


Vital role for primary healthcare providers: urgent need to educate the community about daily nutritional self-care to support immune function and maintain health

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To cite: Calder PC, Bach-Faig A, Bevacqua T, *et al.* Vital role for primary healthcare providers: urgent need to educate the community about daily nutritional self-care to support immune function and maintain health. *BMJ Nutrition, Prevention & Health* 2023;**6**:e000755. doi:10.1136/bmjnph-2023-000755

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Received 21 August 2023
Accepted 22 November 2023
Published Online First
6 December 2023

ABSTRACT

The importance of self-care to improve health and social well-being is well recognised. Nevertheless, there remains a need to encourage people to better understand how their body works, and how to keep it healthy. Because of its important role, part of this understanding should be based on why the immune system must be supported. This highly complex system is essential for defending against pathogens, but also for maintaining health throughout the body by preserving homeostasis and integrity. Accordingly, the immune system requires active management for optimal functioning and to reduce the risk of chronic diseases. In addition to regular exercise, healthy sleeping patterns, cultivating mental resilience, adequate nutrition through healthy and diverse dietary habits is key to the daily support of immune function. Diet and the immune system are closely intertwined, and a poor diet will impair immunity and increase the risk of acute and chronic diseases. To help elucidate the roles of primary healthcare providers in supporting individuals to engage in self-care, an international group of experts reviewed the evidence for the roles of the immune system in maintaining health and for nutrition in daily immune support, and discussed implications for population health and clinical practice.

INTRODUCTION

In recent years, there has been an increased interest in, and focus on, the importance of self-care—one of the oldest and most promising approaches to improving health and quality of life.¹ The WHO defines self-care as ‘the ability of individuals, families, and communities to promote health, prevent disease, maintain health, and to cope with illness and disability with or without the support of a healthcare provider’.² This concept of self-care is particularly important because the current global shortage of healthcare workers is predicted to worsen over the next decade.³ Taking

better care of our own health at every stage of life is vital not only to help prevent disease and improve health outcomes, but also to relieve the enormous pressure on health and social care systems. Self-care encompasses a wide range of actions to improve the body, mind and social well-being²—including, for example, disease prevention through healthy eating and regular exercise to the use of non-prescription interventions to manage symptoms and common ailments.⁴ An increasing number of people are becoming more aware of and informed about the concept of self-care and its potential benefits.

However, not everybody has the self-confidence to manage all aspects of their health.^{5,6} Furthermore, health literacy is often low, even in developed countries.^{4,7} Consequently, there is an urgent need to empower individuals to acquire a greater understanding of how their body works and what it requires to stay healthy, and to enable them to better recognise symptoms and conditions suitable for self-care. Because of its central role in health, increased understanding of the importance of maintaining a healthy immune system should form part of any programme designed to raise awareness. The role of the immune system in defending against pathogens is well recognised, and this has been brought to even greater public attention because of the COVID-19 pandemic. More people than ever have begun to realise that a healthy immune system is better able to provide protection against viruses (and other pathogens) and help safeguard against the threat of future pandemics. Host defence against pathogens is only the tip of the



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immunity iceberg—underneath, the myriad of immune cells, signals, and stimulatory or inhibitory responses involved in defending the body also help to maintain health throughout the body. This highly complex network requires daily active maintenance for optimal functioning, with a particular focus on adequate nutrition through healthy and diverse dietary habits.^{8–10} When combined with other self-care measures (such as regular exercise, body weight management, healthy sleeping patterns, and cultivating mental resilience), such actions can help to fortify the immune system against factors that cannot be easily controlled, including infections, other environmental challenges and the chronic, low-grade inflammation that occurs in response to physiological stimulation of the innate immune system throughout life.

Primary healthcare providers (PCHPs) around the world play a central role in educating communities, and actively support and empower individuals to responsibly engage in self-care.^{11 12} PHCPs, particularly pharmacists, represent a widely available, easily accessible and convenient resource⁴ that can be used to promote self-care strategies for daily immune support—including nutritional recommendations that could help to improve public health; to be accurate and effective, these recommendations need to be evidence-based and given by PHCPs with sufficient training in diet and nutrition as part of self-care. In October 2022, an international group of experts from the fields of primary care and biomedical sciences attended a webinar to review and discuss this topic. Their aim was to: (1) review and discuss the evidence (using scientific literature provided ahead of the webinar and presented by key experts during the webinar) for (a) the central roles of the immune system in maintaining general health beyond host defence and (b) the role of nutrition in daily immune support; (2) discuss the implications for PHCPs in their daily clinical or pharmacy practice. The key outcomes of the webinar were documented and approved by the experts, and are summarised within this review.

A healthy immune system is central to overall health, with roles beyond defending against pathogens

Defending the body against attack by pathogens (such as viruses, bacteria and fungi) is the primary function of the immune system,¹³ and the effects of the immune response are often noticeable. The familiar symptoms of a cold (eg, sneezing, runny or congested nose, sore throat, cough, fatigue and body aches) are all signs that the immediate innate defences (particularly inflammation) and the later adaptive immune responses are working to clear the virus from the body. It is obvious that a robust immune response is important to host defence against pathogens, and it is well described that people with a weakened immune system are at increased risk of infection and of those infections becoming more severe.

In addition to its role in defence against pathogens, the immune system is involved in innumerable and interrelated dynamic actions throughout the body, which work

together to keep physiological processes in balance (homeostasis) and help the body to function and respond to challenges on a daily basis (figure 1).¹⁴ In simple terms, the immune system may be thought of as an information management system, which continually collects, interprets, communicates and stores data, and sets in motion events to maintain or restore homeostasis.¹⁵ In this way, a properly functioning immune system helps to maintain overall health and plays a role in reducing the risk of a range of chronic diseases that might otherwise occur as the body ages.^{14 16}

The inflammatory process: fundamental roles in maintaining whole body homeostasis and integrity

A key component of the innate immune system is the inflammatory response, which goes beyond eliminating infections and repairing tissue injury—two extreme body perturbations that are easily observable. In fact, inflammation also occurs at a lower magnitude in the absence of infection or overt tissue damage to maintain normal cellular, tissue, and systemic homeostasis.¹⁷

Inflammation is vital for enforcing homeostasis and protecting the functional and structural integrity of tissues and organs throughout the body, in both infectious and sterile situations (ie, those occurring in the absence of microorganisms).¹⁷ When normal (non-inflammatory) homeostatic mechanisms are insufficient to overcome a threat to homeostasis (ie, following an alteration in tissue structure or function or dysregulation of physiological processes), a variety of proinflammatory mediators produced by several types of cells induce an ‘inflammatory mode’ until normal homeostatic processes can be restored (figure 1).^{17 18} Once this has been achieved, specific negative feedback mechanisms resolve inflammation and homeostasis is once more regulated by the non-inflammatory physiological processes.¹⁷

To help illustrate the importance of the immune system and the inflammatory response to the normal functioning of the body, specific examples are briefly discussed below.

Metabolic health

Metabolic health can be defined as the ability of the body to respond efficiently to changes in the supply of food and nutrients, and to the dynamic demands for energy sources, chemical substrates, cofactors and building blocks to support cell and tissue function. This is achieved through regulation of physiological processes. Metabolic health is reflected by adequate condition-specific concentrations of a number of metabolic parameters, such as blood glucose, triglycerides and high-density lipoprotein cholesterol, ‘normal’ blood pressure, and a healthy waist circumference—factors that are directly related to the risk of conditions such as type 2 diabetes and cardiovascular disease.¹⁹ The immune system plays an important role in regulating metabolic processes and vice-versa.²⁰ This immuno-metabolic cross-talk is pivotal in promoting metabolic health throughout the entire life course and plays essential roles in the ability of a host to respond to

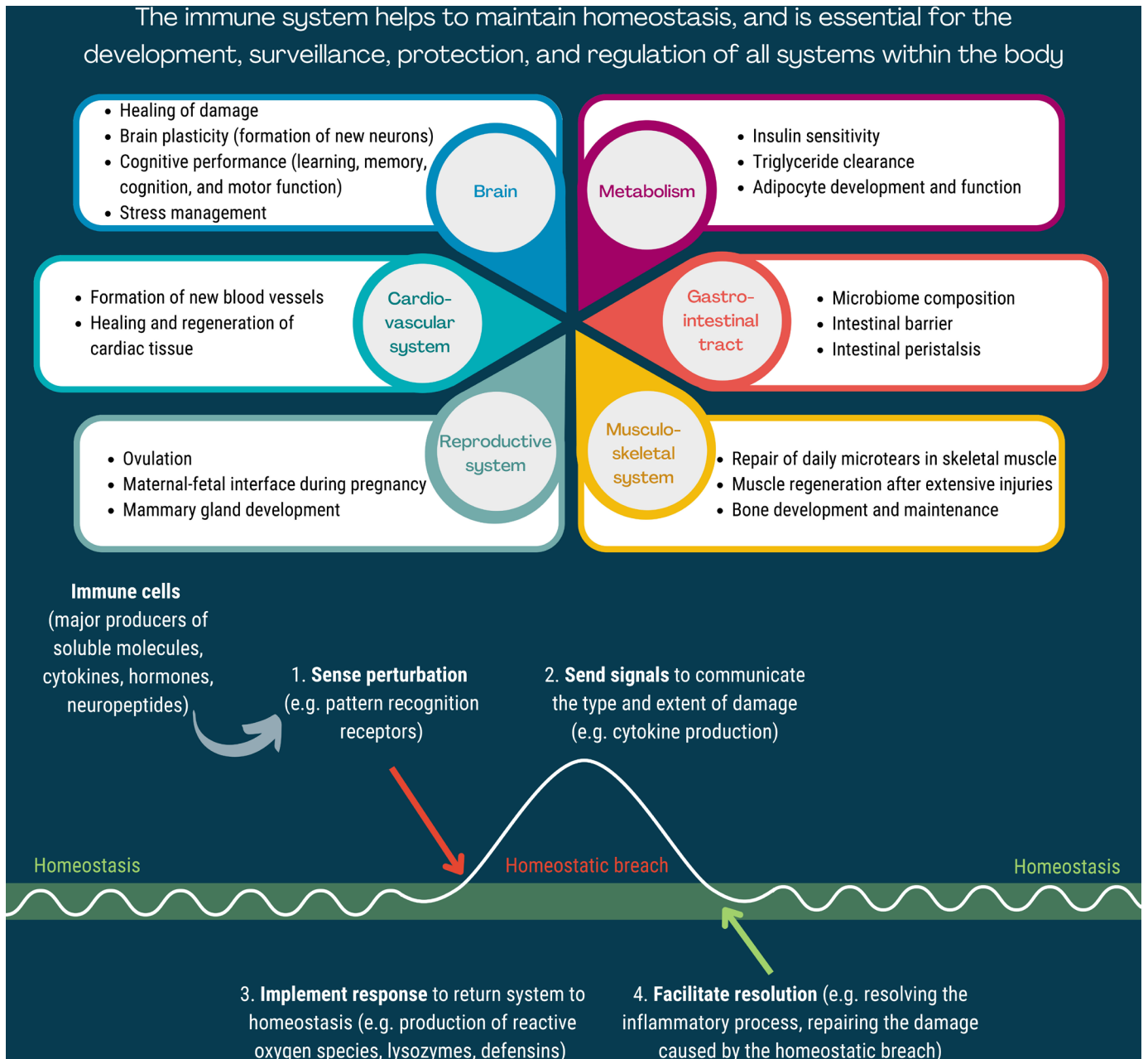


Figure 1 The multifaceted roles of the immune system go beyond host defence.^{13 14 27 48 52–56 119 120} Negative feedback mechanisms normally correct small deviations in the body’s steady-state variables to regulate homeostasis—but these may be insufficient to maintain stability if deviations are too large; when this happens, inflammatory cells and signals support homeostatic regulation until homeostasis is restored.¹⁷

external challenges and dynamic conditions within the body to maintain homeostasis.^{20–23} Metabolism involves sensing the nutrient balance to allow the host to prioritise energy storage against the requirements for energy and substrates to support tissue growth, function and maintenance.²¹ The immune system plays an important role in this sensing.

For example, in adipose tissue (a known ‘immunological niche’²¹) and the liver, immune cells produce signalling molecules that regulate tissue homeostasis and metabolic functions such as the actions of insulin or the breakdown of triglycerides.^{24 25} The immune system

also helps to prevent obesity by orchestrating the transformation of white adipose tissue into beige cells.^{14 26} The development of adipocytes (cells that store fat) and their function (eg, thermogenesis, insulin sensitivity) are supported and maintained by immune cells located in the adipose tissue.¹⁴

The brain

Lifelong maintenance of the brain relies on a healthy immune system. For many years, it was believed that the central nervous system (CNS) was an immune-privileged organ unable to tolerate immune reactivity; thus, the

belief was that any immune responses in the brain would need to be eradicated to prevent neurodegeneration.²⁷ However, immune cells residing in the CNS have been identified, such as the microglia (the brain's resident macrophages) which participate in inflammation and immune responses.¹⁵ It is now clear that the immune system provides homeostatic support to the CNS and helps to maintain the complex and delicate brain environment in optimal condition.^{28 29}

Immune cells recognise the self-components of the CNS and patrol the healthy brain to identify abnormal situations and resolve them before further damage can occur, or facilitate repair if damage has occurred.²⁹ 'Guardian' immune cells and signals form part of the protective barriers that exist between the periphery and the brain.^{27 30–32} In this way, the immune system is essential for preventing and healing damage in the CNS.^{33–36} It also participates in brain plasticity throughout life (ie, the ability of the brain to be restructured to enable it to function in a new way),^{37–39} and is pivotal in supporting learning, memory, cognition and motor function.^{29 38 40–42} Cross-talk between the immune system and the CNS coordinates the body's response to stress, infection, and other challenges.³⁷

Memory skills, the ability to learn and cognitive and motor function begin to decline with age, which reflects the ageing of the brain but also ageing of the immune system.^{29 43 44} Restoring communication between the immune system and the brain can help to restore brain function during the ageing process and may be beneficial in pathologies such as Alzheimer's disease.^{27 43 45} The immune system not only supports cognitive functions, but also influences behaviour. The body's natural resilience mechanisms, which allow a person to cope with and recover from mental stresses, are dependent on a properly functioning immune system^{30 42} that influences emotional and behavioural processes.^{27 42 46 47} Some people are naturally more susceptible to stress, and their ability to manage stress is linked to their inflammatory phenotype; however, it may be possible to improve resilience to stress by changing the inflammatory phenotype.⁴²

Other body systems

The integrated roles of the immune system extend throughout the body. For example, there is a mutualistic relationship between the immune system and gut microbiota. The microbiota is critical to the training and development of the immune system; in turn, around 70% of the body's immune cells reside in the gut wall⁴⁸ to ensure that there is a diversified and balanced microbiome, that commensals do not overuse host resources, and that immune tolerance to innocuous stimuli is maintained.^{49 50} When immune function becomes impaired (eg, when inflammation becomes chronic), this can result in dysbiosis that adversely affects the functioning of the microbial communities and impairs gut function.⁴⁹ Additional roles of the immune system in the gastrointestinal tract have been reported, such as the regulation of intestinal

peristalsis and the gut epithelial barrier through the action of immune cells on epithelial cells and neurons.¹⁴

There is also extensive cross-talk between the interconnected immune and cardiovascular systems.⁵¹ The immune system is essential for formation of new blood vessels, maintaining cardiac composition and function, and healing and regeneration of damaged epithelial and cardiac tissue, thus ensuring homeostasis within the cardiovascular system.^{52 53} In the musculoskeletal system, continual repair of microtears in skeletal muscle after daily use and promoting muscle regeneration after more extensive injury are dependent on the immune system,⁵⁴ while strong skeletal muscles (which develop after regular exercise) have emerged as a potent regulator of immune system function.⁵⁵ The immune system also has complex interactions with bone, and is essential for regulating the activity of bone cells during bone development and maintenance.⁵⁶ In the reproductive system, the immune system has crucial protective activities, participating in ovulation, maintaining the maternal–fetal interface during pregnancy, and regulating mammary gland development.⁵⁷

The immune system is challenged on a daily basis—which can have serious consequences if inflammation is not sufficiently resolved

The immune system orchestrates health when it functions well (figure 2). However, when dysregulated it can lead to uncontrolled, chronic, inflammatory responses that can result in disease.⁵⁸ Throughout life, the body is exposed to a vast array of biological, environmental, social and psychological stressors on a daily basis, including eating food, undertaking physical activity, emotional disturbances, exposure to pathogens and toxins, mechanical damage and temperature fluctuations.¹⁴ Each of these has the potential to disturb homeostasis and trigger the inflammatory response¹⁷ (figure 3). It is important that any inflammatory process is fully resolved each time to avoid pathological consequences.⁵⁹ However, increased concentrations of inflammatory markers⁶⁰ and inadequate resolution of acute inflammation occurs over time,⁶¹ leading to low-grade, chronic inflammation.⁵⁹ This inflammation is associated with numerous chronic diseases^{17 59 62–66} and almost every pathology of the brain,^{27 67} and contributes to all of the well-established hallmarks of ageing.⁶⁸

For example, persistent, low-grade inflammation is a common marker in immune-metabolic disturbances, with roles in cardiovascular diseases, many cancers, obesity, insulin resistance and type 2 diabetes, fatty liver disease, cachexia, etc.^{14 69–73} Disruption of the tight interface between the immune system and the brain when coordinating the body's response to challenges such as stress can also lead to chronic disease.³⁷ Alterations in the neuroprotective immune activities within the brain and CNS can contribute to dementia and other neurodegenerative diseases, which have a further detrimental impact on immunity, causing a vicious cycle.²⁷ If inflammation triggered during tissue repair in the heart is not tightly regulated and quickly resolved, further cardiac damage

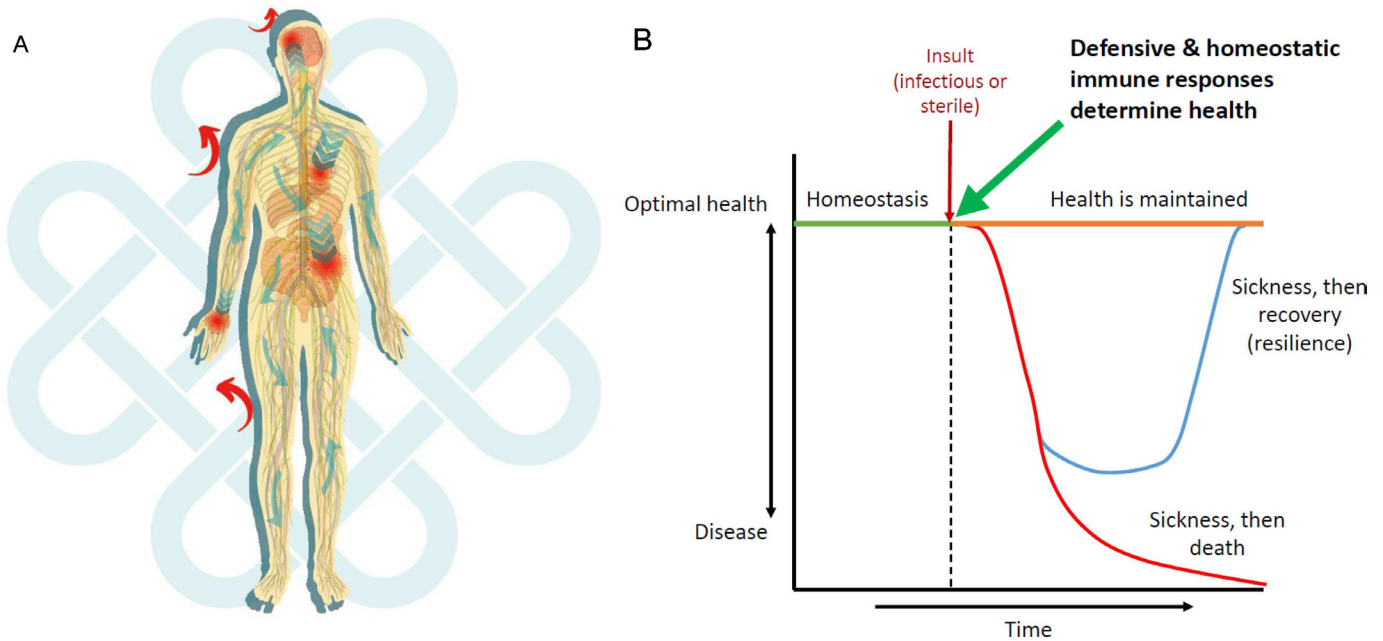


Figure 2 (a) The immune system is integrated throughout every part of the body and is constantly on alert for external threats and for any internal challenges or anomalies that might affect homeostasis. (b) When any irregularities are detected or sickness develops, an appropriate immune response is triggered to respond to the problem, restore homeostasis, and thereby maintain health (partly adapted with permission from Ayres¹²¹).

can occur, increasing the risk of heart disease.⁷⁴ Immunological impairments in one system can damage another; for example, certain neuroendocrine and immunometabolic diseases are known to disrupt endothelial function (a ‘barometer’ of cardiovascular health), which can lead to atherosclerosis and cardiovascular disease.⁵¹

Considering the importance of the immune system to overall health (in terms of both protection against pathogens, for example, and maintenance of body homeostasis and function), the daily challenges it faces from external and internal stressors, and the potential impact that immune dysfunction can have on short-term and long-term health, it is clearly crucial to support the immune system on a daily basis. Self-care forms an important part of maintaining a healthy, well-nourished immune system.

Daily self-care through nutrition is important to support immune function

Maintaining or restoring immune resilience on a daily basis could help to prevent adverse effects in the body, reduce the risk of disease and potentially improve or mitigate the course of disease. Simple lifestyle changes can support immune function by targeting inflammation and maintaining immune cell health, with a potential reduction in the risk of infections and chronic diseases.⁷⁵ It might not be possible to alter certain factors that challenge or impair immunity (such as exposure to pathogens or pollutants, etc)—but it is possible to implement daily self-care measures that are known to have a positive impact on immune function, including regular exercise,^{76–80} good quality sleep,^{81 82} a healthy mindset that is more resilient to stress,^{83–85} and adequate nutrition.^{86 87}

In fact, a healthy diet is a cornerstone of daily immune support; over a lifetime, it plays a critical role in supporting immune functions and helping to improve general health.⁸⁸ The development and optimal functioning of immune cells and immune mechanisms are reliant on an adequate supply of essential fatty acids, proteins (a source of essential amino acids) and micronutrients such as vitamins A, C, D, E, B6, B9 (folate), and B12, and minerals including zinc, copper, iron and selenium.^{8–10 86 87 89–91} When the body becomes malnourished—whether through undernutrition or overnutrition—and nutrient supply is deficient or even insufficient, the production and activity of immune cells becomes impaired⁹⁰ and the immune system cannot function properly,^{89 92} increasing the risk of infections^{8 91} and chronic disease.^{86 87} Non-optimal dietary intake is proven to be a major factor in the global burden of disease^{93 94} and mortality.⁹⁵

Providing adequate nutrients to support immune function is an easily modifiable, high-priority self-care measure that can help to maintain general health.^{93 96 97} Improving nutritional status helps to maximise immune protection against infections and may protect against the development of inflammatory/immune-mediated diseases.^{93 96 98} Although more research is necessary, there is a good rationale based on mechanistic data to postulate that supporting immune function through nutrition on a daily basis could have a beneficial effect on maintaining homeostatic mechanisms throughout the body and may help protect against chronic diseases.^{86 99 100}

Minimally processed, naturally nutrient-dense foods are the preferred way to fill micronutrient gaps, with fruits, berries and vegetables in particular containing

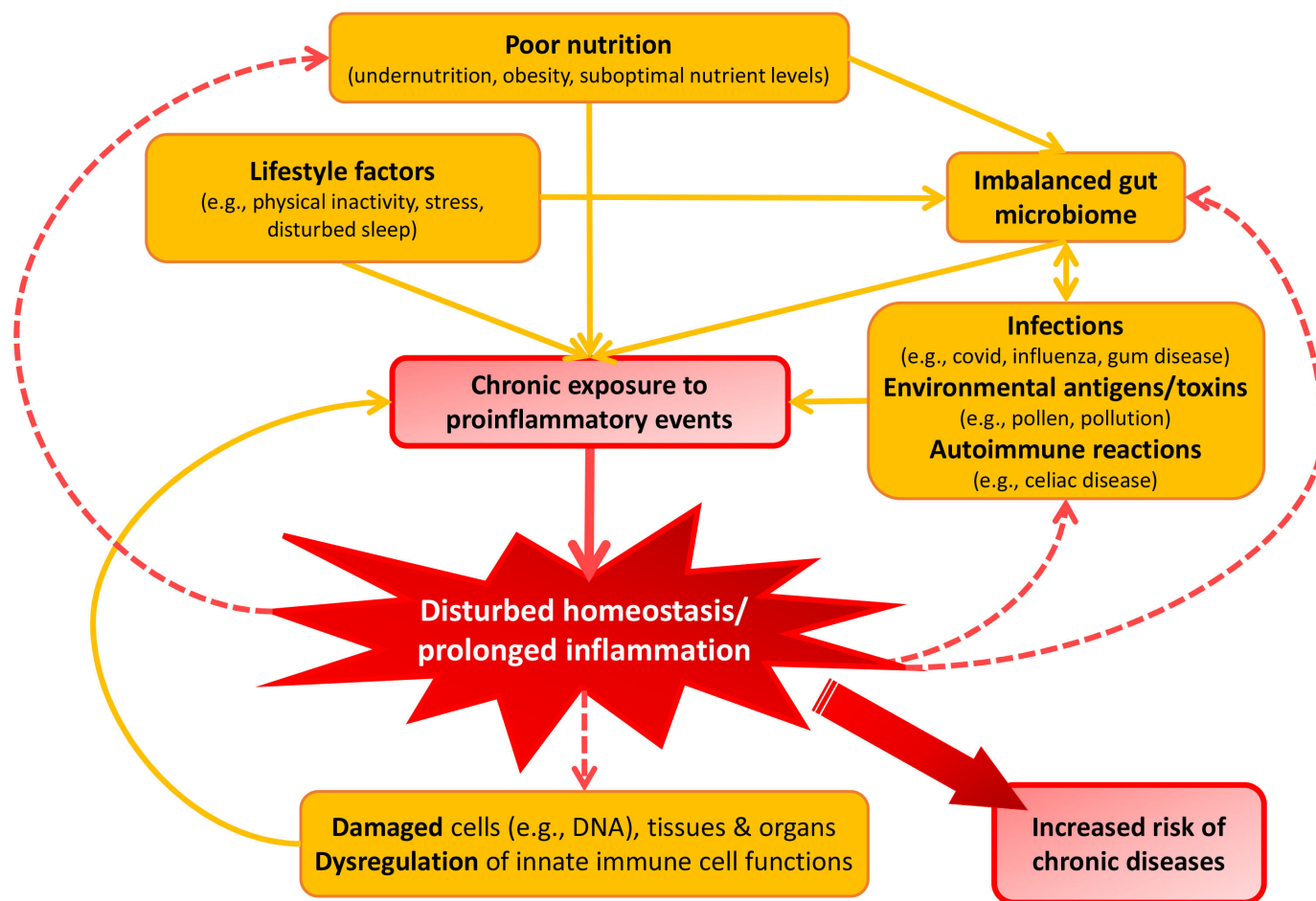


Figure 3 The immune system can be challenged by many factors throughout life, leading to increased inflammation, damaged cells and dysregulation of homeostasis that contribute to chronic and age-related disorders such as type 2 diabetes, cardiovascular and cerebrovascular diseases, dementia, cancer, etc.^{59 122}

numerous micronutrients and several classes of bioactive compounds (eg, polyphenols, carotenoids, etc) that have immunomodulatory effects.^{101–105} However, the body may not be able to obtain all the nutrients it needs from the diet alone, particularly in some subgroups of the population.¹⁰⁶ Geographical, sociological and lifestyle factors, combined with constant exposure to pathogens and other immunological challenges, can contribute to insufficient micronutrient intakes.^{106 107} Even in high-income countries, suboptimal micronutrient levels are common throughout the life course.^{88 108 109} Data indicate that daily intakes of vitamins A, C, D, E and B12, calcium, iron and zinc—all essential for immune function^{8 91}—fall below recommended intakes in some adults^{96 106} and throughout the life course, even in seemingly healthy people.⁸⁸ As increasing dietary diversity to meet daily requirements is desirable but can be hard to achieve in reality for many people, particularly for certain vitamins and minerals. In such cases, a supplement containing multiple micronutrients known to support immune function could be a simple and cost-effective way of complementing the diet and closing some nutritional gaps.^{8 96} A healthcare provider should always be consulted first to ensure that the consumer can safely use a micronutrient supplement,

that they are using a certified product, and that they are not only aware of the potential benefits but also of the upper tolerable limits. Furthermore, it is important that they are advised where they are able to access evidence-based information from credible sources, and to always check the often misleading information contained in social media posts, for example.

PHCPs have a crucial role in encouraging daily self-care through nutrition for immune support

Considering the evidence presented, it is evident that the immune system is the centre of human health and resilience. By protecting the body from external stressors such as pathogens, as well as internal stressors that also challenge and disrupt homeostasis, a well-functioning immune system ensures lifelong, optimal functioning of human body cells, tissues and organs. Hence, immune support through nutrition is a high-priority self-care practice that can help to maximise the health and well-being of the population. In situations of inadequate diet or challenging immune stressors, regular use of a micronutrient supplement in accordance with the manufacturers' instructions seems likely to help support a well-functioning immune system. Accordingly, there is a clear

public health need to empower the community to take care of their immune system and health through nutritional support, given the annual morbidity and mortality from infections in general, the increasing likelihood of respiratory infections from novel viruses, and the global increase in rates of chronic diseases that involve nutrition and immune impairment.^{93 110 111} Many people do not fully understand the link between nutrition, immune function and the potential for a healthier life, and might not see the need to improve their daily diet. Poor health literacy among communities is a barrier in community education. Multiple and complex factors have a strong influence on dietary choices and patterns, which can be hard to overcome.¹¹² Education is needed to enable people to better recognise the direct link between what they eat, the impact on their immune health and the resulting effects on their overall health and well-being. Furthermore, it is essential to raise awareness that, in keeping with other body systems, the immune system requires daily nutritional support, and that diet is really important but may not be sufficient to meet the recommended dietary allowances for all nutrients, particularly micronutrients that are critical for immune function.

PHCPs have a central role in community education and there is a need to engage their help to reach the community. Pharmacists, for example, already recommend self-care activities to the public to improve and preserve optimal health and quality of life, and provide education about the importance of healthy eating, physical activity and mental well-being.¹ PCHPs are trusted, convenient, widely accessible, widely used and can provide (usually) free sources of health information, and thus are in a unique position to further encourage the community to take a more active role in the maintenance of their own nutritional health. Many also have contact with people of all ages, and often whole families, and may know their background, lifestyle and health concerns. This is invaluable, as lifelong immune support through nutrition is essential. Ultimately, enabling better health outcomes in individuals will contribute to the sustainability of health-care systems and have a broader positive impact on society and the economy.

Well-trained PCHPs are ideally suited to use their skills to educate the community about their immune system, provide evidence-based advice on self-care through nutritional support and help overcome barriers to changing dietary habits. Nutritional education can help to improve dietary intake¹¹³ and has the potential for a beneficial impact on public health. Nevertheless, there are multiple factors that may impede the involvement of PHCPs in raising awareness and educating the community. Lack of time and resources for PHCPs, combined with lack of ongoing training for them and their assistants, is a problem that needs to be resolved. In addition, the minimal exposure to nutritional knowledge during the training of all PHCPs is detrimental,¹¹⁴ particularly when combined with insufficient understanding of the broader roles of the immune system beyond host defence

and how to communicate its importance.¹¹⁵ These issues must be addressed before PCHPs can safely and confidently advise the community about basic nutrition and know when they should refer to an expert. Integrating evidence-based nutrition courses into health professional education, using a range of delivery and communication options, can prompt greater competence and confidence when providing nutritional advice.^{116 117} There is a range of solutions that could be used to help educate PHCPs about the impact of nutrition on the immune system and the potential public health benefits of daily immune support through nutrition. These might include, for example, the creation of live and virtual communities for PHCPs, continuous training via online resources or participation in scientific events. Educational materials with guidance to empower PHCPs during discussions about dietary supplements are also already available (such as the Operation Supplement Safety document developed by the US Department of Defense¹¹⁸). The ensuing knowledge, combined with effective community communication tools, can be used by PHCPs to directly inform the community about the benefits of daily nutritional self-care to support immunity. Such community tools might encompass succinct and accessible online and print resources (eg, leaflets, websites and social media posts on topics such as new information on micronutrients, dietary choices during different life stages and effects of nutrition on immune function); practical interactive, and case-based information-sharing sessions that offer bidirectional communication between speakers and audiences; diagnostic aids within pharmacies that are accessible to the community (featuring simple nutritional assessment tools and integration with wearable technologies). These educational initiatives should be supported by a number of stakeholders, such as health systems, PHCP associations, insurance companies and the self-care industry wherever possible, by presenting scientific research on nutrition and immune health, using online resources to reach PHCPs and the public, and helping to monitor and fact-check misinformation online to ensure that people receive accurate advice on why and how to support their immune system through nutrition.

CONCLUSIONS

The immune system is important to the body's function and resilience to challenges, and this goes beyond defence against pathogens. Consequently, immune impairments result in loss of homeostasis and resilience and an increased risk of various diseases. Multiple nutrients are vital to support immune system function. Hence, a poor diet is linked with immune impairments and increased susceptibility to infection. However, such immune impairments are also part of the link between poor diet and many chronic non-communicable diseases. Diet is important in the supply of optimal nutrition; even so, many people—even in well-developed countries—have insufficient intakes of many micronutrients.

Micronutrient supplements can help to fill nutrient gaps for immune support where diet is insufficient. There is a public health need to galvanise the community into taking daily care of their immune system through nutrition support. PHCPs already play a central role in educating the community, and should be encouraged to proactively promote nutritional immune self-care. However, there is a need to empower and assist PCHPs by investing in training and providing succinct and reliable information about the immune system and the vital roles of nutrition—including the use of a multiple micronutrient supplement to help close any nutrient gaps that could impair immune function.

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Acknowledgements The outline of the publication was developed with input from all authors, based on an expert webinar meeting and the subsequent conclusions concerning the role of nutrition in immune support. The draft manuscript was prepared by Deborah Nock (Medical WriteAway, Norwich, UK), who provided editorial support during all review rounds.

Contributors Conceptualisation, all authors; collection, analyses or interpretation of data, all authors; review outline, all authors; writing—original draft preparation, Deborah Nock (medical writer); writing—review and editing: all authors, supported by Deborah Nock; validation, all authors; project administration, AP; funding acquisition, AP. All authors have read and agreed to the published version of the manuscript.

Funding This writing of this article was funded by Bayer Consumer Care, Basel, Switzerland, including the services of the medical writer.

Competing interests PCC acts as an ad hoc adviser/consultant to BASF AS, DSM, Danone-Nutricia, Cargill, Nutrilife, Bayer Consumer Care, Haleon Wellness (formerly GSK Consumer Healthcare), and Fresenius Kabi; has received speaking honoraria from DSM, Danone-Nutricia, Fresenius Kabi, Bayer Consumer Care, GSK Consumer Healthcare, Biogredia, Pepsico, Procter & Gamble and Abbott; has current research funding from Bayer Consumer Care and Tate and Lyle; and is using study materials from DSM and Tate and Lyle in current human trials. AB-F has received fees for oral presentations at Bayer Hispania SL Congresses. DR-F acts as an ad hoc adviser/consultant to Marjan, Mantecorp, Novo Nordisk, Arese, Apsen, Pfizer, Nestlé, Abbot and Cellera. The funder, Bayer Consumer Care, employs AP and had a role in the writing and review of the manuscript and the decision to publish the manuscript. All authors received financial support for participating in the related webinar funded by Bayer Consumer Health AG. TB, CGCL, Z-YC, DC, WLK, SNM and PAS declare no conflicts of interest.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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