The relationship between nutritional deficiencies and mental health

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ABSTRACT
The objective of this mini review was to discuss the relationship between nutritional deficiencies and mental health, and to present a structure that helps to visualize these associations based on a literature review and the scenarios of the COVID-19 pandemic. The study was conducted to demonstrate the effect of the nutritional deficiencies on the occurrence and/or worsening of mental health problems, mainly related to the most drastic measures of social distance during the COVID-19 pandemic. Studies have already shown that a nutritionally unbalanced diet may be associated with greater chances of mental health problems. Insufficient levels of micronutrients can, by regulating the stress response, immune and oxidative systems, negatively affect brain functions and, consequently, cognitive functions and mental health of individuals. The current pandemic of COVID-19 reveals an increase in food and nutritional insecurity, and a worsening of this situation among already vulnerable populations. Micronutrient deficiencies may be exacerbated in a context of increased food insecurity and the COVID-19 pandemic, which may contribute to increased mental health problems.

Keywords: COVID-19; Food Intake; Food Insecurity; Mental Health; Public Health.

RESUMEN
El objetivo de esta revisión fue discutir la relación entre las deficiencias nutricionales y la salud mental, y presentar una estructura que ayude a visualizar estas asociaciones con base en la revisión de la literatura y en los escenarios de la pandemia de COVID-19. El estudio se llevó a cabo para demostrar el efecto de las deficiencias nutricionales en la ocurrencia y/o empeoramiento de los problemas de salud mental, principalmente relacionada con las medidas más drásticas de distancia social durante la pandemia de COVID-19. Los estudios ya han mostrado que una dieta desequilibrada nutricionalmente puede estar asociada con mayores chances de problemas de salud mental. Niveles insuficientes de micronutrientes pueden afectar negativamente las funciones del sistema nervioso y, consecuentemente, las funciones cognitivas y la salud mental de las personas. La pandemia de COVID-19 ha revelado un aumento en la inseguridad alimentaria y nutricional, y ha empeorado esta situación en las poblaciones ya vulnerables. Las deficiencias de micronutrientes pueden ser exacerbadas en un contexto de mayor inseguridad alimentaria y la pandemia de COVID-19, que puede contribuir a aumentar los problemas de salud mental.
INTRODUCTION
Since the beginning of 2020, the world has been facing changes due to the pandemic of a new coronavirus: SARS-Cov-2. As of September 10, 2020, more than 27 million people have been infected and more than 900,000 have died due to COVID-19 in all continents (https://coronavirus.jhu.edu/map.html). Although other coronaviruses have already caused epidemics recently, including the severe acute respiratory syndrome (SARS)\(^1\), in 2002, and the Middle East Respiratory Syndrome (MERS)\(^2\), first reported in 2012, none have spread to so many countries in such a short time and have brought such radical changes around the world.

The implementation of preventive mitigation, such as social distancing, and suppression measures, such as lockdowns, have disrupted the dynamics of daily life\(^3,4\). In addition, the occurrence of COVID-19 triggered a major global economic crisis, consequently affecting countries’ political and social domains\(^5\). Thus, the current scenario leads to unprecedented uncertainties, which can cause distress and social anxiety, and directly affect the mental health of individuals and populations\(^5,6\).

Mental health is a broad theme that involves psychological, emotional, behavioural and mental disorders. It can also cover socio-economic, cultural and, even accessibility aspects\(^7\). Several studies have demonstrated the association between the current COVID-19 pandemic and poorer mental health\(^8\), which in turn can be worsened by factors related to a new eating routine\(^9\). The objective of this mini review was to discuss the relationship between nutritional deficiencies and mental health, and to present a structure that helps to visualize these associations based on a literature review and the current COVID-19 pandemic.

METHODS
The present review was conducted by screening articles on the effect of different levels of nutritional deficiencies on the occurrence and/or worsening of mental health problems, based on the main database of scientific references on health, assessed throughout PubMed. In addition, a search of the bibliographic references of relevant studies and reviews that addressed the topic of interest was conducted. The following key-words were used: nutritional deficiencies, nutritional deficits, food intake, food insecurity, mental health, anxiety, depression, bipolar disorder, schizophrenia, obsessive-compulsive disorder, Alzheimer’s disease, combined with COVID-19, SARS-CoV-2, novel coronavirus and coronavirus.

RESULTS AND DISCUSSION
Using the previously mentioned search, we incorporated 44 studies in this review. The results were addressed considering the following themes: 1) Relationship between food intake and mental health; and 2) Impact of the COVID-19 pandemic on food intake: different realities.

Relationship between food intake and mental health
Studies have shown that a nutritionally unbalanced diet may be associated with increased chances of anxiety, depression, bipolar disorder, schizophrenia, obsessive-compulsive disorder, and Alzheimer’s disease, among others\(^10,11,12\). The mechanisms involved in such associations are diverse, considering also the different level of the nutritional deficiency. The brain uses energy from food to function properly, as it has a high metabolic rate. Nutrients such as amino acids, fatty acids, vitamins and minerals act in the formation and maintenance of structures and in the performance of functions, such as intracellular and extracellular communication\(^13,14\). The important role of neurotrophic proteins in neuronal plasticity and in tissue repair mechanisms is also recognized\(^15,16\).

Some authors suggest that supplements of selected nutrients (isolated or in combination) can be incorporated in the treatment of mental disorders since they act as protagonists of many neurochemical modulatory activities\(^12,17\). Thus, therapy with specific micronutrients can be an alternative to the use of drugs used in mental health disorders, as these can cause a series of unwanted side effects\(^15\). Antioxidant vitamins, B vitamins, vitamin D, polyunsaturated fatty acids (PUFA n-3) and minerals stand out as relevant nutrients for brain function\(^12,18\). Such micronutrients were investigated for their association and/or impact on cognitive development and had direct effects on the quality of life and mental health of individuals\(^12,19\).

Studies on the association between dietary antioxidants and depression show that the intake of vitamin C and beta-carotene are lower in individuals with depression compared to controls\(^20,21\) and suggest that beta-carotene could be
used to manage depression. Beta-carotene has also been shown to be associated with better memory performance and may also be a key molecule for the prevention and therapy of Alzheimer’s disease, due to its ability to inhibit the formation of oligomers and amyloid beta peptide fibrils.

Vitamins B₆ and B₁₂ are involved in the process of single carbon metabolism, directly related to the production of monoamine neurotransmitters and other important methylation reactions in the brain, and low level of both vitamins was associated with higher rates of depression. Vitamins B₆, B₁₂, and folate, in turn, may be associated with the prevention and treatment of Alzheimer’s disease through its supplementation, by inhibiting oxidative stress and decreasing homocysteine concentrations.

Vitamin D can play a role in brain signalling pathways, also related to emotion and changes in anxiety behavior. Data suggest that low concentrations of vitamin D are associated with increased depressive symptoms and the presence of dementia and Alzheimer’s disease. In this sense, the Clinical Practice Guideline of the Endocrine Society recommends the maintenance of vitamin D₃ concentrations above 75 nmol/L to reduce the risk of Alzheimer’s disease. Studies also report that vitamin D supplementation would improve depression symptoms, and significantly improve cognitive performance in individuals with senile dementia.

In addition to their antioxidant properties, PUFA n-3 act on the adjustment of the serotonin system, proinflammatory cytokines and neurotrophic factor derived from the brain. A meta-analysis of 14 studies comparing PUFA n-3 levels in patients with depression and controls showed that levels of EPA, DHA and total PUFA n-3 were significantly lower in patients with depression, giving evidence of the important role of PUFAs n-3 in the depression’s pathogenesis. In addition, some studies have highlighted a possible association between fish intake and PUFA n-3 and a lower risk of dementia, including Alzheimer’s disease.

Among the minerals, zinc has an important role in the migration, synaptogenesis and neurogenesis of neurons. Studies show an association between zinc deficiency and increased depressive symptoms, and that zinc supplementation improves depressed mood. Besides, zinc deficiency has been associated with loss of cognition in Alzheimer’s patients.

In addition to zinc, iron also stands out as a mineral directly related to mental health, since it is involved in the production of myelin and is a cofactor for the synthesis of neurotransmitters. Iron deficiency affects neural processes such as myelination, dendritic afforestation and neural plasticity. Further, iron may play an important role in oxidative stress in Alzheimer’s disease, and an imbalance in iron homeostasis is considered a precursor to this disease. In general, iron supplementation was associated with improved attention and concentration in older children and adults.

In summary, several vitamins and minerals, which are part of a balanced diet, have critical roles in brain metabolism. Therefore, insufficient levels of these micronutrients can, by regulating the stress response, immune and oxidative systems, negatively affect brain functions and, consequently, cognitive functions and mental health of individuals. However, it is necessary to consider that the unbalanced micronutrient reserves can be observed in different levels and, consequently, affect the neuro functions in diverse pathways. Nutritional deficiencies can mildly present themselves, generating unobservable symptoms for example, or even occur in a moderate to severe way, affecting mental functions. In addition, it is possible that nutritional deficiencies have a progressive effect on mental health, depending on the severity of the nutritional deficiency. Therefore, the manifestation of these deficiencies in mental health can take some time to become noticeable and follow-up studies would be necessary to test these long-term effects.

Regardless, an inadequate food intake and its nutritional deficiencies are more likely to occur in a scenario of food insecurity, including a range of restrictions on food access and even more extreme situations, such as hunger. What is known so far is that there were changes in the food consumption profile during the pandemic period, especially among disadvantaged populations from middle- and low-income countries, as reported in the following topic. Such changes can lead to inadequate quality and quantity of food intake and may result in nutritional deficiencies, especially of micronutrients, and worsen cases of poor mental health, already weakened by the current context of social distancing.

Impact of the COVID-19 pandemic on food intake: different realities

In the current pandemic scenario, the diet of individuals can suffer significant changes and may be different from that seen routinely in pre-COVID-19 times. Such changes can have a distinct impact on developing countries and countries with precarious conditions of assistance to health and social protection services. In addition, they may also have a distinct impact on populations in the same country, mainly due to intraregional inequities.

Social distancing and the consequent impact on the economy can compromise income generation and access, resulting in notorious budgetary constraints among the most economically affected people (informal workers, newly unemployed, workers who undergo wage reductions, individual microentrepreneurs, among others). Therefore, those individuals may have difficulty in accessing food, including the purchase of food, thus violating the guarantee of the human right to adequate food (Figure 1). Such difficulty might be even more significant in families that faced food insecurity in the pre-pandemic period. Food insecurity, which is when there is no guarantee of regular and permanent access to food in sufficient quantity and nutritional and sanitary quality, can also compromise other basic needs during the pandemic.

According to the concepts of adequate and healthy food, feeding should include individuals’ biological and social aspects, including both quantitative and qualitative food intake. Food intake is directly influenced by food choices.
and consumption patterns\textsuperscript{48}, which may be influenced by the pandemics' social, political and economic contexts. In this scenario, the excessive concern with hygiene in food acquisition and preparation, the new routines to access markets, the uncertainties about the movement of people on the streets and the fear of a future food shortage can limit food choices and preferences. These reasons can lead people and families to buy easily-purchased food, such as ultra-processed foods (UPF). UPFs are hyper-palatable, require little time to be prepared, and can be stored for a long time. Those reasons bring convenience by reducing the frequency of going to food markets and, consequently, situations of greater exposure to COVID-19 are avoided\textsuperscript{49,50}.

The changes observed in food choices and preferences occur in different population groups but have worse consequences for those socio-economic disadvantaged – previous food insecurity and the economic impacts from COVID-19 tend to be more prominent among these populations.

Another dimension to be considered for adequate and healthy food is permanent and regular access to food, closely related to the presence of food and nutritional security\textsuperscript{48}. Food availability and its supply chain were directly impacted by the pandemic. An example is in agriculture, especially family farming, which had its marketing channels hindered or suspended, in part by the temporary closure of food consumption establishments and due to the reduction/closure of consumption in food markets. Moreover, food prices increased, making it even more difficult to access diversified and nutritionally adequate food\textsuperscript{9}.

Thus, maintaining an adequate diet proves to be an arduous task in a pandemic scenario and can lead to uncertainties concerning to food, such as the acquisition of enough food for all family members. It is also hard to predict whether the pre-pandemic food patterns will be possibly be re-established at some point soon.

Given the above, the presence of food insecurity can be considered more evident in the present times, and the consequent compromise in the quality of the individuals' diet could also contribute to poorer mental health\textsuperscript{51}. On the other hand, a good quality diet can contribute to anti-

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Figure 1: Mechanisms addressing the relationship between nutrition and mental health in COVID-19 crisis.
The relationship between nutritional deficiencies and mental health

Inflammatory and protective effects due to various nutrients and other bioactive components, which optimize brain biochemistry and support cognitive health.

It is important to note that, although there is some evidence about the pandemic’s influence on food access and availability, especially among the most economically affected classes, the relationship between nutritional deficiencies and mental health during the COVID-19 pandemic is not fully understood. Also, the occurrence of mental health problems among these individuals may be underlying the outbreak of COVID-19.

Considering that the COVID-19 pandemic is still ongoing, there is still space for studies to assess the impact of nutritional deficiencies on mental health during this pandemic, which could be beneficial for understanding this relationship and preparing for future effective responses.

CONCLUSION

The current pandemic of COVID-19 reveals a probable increase in food and nutritional insecurity, and a worsening of this situation among already fragile populations. This can compromise food consumption and result in micronutrient deficiencies, which may affect the mental health of individuals already impacted by the social distancing measures and by the world’s fragile political, social and economic situation related with the COVID-19.

Therefore, it is important to maintain or implement, new public policies to guarantee the human right of access to adequate food and contribute to food security in pandemic times. It is especially important to guarantee affordable food prices for the most vulnerable during the pandemic period. Furthermore, in addition to guaranteeing adequate micronutrients consumption, it is also important to provide mental health support during the COVID-19 epidemic.

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