



# Obesity as a Risk Factor Against COVID-19

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**Abstract:** In late 2019, in Wuhan City, China, SARS-CoV2 was identified as the cause of an outbreak of acute respiratory illness called COVID-19 representing its most frequent lethal complication. *Objective:* To analyze, by means of a literature review, obesity as a risk factor for COVID-19. *Methodology:* A systematic review of the literature was carried out in scientific databases such as: Latin American and Caribbean Health Sciences Literature (LILACS); Virtual Health Library (VHL); Wiley Online Library and Medical Literature Analysis and Retrieval System Online (MEDLINE), Scielo, Scopus. The search terms included the study variables. *Results:* According to the analysis of 51 articles, it was determined that obese, male and elderly patients are the profile most prone to present respiratory system failures associated with COVID-19. Their pictures are aggravated by immunological and hormonal physiopathology typical of obesity; in addition, comorbidity in which there is diabetes, hypertension, cardiovascular diseases and obstructive pulmonary disease aggravates the picture of COVID-19 in obese patients. *Conclusions:* The presence of obesity is indeed a risk factor against COVID-19 infection, since it increases the possibility of suffering severe respiratory conditions.

**Keywords:** COVID-19, Obesity, Risk Factors, Comorbidity

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## 1. Introduction

The World Health Organization defines obesity as an abnormal or excessive deposit of fat, so it adopts a simple way to measure obesity, which is the calculation of the Body Mass Index (BMI), which is obtained by weight in kilograms divided by size in square meter; therefore, if a person with a BMI equal to or greater than 30 is considered obese and if it is equal to or greater than 25 is considered overweight [1].

Coronavirus (COVID-19) caused by severe acute respiratory syndrome (SARS-CoV-2) has attracted increasing global attention [2], because its sudden outbreak and global spread represent one of the greatest public health challenges of modern times [3]. Thus, on 30 January 2020, the World Health Organization (WHO) declared the new coronavirus

epidemic, now called coronavirus disease 2019 (COVID-19), a public health condition of international concern [4].

The epidemic has led to worldwide research efforts to identify the population most at risk of developing a critical disease and dying. Initial data indicated that older people are particularly vulnerable, as well as those with diabetes or cardiovascular (including hypertension), respiratory or kidney disease [5]. However, other studies have determined that symptomatology can even affect patients younger than 60 years of age and even involve asymptomatic symptoms [6]. These problems are often concentrated in certain racial groups (e.g., African Americans and Asians) which also appear to be more prone to the worst outcomes of COVID-19 [7]. An increasing number of reports have linked obesity to more serious diseases and death from COVID-19 [4, 5].

The new coronavirus disease (COVID-19) was first reported on 31 December 2019 and has spread worldwide. The mortality rate of patients with COVID-19 increases when the conditions are complicated with conditions such as diabetes, cardiovascular diseases, hypertension and other underlying diseases. Taking into account the large number of elderly people with other diseases in the outbreak areas, the efforts to prevent and control the pandemic have been insufficient and the control of its spread in the world has been an emerging public health problem [8].

### **1.1. Background**

Obesity is very prevalent in the United States and Europe, with an incidence of more than 40% [9, 10]. It can cause diabetes, cardiovascular diseases, vascular diseases and tumors, all associated with the susceptibility or higher mortality of COVID-19 [11, 12].

Studies indicate that obese patients with COVID-19 are more likely to receive mechanical ventilation and have a higher mortality rate [13]. These facts remind us that obesity may be closely related to the worsening of COVID-19. At the same time, at the same time they suggest that there are no differences in body mass index (BMI) between serious and non-serious groups [14, 15].

In the United Kingdom, 72.1% of 775 patients diagnosed with COVID-19 were found to be overweight or obese with a BMI > 30, of whom 60.9% died [15]. In Italy, the prevalence of obesity was identified in 10.0% of a population of 1290 deceased patients, after an analysis of their respective clinical histories [16]. In France, obesity and severe obesity were present in 47.6% and 28.2% of patients requiring invasive mechanical ventilation (IVM) [13].

A study conducted in Cuenca-Ecuador, with 318 individuals of both sexes, presents the prevalence of obesity of 23.6% (27.5% in women and 18.4% in men). Then the risk factor that showed the greatest association was type 2 diabetes mellitus, followed by high blood pressure and high daily calorie consumption [17].

### **1.2. Obesity as a Risk Factor for Complications of COVID-19**

Obesity is considered a factor associated with morbidity and premature mortality in world statistics, while its health consequences are several [18]. In addition, studies have determined that obese people have a higher risk of complications in relation to more than twenty chronic diseases such as type 2 diabetes, hypertension, dyslipidemia, cardiovascular diseases, stroke, sleep apnea and some types of cancer [13, 18, 19]. Obesity is associated with a decrease in the volume of expiratory reserve, functional capacity and distensibility of the respiratory system. In addition, the increase in inflammatory cytokines associated with obesity may contribute to the increased morbidity associated with obesity in COVID-19 infections [20].

Psychosocial stress reactions increase energy intake and individuals with limited social interactions are at increased risk of developing obesity [3]. In addition, health fragility is

known to generate a poor immune response, as well as a decrease in functional reserve [21], so human emotional health is also an important associated factor in the analysis of related conditions.

### **1.3. Sociodemographic Factors of Obese Patients with COVID-19**

Obesity is a global disease with at least 2.8 million people dying each year from the consequences of overweight, according to World Health Organisation figures [22]. In addition, there is growing evidence to suggest that the results of coronavirus disease 2019 (COVID-19) are worse in those with obesity and that a significant proportion of those in need of intensive care are overweight [23].

The prevalence of adult obesity and severe obesity in 2017 to 2018 has increased with respect to measurements from 2009 to 2010 and reached 42% and 9%, respectively [9]. These observations suggest that the proportion of patients with severe obesity and COVID-19 infections will increase, and the disease will likely have a more severe course in these patients [20].

The relationship between sociodemographic characteristics and mortality of patients hospitalized with COVID-19 presents particularities, considering some factors such as racial: it was known that black patients, Mestizos and indigenous people were less frequently admitted to the ICU and were more frequently intubated than white and Asian patients. These populations are more likely to suffer from chronic diseases, which increases their risk of mortality associated with COVID-19 [24].

China's first reports pointed to a gender imbalance in detected cases and lethality rate, however, there is no comprehensive analysis of the underlying causes [25]. While the disease has spread across several continents, the research initiative "Global Health 5050" presented a breakdown of the disease by sex in countries around the world, showing that there would be a similar number of cases in women and men, but higher mortality in men [26].

With regard to age, it is known that the susceptibility to infection in people under 20 years of age is about half that in adults over 20 years of age. Clinical symptoms are evident in 21% of infections in people aged 10-19 years, and increase to 69% in infections in people over 70 years of age [27]. Data from China show that the case fatality rate of COVID-19 increases with age, ranging from 0.4% in patients up to age 40; by 1.3% between the age of 60; by 8% at age 70 and increasing by 14.8% from age 80. In comparison, the overall mortality rate is 2.8% worldwide and 2.7% in the U.S. [28]. This information has implications for the projected global burden of COVID-19, as a result of demographic differences between different environments.

### **1.4. Pathophysiology and Clinical Manifestations of Obesity and Involvement to COVID-19**

In the perspective of identifying and clarifying the main pathophysiological mechanisms that lead to increased

susceptibility and severity of COVID-19 and obesity per se, the following information may be cited.

It has been established that due to secretion of macrophages from adipose tissue of the M1 phenotype, people with obesity have higher circulating levels of proinflammatory cytokines such as IL-1 $\beta$ , IL-6, IL-12, TNF- $\alpha$  and MCP-1 [29]. In addition, the imbalance in the production of leptin and adiponectin also creates an unfavourable hormonal environment that generates and maintains a chronic proinflammatory state [30].

At the immunological level, obesity also affects the response mediated by CD8 T lymphocytes, which are of vital importance for the response to viruses, with the possibility of aggravating the clinical picture. Attached to the immune response, obesity is associated with impaired ventilation of the base of the lungs, decreasing the volume of expiratory reserve, functional capacity and compliance of the respiratory system, which hinders the ventilation of these patients by reducing oxygen saturation. Obesity along with its associated pathologies such as dyslipidemia, type 2 diabetes mellitus, hypertension and cardiovascular disease could play an important role in the immune system of the host infected with SARS-CoV-2 [13, 28, 29].

Among the clinical manifestations of obesity are several gastrointestinal complications such as upper abdominal pain, diarrhea, gastroesophageal reflux disease, vesicular lithiasis, non-alcoholic hepatic steatosis and other less studied chronic gastrointestinal symptoms, such as irritable bowel syndrome and lower abdominal pain. Likewise, the body mass index and abdominal perimeter are risk factors for severity and mortality in patients with acute pancreatitis [31].

It is important to note that, in patients with obesity, when an antigen is present, the activation of macrophages is reduced and the production of proinflammatory cytokines is reduced after the stimulation of macrophages, as well as a poor response of B and T cells, due to chronic low-grade inflammation linked to obesity [30]. Both situations lead to increased susceptibility to viral infection and prolonged viral spread [32].

SARS-CoV-2 contains about 30,000 bases of RNA, the same that uses the protein S (spike) with a glycosylated dense structure to enter host cells and binds with great affinity to the angiotensin converting enzyme receptor (ACE2). This enzyme is found in alveolar cells type II. In the cells of the upper and lower respiratory tract, RNA enters and is converted to viral proteins. This results from two processes: Direct cytopathic effect that deals with viral infection, which prevails in the early stages of the pathology; and the second process is the inflammatory response not controlled by the infected individual, which influences the last stages. The superimposition of these two pathophysiological processes results phenotypically in a 3-stage evolution of the disease: early phase, pulmonary phase and hyperinflammatory phase [33].

The reduction in the stimulation of macrophages at the time of antigen presentation may even explain a possible low vaccination success in viral infections in general [30] and especially in the case of the virus causing COVID-19. The

visible reduction in the effects of the disease will not be a reality until effective vaccines are given to a large part of the world's population, in such a way as to prevent the hospitalization and chronic status of COVID-19 [34].

### **1.5. Comorbidity of Obese Patients Affected by COVID-19**

The first BMI investigations in critical patients hospitalized for COVID-19 infection (although with small samples) determined that approximately 85% of patients with obesity required mechanical ventilation [13]. Preliminary data from New York City showed that obesity (BMI > 40 kg / m<sup>2</sup>) is the second strongest independent predictor of hospitalization, after old age [7].

It has been determined that the cases of severe affection to the human organism by COVID-19 entail bilateral interstitial pneumonias that require assistance in intensive care (ICU) and can evolve to a respiratory distress syndrome, which has a high mortality [35]. The most common comorbidities are hypertension, cardiovascular disease, type 2 diabetes, and obstructive pulmonary disease [35, 36]. Some research has determined that factors such as elevated serum triglycerides, total cholesterol, low-density lipoprotein cholesterol, blood pressure, ferritin, CRP, and low relative lymphocyte count are significant risk factors in obese COVID patients -19. Many studies have evaluated risk factors (age, sex, comorbidities) that may be related to complications and deaths. Studies to date have shown a worldwide predominance of older men, as well as those with cardiovascular disease, in adverse outcomes from COVID-19 [37].

With its increasing prevalence, obesity is an important risk factor for many noncommunicable diseases [38]. A recent meta-analysis has shown that obesity-associated complications are important risk factors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection. In a total of 1,558 COVID-19 patients in 6 studies, the likelihood ratio (LR) was determined for each comorbidity. The following results were obtained: PC in hypertension: 2.29, P < 0.001; CP in diabetes: 2.47, P < 0.00; PC in chronic obstructive pulmonary disease (COPD): 5.97, P < 0.001; PC in cardiovascular disease: 2.93, P < 0.001 and PC in cerebrovascular disease: 3.89, P = 0.002 [39]. Consequently, hypertension, diabetes, COPD,

In obese patients, excess adipocytes can potentiate immune and inflammatory changes [40]. Increased adipose tissue mass is a well-known contributing factor in proinflammatory cascades [41]. SARS-CoV2, which causes the current global COVID-19 pandemic of global proportions, has a high affinity for angiotensin-converting enzyme 2 (human ACE2) [42, 43]. ACE2 receptors show increased gene expression in adipose tissue [44]. Therefore, excess body fat increases ACE2 receptors and may increase the risk of SARS-CoV2 infection and developing a severe form of COVID-19 [25].

## **2. Methodology**

To analyze, through a bibliographic review, obesity as a risk factor for complications of COVID-19, a theoretical and

interpretive approach was used. In this framework, the methodological strategy with which the conceptualizations and findings that delimit the object of study were addressed was the qualitative systematic review of bibliographic sources.

The search and selection of documentary sources was carried out in three phases, based on the application of tracking criteria. These included the following terms: COVID-19; obesity; obesity; socio-demographic factors;

socio-demographic factors; pathophysiology of obesity; pathophysiology of obesity; obese patient comorbidities; comorbidities of obesity.

#### *Phase 1: Use of Boolean operators.*

To track information in databases, two logical operators (Boolean) were used: "AND" to include two or more terms in the same search and "OR" to obtain explorations that include at least one of the terms required.

**Table 1.** Equations and results of the search process.

Applied equation	Results			
	LILACS	VHL	Wiley Online Library	MEDLINE
"COVID-19" AND "obesity"	37	490	14	Four. Five
"COVID-19" AND "obesity"	43	1351	1807	1589
"COVID-19" OR "obesity" AND "socio-demographic factors"	206	2631	22575	281
"COVID-19" OR "obesity" AND "socio-demographic factors"	53	180	21818	0
"COVID-19" AND "obesity" OR "pathophysiology of obesity" OR "comorbidities of obesity"	42	1485	2607	23963
"COVID-19" AND "obesity" OR "obesity pathophysiology" OR "obese patient comorbidities"	0	3	456	2544

#### *Phase 2: Inclusion and exclusion criteria.*

After the initial information tracing with the stated equations, filters were applied to the results obtained; This procedure gave way to the specificity of the publications according to the following inclusion criteria: Scientific articles, published in the last five years, in English and Spanish. Duplicate studies, from repositories, difficult to translate and interpret, that do not present the abstract or the text, or were subscription-based, were excluded.

#### *Phase 3: Exploration techniques.*

The variables that make up the object of study were determined to apply them as bibliographic search terms. COVID-19. Obesity, risk factors, comorbidity. The databases that collect publications related to research in the Health area were investigated. Latin American and Caribbean Health Sciences Literature (LILACS), Virtual Health Library (VHL), Wiley Online Library, Medical Literature Analysis and Retrieval System Online (MEDLINE).

A first information search was carried out on the identified variables, in such a way that the exclusion criteria that led to a more specific search for information could then be defined. A classification matrix of the selected documents was elaborated, which contained descriptive categories of the analyzed information: search equation; publication date; authors; publication title; summary or abstract; guiding question; Methodological approach; results; conclusions; database in which the publication is hosted.

## 3. Results

After applying the inclusion criteria, 91 publications were found, of which 32 required a paid subscription and, therefore, were excluded from the analysis. 59 bibliographies of which 8 did not meet the objectives; Therefore, a total of 51 bibliographies were cited, 2 of these were from web pages such as WHO and PAHO.

**Table 2.** Metadata matrix (20 most recent posts).

No	Magazine	Publication title	Authors	Year of publication	Idiom	Target covered
1	Dovepress Journal.	Impact of Obesity and Its Associated Comorbid Conditions on COVID-19 Presentation	Mehanna, Osama Askary, Ahmad El Ali, Ebtesam Esawy, Basem El	2021	English	"To determine the comorbidities of obese patients affected by COVID-19".
2	The Lancet	Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment.	Olivier J Wouters, Kenneth C Shadlen, Maximilian Salcher-Konrad, Andrew J Pollard, et al.	2021	English	"Identify the sociodemographic factors of obese patients affected with COVID-19".
3	Aging Research Reviews journal	Aging in COVID-19: Vulnerability, immunity and intervention	Chen, Yiyin Klein, Sabra L. Garibaldi, Et al.	2021	English	"Identify the sociodemographic factors of obese patients affected with COVID-19".
4	Public Health	Sociodemographic factors associated with COVID-19 in-hospital mortality in Brazil	Peres, IT Wands, LSL Mayrinck Gelli, JG Marchesi, JF Dantas, LF et al.	2021	English	"Identify the sociodemographic factors of obese patients affected with COVID-19".
5	The Lancet	Obesity could shift severe COVID-19 disease to younger ages	Kass, David A. Duggal, Priya Cingolani, Oscar	2020	English	"Identify the sociodemographic factors of obese patients affected with COVID-19".

No	Magazine	Publication title	Authors	Year of publication	Idiom	Target covered
6	Obesity Medicine journal	The relationship between obesity and other medical comorbidities	Afolabi, Hafeez Abiola Zakariya, Zaidi bin Ahmed Shokri, Amran Bin Mohammad Hasim, et al.	2020	English	“To determine the comorbidities of obese patients affected by COVID-19”.
7	Obesity Medicine journal	Association of high level gene expression of ACE2 in adipose tissue with mortality of COVID-19 infection in obese patients	Al-Benna, Sammy	2020	English	“To investigate the pathophysiology and clinical manifestations of obesity and its involvement in COVID-19”.
8	Obesity Medicine journal	Potential pathophysiological mechanisms leading to increased COVID-19 susceptibility and severity in obesity	Belančić, Andrej Kresović, Andrea Rački, Valentino	2020	English	“To investigate the pathophysiology and clinical manifestations of obesity and the implication to COVID-19”.
9	The Journals of Gerontology: Series A	Unequal Impact of Structural Health Determinants and Comorbidity on COVID-19 Severity and Lethality in Older Mexican Adults: Considerations Beyond Chronological Aging	Bello-Chavolla, Omar Yaxmehen González-Díaz, Armando Antonio-Villa, et al.	2020	English	“Determine the comorbidities of obese patients affected by COVID-19”.
10	The Journal of Clinical Endocrinology & Metabolism	Predicting mortality due to SARS-CoV-2: A mechanistic score relating obesity and diabetes to COVID-19 outcomes in Mexico	Bello-Chavolla, Omar; Bahena-López, Jessica; Antonio-Villa, Neftali; Vargas-Vázquez, et al.	2020	English	“Determine the comorbidities of obese patients affected by COVID-19”.
eleven	Journal of Pathology	Angiotensin-converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19)	Bourgonje, Arno R. Abdulle, Amaal E. Timens, et al et al.	2020	English	“To investigate the pathophysiology and clinical manifestations of obesity and the implication to COVID-19”.
12	Diabetes Care	Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China	Cai, Qingxian Chen, Fengjuan Wang, et al.	2020	English	“To determine the comorbidities of obese patients affected by COVID-19”.
13	Nature Reviews Endocrinology	Will the COVID-19 pandemic worsen the obesity epidemic?	Clemmensen, Christoffer Petersen, Michael Bang Sørensen, Thorkild IA	2020	English	“Identify the sociodemographic factors of obese patients affected with COVID-19”.
14	Obesity	Obesity and its Implications for COVID-19 Mortality	Dietz, William Santos-Burgoa, Carlos	2020	English	“To determine the comorbidities of obese patients affected by COVID-19”.
fifteen	Diabetes Care	Obesity Is a Risk Factor for Greater COVID-19 Severity	Gao, Feng Zheng, Kenneth I. Wang, Xiao Bo Sun, Qing Feng Pan et al.	2020	English	“To determine the comorbidities of obese patients affected by COVID-19”.
16	Obesity Research and Clinical Practice	Obesity and mortality of COVID-19. Meta-analysis	Hussain, Abdulzahra Mahawar, Kamal Xia, Zefeng Yang, et al.	2020	English	“To determine the comorbidities of obese patients affected by COVID-19”.
17	Biology of Sex Differences	Impact of sex and gender on COVID-19 outcomes in Europe	Klein, Sabra L. Morgan, Rosemary	2020	English	“Identify the sociodemographic factors of obese patients affected with COVID-19”.
18	Diabetes and Metabolism	Body mass index and outcome in patients with COVID-19: A dose-response meta-analysis	Pranata, R. Lim, MA Yonas, E. Vania, et al	2020	English	“Determine the comorbidities of obese patients affected by COVID-19”.
19	Obesity	High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective study	Simonnet, Arthur et al.	2020	English	“Determine the comorbidities of obese patients affected by COVID-19”
20	The Lancet		Zhou, Fei Yu, Ting Du, Ronghui Fan, et al.	2020	English	“Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan”.

## 4. Discussion

Obesity has become a global public health problem, with a significant and profound impact on morbidity, mortality, and the cost of healthcare [45]. It has been established that obesity is, indeed, a risk factor for COVID-19, [22] because, on the one hand, it aggravates the chronicity of respiratory diseases by reducing lung function [3, 8], and immunological and inflammatory alterations [20, 21]. Furthermore, the tendency

of obese patients to develop a severe form of COVID-19 due to the accumulation of body fat is denoted [22, 46].

The implications of this disease in obese people include possible difficulties in handling diagnostic tests, as well as in treating COVID-19. It should also be noted that consequences associated with confinement with repercussions on the control and treatment of obesity have been established, so that the affection of this population would confirm their vulnerability to the pandemic [47].

The important role of some socioeconomic aspects has

been demonstrated, although age is a significant predictor, comorbidities and structural health factors also determine the risk of fatality in elderly patients [44]. The COVID-19 pandemic has shown a markedly low proportion of cases among minors, attributed to these populations having a lower susceptibility to infection, a lower propensity to show clinical symptoms, or both. A study evaluated epidemic data by age in 26 countries, finding that clinical symptoms occur in 25% of infections in people aged 10 to 19 years; this figure increases to 76% in those older than 70 years [27].

It was highlighted that the symptoms of patients infected with COVID-19 tend to vary in a wide range; however, elderly men with cardiovascular disease and obesity show greater adverse outcomes from COVID-19 [18, 19]. According to the age factor, it was determined that the cases of contagion and the severity of the symptoms tend to rise in direct relation to the number of years.

The nervous system also appears to be susceptible to SARS-CoV2 denoting an intensified proinflammatory immune response, which can cause severe disturbances in central respiratory function, as well as cerebrovascular disease, seizures, and other symptoms such as loss of taste and smell [48]. The multi-organ involvement that COVID-19 causes includes the nervous system, ventilatory failures are evidenced in which there are no ventilation / perfusion imbalances on their own, but loss of hypoxic vasoconstriction reflexes has also been detected [49]. At the immunological level, obese people are affected in their ability to respond to viruses, as well as a deformed ventilation at the base of the lungs that leads to a serious affection of the respiratory system [50].

Among the most common conditions caused by contagion of COVID-19 were bilateral interstitial pneumonias that entail assistance in intensive care (ICU). In addition, hypertension, cardiovascular disease, type 2 diabetes, and obstructive pulmonary disease [35, 36]. Among the main comorbidities and risk factors associated with mortality in people infected by COVID-19 are: diabetes mellitus (Risk ratio = 1.63); systemic arterial hypertension (Hazard ratio = 1.48); obesity (Risk ratio = 1.37) and chronic kidney damage (Risk ratio = 2.06); it was established that the presence of comorbidities associated with the infection by SARS-CoV-2 actually increases the risk of mortality in people [51].

## 5. Conclusions

The study highlights that men over 65 years of age constitute the predominant profile among patients with the highest level of disease and morbidity. In addition, black, mestizo and indigenous populations have been identified as those most likely to suffer from chronic diseases, increasing their risk of mortality from COVID-19.

Metabolism disorders caused by obesity are related to cases of worsening symptoms of COVID-19. The unfavorable hormonal environment present in obese patients with COVID 19, as well as the immune level of these people make them

more prone to experiencing respiratory system malfunctions.

In comorbidity, the significance of obesity-related conditions was evidenced for patients with COVID-19, especially in cases of diabetes, hypertension, cardiovascular diseases and obstructive pulmonary disease; among the most common conditions caused by contagion of COVID-19 were bilateral interstitial pneumonias that entail assistance in intensive care.

There is evidence of the need to deepen the link between obesity and COVID-19 in order, in this way, to design prevention plans that can reduce the risks that are currently experienced in vulnerable populations.

## Conflicts of Interest

The authors do not report conflicts of interest

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