

Chapter 12

The role of nutrition in respiratory disease and COVID-19 management

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Introduction

The role of nutrition in immune development and disease recovery as well as the impact of infection on one's nutrition is widely known. However, many other evidences on this relationship are not conclusive most especially for emerging diseases such as corona virus disease (COVID-19). This chapter will review existing systematic reviews and meta-analysis literature on the subject of nutrition and infection with special emphasis on respiratory infection and COVID-19. The chapter will look at existing relationships between nutrition and respiratory infections, immunity and infection and patient recovery, nutrition and COVID-19, and the role of nutrition in infection control and management.

Background

The role of nutrition on the human defense system cannot be overemphasized as nutrition, diet, and nutritional status is an important determinant of the body's immunity. Existing evidence has established relationship between disease infectivity, mortality, and micronutrient deficiencies. Reviews of research over the past years on nutrition and immune function have suggested a dire consequence of nutritional deficiency on host immune response to disease infections. Malnutrition has been linked to immune function depression resulting in disease susceptibility (Naja & Hamadeh, 2020). Earlier studies by Maggini, Pierre, and Calder (2018) reported poor nutritional status as a leading cause of immune impairment. Thus adequate nutritional intake has been recommended as a potent intervention to restoring the body's immune function and resistance to infection.

Recent global reports on nutrition have indicated that malnutrition is among the major factors leading to an increase in death rate worldwide. The novel corona virus pandemic to a large extent has exposed our vulnerable food systems, as efforts in containing the spread of infection have resulted in food shortages globally. This consequently has exposed persons with underlying conditions and compromised immune state as a result of a poor nutritional status to disease infection (Global Nutrition Report, 2020).

This chapter is presented in three sections. The first section of the chapter discusses generally the role of nutrition/correlation between nutrition and immunity, infectious cycle, infectivity and disease recovery. The second section of the chapter deals with the association between nutrition and immunity against respiratory diseases, nutrition and infectivity of respiratory diseases and nutrition and recovery from respiratory illnesses. The final section of the chapter focuses on the role of nutrition in the development of the immune system against COVID-19, infectivity of COVID-19, recovery, optimizing nutrition for improved mental health during COVID-19, and management of COVID-19.

Nutrition and immunity

Nutrition has been reported to improve the body's resistance to infection aside modulating immune functions. Nutritional deficiency of certain micronutrients has been found to impair immune responses (Bhaskaram, 2001). Numerous micronutrients, including vitamins A, D, C, E, B6, and B12, folate, zinc, iron, copper, and selenium, are critically essential as they mutually support each other in the immune protection and response process (Gombart, Pierre, & Maggini, 2020). Jayawardena, Sooriyaarachchi, Chourdakis, Jeewandara, and Ranasinghe (2020) highlighted the importance of micronutrients, nutraceuticals, and probiotics to immunity against the COVID-19 pandemic. Poor nutritional status in Chronic Kidney Disease (CKD) patients was reported as a risk to weakened serologic response to Hepatitis B Vaccine (HBV). Patients with an improved nutritional status were better protected against viral infections in a recent study

(Calder, Carr, Gombart, & Eggersdorfer, 2020). In a systematic review to unravel the relationship between immune function and nutritional status among highly active antiretroviral therapy (HAART)-treated patients, it was observed that malnourished patients recorded early deaths due to poor immune function (Sicotte, Langlois, Aho, Ziegler, & Zunzunegui, 2014). Researchers assessed the correlation between parameters such as the composition of microbiota, feeding status, and immunity in a case-control study of Ecuadorian children with Autism Spectrum Disorder. Outcome of the study showed variations in feeding behavior, immune function, and microbiota composition (Zurita et al., 2020). Grueber, Gray, Morris, Stephen, and Senior (2018) identified certain inheritable immune characteristics in offspring that are dependent on the variation in parental nutritional intake. The study measured the outcome of maternal nutrition on child immune status by employing frameworks that defined dietary manipulations with respect to energy and macronutrient compositions. The alteration in maternal dietary intake was observed to affect child's immune function by decreasing the expression of certain inflammatory markers (Grueber et al., 2018).

With the emergence of the Corona virus pandemic, there have been reports that micronutrient interventions could possibly play a key role in patient recovery by improving immune function. Several research findings to a large extent have investigated the immune modulatory effect of vitamin D. Maalmi, Tangour, and Hamzaoui (2012) pointed out the role of vitamin D in the regulation of T cells in younger asthmatic patients. They observed that only 6 out of 39 asthmatic children enrolled for the study had adequate calcifediol levels while sufficient levels were found in the vast majority of healthy controls. Also, it was observed that 17 of the asthmatic patients expressed deficiency in serum vitamin D levels. Healthy participants, however, expressed no signs of serum vitamin D deficiency. The levels of Th1, Th2, and Th17 were found to correspond with the serum concentrations of calcifediol. There have been speculations over how critical lower vitamin D status may influence immune response to influenza vaccines administered in the elderly population. Lee et al. (2018) underscored no substantial link between the vitamin and its immunogenic influence on influenza vaccines. They however noted that specific influenza strains may present peculiarities, lower rate of protection in influenza A virus H3N2 and B strains in vitamin D-deficient patients compared with vitamin D-rich patients (Lee et al., 2018). Probiotics and prebiotics administration have been found to trigger immunogenic response to influenza vaccines in the elderly as the rate of seroprotection in influenza H1N1, H3N2, and B subtypes improved dramatically in subjects who took prebiotics or probiotics (Lei, Shih, & Liu, 2018). The administration of probiotics bacteria has been reported to reduce both upper and lower respiratory tract infections (Campbell, 2020). Probiotic strains could be employed to manipulate these microbiotas, offering new perspectives in the management of respiratory failures (Enaud et al., 2020). Mounting evidence supports a relationship between the gut and lungs, thus more studies to explore the potential role of probiotic in attenuating COVID-19 either through

immunomodulatory actions on systemic inflammation or by direct association with the lungs have been recommended (Bottari, Castellone, & Neviani, 2020; Mak, Chan, & Ng, 2020).

A review of the role of vitamin C and some micronutrient supplementation in triggering changes in immune function in exercising athletes found two trials that backed the use of vitamin C as a preventive agent against Upper Respiratory Tract (URT) infections (Moreira et al., 2007).

In relation to URT infections, a review which included 82 eligible studies that considered the preventive role of vitamin C in immune clusters and in common cold reported that regular supplementation of vitamin C (1 to 2 g/day) reduces cold duration (by 8% in adults and in children by 14%) and the severity of common cold (Rondanelli et al., 2018). There is evidence that a high dose of intravenous vitamin C (HIVC) can inhibit numerous key components of cytokine storms which can eventually degrade the endothelium and alveolar membrane in clinical trials. These trials were conducted on patients with bacterial-induced sepsis and acute respiratory distress syndrome (ARDS) which are conditions that occur in severe critically ill COVID-19 patients (Liu, Zhu, Zhang, Li, & Peng, 2020). Findings from a meta-analysis of 29 controlled trials with 11,306 participants revealed that vitamin C administration shortened the period of being infected with URTIs (Hemilä & Chalker, 2019). In adults, the duration of infections was reduced by 8% and in children by 14% (Hemilä & Chalker, 2019). Considering the fact that critically ill patients are likely to be admitted in intensive care units (ICUs) and the evidence that their vitamin C levels usually reduce drastically (Carr et al., 2017; Hemilä & Chalker, 2019), there is no reason to doubt that vitamin C would not be effective against COVID-19. The potential role of vitamin C in shortening patients stay in ICUs by 8% was reported in a meta-analysis that included 12 trials with 1766 patients in ICU (Hemilä & Chalker, 2019). Likewise, another meta-regression analysis that included eight (8) trials found that vitamin C shortened the duration of mechanical ventilation in patients who required the longest ventilation (Hemilä & Chalker, 2020a, 2020b). Liu et al. (2020) therefore hypothesized that HIVC could be added to the treatment of ARDS and multiorgan dysfunction which are associated with COVID-19.

The role of zinc in enhancing immune function and reducing the risk of infections mainly as a result of its antiinflammatory property has also been reported (de Almeida Brasiel, 2020). A randomized, double-blind, placebo-controlled trial in nursing homes revealed that providing zinc supplements to older adults improved their immune response and provided protection against infection (Barnett et al., 2016). With regard to common colds, intake of zinc supplements was reported to shorten the duration of colds by approximately 33% (Rondanelli et al., 2018). In a meta-analysis that included a number of placebo-controlled zinc lozenge trials, it was revealed in five trials that common cold duration was reduced by 33% among participants who were administered with zinc doses of 80–92 mg/day. There was a further reduction in cold duration

by 2% (i.e., 35%) in two trials in which participants received a higher zinc doses of 192–207 mg/day (Hemilä, 2017). Selenium (Se) is an essential trace mineral which is vital for particularly maintaining a well-balanced immune response. In an European cross-sectional study ($n=1915$), COVID-19 patients showed a pronounced deficiency in total serum Se (mean $\pm$ SD, 50.8 ± 15.7 vs. 84.4 ± 23.4 $\mu\text{g/L}$) and SELENOP (3.0 ± 1.4 vs. 4.3 ± 1.0 mg/L) concentrations. A Se status below the 2.5th percentile of the reference population, i.e., $[\text{Se}] < 45.7$ $\mu\text{g/L}$ and $[\text{SELENOP}] < 2.56$ mg/L, was observed in 43.4% and 39.2% of serum samples of COVID-19 patients, respectively. The Se status was significantly higher in samples from surviving COVID-19 patients as compared with nonsurvivors (Se; 53.3 ± 16.2 vs. 40.8 ± 8.1 $\mu\text{g/L}$, selenoprotein P (SELENOP); 3.3 ± 1.3 vs. 2.1 ± 0.9 mg/L (Moghaddam et al., 2020). Although the potential role of these micronutrients has been individually discussed, it is important to indicate their complementary roles in nutritional health, that is, they do not work in isolation, but rather mutually support and depend on each other.

Essential micronutrients and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid are known to have the capacity to boost immunity against viral infections (Calder et al., 2020). Specifically, omega-3 PUFAs, mainly α -linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid, inhibit the activation of immune cells while also actively enhancing specific immune functions like phagocytosis and neutrophil differentiation. This suggests that omega-3 PUFAs play a role in mediating immune function and thus may be vital as a supportive dietary therapy for prevention and treatment of flu-like viral infections, including COVID-19 (Akhtar et al., 2020).

Growing evidence suggests that functional foods which are products that contain different biologically active compounds when consumed, contributes to maintaining the optimal state of physical and mental health of the population. Functional foods contain biologically active compounds with the potential to improve health or to reduce the risk of disease (Butnariu & Sarac, 2019). These functional foods include tea components that may help optimize immunological responses such as improving defense functions and resistance to infections. Tea components such as Epigallocatechin-3-Gallate (EGCG) and garlic (*Allium sativum* L.) have been described as being gatekeepers of immune function (Wu, Lewis, Pae, & Meydani, 2019). Garlic contains diverse bioactive compounds, such as allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and S-allyl-cysteine which have been shown to exhibit antiinflammatory, antibacterial, antifungal, immunomodulatory properties (Phan, Netzel, Chhim, Netzel, & Sultanbawa, 2019; Shang et al., 2019). Recently, the protective role of EGCG in diseases with uncontrolled immune activation such as the novel COVID-19 has been explored (Menegazzi et al., 2020). Menegazzi et al. (2020) argued and recommended that since EGCG can regenerate the natural immunological homeostasis in many autoimmune diseases it can be considered a potential safe natural supplement to counteract hyperinflammation development in COVID-19 patients.

Nutrition infection cycle

Nutrition has been reported to be closely associated with infection. Globally, nutritional deficiencies have been linked to a number of disease infections. Malnutrition is known to trigger immunodeficiency, predisposing the malnourished to several infectious diseases. [Savino \(2002\)](#) reported that thymus development is significantly affected in severely malnourished children leading to a compromised immune state and consequently a lasting reduction in peripheral lymphocyte counts ([Savino, 2002](#)). Both innate host defense mechanisms as well as acquired immunity (lymphocyte functions) are affected in patients with poor nutritional status ([Schaible & Stefan, 2007](#)). Consequently, this immunodeficiency results in the susceptibility to infections ([Beisel, 1996](#)) particularly those triggered commonly in persons with HIV/AIDS by opportunistic pathogens ([Cegielski & McMurray, 2004](#); [Field et al., 2001](#)).

The multifaceted interaction of malnutrition and infections generates a prolonged unfriendly environment of a vicious cycle which mutually favors the two entities. This vicious cycle of nutrition and infection is usually associated with a reduction in inflammatory response, a decrease in the ability to produce specific antibodies as well as a decline in the activity of macrophages ([Rodríguez-Morales, Bolívar-Mejía, Alarcón-Olave, & Calvo-Betancourt, 2016](#)). Observations from epidemiological data have supported the contention that malnutrition and infection exacerbate each other. However, not all infections are influenced equally by nutrition ([Chandra, 1983](#); [Scrimshaw et al., 1968](#)). There is sufficient evidence suggesting that certain infections like tuberculosis, diarrhea, and measles clinical outcomes are affected significantly by poor nutritional status while others like tetanus and viral encephalitis are minimally influenced ([Chandra, 1996](#)).

Two possible outcomes of the complex interaction between nutrition and infection are synergist and antagonistic effects. The former occurs when infection degenerates malnutrition or when poor nutrition status decreases immune response to infection. The latter occurs when the agent of multiplication is decreased by malnutrition ([Rodríguez-Morales et al., 2016](#)).

With regard to COVID-19, available data on the effect of nutrition on this infection is scarce. However, considering the key clinical features of COVID-19 which include cough, fever, sore throat, headache, fatigue, headache, and breathlessness suggest that it has similar features to a seasonal influenza infection ([Guan et al., 2020](#)). Hence, specific nutritional deficiencies in vitamins—A, C, D, and E—zinc, selenium, and omega-3 fatty acids may result in immune system dysfunction increasing one's susceptibility to COVID-19 infection. Vitamin D is involved in maintaining immunity and its deficiency has been reported to be associated with an increased risk of respiratory infection. This has led some researchers to hypothesize that vitamin D supplementation could hold promise as a preventive or therapeutic agent for COVID-19 ([Martineau & Forouhi, 2020](#)). Epidemiological studies assessing the relationship between vitamin D status and incidence and severity of COVID-19 are currently scarce

in number (Martineau & Forouhi, 2020). In two ecological studies, an inverse association was reported between national estimates of vitamin D status and COVID-19 incidence and mortality in European countries (Ilie, Stefanescu, & Smith, 2020; Laird, Rhodes, & Kenny, 2020). Findings from a retrospective longitudinal study from Israel revealed an independent correlation between low vitamin D levels and subsequent incidence and severity of COVID-19 (Merzon et al., 2020).

Nutrition and infectivity

Beside genetic and environmental conditions which have been ascribed as an underlining factor leading to disease infections, recent findings have suggested that malnutrition is also another underestimated risk factor. In the quest to identify possible risk factors leading to autoimmune disease conditions, the vitamin D status of patients battling autoimmune gastritis was equated to those present in patients with *Helicobacter pylori*, lymphocytic gastritis, and in healthy controls. The analysis contended that low vitamin D was a possible risk factor for autoimmune diseases (Antico, Tozzoli, Giavarina, Tonutti, & Bizzaro, 2012). In probing the potency of multivitamin supplementation in mitigating disease infections in the aged population, Alexander et al. (2020) found that multivitamins effectively fight against infection in the aged population by reducing to a large extent, the length of infection (by a factor of 17.5). Contrarily the frequent usage of the supplement by the aged population in reducing incidence of infection was seen as insignificant and inconsistent in relation to its efficacy (El-Kadiki & Sutton, 2005).

Low calcifediol in the plasma has been linked with a possible high incidence of Inflammatory Bowel Disease (IBD) and related complications (Ananthakrishnan et al., 2013). This assertion follows after several databases were searched thoroughly for a possible association. After a meta-analysis of the existing literature, it was affirmed that there was over 60% incidence of vitamin D deficiency in IBD patients in comparison to healthy subjects (Del Pinto, Pietropaoli, Chandar, Ferri, & Cominelli, 2015). The role of vitamin A in fighting lower respiratory tract infections in infants below eight was evaluated. Reports from most studies suggested that retinol had no effect on prevalence of symptoms or occurrence of acute lower respiratory tract infections (LRTI). Chen et al.'s (2008) review of the effectiveness and safety of vitamin A for prevention of acute LRTI concluded that vitamin A has only a limiting effect in preventing LRTI; however, they do acknowledge its effect on populations with acute and chronic undernutrition and thus recommend against supplementation in all children to prevent acute LRTI (Chen et al., 2008). To validate claims suggesting a correlation between hypovitaminosis of calcifediol levels and severe acute lower respiratory infection, a total of 150 Indian children below age 5 were recruited. The study revealed that low vitamin D status in young infants coupled with a lack of exclusive breast feeding after the first trimester

of birth triggered acute lower respiratory infection (ALRI) in children (Wayse, Yousafzai, Mogale, & Filteau, 2004).

A meta-analysis and meta-regression of ten (10) randomized trials revealed that zinc supplementation reduced the incidence of ALRI defined by specific clinical criteria [IRR 0.65, 95% confidence interval (CI) 0.52–0.82] (Roth, Richard, & Black, 2010). Similarly, Lassi, Moin, and Bhutta's (2016) systematic review reported that zinc supplementation reduced the incidence of pneumonia by 13% (fixed-effect risk ratio (RR) 0.87; 95% confidence interval (CI) 0.81 to 0.94, six studies, low-quality evidence) and prevalence of pneumonia by 41% (random-effects RR 0.59; 95% CI 0.35 to 0.99, one study, $n=609$, low-quality evidence). A study among Indian young children aged between 6 and 30 months found that the risk of ALRI was significantly higher among vitamin-D deficient (OR 1.26; 95% CI: 1.03 to 1.55) compared to vitamin-D-replete children in a six-month follow-up period (Chowdhury et al., 2017).

Nutrition and disease recovery

Timely provision of adequate nutrition in early phase of critical illness to minimize protein energy deficit has been suggested to improve clinical outcomes, particularly in lean and obese patients (Alberda et al., 2009). Heyland et al. (2015) postulate a possible greater impact of nutrition and exercise on physical recovery of survivors of critical illness but recommend the need for randomized trial testing in proving this relationship.

Earlier studies by Heighes, Doig, Sweetman, and Simpson (2010) highlighted evidence in favor of the timely supply of enteral nutrition in the terminally ill patients. The study reported a sharp decline in intestinal surgery-related deaths following the timely administration of enteral nutritional supports. Although existing data are limited and also inconsistent, data backing the crucial impacts of enteral nutrition and its outcome on severely sick patients cannot be overlooked Heighes et al. (2010).

Hyltander et al.'s (2005) study on timely enteral (EN) and parenteral (PN) feeding support and oral nutrition on recovery time during cancer treatment found the supply of supportive enteral and parenteral nutrition had no greater effect in contrast to oral nutrition when directed by a health care giver. The impact of the combination of PN and EN as against EN only was assessed in some terminally ill patients. Severely sick patients receiving EN alone saw a decline in length of hospitalization and infection. Subjects who received a combination of PN and EN saw no combined consequence following intake of one of the artificial nutritional supplement on death rate, duration in ICU, ventilation time, prealbumin and albumin (Shi, Wei, Huang, & Liao, 2018).

The potential role of healthy nutrition in enhancing recovery, reducing recurrence of terminal diseases, and thus increasing one's survival rate in conditions such as breast cancer (Reeves, Terranova, Eakin, & Demark-Wahnefried, 2014; Rock et al., 2015), endometrial cancer (Kitson et al., 2018; Koutoukidis,

Knobf, & Lanceley, 2015), and ovarian cancer (Beavis, Smith, & Fader, 2016; Thomson et al., 2014) has also been reported. With regard to the COVID-19 pandemic, it has been asserted that wider access to healthy foods should be a top priority and individuals should be mindful of healthy eating habits to reduce their susceptibility and also enhance recovery rate. In the case of severe COVID-19 patients who may have to be on admission in ICU for approximately 2 weeks or more, their dietary intakes become a key determinant for maintaining skeletal muscle and avoiding metabolic disturbances.

Additionally, severe COVID-19 patients suffer respiratory difficulties that result in another extra layer of complexity, preventing such patients from eating well.

Nutrition and respiratory illness

Several research works have reported some promising relationships among respiratory infection and nutritional status. Esposito, Baggi, Bianchini, Marchisio, and Principi (2013) summarized the vital role played by certain micronutrients in facilitating the body's production of antibiotics which goes a long way to protect the body against ARI. Low calcifediol levels in the plasma have been reported to be a potential risk factor contributing to an enhanced susceptibility to disease infection, particularly those associated with the respiratory system (Gibney et al., 2008; Laaksi et al., 2007; Roth et al., 2010). Gunville, Mourani, and Ginde (2013) reported that the modulatory effect of vitamin D on the body's function follows a cascade of events, where first an immune function is enhanced which in turn triggers antibody production which functions to resist and fight against infections.

Esposito and Lelii's (2015) review of studies also revealed that a concentration of between 20 ng/mL and 50 ng/mL of hydroxycholecalciferol (25[OH]D) is considered adequate to provide an immunomodulatory effect in childhood respiratory tract infections such as pediatric tuberculosis, acute otitis media, bronchiolitis, pharyngotonsillitis, and pneumonia. Zhang and coauthors reported the deficiency of fat-soluble vitamins such as vitamin D, A, and E as a possible risk factor for recurrent respiratory tract infections in children below 15 years of age considering the significantly low levels of micronutrients in recurrent RTI subjects (Zhang et al., 2016). Beside its role in encouraging weight gain in malnourished Chronic Obstructive Pulmonary Disease (COPD) patients, nutritional supports have been reported to also improve respiratory status and good health in a COPD population (Ferreira, Brooks, White, & Goldstein, 2012).

Nutrition and respiratory infectivity

Accumulated evidence over the past few decades from different sources suggests that micronutrients mediate host resistance infection. Several efforts have been directed at studying the possible effect of vitamin A intake on immune response to infections (Stephensen, Blount, Schoeb, & Park, 1993). Low

vitamin A levels in experimental mouse models were observed to affect immune regulatory activities of the macrophages and neutrophils, as well as alter the barrier lining the epithelial tissues (Stephensen, 2001).

Chen et al. (2008) review of randomized control trials assessing the role of retinol in fighting LRTIs in children found no important influence of vitamin A on the incidence or occurrence of symptoms of LRTIs, following observations of eight different studies.

A case-control study to analyze the correlation between acute lower respiratory infection and vitamin D deficiency in neonates found low vitamin D status as a potential factor contributing to the risk of ALRI in newborns. They recommended adequate vitamin D supplementation during pregnancy especially in the winter (Karatekin, Kaya, Salihoğlu, Balci, & Nuhoglu, 2009).

Similarly, a review on the efficacy of vitamin D supplements in fighting against the incidence of LRTIs and the modulating factors found to a large extent the effect of vitamin D intake in mitigating the risk of acute respiratory tract infections (Martineau et al., 2017). Subjects who received a routine supply of vitamin D supplements lacking extra bolus doses were shielded from ALRI during the analysis while those who received at least one bolus dose did not express protection against respiratory infections (varying odds fraction 0.86–1.10, 0.97; P for contact=0.05). However, varying degree of protection was observed among study subjects who received vitamin D in every day of the week. Participants with baseline calcifediol levels less than 25 nmol/L (varying odds fraction 0.17, 0.30–0.53) experienced stronger degree of protection than in those with baseline calcifediol levels greater than or equal to 25 nmol/L (varying odds fraction 0.60, 0.75–0.95; P for contact=0.006) (Martineau et al., 2017). Jolliffe, Griffiths, and Martineau (2013) reported vitamin D deficiency to be strongly associated with an enhanced vulnerability to respiratory-related infections although results of the RCT showed inconsistencies in variations in dosing regimens between participants. Conversely, after administering vitamin D supplements to children previously diagnosed with ARI, the results suggested that these nutritional interventions were not associated with the reduction of the incidence of ARIs. Notwithstanding, children previously diagnosed with asthma saw over 70% decrease in the event of asthma exacerbation after being exposed to vitamin D supplementation (Xiao et al., 2015).

Nutrition and immunity against respiratory illness

For more than a century now, greater consideration has been given to the role played by micronutrients on bodily functions. While their availability is known to improve immunity against infections, their deficiency has been reported to be correlated with an increase in the susceptibility to disease infection. The role of serum vitamin D levels' in disease activity was investigated in 39 participants suffering from asthma. Over 40% of asthmatic subjects recruited showed deficiency in serum vitamin D levels, while only 15% had adequate levels. The

control participant did not express lower levels of the vitamin. The study suggested a negative association between vitamin D and interleukin-17 levels in young asthmatics and also described the availability of vitamin D in serum as a key factor in promoting the regulation of *in vivo* T cells between asthmatics (Maalmi et al., 2012). Probiotics and prebiotics administration have been found to trigger immunogenic response to influenza vaccines in the elderly as the rate of seroprotection in influenza H1N1, H3N2, and B subtypes improved dramatically in subjects who took prebiotics or probiotics (Lei et al., 2018). Lee and coauthors investigated the immunogenic influence of vitamin D against influenza. They observed no important effect of the vitamin on influenza infection, but conceded that it may have peculiar effects on immune response to different strains of the virus (Lee et al., 2018).

Fortes et al.'s (1998) randomized, controlled trial investigated the effect of vitamin A and zinc intake on immune function in aged population. Immune response to factors such as chronic diseases, depression, acute respiratory diseases, and smoking was assessed by performing immune test on counts of leukocytes, T-cell subsets, and lymphocytes. Zinc supplementation was found to increase the number of cytotoxic T-lymphocytes and CD4⁺DR⁺ T-cells while vitamin A intake decreased the number of CD4⁺ T-cells and CD3⁺ T-cells. The authors concluded that vitamin A supplementation had a deleterious effect in aged population.

A randomized control trial studying the effect of daily combination of vitamin E and multivitamin-mineral supplements on the severity and prevalence of respiratory tract infections among the elderly of over 60 years of age found the administration of both vitamin E and multivitamin-mineral to have a positive effect on the frequency and impact of acute respiratory infection among unhospitalized aged. However, an adverse effect of vitamin E was observed with disease severity (Graat, Schouten, & Kok, 2002). Meydani, Han, and Wu's (2005) review of the effect of the administration of vitamin E on immune response among aged revealed that vitamin E improved immune function as well as enhance the production of antibodies in response to the administration of vaccines. These improvements in immune function were linked to an enhanced resistance to influenza infection and a decreased risk factor for contracting upper respiratory infections in adult mice and human population. In a related study, a total of six hundred and seventeen (617) aged home residents were recruited in a clinical controlled trial which aimed at evaluating the impact of 1-year vitamin E administration on immune function, infection length, and incidence. The result showed to a large extent an improvement in immune response and the response to vaccines. Vitamin E administration was also found to be associated with a significant decrease in the occurrence of common cold and as well as a decline in the number of common cold cases among the adults (Meydani et al., 2004).

Over the past 2 decades, zinc supplements have been administered in an attempt to improve immunity against respiratory disease infections. Overbeck, Rink, and Haase (2008) review of existing literature summarizing the possible

mechanism by which zinc affected various disease infections and response to vaccination reported that zinc administration affected immune function. The review, however, could not distinguish whether zinc solely modulated immune function and to what extent. Additionally, it was observed that zinc was ineffective in many vaccination trials as its effect on common cold and malaria is still not conclusive ([Overbeck et al., 2008](#)).

In an attempt to investigate the relationship between serum levels of trace elements and the susceptibility to asthma in adult population, a total of 270 adults comprising of 100 asthmatic patients and healthy individuals were enrolled. Serum levels of Zn, Mg, Cu, and Se were measured. The case-control study revealed higher levels of serum Cu and Se in healthy subjects than in asthmatic patients. On the contrary, serum zinc levels were found to be lower in controls than in asthmatics. It was concluded that the decrease in serum selenium and copper levels against increased zinc levels affected the function of antioxidant enzymes by decreasing to an extent the antioxidant capacity in asthmatic patients ([Hussein, Yousif, & Saeed, 2008](#)).

Nutrition and recovery from respiratory illness

Proactive management of infection has recently become a focal point in medical practice. Among the various approaches employed by health professionals which have been reported to be effective in mitigating complications arising from respiratory-related infections have always included the provision of specialized nutritional supports. [Jackson, Lesho, and Peterson's \(2000\)](#) meta-analysis of randomized control trials on zinc gluconate and common cold concluded a gap in evidence of its effectiveness. In order to synthesize evidence regarding the effectiveness of nutritional support in mitigating the incidence, morbidity, and mortality of childhood ALRI, a meta-analysis on RCT of nutritional interventions, antenatal and breastfeeding promotion, which measured one or more childhood ALRI outcome was conducted. The study revealed a drop in hospitalizations related to respiratory diseases. It was proposed that (1) zinc supplements are crucial in averting about a quarter of incidence of ALRI and ALRI-related mortality in zinc-deficient populations, (2) promoting exclusive breastfeeding lessens ALRI-related morbidity, (3) providing only iron supplements is ineffective in reducing ALRI incidence, and (4) ALRI incidence or mortality is unaffected by the supplementation of vitamin A outside the neonatal period ([Roth, Caulfield, & Black, 2008](#)).

The duration of illness in subjects who developed common acute respiratory infections was assessed after routine probiotics administration. Meta-analysis revealed that the incident of illness reduced significantly after respondents received probiotics. Similarly, the length of infection reduced significantly in participants who were administered than in subjects who took a placebo ([King, Glanville, Sanders, Fitzgerald, & Varley, 2014](#)). A review of the effect

of probiotics on respiratory and gastrointestinal and nutritional outcomes in patients with Cystic Fibrosis (CF) concluded that, the routine administration of probiotics in a stable CF population is key in improving nutritional, gastrointestinal, and respiratory outcomes (Anderson, Miles, & Tierney, 2016).

Nutrition and COVID-19

Contemporary evidence on nutrition and COVID-19

The emergence of the novel corona virus disease has exposed lapses in nutrition and food security in many a population. Several schools of thought have recommended nutritional interventions as key in promoting patient recovery in the fight against the disease. It has also been suggested that an improved nutritional status reduces the risk of infection to a large extent (Beck, Handy, & Levander, 2004). Even though new vaccines are available, administration to everybody across the world will take sometime. The administration of nutrition supports therefore would be needed for better outcomes due to its availability and the established knowledge concerning its contribution to the fight against infection. There is enough evidence suggesting that an improved nutritional status promotes immunity to infections (Zabetakis, Lordan, & Norton, 2020). Maintaining a robust immune system at this material times is thus crucial to the fight against the pandemic. The possible effects of serving extra micronutrient supplementation to COVID-19 infected patients have been recently reviewed. Fortifying nutrition support with micronutrients or conditional amino acids has been suggested to improve outcome in COVID-19 infected individuals although evidences accentuating these facts are lacking (Rozga, Cheng, Moloney, & Handu, 2020). Vitamin D was confirmed as having antiviral properties responsible for protecting against respiratory-related infections such as COVID-19 (Hribar, Cobbold, & Church, 2020). Another study found that the continual administration of vitamin D triggers the antioxidant activity of glutathione enzymes (Lei et al., 2018) and facilitates the production of glutathione which is crucial in the treatment and prevention of COVID-19 (Mousavi, Bereswill, & Heimesaat, 2019; Colunga Biancatelli, Berrill, Catravas, & Marik, 2020; Wimalawansa, 2020). Interestingly, although several calls have been made with reference to the intake of probiotics with the hope of fighting COVID-19 infection, no clinical trial has backed these assertions till date. A possible correlation between pulmonary-related infections and microbiomes in the lung has been, however, underscored which relates bacterial metabolites to diets with a classical example being short chain fatty acids and lung microecological niche (Yang, Xing, Song, & Qian, 2020). Stachowska, Folwarski, Jamioł-Milc, Maciejewska, and Skonieczna-Żydecka (2020) proposed the administration of probiotics as a supportive intervention to coronavirus-infected patients who require antibiotic therapy but present symptoms of gastrointestinal infection.

Nutrition and immune development in COVID-19

It is well known that nutrition plays an important role in promoting immunity and protecting the body against diseases. [Maggini et al. \(2018\)](#) described the relationship between nutrition, immunity, and infection to be bidirectional in nature, and suggested that changing the components in any had a greater impact on the rests. Fruits and vegetables have been reported as important sources of phytonutrients and micronutrients which provides antiinflammatory and antioxidants agents vital in improving immune responses to disease infections ([Calder et al., 2020](#); [Zhang, Taylor, Bennett, Saad, & Rayman, 2020](#)). In this period of the coronavirus outbreak, improving immune function against respiratory infections by administering nutrients with better prospects may be part of the needed solution in controlling the situation. Most recently, the role of vitamin D interventions as a booster of immune function in the resistance of respiratory infection was analyzed by conducting RCTs. The result confirmed the vitamin to boost immune function in deficient individuals against ARTIs ([Martineau et al., 2017](#)). Similarly, [Zabetakis et al. \(2020\)](#) recommended vitamin D as potent in reducing the incident of infections, including the novel coronavirus infection.

Nutrition and COVID-19 infectivity

In order to authenticate the numerous calls in the early parts of this year concerning the prospects of vitamin D supplementation on COVID-19 infectivity, publications on works featuring COVID-19 influenza and vitamin D were meticulously searched. Generally, epidemiological studies have reported that vitamin D deficiency is associated with viral respiratory tract infections ([Ebadi & Montano-Loza, 2020](#)). In most of the trials, vitamin D intake was linked to a decreased incidence of influenza while few reported otherwise. It was observed that coronavirus begun around the winter period, where serum calcifediol levels diminished considerably, on the other hand, cases of the infection were low during the summer period. Another observation was that a large portion of the aged population were victims of the infection, probably because most aged persons are more likely to be deficient in vitamin D as a result of being housebound or institutionalized and thus may not be exposed to sunlight in order for the skin to synthesize some invitro vitamin D. A meta-analysis incorporating data from 21,000 subjects across eight observational studies found that those with a serum vitamin D level $<20\text{ ng/mL}$ (i.e., $<50\text{ nmol/L}$) had a 64% increased risk of community-acquired pneumonia ([Zhou, Luo, & Qin, 2019](#)). Vitamin D agonist, calcitriol, exhibited defensive mechanisms against acute lung injury by modifying and controlling the expression of members of the renin-angiotensin system such as ACE2 in lung tissue ([Xu et al., 2017](#)). This supports and suggests that vitamin D deficiency can be a pathogenic factor in COVID-19 ([Ebadi & Montano-Loza, 2020](#)).

Likewise, persons who are deficient in vitamin D are predisposed easily to chronic diseases such as diabetes and cardiovascular diseases ([Papandreou & Hamid, 2015](#)). These observations were found to correspond with vitamin D

deficiency and thus a recommendation in favor of vitamin D as a potent supplement in mitigating death rate and incidence of coronavirus and influenza infections (Grant et al., 2020; Han et al., 2016).

Selenium deficiency has been reported as crucial to viral infections (Guillin, Vindry, Ohlmann, & Chavatte, 2019). Fakhrolmobasheri, Nasr-Esfahany, Khanahmad, and Zeinalian (2020) reported that selenium may be relevant to the cause of COVID-19. The administration of this micronutrient is known to have positive impacts on immune function (Calder et al., 2020). It has been reported that subjects with low serum selenium levels are at risk of viral infections owing to higher pathogenic mutation rates which ultimately lead to a rapid evolution in pathogenic viral strains (Beck, 2006). Alexander et al.'s (2020) review on the need for possible micronutrient intervention to avert the risk of a chronic coronavirus infection with emphasis on vitamin D, zinc, and selenium found limited evidence for an association between the aforementioned micronutrients and coronavirus disease. It was however argued that since these micronutrients are known to be vital in promoting immune function, resisting viral infection, and reducing inflammations, their administration might offer protection against the novel coronavirus disease.

The protective role of zinc amid the COVID-19 pandemic has been discussed to a large extent. The micronutrient has been envisioned as a potential supportive intervention to overcome the current global crisis. This stems from the fact that zinc possesses immune modulatory characteristics coupled with an antiviral activity (Zhang et al., 2020). The combined effect of the cation form of the mineral (Zn^{2+}) with its ionophore pyrithione has been reported to alter SARS-coronavirus RNA polymerase activity and thereby decreasing its replication process (Te Velthuis et al., 2010).

It has been suggested that vitamin C administration may be effective in boosting the body's immune response to coronavirus infection (Khan, Parikh, Megala, & Predeteanu, 2020). Intravenous administration has been recommended for severe cases of COVID-19 infections, while the oral intake has been suggested to be effective in protecting against infection (Nilashi et al., 2020). Though various claims have been made in favor of vitamin C intake to battle COVID-19 infections, there is limiting evidence to buttress these speculations. Similarly, no current empirical data exist to validate claims that a higher intravenous dosage of vitamin C is effective in the management of COVID-19.

Nutrition and recoveries from COVID-19

A retrospective multicenter study of 212 cases by Alipio and Alipio (2020) to assess the possible clinical outcome of vitamin D supplementation on COVID-19 patient found serum calcifediol levels to significantly affect outcomes in the vast majority of cases with suboptimal vitamin D levels. Multinomial logistics regression analysis showed 8 times increase in the event of mild clinical outcome over a severe outcome as serum calcifediol levels increase ($P < 0.001$,

OR=0.126), and an approximated 20 times increase in the event of mild clinical outcome over a critical clinical outcome. It was inferred that a drop in serum levels of calcifediol could exacerbate clinical outcomes, while a rise in levels enhances outcomes in COVID-19 infected subjects (Alipio & Alipio, 2020).

Vitamin C is highly acclaimed for its antioxidant properties in scavenging free radicals in the body and thereby protecting against oxidative damage. Its role also includes supporting the immune function of the body. Infection has the ability to decrease the levels of vitamin C and increase a person's requirement as the severity of the infection increases (Carr et al., 2017). In a review, Colunga Biancatelli, Berrill, and Marik (2020) suggest a combined prophylactic administration of vitamin C and quercetin in the prevention and early treatment of COVID-19. Currently, various studies are underway to determine the effectiveness of vitamin C on disease outcome among COVID-19 patients. However, in a recently published case series, it was noted that administration of 1 g of vitamin C every 8 h for 3 days significantly decreased inflammatory markers such as ferritin and D-dimer (Hiedra et al., 2020). Also, in a case report, a 74-year-old woman critically ill with COVID-19 recovered unusually early upon intravenous administration of high dose of vitamin C (Khan et al., 2020). The researchers postulated that vitamin C could be helpful in achieving rapid recovery, reducing length of time on a ventilator and stay at the ICU.

Selenium status was reported to be associated with a higher recovery rate from coronavirus infection early this year in China (Zhang et al., 2020). In a recent study, the association between serum selenium levels and the risk of COVID-19 related mortality was assessed. An X-ray fluorescence and selenoprotein analysis was performed on the serum samples obtained from a total of 33 coronavirus-infected subjects. Deficient levels of serum selenium levels were observed in the samples. Additionally, when serum levels were compared between COVID-19 survivors and nonsurvivors, the former showed higher Se levels than the latter. Serum levels in survivors were restored to normal levels while nonsurvivors saw a sharp decline in Se levels (Moghaddam et al., 2020). In a similar study, the relationship between regional selenium status and COVID-19 outcomes was investigated. The study employed Stata prtest to compare COVID-19 related recovery and death rates and assessed the association between recovery rates and regional Se serum levels using linear regression models. Interregional differences in cure rate were observed: regions with low selenium consumption rates had lower cure rates compared to other provinces. Higher death rates were, however, recorded in regions with low consumption. Thus it was concluded that selenium administration was crucial in COVID-19 recovery rate (Zhang et al., 2020).

Nutrition for optimal mental health during COVID-19

The current COVID-19 pandemic brings specific challenges and problems associated with the mental health status of both affected and healthy persons and

even frontline health professionals who care for COVID-19 patients. The pandemic has been reported to have taken a heavy toll on the dietary intakes and nutritional status of people, mainly a result of not only being affected but the psychological trauma that accompanies being affected with COVID-19. Poor diet can be detrimental to mental health and as such dietary interventions hold promise for reducing symptoms of depression across the population. Therefore this section considers the critical role that certain foods and nutrients play in the prevention, management, and recovery from the common mental health-related problems associated with COVID-19.

COVID-19 patients may be confronted by emotional disorders, anxiety, distress, eating disorders, and depression which can take its toll on their sleeping patterns (insomnia), nutritional status, and rate of recovery. A study that evaluated the symptoms of patients with eating disorders during the pandemic found that 37.5% reported symptoms of worsening eating disorder and 56.2% reported additional anxiety symptoms (Fernández-Aranda et al., 2020),

Rogers and colleagues' systematic review revealed that COVID-19 patients on admission in health facilities experienced psychological problems. They included confusion (36 [27.9%; 95% CI 20.5–36.0] of 129 patients), depressed mood (42 [32.6%; 24.7–40.9] of 129), anxiety (46 [35.7%; 27.6–44.2] of 129), impaired memory (44 [34.1%; 26.2–42.5] of 129), and insomnia (54 [41.9%; 22.5–50.5] of 129). Even after recovery (postillness stage) there were still such experiences of depressed mood (35 [10.5%; 95% CI 7.5–14.1] of 332 patients), insomnia (34 [12.1%; 8.6–16.3] of 280), anxiety (21 [12.3%; 7.7–17.7] of 171), irritability (28 [12.8%; 8.7–17.6] of 218), memory impairment (44 [18.9%; 14.1–24.2] of 233), and fatigue feeling (61 [19.3%; 15.1–23.9] of 316) (Rogers et al., 2020).

It is also possible that affected persons who are cared for in the ICU are very likely to develop certain psychological trauma. These include feelings of anger, sadness and helplessness, severe irritation, problems with sleeping, and extreme stress. Findings from previous studies indicate that COVID-19 patients reported gloomy feelings, lack of interest in happening in their immediate environment, and losses in their appetite. A systematic review on COVID-19 and mental health consequences reported a high level of posttraumatic stress symptoms (PTSS) (96.2%) and significantly higher level of depressive symptoms ($p=0.016$) among COVID-19 patients (Vindegard & Benros, 2020).

A broad body of studies associate social isolation and loneliness to both poor mental health outcomes, especially because of the challenge of overcoming the difficulties associated with adapting to the new lifestyle of the quarantine. In addition, research on the psychological impact of quarantine outbreaks of diseases suggests that such isolations and confinements can result in negative mental health outcomes. Specifically, there is also a cause for alarm considering the possibility of suicidal ideation during this time, given that isolation is a risk factor for suicide.

Research that has been conducted to elucidate the relationship between diet and mental health is scarce (Choda et al., 2020). However, some studies have

reported that increased consumption of fruits, vegetables, fish, poultry, dairy products, unprocessed meat, and whole grains is associated with a reduced susceptibility to depression (Lai et al., 2014; Lang, Beglinger, Schweinfurth, Walter, & Borgwardt, 2015; Schefft, Kilarski, Bschor, & Koehler, 2017). Several nutrients such as calcium, magnesium, zinc, folate, vitamins D and B12, and n-3 polyunsaturated fatty acids (PUFA) have been suggested to be effective in the management of depression (Lang et al., 2015; Schefft et al., 2017). For example, in a recent prospective cohort study that was conducted among 4701 participants who were followed for 5 years, it was revealed that regular intake of rich food sources of calcium such as dairy products resulted in better mental health outcomes among Japanese adults (Choda et al., 2020). Another systematic review revealed twelve (12) antidepressant nutrients that are associated with the prevention and treatment of depressive disorders (LaChance & Ramsey, 2018). The twelve (12) nutrients are folate, iron, long-chain omega-3 fatty acids (EPA and DHA), magnesium, potassium, selenium, thiamine, vitamin A, vitamin B6, vitamin B12, vitamin C, and zinc. These nutrients are present in food sources such as oysters and mussels, various seafoods, and organ meats for animal foods. They also include plant food sources such as leafy greens, lettuces, peppers, and cruciferous vegetables (cabbage, cauliflower, broccoli, brussels sprouts) (LaChance & Ramsey, 2018). With regard to meat consumption, in a systematic review, eleven (11) out of eighteen (18) studies demonstrated that meat abstention was associated with poorer psychological health. The most rigorous studies demonstrated that the prevalence or risk of depression and/or anxiety were significantly greater in participants who avoided meat consumption (Dobersek et al., 2020).

A systematic review and dose-response meta-analysis of prospective studies found that high-quality diet, regardless of type (i.e., healthy/prudent or Mediterranean) which contained vegetables and fish sources, was associated with a lower risk of depressive symptoms over time (odds ratios ranged 0.64–0.78 in a linear dose-response fashion [$P < 0.01$]) (Molendijk, Molero, Sánchez-Pedreño, Van der Does, & Martínez-González, 2018). A meta-analysis involving sixteen (16) eligible randomized controlled trials reported that dietary interventions significantly reduced depressive symptoms ($g = 0.275$, 95% CI = 0.10 to 0.45, $P = 0.002$). Similar effects were observed among high-quality trials ($g = 0.321$, 95% CI = 0.12 to 0.53, $P = 0.002$) and when compared with both inactive ($g = 0.308$, 95% CI = 0.02 to 0.60, $P = 0.038$) and active controls ($g = 0.174$, 95% CI = 0.01 to 0.34, $P = 0.035$) (Firth et al., 2019).

Nutrition in management of COVID-19

Malnutrition is known to extend the length of infection as well as increase the overall number of times spent in a health center during an ailment. As vaccines trials are still underway, and much attention is being given to nutritional interventions as possible remedies in the fight against COVID-19, rehabilitation

departments must step up their game in the diagnosis, treatment, and prevention of malnutrition in hospitalized coronavirus-infected patients, so as to improve prognosis and patient recovery (Barazzoni et al., 2020; Volkert et al., 2019). Any attempt to underestimate the intervening role of nutrition in the fight against coronavirus infection must be downplayed since the recovery and chances of survival as well as the rehabilitation of patient is also dependent on nutritional support (Brugliera et al., 2020).

San Raffaele Scientific Institute, early this year, hosted some 50 COVID-19 infected patients at its Rehabilitation Centre. Participants, after testing positive for functional independence measure and nasopharyngeal swab test, were recruited for admission with the aim of assessing the managerial effect of nutrition on COVID-19 patient. A multidisciplinary team took care of patient's nutritional status and swallowing function during the rehabilitation period. The cohort expressed an approximated average Functional Independence Measure (FIM) value of 77.0 with some degree of dysphagia in more than 90% of COVID-19 infected patients. A dysphagia rate of about 50% was reported in a previous communication after orotracheal intubation. While less than 30% of patients exhibited a minimal incidence of malnutrition, 45% of the recruited patients expressed an elevated risk indicating that the recovery of COVID-19 patients was also dependent on nutritional supplementations coupled with effective swallowing training techniques (Brugliera et al., 2020).

A systematic review performed between February and April 2020 revealed that micronutrient deficiencies, especially vitamins A, B complex, C, and D, zinc, iron, and selenium, are common among COVID-19 patients and could plausibly increase their risk of death. A recommendation was made to consider the judicious use of need-based micronutrient supplementation, alongside existing micronutrient fortification program, in the management of this global pandemic (Akhtar et al., 2020). For COVID-19 patients in rehabilitation centers, it has been recommended that another supportive therapy that must be considered is the use of probiotics, particularly in case of intestinal issues among some COVID-19 patients. In addition, adequate hydration must be maintained particularly in patients confronted by frequent episodes of diarrhea and vomiting in order to prevent electrolyte imbalances (Brugliera et al., 2020).

Conclusion

The role of nutrition in the human defense system cannot be overemphasized as nutrition, diet, and nutritional status is an important determinant of the body's immunity. Malnutrition is known to trigger immunodeficiency, predisposing the malnourished to several infectious diseases.

Existing evidence has established relationship between disease infectivity, mortality, and micronutrient deficiencies. Numerous micronutrients, including vitamins A, D, C, E, zinc, iron, copper, and selenium, are critically essential as they mutually support each other in the immune protection and response

process. The role of vitamin C in the prevention and management of respiratory infections cannot be overemphasized. Zinc's role in enhancing immune function and reducing the risk of infections mainly as a result of its antiinflammatory property has also been established. Selenium (Se) is an essential trace mineral which is vital for particularly maintaining a well-balanced immune response. Although the potential role of these micronutrients has been individually discussed, it is important to note their complementary roles in nutritional health as they do not work in isolation. Growing evidence suggests that functional foods which include tea components may help optimize immunological responses such as improving defense functions and resistance to infections. The effect of probiotics and prebiotics on health is also known.

The COVID-19 pandemic is a stressful time and it can be especially challenging when managing concerns around eating. With the occurrence of such pandemics and its associated psychological problems, dietary interventions may be immensely helpful and effective as part of the prevention, management, and treatment strategies. This review has highlighted the need to consume adequate amounts of particular nutrients and foods, especially calcium, dairy products, vegetables, vitamin D, carotene, and n-3 PUFA which have been found to lead to better mental health.

Timely provision of adequate nutrition in early phase of critical illness to minimize protein energy deficit has been suggested to improve clinical outcomes, particularly in lean and obese patients. With regard to the COVID-19, a wider access to healthy foods should be a top priority and individuals should be mindful of healthy eating habits to reduce their susceptibility and also enhance recovery rate.

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