutrition and care for children. In 2006, the ESPGHAN committee of nutrition stated that early infant feeding not only influences physical growth and development but also the incidence of GI, respiratory, and allergic disease in early childhood, as well as possibly metabolism and health in late childhood and adulthood [27].

Taking action to reduce the risk of childhood obesity is crucial. This should begin as early as fetal life by reducing obesity in pregnant women [28]. Promoting breastfeeding is another important measure, as it is considered the best nutrition for infants [28]. For those who are formula-fed, it is essential to choose a

formula with an appropriate protein content. High protein intake in infant formula during the first year of life has been associated with insulinogenic and adipogenic effects, leading to greater fat mass in children aged 2–6 years. Lowering protein content in infant formula may result in healthier body composition during early childhood [29].

Supplementing formula with HMOs is also beneficial. HMOs play a role in maintaining a healthy intestinal microbiota, preventing dysbiosis, and mitigating the risk of obesity and metabolic syndrome [30].

Moreover, healthy weaning practices and the adoption of a healthy diet for toddlers and children are essential. This includes limiting the consumption of sugary and fatty foods and beverages, as well as curbing their promotion through television and digital media [31]. Governments should consider implementing clear labeling of foods containing high sugar, high fat, trans fat, saturated fat, and artificial sweeteners. Additional measures, such as banning the sale of unhealthy foods in schools and increasing taxes on producers, can help reduce their consumption [31].

Encouraging physical activity and promoting regular exercise for children and their parents are important strategies. Adequate sleep is also crucial in maintaining a healthy lifestyle [31].

Furthermore, monitoring healthy nutrition throughout the lifecycle, from infancy to childhood, adolescence, and beyond, should involve pediatricians and society as a whole [32]. Various governmental, organizational, and societal support, including WHO, UNICEF, PAHO, and WABA, have implemented important action plans to combat obesity, as summarized by Sotiraki et al. [33].

Conclusions

Globesity, the global obesity, is a rising epidemic affecting individuals across different age groups, from infancy to the elderly. It has deleterious impacts on various body organs and systems. Efforts should be undertaken to address and halt this problem. Early intervention, starting as early as fetal life and continuing into early infancy, where plasticity is highest and side effects are minimized, is highly recommended. Early nutrition supporting breast feeding is the best strategy in infants. In formula-fed babies, appropriate formula feeding with low protein content and HMO supplementation are beneficial strategies. Healthy weaning, promoting good sleep habits, regular exercise, and continuous follow-up throughout the life cycle are essential cornerstones in combating globesity.

Conflict of Interest Statement

The author declares no competing interests.

Author Contributions

Naglaa M. Kamal, Sara A. Abosabie, and Salma A.S. Abosabie contributed significantly to manuscript writing, reviewing the literature, the acquisition, and interpretation of data; drafting the article, revising it critically for important intellectual content; and final approval of the version to be published.

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Nutrition and Immunity: Key Nutrients and Trends in Nutrient Supplementation in Women and Children

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Abstract

Nutrition plays a critical role in promoting good immunity and health. One third of the population has at least one micronutrient deficiency, with higher vulnerability observed in women and children. A healthy diet is critical to guarantee an adequate micronutrient status and good immune response. Food components (high-quality fats and carbohydrates; many micronutrients) have been associated with antioxidant, anti-inflammatory, and immune-modulating properties. All pregnant women should be supplemented with folic acid and iron, and some may require calcium supplementation for the prevention of preeclampsia. Some women may benefit from multiple micronutrient supplementation (MMS), vitamin D, and/or omega 3. In breastfeeding babies, vitamin D supplementation is indicated for preventing deficiency, and, in areas of high vitamin A deficiency prevalence, children may need vitamin A supplementation to prevent morbidity and mortality. In adults, some evidence has shown that vitamin D or C supplementation may decrease the risk of respiratory infections and/or duration of symptoms. For COVID-19, there is some evidence of a reduction of complication events, mainly ICU admissions in adults supplemented with vitamin D, but studies show high heterogeneity. During the COVID-19 pandemic, some countries have reported an increase in the use of dietary supplements. A need for better nutrition education for the general public and health professionals is evident, as well as better targeting nutrition interventions according to adequate nutritional assessment. Countries should focus on increasing the nutrient density of the food supply, and improve food access, while decreasing the availability of ultraprocessed foods to promote health and optimal immunity.

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Introduction

Micronutrient deficiencies still represent a significant public health issue around the world. One-third of the population has at least one form of micronutrient deficiency. Inequities in the burden of micronutrient deficiencies are evident, where pregnant women and children are at higher risk [1]. Recent data from the Global Micronutrient Deficiencies Research Group showed that 56% of preschool children and 69% of nonpregnant women of reproductive age have at least one of three micronutrient deficiencies. The prevalence of micronutrient deficiencies is higher in low- and middle-income countries (LMICs), but high-income countries may also be affected. Fifty percent of women and children from high-income countries have at least one micronutrient deficiency. Regions with the highest prevalence are Sub-Saharan Africa, East and South Asia, and the Pacific [2].

Iron deficiency is the most common micronutrient deficiency, with one third of the population affected by it [1]. In 2016, approximately 40% of children and pregnant women had iron deficiency [3]. Iron deficiency anemia (IDA) is the dominant cause of anemia globally (>50%), and increases morbidity and mortality. In pregnancy, IDA increases the risk of preterm birth, low birth weight (LBW) and mortality. In children, it is associated with mental and motor development problems [4]. Vitamin A deficiency is also one of the most prevalent micronutrient deficiencies, which mainly affects children 1–4 years old. It is the leading cause of preventable blindness and increases the risk of severe infections, including diarrhea and measles [1]. Iodine deficiency is also prevalent in some countries (Europe, South East Asia, Sub-Saharan Africa), with higher prevalence observed in women and adults (30–34 years of age) [1, 5]. In a study where the estimated annual percentage change in the prevalence of iron, vitamin A, and iodine deficiencies was calculated (1990–2019), an upward trend was observed in some countries, including the Philippines, Pakistan, South Sudan, Madagascar, Somalia, Andorra, Portugal, Mexico, Monaco, and San Marino [1]. Vitamin D deficiency is also very prevalent worldwide, with a higher risk in women. Countries most affected include North America, some Middle East countries, Northern Europe and North Africa, and other very high-latitude countries [6].

In this context, and particularly, in the COVID-19 pandemic, attention has been given to achieve an optimal nutritional status, including adequate micronutrient status, to promote a healthy immune system. Healthy diets, food fortification, and nutrient supplementation are key for optimal immunity. This review is aimed to describe the important role that nutrition has on immunity, to show the evidence of micronutrient supplementation for improving health and protecting against respiratory infections in women, pregnant women and children, and the trend of micronutrient supplement use in recent years.

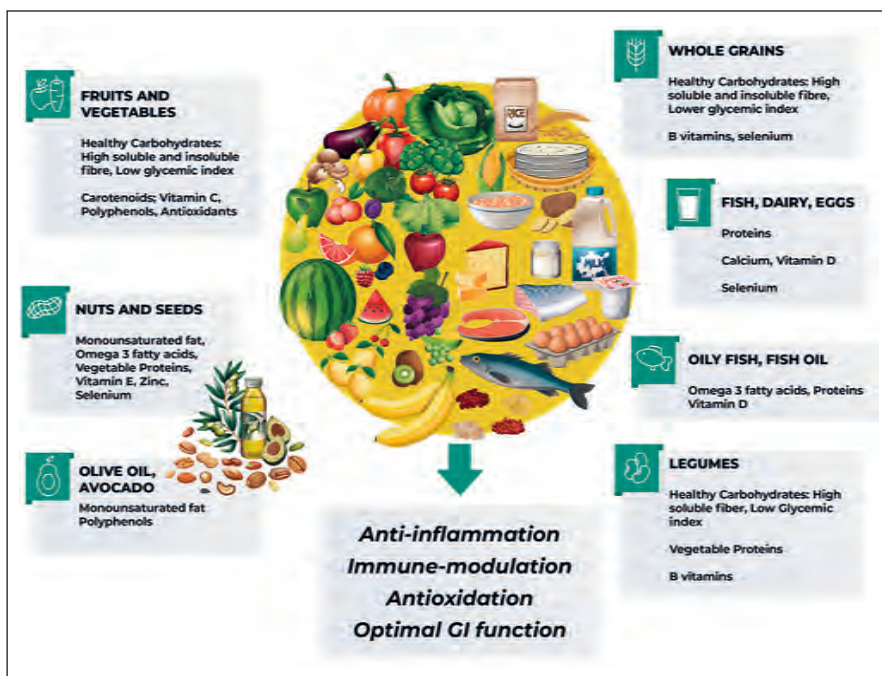


Fig. 1. Healthy dietary pattern food components and their role in promoting healthy immunity.

Role of Nutrition in Promoting a Healthy Immune System

Healthy diets should be accessible and consumed by all individuals, and should provide a balance of macro and micronutrients, considering they have different roles in immunity. In general, a healthy dietary pattern is considered one with a high content of fruits, vegetables, grains, and legumes. It includes fish, dairy, eggs, and healthy fats (i.e., nuts and seeds, olive oil/other oils, other monounsaturated fat sources) and limits red meat, processed meats, as well as added sugars and ultraprocessed foods. Some healthy dietary patterns that have been studied in randomized clinical trials (RCTs) include the Mediterranean-type diet and the DASH diet; both have been associated with the improvement of multiple metabolic parameters [7, 8], as well as with a decrease in inflammation and oxidative stress [9, 10] (Fig. 1). Regarding macronutrient intake, it is important to guarantee an adequate protein intake to reduce the risk of infections. Amino acids are essential for antibody and cytokine production and participate in regulating the activation of macrophages, natural killer cells, B-, and T lymphocytes [11]. The type and quantity of lipid intake may also alter immunolog-

ic function. High-fat diets have been associated with macrophage dysfunction and with impaired signaling within the immune response. Excessive saturated fat intake has been related with increased levels of C-reactive protein (CRP) and fibrinogen and with higher low-grade chronic inflammation [12]. An imbalance between omega 6 and omega 3 polyunsaturated fatty acids intake may promote inflammation; where omega 3 fatty acids (eicosapentaenoic acid-EPA and docosahexaenoic acid-DHA) have an antiinflammatory role. Omega-3 fatty acids change the composition of the phospholipid bilayer of the host cell membrane, thereby preventing viral entry. The ideal omega 6/omega 3 fatty acid intake ratio is 1:1–4:1, which is much higher in current “Western” diets [11]. Omega 3 fat intake is low in most regions around the world. The DHA intake recommendation of 250–500 mg per day appears to be met only in East Asia. In a recent report, low levels of %EPA+DHA of total fatty acids in erythrocytes or erythrocytes equivalents were observed in different world areas, with adequate levels found in very few high latitude countries [13, 14].

Carbohydrate intake may also exert inflammatory effects. High glycemic index and/or high glycemic load diets are associated with higher CRP levels and have correlated positively with inflammatory cytokines (tumor necrosis factor (TNF)-alpha, interleukin-6). On the other hand, low glycemic index diets may decrease inflammatory responses. High-fiber diets have also been associated with lower CRP and TNF-alpha levels; the associations appear to be related with the increase in short chain fatty acids (SCFAs) that result from fiber fermentation in the gut [12, 15]. SCFA enhances mucus secretion and increases antimicrobial peptides. A high-fiber and prebiotic diet promotes the growth of less opportunistic bacteria and bacterial metabolites and decreases lipopolysaccharide and proinflammatory cytokines, while increasing the growth of more beneficial bacteria, resulting in a more functional intestinal barrier and a better regulated immune response [16].

Micronutrients also have multiple roles in maintaining a healthy immune system. Vitamin C, vitamin E, B carotenes, and phenolic compounds are potent antioxidants and participate in quenching reactive oxygen species and/or reactive nitrogen species, which is essential to reduce macronutrient oxidation or nitration. Zinc and selenium promote antioxidant responses participating as cofactors of antioxidant enzymes and transcription factors. Zinc appears to interfere with the viral replication cycle. Carotenoids also interact in translocation of transcription factors involved in inflammation and oxidative stress regulation. Carotenoids can influence monocyte macrophage differentiation, as well as regulate metabolism by activating specific nuclear receptors [11, 12, 17]. Vitamin D is an immunomodulator that improves microbial activity against pathogens, including respiratory viruses. It attenuates the innate inflammatory

response and promotes antimicrobial peptides and defensins. Vitamin D also affects adaptive immunity by enhancing CD4 T cells, suppressing T helper 17 cells, and promoting the production of virus-specific antibodies by activating T-cell-dependent cells [18]. There is plenty of evidence of the role of nutrients in decreasing inflammation, oxidative stress, and promoting good immune response.

Ideally, macronutrient and micronutrient intake requirements should be met with a healthy diet. Even though the estimated prevalence of inadequate micronutrient intakes has been reduced globally, through the increase in food supply and/or improvement in micronutrient density, inadequate intakes of many nutrients are still prevalent in many countries. Most frequent inadequate intakes include calcium, iron, zinc, vitamin A, and vitamin C [5]. The high intake of ultraprocessed foods and high energy dense diets in many countries are associated with lower intake of micronutrients and fiber [19]; a diet high in ultraprocessed foods has been associated with oxidative stress, inflammation, and intestinal dysbiosis [20]. The high prevalence of food insecurity in some regions may account for inadequate intakes as well.

In the COVID pandemic, promoting a good nutritional status should be a priority. On one hand, it is well known that an inadequate nutrition and metabolic status (obesity, hypertension, diabetes, anemia) are risk factors for COVID-19 and may increase the risk of complications and/or mortality [21]. High prevalence of malnutrition has been observed in COVID-19 patients [22]. Some evidence has shown an altered microbiota profile in infected individuals, probably affecting the magnitude of COVID-19 severity via modulating host immune responses [23]. It is urgent to improve dietary intake and guarantee access of healthy food for everyone, improve food fortification strategies, and recommend micronutrient supplementation in those who need it.

Micronutrient Supplementation in Women of Reproductive Age and during Pregnancy

Considering the current nutritional status of women around the world, nutrient supplementation is needed in some life cycle stages and in conditions that increase the risk for deficiencies. Early optimal nutrition has become a priority considering the evidence of its effect on fetal programming of metabolic diseases. It is well known that diet, lifestyle factors, and nutrition and metabolic status during conception and in pregnancy affect different fetal organs modifying the risk of adverse perinatal outcomes and the long-term risk of NCDs [24, 25] (Fig. 2).

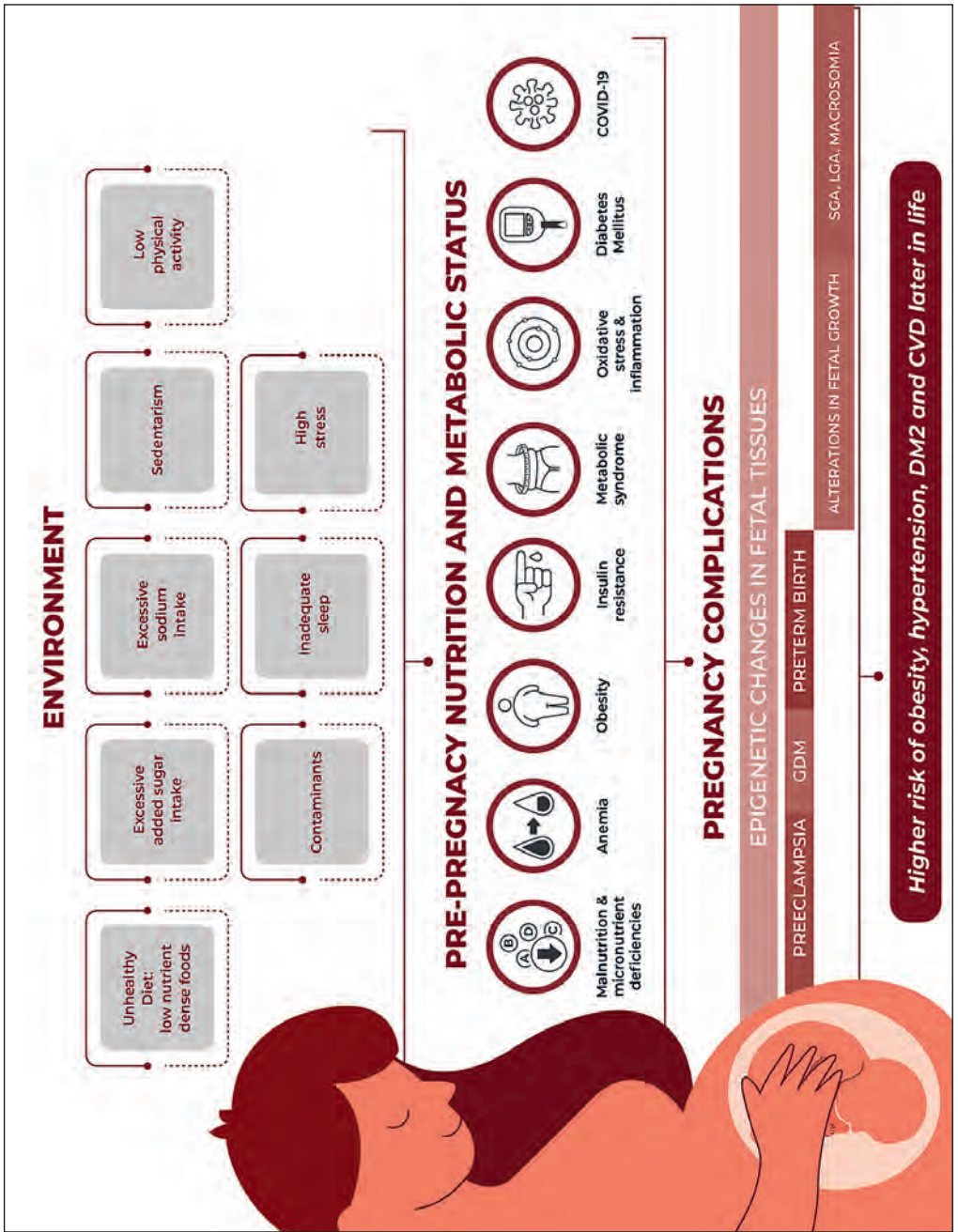


Fig. 2. Maternal nutrition and lifestyle determinants of fetal programming of metabolic diseases.

Iron supplementation appears to be important in women of reproductive age that live in areas with high prevalence of anemia. A recent Cochrane review showed that in menstruating women, the intermittent supplementation of iron reduces significantly the risk of anemia and improves the level of hemoglobin, with similar effects to daily supplementation [26]. Daily iron supplementation may increase Hb levels and reduce the risk of anemia and IDA in infants, pre-school and school-aged children, and pregnant and nonpregnant women [27].

The WHO guidelines for prenatal care recommend that all women of reproductive age should take folic acid (400 µg per day) to decrease the risk of neural tube defects (NTDs) [28]. Women with high risk of developing NTDs should take higher doses [29] (Table 1). During pregnancy, the WHO recommends daily folic acid and iron supplementation (30–60 mg per day) for all women in all contexts. For women reporting side effects due to oral iron intolerance, a weekly supplementation of 120 mg per day of iron and 2.8 mg per day of folic acid may be recommended, which has been shown to have similar benefits [28].

Considering recent evidence, an update of the WHO recommendations (2020) includes MMS (3–4 micronutrients including folic acid and iron and up to 15 micronutrients) for LMIC women [30]. Women in areas with food insecurity, nutrition deficiencies, or vulnerable populations may benefit from MMS [30]. Good quality evidence from meta-analysis has shown a reduced risk of LBW and small for gestational age (SGA) newborns in women from LMICs receiving MMS (containing iron and folic acid) when compared to placebo [31, 32]. A reduction in the risk of preterm birth has also been observed in some studies [31]. MMS supplementation has not been associated with higher perinatal or neonatal mortality [31, 32].

There is no consensus for other routine micronutrient supplementation for all pregnant women. However, there are individual conditions that may require the supplementation of some other nutrients in some women. In women with high risk of preeclampsia and low calcium intakes, calcium supplementation should be started [33]. In women with plant-based diets, who are vegan or vegetarian, or have inadequate intakes, supplementation of zinc, vitamin B₁₂, vitamin D, iron, and DHA and EPA may be required. Routine and specific nutrient supplementation recommendations during pregnancy are shown in Table 1.

Controversy exists about vitamin D supplementation in pregnancy and the ideal doses to be prescribed. Intake recommendations are highly variable between international and regional guidelines. Considering the high prevalence of vitamin D deficiency in many countries, many women may need to be supplemented. Risk factors for deficiency include living in high latitude countries or

Table 1. Nutrient supplementation recommendations in pregnancy and evidence of its effect on perinatal and child health

Nutrient and DRI (IOM)	Supplementation: pregnant women, all women (WHO)	New evidence	Maternal and fetal outcomes
Folic acid (preconceptionally) 600 µg/day	400 µg/day	Canadian obstetrics and gynecology guidelines ^a : High risk: 4–5 mg/day (until 12 weeks) Moderate risk: 1 mg/day (until 12 weeks) Low risk: 400 µg/day Recommended within a multivitamin containing 14–20 mg/day iron and 2.6 µg/day of vitamin B ₁₂	Decrease the risk of neural tube defects
Iron 27 mg/day	30–60 mg/day elemental iron In women with oral iron intolerance, intermittent supplementation may be recommended (120 and 2.8 mg/week of iron and folic acid)		Decrease the risk of low birthweight, anemia, and iron deficiency
Calcium 1,000 mg/day	In women with high risk of preeclampsia and with low calcium intakes: 1.5–2.0 g/day elemental calcium	Some recent evidence has shown a protection with lower doses (<1 g/day)	Decrease the risk of hypertension and preeclampsia in high-risk women with low intakes Shows protection against severe maternal morbidity and mortality
Multiple micronutrients (containing folic acid and iron)	In context of rigorous research In LMICs women, women with malnutrition and/or food insecurity	Several studies, mainly in LMICs, have been done with MMS containing folic acid and iron (≥3 micronutrients) compared to folic acid and iron alone	In LMICs, probably decrease the risk of LBW, SGA, and preterm birth May decrease stillbirth risk, particularly in LMICs Improves maternal micronutrient status
Vitamin D 600 IU/day	Not routinely	According to vitamin D deficiency prevalence and the presence of risk factors for deficiency, supplementation may be required	Probably reduce the risk of GDM, LBW, and SGA (see Table 2)
Vitamin B ₁₂ 2.6 µg/day	Not routinely	Should complement folic acid supplementation Additional supplementation may be needed in women with plant-based diets (vegan, vegetarian) and/or food insecurity	Very few RCTs
Zinc	Not routinely	Supplementation may be needed in women with plant-based diets (vegan, vegetarian) and/or food insecurity Iron, folic acid, and calcium supplementation may reduce zinc bioavailability	Controversy, if decreases the risk of preterm birth More research is needed
Omega 3 (DHA-EPA)	Not routinely	If inadequate intakes, supplementation with intake recommendation (DHA 200–300 mg/day)	Decrease the risk of preterm birth and LBW
Myoinositol	Not routinely		Possibly reduced the risk of GDM

DRI, dietary reference intake; IOM, Institute of Medicine dietary reference intake recommendations; WHO, World Health Organization; LMICs, Low- and middle-income countries; LBW, low birth weight; SGA, small for gestational age; RCTs, randomized clinical trials; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GDM, gestational diabetes mellitus.

^aIndividualized supplementation taking into account risk of neural tube defects. High risk: previous pregnancy, personal history, or a first-degree relative with a neural tube defect; moderate risk: folate sensitive congenital anomalies or women with complex medical/surgical conditions with high risk of folate deficiency (diabetes mellitus, obesity, malabsorption, gastric bypass, hepatic disease, metformin use, anticonvulsive medications, renal disease with dialysis).

not being exposed to sunlight, having obesity, dark skin pigmentation, and low dietary intakes [6].

Evidence from meta-analysis of RCT of vitamin D supplementation during pregnancy and its effect on maternal, neonatal and child health is presented in Table 2. Vitamin D supplementation increases maternal and neonatal 25-hydroxyvitamin D (25-OH-D) concentrations [34]. Evidence has shown a lower risk of developing gestational diabetes mellitus, and apparently higher birth weight and lower risk of LBW and SGA in supplemented women. Controversy exists about its effect on decreasing the risk of preeclampsia and preterm birth [34–42]. The supplementation with 4,000 IU per day has not been associated with adverse effects (hypocalcemia, hypercalcemia, hypercalciuria, hypervitaminosis), but it does not appear to be beneficial in reducing adverse perinatal outcomes [42].

Recent evidence in women planning a pregnancy and in pregnant women has shown that myoinositol supplementation versus control possibly reduced the risk of gestational diabetes mellitus. However, the evidence is still graded as low quality [43].

Micronutrient Supplementation in Children

All children need to meet the vitamin D intake recommendation of 400 IU per day during the first year of life to maximize bone health [44]. It is recommended to supplement exclusively or partially breastfed babies, or that the breastfeeding mom receives supplementation to prevent developing vitamin D deficiency [45]. In children, there is not enough evidence to routinely recommend micronutrient supplementation. A thorough clinical and nutritional evaluation is necessary in clinical practice or at community or regional levels.

To prevent mortality and morbidity associated with vitamin A deficiency (measles, night blindness), in 2011, the WHO recommended large oral doses of vitamin A for children living in areas with a high prevalence of vitamin A deficiency. In infants aged 6–11 months, the recommendation is a single dose of 30,000 µg RAE (100,000 IU), and for 1–5-year-old children, 60,000 µg RAE (200,000 IU) is recommended every 4–6 months [46].

High certainty evidence from a recent Cochrane review (2022) of 47 RCTs from 19 countries in children living in the community reported a significant 12% reduction in all-cause mortality and a 12% reduction in mortality due to diarrhea in children supplemented with vitamin A, when compared to a control group [47].

In terms of growth, a recent meta-analysis showed that zinc supplementation in healthy term infants <6 months of age resulted in significant increases in

Table 2. Summary of meta-analysis of vitamin D supplementation studies and its effect on main perinatal outcomes and neonatal growth

Meta-analysis of RCTs	Studies (heterogeneous vitamin D intervention)	Effect size Relative risk/odds ratio (95% confidence interval)
<i>Gestational diabetes</i>		
Palacios et al. 2019 [35]	4 RCTs (vitamin D vs. placebo)	RR: 0.51 (95% CI: 0.27–0.97) , moderate-certainty evidence
Pérez-López et al. 2015 [36]	2 RCTs	RR: 1.05 (95% CI: 0.60–1.84)
Roth et al. 2017 [37]	14 comparisons	RR: 0.61 (95% CI: 0.45–0.83)
Palacios et al. 2019 [42]	5 RCTs 1,446 women (601 IU/day vs. ≤600 IU/day)	RR: 0.54 (95% CI: 0.34–0.86)
<i>Preeclampsia</i>		
Palacios et al. 2019 [35]	4 RCTs 499 women	RR: 0.48 (95% CI: 0.30–0.79) , moderate-certainty evidence
Aguilar-Cordero et al. 2020 [38]	7 RCTs	OR: 0.68 (95% CI: 0.49–0.95)
Gallo et al. 2020 [34]	5 RCTs	OR: 0.7 (95% CI: 0.4–1.4), grade II evidence
Pérez-López et al. 2015 [36]	3 RCTs	RR: 0.88 (95% CI: 0.51–1.52)
Roth et al. 2017 [37]	16 comparisons	RR: 0.82 (95% CI: 0.63–1.07)
<i>Preterm birth</i>		
Palacios et al. 2019 [35]	7 RCTs	RR: 0.66 (95% CI): 0.34–1.30, low certainty evidence
Aguilar-Cordero et al. 2020 [38]	5 RCTs	OR: 0.62 (95% CI: 0.40–0.97)
Bi et al. 2018 [39]	7 RCTs	RR: 0.98 (95% CI: 0.77–1.26)
Pérez-López et al. 2015 [36]	3 RCTs	RR: 1.26 (95% CI: 0.60–2.63)
Roth et al. 2017 [37]	15 comparisons	RR: 1.0 (95% CI: 0.77–1.30)
Thorne-Lyman and Fawzi 2012 [40]	2 RCTs	RR: 0.77 (95% CI: 0.35–1.66)
<i>Birthweight</i>		
Maugeri et al. 2019 [41]	13 RCTs	+103.17 g (95% CI: 62.29–144.04)
Bi et al. 2018 [39]	17 RCTs	+75.38 g (95% CI: 22.88–127.88)
Gallo et al. 2020 [34]	9 RCTs	+114.2 g (95% CI: 63.4–165.1)
Roth et al. 2017 [37]	37 comparisons	+58 g (95% CI: 18.88–97.78)
Pérez-López et al. 2015 [36]	8 RCT 10 comparisons	+107.6 g (95% CI: 59.9–155.33)
<i>Low birth weight</i>		
Palacios et al. 2019 [35]	5 RCTs	RR: 0.55 (95% CI: 0.35–0.87) , moderate certainty evidence
Maugeri et al. 2019 [41]	3 RCTs	RR: 0.40 (95% CI: 0.22–0.74)
Thorne-Lyman and Fawzi 2012 [40]	3 RCTs	RR: 0.40 (95% CI: 0.23–0.71)
Pérez-López et al. 2015 [36]	4 RCTs	RR: 0.72 (95% CI: 0.44–1.16)
Roth et al. 2017 [37]	8 RCTs	RR: 0.75 (95% CI: 0.49–1.15)
<i>Small for gestational age</i>		
Pérez-López et al. 2015 [36]	3 RCTs	RR: 0.78 (95% CI: 0.50–1.21)
Bi et al. 2018 [39]	6 RCTs	RR: 0.72 (95% CI: 0.52–0.99)
Roth et al. 2017 [37]	7 comparisons	RR: 0.60 (95% CI: 0.40–0.90)
Thorne-Lyman and Fawzi 2012 [40]	2 RCTs	RR: 0.67 (95% CI: 0.40–1.11)
Maugeri et al. 2019 [41]	5 RCTs	RR: 0.69 (95% CI: 0.51–0.92)

RCT, randomized clinical trial. Effect sizes in bold are considered statistically significant.

weight-for-age Z-scores and weight-for-length Z-scores compared to placebo [48].

In a meta-analysis of intervention studies in LMICs children under five, the risk of anemia was reduced with different nutrient supplementation schemes: iron, iron and folic acid and MMS, as well as with other nutrition interventions [49].

Micronutrient Supplementation and Respiratory Infections and COVID-19

In terms of prevention of respiratory infections, including COVID, and/or modifying complications associated with the disease, some meta-analyses of RCTs and observational studies evaluating micronutrient supplementation have been done. Due to its important immune-modulating role, vitamin D supplementation has been widely studied. In Table 3, a summary of the effect of vitamin D supplementation on COVID infection, severity of disease, ICU admission, and mortality is presented. In general, there is some evidence of reduction of complication events, mainly ICU admissions. Many of these meta-analyses reported high heterogeneity between studies, including different doses, different degrees of severity of the disease, different exposure time to supplementation, and differences in baseline vitamin D status [50–55]. Thus, more evidence from RCT studies is needed before recommending vitamin D supplementation to decrease COVID-19 risk and/or as an adjunct therapy in infected patients.

Studies have also evaluated the effect of other vitamins or MMS on the incidence of respiratory infections and/or duration of symptoms. Some studies of vitamin D supplementation have shown a reduced risk of respiratory infections and in the duration of symptoms; but controversy exists between studies. Supplementation appears to be particularly beneficial in North America. The effect of vitamin C supplementation is also controversial, where some studies have shown protection against respiratory infections and/or duration of symptoms, but others have not. Zinc supplementation has shown a decreased risk of respiratory infections in children living in Asia, but not in other regions [56, 57]. Low-quality evidence has shown also a protection of zinc supplementation on the risk of pneumonia in children [58].

In summary, according to recent evidence, it is difficult to translate the data for clinical practice. In many studies, the baseline micronutrient status is not measured or taken into account, and the effect on individuals with deficient states is different. There is also a need for more high-quality evidence, particularly for infections and COVID-19.

Table 3. Effect of vitamin D supplementation on the risk of COVID-19 infection, complications, and mortality: evidence from meta-analysis of RCTs

Study	Study design	Effect of vitamin D supplementation
<i>Primary prevention (risk of infection)</i>		
Hosseini et al. 2022 [50]	5 studies (1 RCT, 4 non-RCTs)	No significant effect on COVID infection RR: 0.28 (95% CI: 0.01–6.43, $n = 33$ subjects)
<i>Secondary prevention (severity of symptoms, hospitalization, etc.)</i>		
Varikasavu et al. 2022 [51]	6 RCTs $n = 551$ patients	Lower symptom severity RR: 0.46 (95% CI: 0.23–0.93, $p = 0.14$, 6 studies, $I^2 = 52%$, $p = 0.06$) Lower COVID-19 positivity at 14 days (RT-PCR) RR: 0.46 (95% CI: 0.24–0.89, $p = 0.02$, $I^2 = 0%$)
Hosseini et al. 2022 [50]	5 studies (2 RCTs, 3 non-RCTs)	1 RCT: less severe symptoms; <3 severe symptoms at 14 days
<i>Tertiary prevention (ICU admission, mortality)</i>		
Varikasavu et al. 2022 [51]	6 RCTs $n = 551$ patients	No significant effect on mortality RR: 0.78 (95% CI: 0.25–2.40, $p = 0.66$, $I^2 = 33%$, $p = 0.21$) Lower total events ^a RR: 0.60 (95% CI: 0.40–0.92, $p = 0.03$, $I^2 = 48%$, $p = 0.03$)
Stroehlein et al. 2021 [52]	3 RCTs $n = 356$ patients	No significant reduction in all-cause mortality at discharge (very low certainty evidence) 1 RCT: RR: 0.11, 95% CI: 0.01–2.13 1 RCT: RR: 1.49, 95% CI: 0.55–4.04 No significant reduction in mechanical ventilation (low certainty evidence) 1 RCT: RR: 0.52, 95% CI: 0.24–1.13)
Hosseini et al. 2022 [50]	5 studies (2 RCTs, 3 non-RCTs)	Lower mortality RR: 0.52 (95% CI: 0.36–0.75, 11 studies, 3,391 patients, $I^2 = 54%$) Lower ICU admission RR: 0.35 (95% CI: 0.20–0.62, 7 studies, $I^2 = 75%$) No differences observed between RCT and non-RCT
Tentolouris et al. 2022 [53]	10 studies (2 RCTs, 8 non-RCTs)	No significant effect on mortality (REM OR: 0.597, 95% CI: 0.318–1.121, $p = 0.109$, 9 studies, 2,078 patients, $I^2 = 62.4%$, $p = 0.006$) Lower ICU admission (REM OR: 0.326, 95% CI: 0.149–0.712, $p = 0.005$, 6 studies, 860 patients, $I^2 = 60%$, $p = 0.02$) Stratification by doses: High dose vitamin D – no significant effect on mortality or ICU admission Low dose vitamin D – lower mortality and lower ICU admission
Szarpak et al. 2022 [54]	8 studies (2 RCTs, 6 non-RCTs) $n = 2,322$ patients	No significant reduction in 14 d mortality or in-hospital mortality 14 d OR: 0.51, 95% CI: 0.12–2.19, $p = 0.36$ In-hospital OR: 0.56, 95% CI: 0.23–1.37, $p = 0.20$ Lower ICU admission OR: 0.19, 95% CI: 0.06–0.54, $p = 0.002$, $I^2 = 77%$ Lower need of mechanical ventilation OR: 0.36, 95% CI: 0.16–0.801, $I^2 = 48%$, $p = 0.01$
Rawat et al. 2021 [55]	5 studies (2 RCTs, 3 quasiexperimental) $n = 467$ patients	No significant effect on mortality (very low certainty evidence) RR: 0.55 (95% CI: 0.22–1.39, $p = 0.21$) No significant effect on ICU admission (very low certainty evidence) RR: 0.20 (95% CI: 0.01–4.26, $p = 0.3$) No significant effect on mechanical ventilation (very low certainty evidence) RR: 0.24 (95% CI: 0.01–7.89, $p = 0.42$)

RCT, randomized clinical trial; RR, relative risk; OR, odds ratio; Non-RCT, nonrandomized clinical trial; REM, random effect model; ICU, intensive care unit. ^aIncluding symptom severity, positivity RT-PCR, seropositivity, IgM/IgG, and mortality.

Trends in Micronutrient Supplementation Use

In line with the above, the use of micronutrient supplements appears to be increasing around the world. According to the National Health and Nutrition Survey data in the United States, from 2007 to 2018, the use of dietary supplements increased from 50% to 56%, micronutrient containing supplements increased from 46% to 49% and the use of single nutrient supplements also increased. However, the use of multivitamin decreased from 70% to 56% [59]. In women of reproductive age, a decrease from 32.7% to 23.6% in the use of multivitamins was observed between 2006 and 2016 [60].

It has been reported that people who use supplements tend to be female, older, have higher education, higher income, and healthier lifestyles. Some studies have shown a better diet quality in dietary supplement users. It is well known that the use of nutrient supplements reduces the prevalence of inadequate intakes for most nutrients, but may increase the risk of excessive intakes in some cases [61]. In the United States, it has been reported that adults who use supplements may have <5% of excessive intake of nutrients. However, in supplemented toddlers, 97% of vitamin A excessive intake and 46% of excessive zinc intake have been observed [62]. In Canada, excessive intakes of niacin and vitamin A were reported in 80% of supplemented children (1–3-year-old) [63].

There is a lack of information about supplement use in many countries. From existing data, the use of supplements appeared to be lower in the United Kingdom, South Korea, Spain, and Greece compared to the US population [61]. However, in the COVID-19 pandemic, some cross-sectional studies were conducted in different countries to evaluate the change in nutrition behaviors, including supplementation. Most studies used surveys to collect data. In Poland, 13% of the respondents started supplementation because they wanted to improve immunity and to be protected against COVID [64]. In Saudi Arabia, 93% of the population used natural or herbal products to improve their immunity. The reported increase in people who regularly used these products was from 7.3% to 46%. In the United Arab Emirates, a high proportion of participants (56%) stated they used supplements for prevention or treatment of COVID-19. In Lithuania, 25% of the respondents increase their use of dietary supplements during the pandemic, which were commonly used in COVID-19 patients or in family members or friends of infected people. The main reason of supplement use was to strengthen the immune system [65]. In Spain, 24% of participants reported to use dietary supplements, where only 4% used them before the pandemic [66].

It is clear that micronutrient supplementation is one of many other nutrition interventions that may improve immunity, reduce individual susceptibility to infection, and delay the progression of symptoms. The COVID-19 pandemic

has brought public attention to improve immunity and health. Dietary supplements have been linked to better immunity and over-the-counter use appears to be increasing in different countries. Many people that do not need supplementation are taking dietary supplements. Nutrition communication to the public has been ineffective and the role of health professionals in taking decisions and individualizing nutrient supplementation schemes seems to be weak. Many myths regarding nutrition exist for COVID-19 prevention and treatment, as well as for respiratory infections [21]. There is a high need of education to the public and to health professionals in terms of healthy eating and the individual use of micronutrient supplementation. Better well-targeted efforts should be made to implement micronutrient supplementation programs in different countries.

Conclusion

There is a high prevalence of micronutrient deficiencies and inadequate micronutrient intakes around the world that are related with unhealthy diets, lack of fortification strategies in some countries, and food insecurity. This causes a global burden of morbidity and mortality in vulnerable populations, as well as disability. It is important to promote optimal vitamin and mineral intakes in the general population to promote health and for optimal immunity. More emphasis should be placed on increasing the nutrient density of the food supply (diversification, fortification) and improving access and utilization of nutrient dense foods.

Nutrition assessment, including dietary intake and micronutrient status, is essential, at individual or community level, to individualize micronutrient supplementation schemes, using the best evidence available. Individualization is key, considering many factors that affect micronutrient status. If deficiencies are documented by biochemical and/or clinical markers, supplementation should be recommended according to regional practice guidelines to normalize serum concentrations and micronutrient stores.

The involvement of health professionals and nutrition experts in recommending micronutrient supplementation and/or fortification in different regions or communities, as well as in clinical practice, is essential. More education is needed aiming to increase knowledge in the general public to reduce over-the-counter supplement use and increase awareness and competencies among health professionals.

More high-quality studies are needed regarding the effect of micronutrient supplementation in reducing infections, including COVID-19. Current data are difficult to interpret due to the high heterogeneity between studies in terms of doses, supplementation timing, baseline nutrient status, and severity of diseases.

Conflict of Interest Statement

Otilia Perichart-Perera is a speaker/consultant of the Nestlé Nutrition Institute.

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Social Media: The Weapon in the Armory

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Abstract

Social media is the way we communicate today around the world to convey emotions, messages, and social messages that need to be spread far and wide in the quickest possible form to reach the masses. A “blink” or a “wink” can be conveyed as soon as it happens, and Medics are using this as the best method of networking to spread the good word. Some of the frequently discussed topics on YouTube, such as pediatric nutrition, function as the epicenter to spread cheer, awareness, importance, and the need to focus on the “first 1,000 days (about 2 and a half years) of life” and after in ensuring the best for the child now and later in life. The top points of discussion in this chapter will be surrounding “No salt, No sugar, No cow's milk, No biscuits before 1 year,” familial or cultural culinary habits, feeding practice during diarrhea, introduction of animal protein in weaning diet of infants, vitamin D deficiency, the coming of age for millets, avoidance of unpasteurized cow's milk, the danger of “hidden hunger”, and social media in medical education.

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Introduction

In recent years, health communication via social media has increased due to the ever-growing number of technology users globally [1]. Social media use in nutrition and public health education can reduce the barriers that affect access to healthcare resources and support. Despite the potential advantages of social media, this also poses challenges such as misinformation, disinformation, and the lack of a standard information verification system [2]. As public health promo-

tion becomes more deeply rooted in internet-based programming, nutrition and health educators are required to become more competent in navigating social media messaging that impacts both online and offline consumer health experiences [1]. Additionally, there are a variety of food and nutrition trends [3] on social media platforms, whereby experts, industry, marketing agencies, and influencers engage audiences in the hot topics. Some key topics explored in this review include salt, sugar, and vitamin D deficiency among others.

With the increasing demand for healthcare services, social media platforms have become a necessary tool for healthcare providers to share information with the public. This chapter explores key hot topics on social media platforms including complementary feeding, among others. The context of India is utilized as a case study to provide insight into practice relevant examples.

Complementary Feeding

In some communities, complementary feeding starts earlier than recommended and this is thought to be a contributing factor to an increased risk of noncommunicable diseases, impaired growth, and allergies [4–7]. In a study conducted by Brion et al. [8], the introduction of salt at about four months was linked to a high systolic blood pressure at the age of seven. Consumption of excessive amounts of salt and fat has been linked to both cardiovascular diseases and stroke in adulthood. Several countries have successfully implemented strategies to campaign on reduction of salt and fat consumption [9–11]. Similarly, several studies have shown the link between high sugar consumption and cardiovascular diseases. The National Health and Nutrition Examination Survey, 2009–2014 survey, shows that although sugars should contribute to only 10% of total energy intake, the consumption of sugar had significantly increased beyond the recommendations by the second birthday among infants in the United States of America [12]. These dietary factors demonstrate a significant correlation between infant health and future comorbidities [13]. As a result, examples of taglines used in social media to raise awareness on this issue include: “No Salt,” “No Sugar,” “No Cow’s Milk,” “No biscuits before 1 year.”

Familial or Cultural Culinary Habits

Exemplifying sociocultural factors in the context of India as a case study, according to the National Family Health Survey-5 (NFHS) [14] conducted in 2019–2020, a large proportion of children remain undernourished, despite very significant

global economic progress in recent years, and concurrently there is a steady increase in the number of children with obesity due to minimal access to healthier foods. Additionally, lack of exercise during the COVID pandemic exacerbated the rates of obesity ranging from adolescents to adults from 15 to 45 years.

Among children, low height for age and low weight for age remain significant issues and are proportionately worse in certain geographical areas. Stunting or chronic malnutrition (i.e., low height with respect to age) has increased in 11 of the 17 states. In comparison with the NFHS-4 done during 2015–2016, the proportion of severely wasted children has increased in 13 of the 17 states [14]. More nutrition specific and sensitive interventions are needed to improve the cultural culinary habits and nutrition/health outcomes [14].

Feeding Practices during Diarrhea

Once again in the context of India, for years many carers have believed the myth that children should be fed less when having a diarrhea episode. Most children are fed alternatives such as arrowroot powder, rice, and lentil powder as the staple diet during an episode of acute gastroenteritis. According to NFHS-5 [15], the population has not fully embraced the World Health Organization and Indian government recommendations on giving oral rehydration solution to children during acute gastroenteritis episodes. The survey highlights that to reduce cases of dehydration and minimize the effects of diarrhea on nutritional status, mothers are encouraged to continue normal feeding of children with diarrhea and to increase the amount of fluids. In the two weeks before the survey, only 5% of children under 5 years of age with diarrhea were given more liquids than their usual intake, as recommended. Thirty-one percent received the same amount of liquids. Of greater concern, 59% of children with diarrhea were given less to drink and 5% were not given anything to drink. Only 30% of children with diarrhea were fed according to the recommended practice of giving the same amount of food or more food to the sick child. 60% of children were given less food than usual, while 2% who had previously been given food received no food while having diarrhea [15].

Introduction of Animal Protein in Weaning Diet of Infants

Introduction of animal proteins remains variable across the globe with hesitation and habits/cultural practices being the main obstacles in the complementary diet of infants. Various societies have recommended the introduction of animal pro-

tein into the infant diet even as early as four months of age. The European Society for Paediatric Gastroenterology, Hepatology, and Nutrition [16] recommends the use of lean meat as early as 4 months of age. Despite various reassurances from experts in the medical field, it remains a major challenge to reinforce this thought and practice in the minds of parents/carers. Iron deficiency anemia remains a global challenge and dietary deficiency is attributed as the major cause. Evidence [17] highlights that the consumption of animal protein as part of a balanced diet in the early weaning of infants along with green leafy vegetables as a preventative measure. Consuming animal proteins at least three times per week or 50 g per day meets the minimum requirements for iron in children [17].

Vitamin D Deficiency

Studies conducted in multiple countries report vitamin D deficiency as a major deficiency. Government agencies have made major changes to the diet consumed by the public to tackle this cause. The US Food and Drug Agency [18] has fortified vitamin D in various consumables for the end consumer to reap the benefits and has added surplus to the help it sustains the shelf life. A study conducted in Chennai, India [19], has shown that there is a high prevalence of hypovitaminosis D among healthy children and adolescents. Among the 45 children studied, 66.7% had normal vitamin D levels and 33.3% had hypovitaminosis D (p value < 0.05) [19]. Encouraging playing outside in sunlight for about a minimum 20 min per day and consumption of oily fish or fish oil capsules/syrup, and natural sources such as papaya and eggs will help in achieving the Recommended Daily Allowance of Vitamin D of 400 IU per day for children. The American Academy of Pediatrics advises that children should be supplemented with 800 IU per day until the age of 5 years [20].

The Coming of Age for Millets

As shown by the archaeological evidence [21], millets are among the archaeological crops in the Vindhyan region (Table 1). Millets have been consumed by people of all ages since the prehistoric era in various forms throughout civilization. Millets contribute to a balanced diet as they are rich in carbohydrates, micronutrients, and dietary fiber. They serve as a prebiotic source in the diet (Table 1) which acts as a good substrate for the gut microbiota and helps in the bulking of stools and contributes to a significant amount of fiber in the pediatric population [21]. The United Nations General Assembly in its 75th session in March 2021, declared 2023 the Internation-

Table 1. Archaeological crops in the Vindhyan region as shown by the archaeological evidence and their prebiotic precursor content

Crop	Available from	Fraction contributing to prebiotic precursor/action
Cultivated rice	Neolithic	Arabinoxylan
Hulled barley	Neolithic	Arabinoxylan and glucan
Bread wheat	Neolithic	Arabinoxylan, resistant starch
Dwarf wheat	Neolithic	Arabinoxylan, resistant starch
Ragi millet	Neolithic	Arabinoxylan
Lentil	Neo and Chalcolithic	Resistant starch
Field pea	Chalcolithic	galactosides
Chick pea	Neolithic	Resistant starch
Horse gram	Neolithic	Resistant starch
Green gram	Early Iron Age	Resistant starch
Black gram	Chalcolithic	Resistant starch
Cow pea	Neolithic	Resistant starch
Moth bean	Early Iron Age	Resistant starch
Pigeon pea	Late Iron Age (AD 300)	Resistant starch and oligofructose and inulin
Onion	Early Iron Age	Inulin and galactosides
Garlic	Late Iron Age (AD 300)	Inulin

Source: Kesavelu and Franklyn [21].

al Year of Millets [22]. Millets remain indigenous to the geographical location and are a staple food for millions of people in Sub-Saharan Africa and Asia. The commonly consumed millets are Pearl; Proso; Foxtail; Barnyard; Little; Kodo; Browntop; Finger; Guinea millets; Fonio; Sorghum (or great millet); Teff. The Food and Agriculture Organization (FAO) predicts an ongoing food shortage due to conflicts and extreme weather conditions in 45 countries, including 33 in Africa, 9 in Asia, 2 in Latin America and the Caribbean, and 1 in Europe. Following this prediction, it is expected that measures will be put in place to mitigate challenges [23].

Avoidance of Unpasteurized Cow's Milk

The Centers for Disease Control and Prevention [24] reports that from 1993 to 2012, about 127 outbreaks linked to raw milk or raw milk products like ice cream, soft cheese, or yogurt were reported which led to 1,909 patients being reported sick with 144 hospitalized. In a similar study conducted recently [25] from 2013 to 2018, 75 outbreaks with 675 illnesses occurred that were linked to unpasteurised milk; of these, 325 illnesses (48%) were among young people aged 0–19 years. The outbreaks were higher in states which allowed the sales of unpasteurized milk. This

Table 2. Examples of micronutrient deficiencies and their effects

Micronutrient deficiencies	Effects include
Iodine	Brain damage in newborns, reduced mental capacity, goiter
Iron	Microcytic hypochromic anemia, impaired motor development and cognition, recurrent infections, increased mortality and morbidity
Vitamin A	Night blindness, visual impairment (mild to severe), recurrent infection risk
Zinc	Reduced immune response, recurrent infections, risk of co-morbidities and mortality

study established a causal relationship between consumption of unpasteurized bovine milk and outbreak of associated illnesses. Widespread consumption of unpasteurized milk and its direct causal relationship in contracting bovine tuberculosis is well known. The risk of transmission remains phenomenally high with the overall prevalence summarized at 5% (95% CI: 3%–7%) [26]. Additionally, zoonotic transmission remains significantly high in milk and milk products made with raw milk [26].

The Danger of “Hidden Hunger”

Hidden hunger is a form of undernutrition that occurs when the intake and absorption of vitamins and minerals (e.g., iodine, iron, zinc) are too low to maintain good health and development [27]. Hidden hunger affects more than two billion people globally, i.e., one in three people in addition to the 505 million people who are in calorie deficit (FAO, IFAD, and WFP 2014 [27]). Table 2 highlights the wide variation and global incidence of hidden hunger of micronutrient deficiency. The “double burden” of malnutrition-undernourishment and obesity with concurrent micronutrient deficiencies is the shifting paradigm that the “developed countries face, while the developing countries face “hidden hunger” [28].

Social Media in Medical Education

Studies have assessed the effectiveness of using social media to educate doctors and medical students together with its limitations [29]. In the pre-COVID era, Cheston et al. [30] analyzed the potential of social media in connecting the medics throughout the United States and concluded that it was the next to best

move in real life. In a systematic review, Erika et al. [31] highlight that there is an increasing use of social media by parents to find authentic information online. The review encourages doctors to utilize social media as an effective method to reach parents/carers in delivering health care to children and young adults. Katz and Nandi [32] mention that social media is an ever-evolving platform, but it remains a very potent tool in conveying medical information to the public and the impact on modern society remains invaluable. Another study [33] explains how “social media can harness” medical educators and trainees alike in modernizing the healthcare system for healthcare education and transition.

D’souza et al. [34] describes social media as a double edge sword which is “here to stay” – connecting people worldwide with rapid pace and without the need for a separate platform or meeting venues. The risk of false information spreading should also be taken as a “short straw” with increasing fake news and accounts which may wrongly question the credibility of the healthcare professional in the modern era [34].

Live Local, Buy Local, and Eat Local

With the increasing campaigns on sustainable food systems, more people are finding it necessary to purchase and consume locally produced meals. For most families with children, the staple food can be found in food items that are available in their locality. These foods include potatoes, cereals, animal protein, poultry products, millets, and vegetables. Some foods also tend to be labelled according to the geographical area in which they are produced and where possible consuming locally sourced products can be advantageous from a sustainability perspective [35]. Categorically, the nutritional component of the foods varies and so does the micronutrient composition depending on the soil and weather. Due to the wide variety from which consumers need to choose, sometimes it may feel overwhelming when selecting foods that are favorable for a growing child in the first 1,000 days (about 2 and a half years) of life and after.

Conclusion

The above key topics are just a few examples of ‘trending’ discussions on food and nutrition across social media platforms. When harnessed properly, social media is a great tool for healthcare providers to disseminate their findings and

share health resources with the public. Additionally, healthcare providers need to understand the drawbacks to using social media in the field and produce strategies for overcoming challenges to using social media in health promotion as well as the best practices for designing, implementing, and evaluating social media forums in communicating public health information.

Conflict of Interest Statement

No conflict of interest.

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It is more important than ever to consider trends in nutrition across the world, especially after the COVID-19 pandemic highlighted the wide discrepancies in access to healthcare, good nutrition, and health outcomes. The 98th Nestlé Nutrition Institute Workshop was delivered in October 2022 in collaboration with the International Academy of Nutritional Educators and NNedPro Global Institute for Food, Nutrition and Health, and focussed on the personal and research experiences of the speakers.

Speakers included international leaders in nutrition throughout the lifespan, with a focus on optimising dietary quality to promote health and wellbeing. Good nutrition is vital in the first 1,000 days of life, particularly for shaping immune responses but this extends through to much later in life, when appropriate nutritional support can help keep vulnerable people out of hospital and living independently at home. The pandemic also made us take stock of the burden of malnutrition, both over and under nutrition, and health inequalities worldwide.

This multidisciplinary workshop provided a platform to reflect on, and discuss what we have learned previously, as well as looking forwards to the future of global health and nutrition and considering how innovative digital technologies could be harnessed to progress this field.

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