



Nutrition planning during the COVID-19 pandemic for aging immunity

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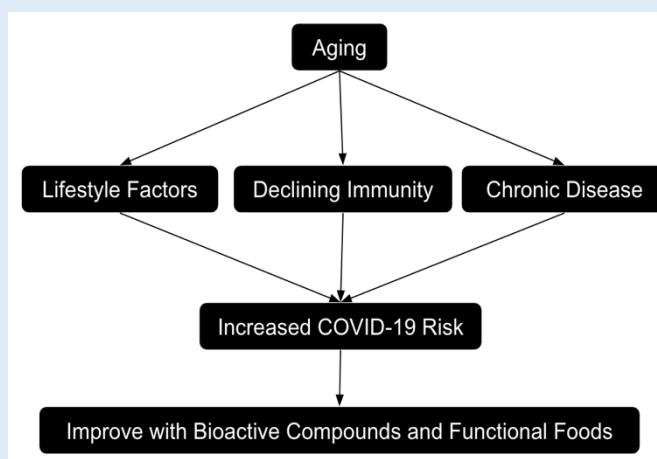
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ABSTRACT

The disease COVID-19, caused by the SARS-CoV-2 coronavirus, disproportionately targets individuals with aging or otherwise dysfunctional immunity. Since nutrition is shown to have a massive effect on the immune system—and other body systems that can both improve protection and ability to fight against the SARS-CoV-2 virus—we conducted a literature review of nutrition recommendations and their antiviral effects in

older adult populations. Certain bioactive compounds and functional foods have been shown in the past to improve the body's immune function and prevent viral infection. We organize our recommendations by food groups, as delineated by the MyPlate nutritional program, to create guidelines for senior citizens, public health experts, nutritionists, caretakers, and nursing homes. We hope this research will assist in improving the age disparity in vulnerability to the disease COVID-19 during the pandemic.

Keywords: COVID-19, SARS-CoV-2, coronavirus, infection, pandemic, deficiency, health, nutrition, immunity, diet, elderly, aging, senior citizens



INTRODUCTION

The outbreak of COVID-19, a disease caused by a novel coronavirus (2019-nCoV) named SARS-CoV-2, was officially declared a pandemic in March 2020 [1]. By July 1, 10,680,651 cases and 516,268 deaths worldwide have been reported [2]. Since this virus is so new, there has not been enough time to run extensive clinical research regarding its behavior, incidence, and symptomatology yet. However, since the coronavirus SARS-CoV-2 has a few pathogenic siblings including SARS-CoV and MERS-CoV, we may use data and findings from these recent past outbreaks when data on SARS-CoV-2 is not available [3].

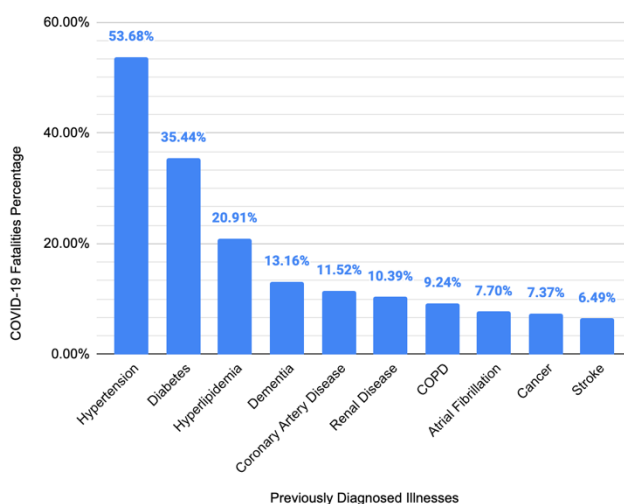
The highest indication of susceptibility to COVID-19 infection is age and age-related chronic conditions, like diabetes, heart disease, and hypertension. A recent clinical study of 1591 COVID-19 patients in Italy found that the mean age of patients was 63 years, almost two decades higher than the average Created from data from New York State Department of Health 2020 population age [4]. The elderly are at huge risk of contracting SARS-CoV-2 and suffering poor health outcomes once infected because of weakened immune and other organ systems. Immunity has been proven to decline with age due to high levels of chronic inflammation, dysregulation of innate immunity, and altered T-cell and B-cell development [5]. This phenomenon places older people at a huge disadvantage when fighting viruses like SARS-CoV-2.

Figure 1 shows the proportions of New York COVID-19 fatalities that were diagnosed with a comorbidity, most commonly diseases of the cardiovascular and pulmonary systems, which are all more likely to appear with increase in age.

This review article aims to address this age disparity in COVID-19 outcomes from within the

context of nutrition. Although many clinical studies haven't been done yet regarding SARS-CoV-2, numerous studies in the past have been found to demonstrate the relationship of food consumption to viral infection. Nutrition and diet are found to affect susceptibility in two ways: (1) by leading to chronic diseases or comorbidities that weaken the body—as 89.8% of fatalities from the disease had at least one comorbidity—or (2) by directly affecting the body's immune system and ability to fight off viruses [6]. Since the elderly already have declining immunity, it is substantially more important for them to receive all essential nutrients in recommended quantities while also managing chronic conditions using lifestyle changes and pharmaceuticals.

Figure 1: New York State Comorbidities in COVID-19 Fatalities



Created from data provided in New York State Department of Health 2020 [6]

However, many older people in the United States live in group housing like assisted living or nursing homes, which, due to a strict business model and high volumes, prepare residents' meals in a commercial kitchen with subpar products to fit a specific budget [7]. Even outside of the group setting, individuals who are elderly, immunocompromised, or ill are less likely to have access to fresh foods, due to

not having availability or ability to obtain transportation to grocery stores.

Utilizing an examination using evidence published regarding immunity and functional foods thus far, we will create a nutritional plan for nursing home contractors, caretakers, food scientists, nutritionists, and senior citizens to consider during the pandemic. Keywords “bioactive compound”, “nutrition”, “COVID-19” were used in PubMed and FFHD Journal to find relevant biochemical and clinical studies.

Recommendation Model: Prevention and management of both chronic diseases and infectious diseases, such as SARS-CoV-2, can be tackled through early dietary intervention and use of functional foods. Functional foods are “natural or processed foods that contain biologically-active compounds; which, in defined, effective, and non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers for the prevention, management, or treatment of chronic disease or its symptoms” [8].

In the United States, the Department of Agriculture (USDA) published a nutrition guide known as MyPlate (Figure 2) which serves as an educational tool to help citizens make healthy food choices [9]. A study conducted on adults over 50 years of age found that following the MyPlate program actually improved dietary intake and long-term health [10]. Nutrition has always been a major problem for the elderly as up to 85% nursing home residents suffer from malnutrition or nutrient deficiencies [11]. Looking beyond general health, this guide is an excellent model to study each food group against the backdrop of improving immune function and preventing COVID-19 infection in older populations. The recommendations listed can be used for

healthcare workers or dietitians who are creating nutritional plans for their patients or by public health experts and content creators to target and educate specific populations.

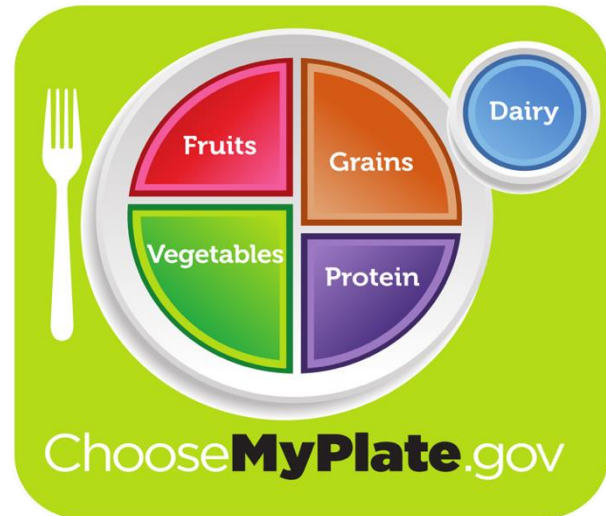


Figure 2: MyPlate Graphic to organize food groups By United States Department of Agriculture 2011 [12]

Rather than only specific food type recommendations, food quantity recommendations are also important to consider. Both undereating and overeating are damaging to health. Nursing home residents and the elderly population are susceptible to loss of appetite due to increased levels of depression, cancer, cardiac or GI disorders, and pharmaceutical medications that may cause nausea or vomiting. All of these factors lead to unintentional weight loss which can cause infection, depression, or death in the elderly [13]. Additionally, studies show that during viral infection, patients display approximately 10% greater resting energy usage. This means that for an infected individual, despite appetite suppression, normal calorie intake should increase by 10% to maintain the patient’s energy and weight [14].

At the same time, due to the pandemic, many immunocompromised older people must stock up on

non-perishable snack foods and spend large amounts of time alone and sedentary at home. Due to these sudden lifestyle changes, much of the quarantined (but non-infected) population is in danger of overeating and weight gain [15], [16]. Moreover, stress and anxiety stemming from financial, health, or social factors causes the body to release the steroid hormone cortisol as an emergency measure, further increasing some individuals' risk of stress-eating, immune dysfunction, obesity, cardiovascular disease, and diabetes [17], [18]. To prevent these negative effects during quarantine, overeating should be prevented and a regular physical exercise regimen should be followed.

Protein: Proteins are defined as meat, poultry, seafood, beans and peas, eggs, processed soy products, nuts, and seeds [12]. A balanced diet should contain a good variety of these listed protein sources. The anti-inflammatory protein adiponectin, which breaks down fatty acids, could be useful to prevent SARS-CoV-2 infection and treat or improve patient outcomes. There is evidence that shows some diets, especially those that are Mediterranean, help in increasing adiponectin gene expression and plasma levels [19]. The Mediterranean diet consists of cardioprotective foods such as fish, legumes, and nuts [20]. This type of diet that promotes high adiponectin is also associated with improved obesity levels and cardiovascular health, especially in the elderly [21], [22]. These and other foods should be consumed in moderation (avoiding either under- or over-consumption).

We will first discuss the benefits and effects of seafood in the body. Since there is evidence of health benefits due to bioactive lipids and polyunsaturated fatty acids, a diet consisting of seafood, or a supplement of fish oil, can be important for

individuals above around 65 years of age [23], [24]. In addition to working against cardiovascular disease and obesity, polyunsaturated fatty acids are shown to be effective in the immune system. They can decrease microbial load by inactivating enveloped viruses such as the SARS-CoV-2 virus [25], [26]. They are also shown to inhibit production of inflammatory mediators like eicosanoids, pro-inflammatory cytokines (IL-1 β , TNF- α , IL-6), chemokines (IL-8, MCP-1), adhesion molecules (ICAM-1, VCAM-1, selectins), and reactive oxygen species [27]. Evidently, polyunsaturated fatty acids are crucial in a diet during a pandemic [26]. According to the U.S. Department of Health and Human Services, polyunsaturated fatty acids can be found in walnuts, sunflower seeds or oil, flax seeds or oil, and most importantly, fish, including salmon, mackerel, herring, albacore tuna, and trout [28].

Nutrients found in meat can also be valuable. Taurine, creatine, carnosine, anserine and 4-hydroxyproline have been shown to help kill pathogenic bacteria, fungi, parasites, and viruses (including coronaviruses like SARS-CoV-2). There is also evidence of these compounds activity against chronic disease such as obesity, cardiovascular disease, and other aging-related disorders which serve as comorbidities during a SARS-CoV-2 infection [29]. Since red meat (including beef) contains each of these beneficial compounds, after further studying optimal dosage amounts and possible negative side effects or other metabolic effects, it can be considered as a functional food for immunity during the COVID-19 pandemic.

Aside from animal sources, plant sources of protein are also vital. Infection with SARS-CoV-2 virus generates acute respiratory syndrome which releases pro-inflammatory cytokines, including IL-6 and TNF- α

[30]. It is shown that a diet rich in legumes, a vegetarian protein source, can inhibit IL-6 and TNF- α and assist in prevention or faster relief from SARS-CoV-2 infection [31]. Specific legumes like fava beans have been studied for years due to their antiviral effects [32]. This functional food is shown to have chemical compounds similar to quinine-based antimalarials such as hydroxychloroquine—which is currently being used in COVID-19 treatment [33]. Consumption of fava beans may have beneficial antiviral effects without the possible side-effects of taking a pharmaceutical like hydroxychloroquine. There is also evidence to show the importance of vegetarian proteins in prevention of other chronic diseases like type 2 diabetes, hypertension, and cardiovascular disease—all common COVID-19 comorbidities. A longitudinal study of aging clinical patients found a reduction in chronic disease biomarkers such as inflammation and oxidative stress when greater proportions of plant-based proteins are consumed in a long-term diet [34]. Evidently, it is important to consume a combination of vegetarian and non-vegetarian sources of protein in order to obtain the optimal combination of nutrients for proper immune system and body function.

Dairy: According to the USDA, the dairy food group consists of fluid milk products and foods made from milk [12]. In addition to containing some protein, dairy products frequently contain an excellent source of essential vitamins and minerals—most notably, calcium.

Minerals found in milk like calcium, zinc, selenium, magnesium, and potassium are valuable in maintaining a healthy immune system in order to fight off the SARS-CoV-2 virus [35]. For example, zinc is used to maintain immune system homeostasis and its deficiency has been proven to impair innate and

adaptive immunity [27]. Supplementation studies have shown that zinc can specifically inhibit viral replication (by preventing viral membrane fusion) and improve antiviral response and symptomatology [36]. A nutritious diet should incorporate all essential minerals to maintain a proper defense.

The American Dairy industry currently fortifies milk with Vitamins A and D, two essential vitamins in maintaining the body's immunity [37]. Vitamin A can play a huge role in reducing susceptibility to pathogens [38]. A clinical study of the Ebola virus epidemic in West Africa showed that Vitamin A could be used as a therapeutic supplement in populations with high likelihood of nutritional deficiencies because it was likely to decrease mortality and improve disease outcomes [39]. Vitamin A actually leads to production of a molecule called isotretinoin, which down-regulates the ACE2 receptor. Since ACE2 is what SARS-CoV-2 virus attaches to in the victim's respiratory tract, this effect of Vitamin A can lead to an inability for viral attachment and infection, decreasing susceptibility of contracting COVID-19 [40].

An especially interesting phenomenon to study is risk for Vitamin D deficiency, which is shown to become more problematic with increase in age [41]. The elderly—who are already vulnerable to COVID-19—are also vulnerable to Vitamin D deficiency, which can compound COVID-19 infection risk. Supplementation with Vitamin D2 or D3 has been shown to offer protection from acute respiratory infections like COVID-19 [42].

The digestive system's natural microbiome plays a large role in immunomodulation and maintaining a defense against infectious disease. The use of probiotics, therefore, which promote and restore a healthy gut microbiome, can assist in providing a secure defense against SARS-CoV-2 [43]. Numerous

clinical studies show evidence of probiotic effectiveness against viruses like malaria and H1N1 [44], [45], [46]. Table 1 below shows immune system effects of several probiotic bacteria to provide evidence that probiotic-containing foods could be recommended as a prophylactic treatment to vulnerable older populations—who already have lower levels of intestinal flora—as a way to prevent or treat COVID-19 [47], [48].

These previous studies on other viruses inspired some initial clinical trials in COVID-19 patients in 2020. Although three new bacteriotherapy and prevention studies are currently recruiting and ongoing at the time of this publication, findings may be promising if the biomarkers measured show improvement for probiotic dietary supplements (such as one called SivoMixx) against a placebo [49].

Foods composed of live, active cultures of non-pathogenic and non-toxic bacteria, namely *Lactobacillus* and *Bifidobacterium*, are regarded as safest and can even be found naturally in foods like yogurt, sour cream, cheese, and other dairy products [50]. There is evidence that suggests probiotics and fermented dairy products are also valuable against several chronic diseases that serve as SARS-CoV-2 comorbidities such as obesity, hypertension, and diabetes as shown in studies charted below in Table 2 [51]. Especially in the vulnerable and those with underlying chronic health problems, restoring healthy microbiota through methods like probiotic effects of the SARS-CoV-2 virus [52].

The data in these clinical studies leads toward evidence that yogurt or consumption is highly important in mitigating the fermented dairy can be formed into a functional food product if dosages are

established and further studies confirm the clinical relevance for chronic disease by measuring biomarkers for these diseases .

Grain: Grains in USDA's MyPlate are foods made from wheat, rice, oats, cornmeal, barley or another cereal grain. Examples include bread, pasta, oatmeal, breakfast cereals, tortillas, grits and can be classified as whole grains and refined grains [12].

Depressed immune function due to rise in stress hormones such as cortisol during chronic disease or SARS-CoV-2 infection can be harmful for many patients in their recovery. Studies show that consuming adequate carbohydrate reduces these stress hormones and limits immune depression [59]. Mood-boosting foods, the most prominent of which is chocolate, are proven to decrease cortisol levels [60]. However, too much sugar consumption is directly correlated to the chronic diseases type 2 diabetes, cardiovascular disease, obesity, autoimmune disease, and more [61]. It is important for populations vulnerable to SARS-CoV-2 to ensure that they are getting enough complex carbohydrate content (keeping the body feel full for longer) in their diets without consuming excess simple sugars or carbohydrates. This can be done by making simple substitutions like fruit for candy, wheat bread for white bread, and dark chocolate for milk chocolate. Additionally, whole grains and other high fiber foods have been shown to exhibit antiviral effects by reducing inflammation and alleviating symptoms.

The mechanism of action enables complex carbohydrates to be fermented in the gut by bacterial species—e.g. *Bacteroides spp.*, *Bifidobacterium spp.*,

Table 1: Clinical data on relationships between probiotics and chronic diseases

Probiotic Source	Outcome
<i>Lactobacillus acidophilus</i>	Enhanced inflammatory signals; enhanced antiviral immune reaction
<i>Lactobacillus rhamnosus</i>	Enhanced antiviral immune reaction; enhanced vaccine immune efficacy
<i>Lactobacillus casei</i>	Enhanced phagocytic and killing activity of alveolar macrophages; increased levels of IgA, IFN- γ , and TNF- α
<i>Bifidobacterium</i>	Enhanced vaccine immune efficacy

Table adapted from He et al 2020 [47]

Table 2: Clinical Data on relationships between probiotics and chronic diseases

Disease	Probiotic Source	Study	Outcome	Reference
Hypertension	Lactotripeptides (milk peptides)	Meta-analysis of 30 randomized clinical trials; N = 2200	Found significant negative association between BMI and blood pressure lowering effects of lactotripeptides ($p \leq 0.001$)	Fekete et al 2015 [53]
Obesity	Yogurt	Meta-analysis of 3 prospective studies; N = 120,877	Yogurt consumption was negatively associated with a 4-year weight gain ($P < 0.001$)	Mozaffarian et al 2011 [54]
Type 2 Diabetes	Yogurt	20-year prospective; N = 194,458	Consumption of one serving of yogurt per day was inversely correlated with type 2 diabetes ($P < 0.001$)	Chen et al 2014 [55]
Type 2 Diabetes	Yogurt	4-year prospective; N = 3,454 (elderly)	Total yogurt consumption was associated with a lower type 2 diabetes risk ($P = 0.002$)	Díaz-López et al 2016 [56]
Mortality	Fermented Dairy Product	10-year prospective; N = 4,526	Fermented dairy consumption was inversely associated with overall mortality ($P < 0.01$)	Soedamah-Muthu et al 2013 [57]

Table adapted from Marco et al 2017 [58]

and *Prevotella spp.*—which create metabolite bioproducts in the bloodstream to signal and release anti-inflammatory cytokines and maintain the mucosal barrier [62], [63]. An increased intake of dietary fiber and complex carbohydrates can improve outcomes for patients in danger of contracting COVID-19.

One food widely used for prevention and treatment of SARS-CoV-2 in Chinese provinces is barley malt, containing additional bioactive compounds such as β -glucans, arabinoxylan, tocols, resistant starch, and polyphenols [63]. If it can be studied further in clinical trials against specific conditions (notably COVID-19) and other chronic diseases in defined dosages, barley malt might be eligible to be a functional food in the United States.

Fruits and Vegetables: The MyPlate program recommends every meal have almost 50% fruit and vegetable content [12]. The benefits of fruits and vegetables have been studied and known for years; plant-based foods are found to contain a multitude of bioactive micronutrients and antioxidants. With aging comes a dramatic decline and dysregulation of immunity, and fruits and vegetables are often the best sources of nutrients to prevent this decline. One randomized controlled experiment compared a group of 65 to 85 year olds that consumed 2 portions of fruits and vegetables a day to another group that consumed 5 portions. The study eventually found that the 5 portions a day participants had a much better antibody response to vaccination against respiratory infections—like the ones caused by the COVID-19 disease—such as pneumonia and meningitis, as well as lower instances of new illness or infection reports; this can be attributed to increases in micronutrients (such as Vitamin C, Lutein, Zeaxanthin, b-Cryptoxanthin, a-Carotene, b-

Carotene, and Lycopene) in the course of 6 to 16 weeks in the group that consumed more fruits and vegetables [64]. Further similar studies should be done to determine the exact number of weeks that can create a statistically significant difference between groups, whether additional biomarkers in the immune system are also affected, or what the effects of modifying dosages and types of produce can have.

Studies show that improvement in consumption of certain vitamins can be invaluable to those that are at-risk to the SARS-CoV-2 virus. Multiple vitamins are shown to be essential in improving immunity and fighting off infections [65]. Vitamin C, or ascorbic acid, is known to prevent lower respiratory tract infection, which can be caused by COVID-19 [66], [67]. Consumption of adequate Vitamin C in diet may improve COVID-19 prevention or prognosis. The dietary recommendation may be achieved through natural foods such as citrus fruits, kiwi, broccoli and other produce [33]. Additionally, there is data to show that an increase in consumption of Vitamin E can also improve viral resistance [68]. Vitamin E enhances T-cell mediated function and has been shown in multiple clinical studies to lower incidence of upper respiratory infection [27], [69]. In the elderly specifically, Vitamin E supplementation has been able shown to enhance immune response and increase resistance to oxidative injury [70].

Antioxidants are also shown to be active against RNA viruses and coronaviruses. Some antioxidant nutraceuticals have been extensively studied in regard to their effects in anti-inflammation (especially in the lungs) and protection against viral infection. Examples include ferulic acid, lipoic acid, spirulina, n-acetylcysteine, selenium, glucosamine, zinc, yeast beta-glucan, elderberry [71]

Table 3: Daily dosage supplement suggestions of various antioxidants and immune effects

Compound	Daily dosage suggestion	Effect on immunity	Reference(s)
Ferulic acid	500–1,000 mg	Boosts type 1 interferon response by promoting induction of HO-1 and activating toll-like receptor 7 (TLR7)	McCarty and Assanga 2018 [72], Ma et al 2011 [73]
Lipoic acid	1,200–1,800 mg (in place of ferulic acid)	Boosts type 1 interferon response by promoting induction of HO-1 and activating toll-like receptor 7 (TLR7)	Ogborne et al 2005 [74]
Spirulina	15 g (or 100 mg phycocyanobilin)	Boosts type 1 interferon response by mimicking the NADPH oxidase inhibiting activity of unconjugated bilirubin	McCarty 2007 [75], Zheng et al 2013 [76], Chen et al 2016 [77]
N-Acetylcysteine	1,200–1,800 mg	Replenish and produce glutathione which declines with age	Ungheri et al 2000 [78], Ghezzi and Ungheri 2004 [79], De Flora et al 1997 [80]
Selenium	50–100 mcg	Deficiency of this essential cofactor for certain peroxidases promotes pathogenic viruses	Luo et al 1985 [81], Nelson et al 2001 [82]
Glucosamine	3,000 mg or more (due to inefficient absorption through oral administration)	Boosts type 1 interferon response by activating mitochondrial antiviral-signaling protein (MAVS)	McCarty et al 2019 [83], Kato et al 2017 [84]
Zinc	30–50 mg	Supports the effective function and proliferation of various immune cells	Prasad et al 2007 [85], Bao et al 2010 [86], Clemons et al 2004 [87]
Yeast Beta-Glucan	250–500 mg	Immunostimulant which amplifies dendritic cell activation via dectin-1 and CR3 receptors	Vetvicka et al 2019 [88]
Elderberry	600–1,500 mg	Source of anthocyanins and symptomatically beneficial in influenza and the common cold	Hawkins et al 2019 [89]
Quercetin	500–1,000 mg (up to 1,250 mg in athletes)	Especially in older populations, improves outcomes of patients suffering from upper respiratory tract infections	Andres et al 2018 [90], Heinz et al 2010 [91]

Table adapted from McCarty and DiNicolantonio 2020 [71], Andres et al 2018 [90]

Their recommended daily dosage and effects are charted above in Table 3.

Fruits and vegetables, especially cherries and citrus fruits like lemons, grapefruits, and sweet oranges are most commonly cited as having effects against virus infection [33], [92], [93]. There is evidence to show that apigenin, found in parsley, and rutin, found in apples and tea leaves, are also effective in improving immunity [94], [95]. Antiseptic foods like garlic, onion, shallot, leek, chive have long been used in traditional medicine to fight viruses and improve the heart [65]. Garlic and onions contain allicin, or diallylthiosulfinate, which serves as a bioactive compound that can kill cells and bacteria and prevent viral proliferation [96]. Additionally, the compound glycyrrhizin, previously used to treat HIV-1 and Hepatitis C infection, has shown in studies to prevent coronavirus replication with few side effects. This sweet bioactive compound is found in liquorice roots and processed products like candy, gum, and tea [97], [98]. Furthermore, ginseng, an Asian root plant used as an herbal supplement for immunity, can improve energy metabolism and improve the usable capacity of lungs among a great number of other benefits [33]. Public health officials should be recommended to further study and include these nutritional compounds in their strategies to improve immunity and overall health during the COVID-19 pandemic.

CONCLUSION

Despite identifying compounds or developing functional foods that can be used as prevention and to take action against the SARS-CoV-2 virus, another problem remains. Public health officials, who can play a huge role in advocating for consumption and

accessibility of these foods, must figure out how to get this advice out large-scale. Some suggestions for the elderly to obtain adequate accessibility and consumption of specific compounds include: improving access to groceries or meal delivery services, establishing adult nutrition education programs, and developing additional functional foods. For groups like the elderly or immunocompromised quarantining at home, these initiatives could improve the frequency of consumption of healthy or fresh foods. For cases where it is impractical to obtain daily recommended amounts of essential nutrition through fresh food products, affordable processed functional foods can be important discoveries in an accessible and nutritious diet. For the most vulnerable populations—to prevent both malnutrition and COVID-19—food scientists should work to develop and market fortified supplements and food items. The elderly should be empowered to make their own health decisions based on up-to-date and accurate knowledge. The goal is to change the way constituents think about food or exercise and create lasting health changes rather than temporary dependence on providers and dieticians during the pandemic. Long-term nutrition and chronic disease management can create numerous opportunities for healthy lifestyles in senior citizens.

Ultimately, senior citizens are most vulnerable to COVID-19 due to nutrition deficiencies and aging-associated chronic diseases and immunity decline. For vulnerable elderly, it is of utmost importance to continue to consider nutrition as a driving factor in protecting against infectious disease contraction or mortality. Further clinical studies must be done to establish support for use of these and other compounds against SARS-CoV-2 infection, but the

recommendations for bioactive compounds and functional foods are an excellent first step in creating a prophylactic nutritional plan for populations that need it most. Structural recommendations (such as those in policy, public health, education, urban planning, economics, etc.) may also be used to improve accessibility to essential nutrition and healthy diets. The relationship between SARS-CoV-2 viral infection, immunity decline in the elderly, and nutrition have been studied in order to supply comprehensive, non-pharmaceutical recommendations to fight the SARS-CoV-2 virus. The findings provided are invaluable in working to alleviate the health disparities and negative outcomes during the COVID-19 pandemic.

Abbreviations: Coronavirus disease 2019 (COVID-19), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Angiotensin converting enzyme 2 (ACE2), Interleukin (IL), Tumor Necrosis Factor (TNF), Membrane cofactor protein (MCP), Intercellular Adhesion Molecule (ICAM), Vascular cell adhesion protein (VCAP), Ribonucleic acid (RNA), US Department of Agriculture (USDA), Body mass index (BMI), Human immunodeficiency virus (HIV)

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REFERENCES

1. Eurosurveillance Editorial T: Note from the editors: World Health Organization declares novel coronavirus (2019 nCoV) sixth public health emergency of international concern. Euro Surveill 2020, 25. <https://doi.org/10.2807/1560-7917.ES.2020.25.5.200131e>

2. "Coronavirus Cases:" Worldometer, Accessed July 1, 2020. www.worldometers.info/coronavirus/#countries
3. Xu J, Zhao S, Teng T, Abdalla AE, Zhu W, Xie L, Wang Y, Guo X: Systematic comparison of two animal-to-human transmitted human coronaviruses: SARS-CoV-2 and SARS-CoV. Viruses 2020, 12(2): 244. <https://doi.org/10.3390/v12020244>
4. Grasselli G, Zangrillo A, Zanella A, et al: Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA 2020, 323(16): 1574–1581. <https://doi.org/10.1001/jama.2020.5394>
5. Pinti M, Appay V, Campisi J, Frasca D, Fülöp T, Sauce D, Larbi A, Weinberger B, Cossarizza A: Aging of the immune system: focus on inflammation and vaccination. European journal of immunology 2016, 46(10):2286-301. <https://doi.org/10.1002%2Ffeji.201546178>
6. New York State Department of Health: "Fatalities" NYS COVID19 Tracker, Accessed June 1, 2020. <https://covid19tracker.health.ny.gov/views/NYS-COVID19-Tracker/NYSDOHCOVID-19Tracker-Fatalities?%3Aembed=yes&%3Atoolbar=no&%3Atabs=n>
7. Strathmann S, Lesser S, Bai-Habelski J, Overzier S, Paker-Eichelkraut HS, Stehle P, Hesecker H: Institutional factors associated with the nutritional status of residents from 10 German nursing homes (ErnSTES study). The journal of nutrition, health & aging 2013, 17(3): 271-6. <https://doi.org/10.1007/s12603-012-0410-8>
8. Gur J, Mawuntu M, Martirosyan D: FFC's Advancement of Functional Food Definition. Functional Foods in Health and Disease. 2018, 8(7): 385-97.
9. Center for Nutrition Policy and Promotion: USDA's MyPlate. United States Department of Agriculture 2011. <https://www.choosemyplate.gov/>
10. Vernarelli J, DiSarro R: Forget the Fad Diets: Use of the USDA's MyPlate Plan Is Associated with Better Dietary Intake in Adults over Age 50 (OR14-06-19). Current developments in nutrition. 2019, 3(Supplement_1): nzz039-OR14. <https://doi.org/10.1093%2Fcdn%2Fnzz039.OR14-06-19>
11. Rowe JW, Kahn RL: Successful aging. The gerontologist 1997, 37(4): 433-40. <https://doi.org/10.1093/geront/37.4.433>
12. United States Department of Agriculture - MyPlate Graphic Resources, Public Domain, 2011. <https://commons.wikimedia.org/w/index.php?curid=38658432>
13. Huffman GB: Evaluating and treating unintentional weight loss in the elderly. American family physician 2002, 65(4): 640.

14. Kosmiski L: Energy expenditure in HIV infection. The American journal of clinical nutrition. 2011, 94(6): 1677S-82S. <https://doi.org/10.3945/ajcn.111.012625>
15. Abbas AM, Kamel MM: Dietary habits in adults during quarantine in the context of COVID-19 pandemic. Obesity Medicine 2020. <https://doi.org/10.1016%2Fj.obmed.2020.100254>
16. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, Rubin GJ: The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The Lancet 2020. [https://doi.org/10.1016/S0140-6736\(20\)30460-8](https://doi.org/10.1016/S0140-6736(20)30460-8)
17. Gluck ME, Geliebter A, Hung J, Yahav E: Cortisol, hunger, and desire to binge eat following a cold stress test in obese women with binge eating disorder. Psychosomatic Medicine 2004, 66(6): 876-81. <https://doi.org/10.1097/01.psy.0000143637.63508.47>
18. Campana B, Brasiel PG, de Aguiar AS, Luquetti SC: Obesity and food addiction: similarities to drug addiction. Obesity Medicine 2019, 100136. <https://doi.org/10.1016/j.obmed.2019.100136>
19. Reis CEG, Bressan J, Alfenas RCG: Effect of the diet components on adiponectin levels. Nutricion hospitalaria 2010, 25(6): 881-888.
20. Widmer RJ, Flammer AJ, Lerman LO, Lerman A: The Mediterranean diet, its components, and cardiovascular disease. The American journal of medicine 2015, 128(3): 229-38. <https://doi.org/10.1016/j.amjmed.2014.10.014>
21. Fragopoulou E, Panagiotakos DB, Pitsavos C, Tampourlou M, Chrysohoou C, Nomikos T, Antonopoulou S, Stefanadis C: The association between adherence to the Mediterranean diet and adiponectin levels among healthy adults: the ATTICA study. The Journal of nutritional biochemistry 2010, 21(4): 285-9. <https://doi.org/10.1016/j.jnutbio.2008.12.013>
22. Connaughton RM, McMorrow AM, McGillicuddy FC, Lithander FE, Roche HM: Impact of anti-inflammatory nutrients on obesity-associated metabolic-inflammation from childhood through to adulthood. Proceedings of the Nutrition Society 2016, 75(2): 115-24. <https://doi.org/10.1017/S0029665116000070>
23. Simopoulos AP: Omega-6 and omega-3 fatty acids: Endocannabinoids, genetics and obesity. OCL 2020;27: 7. <https://doi.org/10.1051/ocl/2019046>
24. Solomando JC, Antequera T, Perez-Palacios T: Evaluating the use of fish oil microcapsules as omega-3 vehicle in cooked and dry-cured sausages as affected by their processing, storage and cooking. Meat Science 2020, 162: 108031. <https://doi.org/10.1016/j.meatsci.2019.108031>
25. Kris-Etherton PM, Harris WS, Appel LJ: Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. circulation 2002, 106(21): 2747-57. <https://doi.org/10.1161/01.CIR.0000038493.65177.94>
26. Das UN: Can Bioactive Lipids Inactivate Coronavirus (COVID-19)? Archives of Medical Research. 2020. <https://doi.org/10.1016/j.arcmed.2020.03.004>
27. Wu D, Lewis ED, Pae M, Meydani SN: Nutritional modulation of immune function: analysis of evidence, mechanisms, and clinical relevance. Frontiers in immunology. 2019, 9: 3160.
28. US Department of Health and Human Services: US Department of Agriculture. 2015–2020 dietary guidelines for Americans. 2015, 8th Edition. [health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines.pdf](https://www.health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines.pdf)
29. Wu G: Important roles of dietary taurine, creatine, carnosine, anserine and 4-hydroxyproline in human nutrition and health. Amino Acids 2020, 18: 1-32. <https://doi.org/10.1007/s00726-020-02823-6>
30. Messina G, Polito R, Monda V, Cipolloni L, Di Nunno N, Di Mizio G, Murabito P, Carotenuto M, Messina A, Pisanelli D, Valenzano A: Functional Role of Dietary Intervention to Improve the Outcome of COVID-19: A Hypothesis of Work. International Journal of Molecular Sciences. 2020, 21(9): 3104. <https://doi.org/10.3390/ijms21093104>
31. Hosseinpour-Niazi S, Mirmiran P, Fallah-Ghohroudi A, Azizi F: Non-soya legume-based therapeutic lifestyle change diet reduces inflammatory status in diabetic patients: a randomised cross-over clinical trial. British Journal of Nutrition. 2015, 114(2): 213-9. <https://doi.org/10.1017/S0007114515001725>
32. Kitayaporn D, Nelson KE, Charoenlarp P, Pholpothi T: Haemoglobin-E in the presence of oxidative substances from fava bean may be protective against Plasmodium falciparum malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene 1992, 86(3): 240-4. [https://doi.org/10.1016/0035-9203\(92\)90292-K](https://doi.org/10.1016/0035-9203(92)90292-K)
33. Kalantar-Zadeh K, Moore LW: Impact of Nutrition and Diet on COVID-19 Infection and Implications for Kidney Health and Kidney Disease Management. Journal of Renal Nutrition. 2020, 30(3): 179-81. <https://doi.org/10.1053%2Fj.ijn.2020.03.006>
34. Hruby A, Jacques PF: Dietary protein and changes in biomarkers of inflammation and oxidative stress in the Framingham Heart Study Offspring cohort. Current Developments in Nutrition 2019, 3(5). <https://doi.org/10.1093/cdn/nz019>
35. Calder PC, Carr AC, Gombart AF, Eggersdorfer M: Optimal nutritional status for a well-functioning immune system is

- an important factor to protect against viral infections. *Nutrients*. 2020, 12(4): 1181. <https://doi.org/10.3390/nu12041181>
36. Read SA, Obeid S, Ahlenstiel C, Ahlenstiel G: The role of zinc in antiviral immunity. *Advances in Nutrition* 2019, 10(4): 696-710. <https://doi.org/10.1093/advances/nmz013>
37. Yeh EB, Barbano DM, Drake M: Vitamin fortification of fluid milk. *Journal of food science*. 2017, 82(4): 856-64. <https://doi.org/10.1111/1750-3841.13648>
38. Huang Z, Liu Y, Qi G, Brand D, Zheng SG: Role of vitamin A in the immune system. *Journal of clinical medicine* 2018, 7(9): 258.
39. Aluisio AR, Perera SM, Yam D, Garbern S, Peters JL, Abel L, Cho DK, Kennedy SB, Massaquoi M, Sahr F, Brinkmann S: Vitamin A supplementation was associated with reduced mortality in patients with Ebola virus disease during the West African outbreak. *The Journal of nutrition* 2019, 149(10): 1757-65. <https://doi.org/10.1093/jn/nxz142>
40. Sinha S, Cheng K, Aldape K, Schiff E, Ruppin E: Systematic cell line-based identification of drugs modifying ACE2 expression. 2020.
41. Carter SJ, Baranaukas MN, Fly AD: Considerations for obesity, vitamin D, and physical activity amidst the COVID-19 pandemic. *Obesity* 2020. <https://doi.org/10.1002/oby.22838>
42. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, Dubnov-Raz G, Esposito S, Ganmaa D, Ginde AA, Goodall EC: Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *British Medical Journal* 2017, 356: i6583. <https://doi.org/10.1136/bmi.i6583>
43. Bajaj A, Purohit HJ: Understanding SARS-CoV-2: Genetic Diversity, Transmission and Cure in Human. *Indian J Microbiol* 2020. <https://doi.org/10.1007/s12088-020-00869-4>
44. Villarino NF, LeClerc GR, Denny JE, Dearth SP, Harding CL, Sloan SS, Gribble JL, Campagna SR, Wilhelm SW, Schmidt NW: Composition of the gut microbiota modulates the severity of malaria. *Proceedings of the National Academy of Sciences* 2016, 113(8): 2235-40. <https://doi.org/10.1073/pnas.1504887113>
45. Ngwa CJ, Pradel G: Coming soon: probiotics-based malaria vaccines. *Trends in parasitology*. 2015, 31(1): 2-4. <https://doi.org/10.1016/j.pt.2014.11.006>
46. Lei H, Xu Y, Chen J, Wei X, Lam DM. Immunoprotection against influenza H5N1 virus by oral administration of enteric-coated recombinant *Lactococcus lactis* mini-capsules. *Virology*. 2010 Nov 25;407(2):319-24. <https://doi.org/10.1016/j.virol.2010.08.007>
47. He LH, Ren LF, Li JF, Wu YN, Li X, Zhang L. Intestinal Flora as a Potential Strategy to Fight SARS-CoV-2 Infection. *Frontiers in Microbiology*. 2020;11. <https://doi.org/10.3389/fmicb.2020.01388>
48. Nagpal R, Mainali R, Ahmadi S, Wang S, Singh R, Kavanagh K, et al: Gut microbiome and aging: physiological and mechanistic insights. *Nutr Healthy Aging* 2018, 4(267-285). <https://doi.org/10.3233/NHA-170030>
49. Infusino F, Marazzato M, Mancone M, Fedele F, Mastroianni CM, Severino P, Ceccarelli G, Santinelli L, Cavarretta E, Marullo AG, Miraldi F: Diet Supplementation, Probiotics, and Nutraceuticals in SARS-CoV-2 Infection: A Scoping Review. *Nutrients* 2020, 12(6): 1718.
50. Serna-Thomé G, Castro-Eguiluz D, Fuchs-Tarlovsky V, Sánchez-López M, Delgado-Olivares L, Coronel-Martínez J, Molina-Trinidad EM, de la Torre M, Cetina-Pérez L: Use of functional foods and oral supplements as adjuvants in Cancer Treatment. *Revista de Investigación Clínica* 2018, 70(3): 136-46. <https://doi.org/10.24875/RIC.18002527>
51. Tapsell LC: Fermented dairy food and CVD risk. *British Journal of Nutrition*. 2015, 113(S2): S131-5. <https://doi.org/10.1017/S0007114514002359>
52. Kalantar-Zadeh K, Ward SA, Kalantar-Zadeh K, El-Omar EM. Considering the Effects of Microbiome and Diet on SARS-CoV-2 Infection: Nanotechnology Roles. *ACS nano*. 2020. <https://doi.org/10.1021/acsnano.0c03402>
53. Fekete ÁA, Givens DI, Lovegrove JA: Casein-derived lactotripeptides reduce systolic and diastolic blood pressure in a meta-analysis of randomised clinical trials. *Nutrients* 2015, 7(1): 659-81. <https://doi.org/10.3390/nu7010659>
54. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB: Changes in diet and lifestyle and long-term weight gain in women and men. *New England Journal of Medicine* 2011, 364(25): 2392-404. <https://doi.org/10.1056/nejmoa1014296>
55. Chen M, Sun Q, Giovannucci E, Mozaffarian D, Manson JE, Willett WC, Hu FB: Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *BMC medicine*. 2014, 12(1): 215. <https://doi.org/10.1186/s12916-014-0215-1>
56. Díaz-López A, Bulló M, Martínez-González MA, Corella D, Estruch R, Fitó M, Gómez-Gracia E, Fiol M, de la Corte FJ, Ros E, Babio N: Dairy product consumption and risk of type 2 diabetes in an elderly Spanish Mediterranean population at high cardiovascular risk. *European journal of nutrition* 2016, 55(1): 349-60. <https://doi.org/10.1007/s00394-015-0855-8>
57. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, Brunner EJ: Consumption of dairy products and associations

- with incident diabetes, CHD and mortality in the Whitehall II study. *British journal of nutrition* 2013, 109(4): 718-26. <https://doi.org/10.1017/S0007114512001845>
58. Marco ML, Heeney D, Binda S, Cifelli CJ, Cotter PD, Foligné B, Gänzle M, Kort R, Pasin G, Pihlanto A, Smid EJ: Health benefits of fermented foods: microbiota and beyond. *Current opinion in biotechnology* 2017, 44:94-102.
59. Gleeson M: Nutritional support to maintain proper immune status during intense training. *Nutritional Coaching Strategy to Modulate Training Efficiency*, Karger Publishers 2013, 75: 85-97. <https://doi.org/10.1159/000345822>
60. Tsang C, Hodgson L, Bussu A, Farhat G, Al-Dujaili E: Effect of Polyphenol-Rich Dark Chocolate on Salivary Cortisol and Mood in Adults. *Antioxidants* 2019, 8(6): 149. <https://doi.org/10.3390/antiox8060149>
61. Moling O, Gandini L: Sugar and the Mosaic of Autoimmunity. *The American journal of case reports* 2019, 20: 1364. <https://doi.org/10.12659/ajcr.915703>
62. Conte L, Toraldo DM: Targeting the gut–lung microbiota axis by means of a high-fibre diet and probiotics may have anti-inflammatory effects in COVID-19 infection. *Therapeutic Advances in Respiratory Disease* 2020, 14(1-5). <https://doi.org/10.1177/1753466620937170>
63. Zeng Y, Pu X, Du J, Yang X, Li X, Mandal M, Nabi S, Yang T, Yang J: Molecular Mechanism of Functional Ingredients in Barley to Combat Human Chronic Diseases. *Oxidative Medicine and Cellular Longevity*. 2020, 2020. <https://doi.org/10.1155%2F2020%2F3836172>
64. Gibson A, Edgar JD, Neville CE, Gilchrist SE, McKinley MC, Patterson CC, Young IS, Woodside JV: Effect of fruit and vegetable consumption on immune function in older people: a randomized controlled trial, *The American Journal of Clinical Nutrition* 2012, 96(6): 1429–1436. <https://doi.org/10.3945/ajcn.112.039057>
65. Wu J, Zha P. Treatment Strategies for Reducing Damages to Lungs in Coronavirus and Other Lung Infections. 2020. <http://doi.org/10.2139/ssrn.3533279>
66. Carr AC, Maggini S: Vitamin C and immune function. *Nutrients* 2017, 9(11): 1211.
67. Hemilä H: Vitamin C intake and susceptibility to the common cold. *British Journal of Nutrition*. 1997, 77(1): 59-72. <https://doi.org/10.1017/S0007114500002889>
68. Wang LS, Wang YR, Ye DW, Liu QQ: A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. *International journal of antimicrobial agents*. 2020, 105948. <https://doi.org/10.1016/j.ijantimicag.2020.105948>
69. Meydani SN, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF, Hamer DH: Vitamin E and respiratory tract infections in elderly nursing home residents: a randomized controlled trial. *Jama* 2004, 292(7): 828-36.
70. Meydani M: The Boyd Orr Lecture: Nutrition interventions in aging and age-associated disease. *Proceedings of the Nutrition Society* 2002, 61(2): 165-71. <https://doi.org/10.1079/PNS2002144>
71. McCarty MF, DiNicolantonio JJ: Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus. *Progress in Cardiovascular Diseases* 2020. <https://doi.org/10.1016/j.pcad.2020.02.007>
72. McCarty MF, Assanga SB: Ferulic acid may target MyD88-mediated pro-inflammatory signaling—Implications for the health protection afforded by whole grains, anthocyanins, and coffee. *Medical hypotheses*. 2018, 118: 114-20.
73. Ma Z, Hong Q, Wang Y, Liang Q, Tan H, Xiao C, Tang X, Shao S, Zhou S, Gao Y: Ferulic acid induces heme oxygenase-1 via activation of ERK and Nrf2. *drug discoveries & therapeutics* 2011, 5(6): 299-305. <https://doi.org/10.5582/ddt.2011.v5.6.299>
74. Ogborne RM, Rushworth SA, O'Connell MA: α -lipoic acid-induced heme oxygenase-1 expression is mediated by nuclear factor erythroid 2-related factor 2 and p38 mitogen-activated protein kinase in human monocytic cells. *Arteriosclerosis, thrombosis, and vascular biology* 2005, 25(10): 2100-5. <https://doi.org/10.1161/01.ATV.0000183745.37161.6e>
75. McCarty MF: Clinical potential of Spirulina as a source of phycocyanobilin. *Journal of medicinal food*. 2007, 10(4): 566-70. <https://doi.org/10.1089/imf.2007.621>
76. Zheng J, Inoguchi T, Sasaki S, Maeda Y, McCarty MF, Fujii M, Ikeda N, Kobayashi K, Sonoda N, Takayanagi R: Phycocyanin and phycocyanobilin from *Spirulina platensis* protect against diabetic nephropathy by inhibiting oxidative stress. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2013, 304(2): R110-20. <https://doi.org/10.1152/ajpregu.00648.2011>
77. Chen YH, Chang GK, Kuo SM, Huang SY, Hu IC, Lo YL, Shih SR: Well-tolerated Spirulina extract inhibits influenza virus replication and reduces virus-induced mortality. *Scientific reports* 2016, 6(1): 1-1. <https://doi.org/10.1038/srep24253>
78. Ungheri D, Pisani C, Sanson G, Bertani A, Schioppacassi G, Delgado R, Sironi M, Ghezzi P: Protective effect of n-acetylcysteine in a model of influenza infection in mice. *International journal of immunopathology and pharmacology* 2000, 13(3): 123-8.
79. Ghezzi P, Ungheri D: Synergistic combination of N-acetylcysteine and ribavirin to protect from lethal influenza viral infection in a mouse model. *International journal of*

- immunopathology and pharmacology 2004, 17(1): 99-102.
<https://doi.org/10.1177%2F039463200401700114>
80. De Flora S, Grassi C, Carati L: Attenuation of influenza-like symptomatology and improvement of cell-mediated immunity with long-term N-acetylcysteine treatment. *European Respiratory Journal* 1997, 10(7): 1535-41.
81. Luo X, Wei H, Yang C, Xing J, Qiao C, Feng Y, Liu J, Liu Z, Wu Q, Liu Y, Stoecker BJ: Selenium intake and metabolic balance of 10 men from a low selenium area of China. *The American journal of clinical nutrition* 1985, 42(1): 31-7.
<https://doi.org/10.1093/ajcn/42.1.31>
82. Nelson HK, Shi Q, Van Dael P, Schiffrin EJ, Blum S, Barclay D, Levander OA, Beck MA: Host nutritional selenium status as a driving force for influenza virus mutations. *The FASEB Journal* 2001, 15(10): 1846-8. <https://doi.org/10.1096/fj.01-0115fie>
83. McCarty MF, O'Keefe JH, DiNicolantonio JJ: Glucosamine for the treatment of osteoarthritis: The time has come for higher-dose trials. *Journal of dietary supplements* 2019, 16(2): 179-92.
<https://doi.org/10.1080/19390211.2018.1448920>
84. Kato H, Kai H, Harada H, Niiyama H, Ikeda H: Oral administration of glucosamine improves vascular endothelial function by modulating intracellular redox state. *International heart journal* 2017, 58(6): 926-32.
<https://doi.org/10.1536/ihj.16-534>
85. Prasad AS, Beck FW, Bao B, Fitzgerald JT, Snell DC, Steinberg JD, Cardozo LJ: Zinc supplementation decreases incidence of infections in the elderly: effect of zinc on generation of cytokines and oxidative stress. *The American journal of clinical nutrition* 2007, 85(3): 837-44.
<https://doi.org/10.1093/ajcn/85.3.837>
86. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, Singh T, Cardozo LJ: Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent. *The American journal of clinical nutrition* 2010, 91(6): 1634-41.
<https://doi.org/10.3945/ajcn.2009.28836>
87. Clemons TE, Kurinij N, Sperduto RD: Associations of mortality with ocular disorders and an intervention of high-dose antioxidants and zinc in the Age-Related Eye Disease Study: AREDS Report No. 13. *Archives of Ophthalmology* 2004, 122(5): 716.
<https://dx.doi.org/10.1001%2Farchophth.122.5.716>
88. Vetvicka V, Vannucci L, Sima P, Richter J: Beta glucan: Supplement or drug? From laboratory to clinical trials. *Molecules* 2019, 24(7): 1251.
<https://doi.org/10.3390/molecules24071251>
89. Hawkins J, Baker C, Cherry L, Dunne E: Black elderberry (*Sambucus nigra*) supplementation effectively treats upper respiratory symptoms: A meta-analysis of randomized, controlled clinical trials. *Complementary therapies in medicine* 2019, 42: 361-5.
<https://doi.org/10.1016/j.ctim.2018.12.004>
90. Andres S, Pevny S, Ziegenhagen R, Bakhiya N, Schäfer B, Hirsch-Ernst KI, Lampen A: Safety aspects of the use of quercetin as a dietary supplement. *Molecular nutrition & food research* 2018, 62(1): 1700447.
<https://doi.org/10.1002/mnfr.201700447>
91. Heinz SA, Henson DA, Austin MD, Jin F, Nieman DC: Quercetin supplementation and upper respiratory tract infection: A randomized community clinical trial. *Pharmacological research* 2010, 62(3): 237-42.
<https://doi.org/10.1016/j.phrs.2010.05.001>
92. Hsu CC, Lin MH, Cheng JT, Wu MC: Diosmin, a citrus nutrient, activates imidazoline receptors to alleviate blood glucose and lipids in type 1-like diabetic rats. *Nutrients* 2017, 9(7): 684. <https://doi.org/10.3390/nu9070684>
93. Adem S, Eyupoglu V, Sarfraz I, Rasul A, Ali M: Identification of potent COVID-19 main protease (Mpro) inhibitors from natural polyphenols: An in silico strategy unveils a hope against CORONA. Preprints 2020.
<https://doi.org/10.20944/preprints202003.0333.v1>
94. Ganeshpurkar A, Saluja AK: The pharmacological potential of rutin. *Saudi Pharmaceutical Journal* 2017, 25(2): 149-64.
<https://doi.org/10.1016/j.jsps.2016.04.025>
95. Meyer H, Bolarinwa A, Wolfram G, Linseisen J: Bioavailability of apigenin from apiin-rich parsley in humans. *Annals of Nutrition and Metabolism*. 2006, 50(3): 167-72.
<https://doi.org/10.1159/000090736>
96. Borlinghaus J, Albrecht F, Gruhlke MC, Nwachukwu ID, Slusarenko AJ: Allicin: chemistry and biological properties. *Molecules* 2014, 19(8): 12591-618.
<https://doi.org/10.3390/molecules190812591>
97. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW: Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *The Lancet* 2003, 361(9374): 2045-6.
[https://doi.org/10.1016/S0140-6736\(03\)13615-X](https://doi.org/10.1016/S0140-6736(03)13615-X)
98. Deutch MR, Grimm D, Wehland M, Infanger M, Krüger M: Bioactive Candy: Effects of Licorice on the Cardiovascular System. *Foods* 2019, 8(10): 495.
<https://doi.org/10.3390/foods8100495>