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#### **VIEWPOINT**

# Quarantine during COVID-19 outbreak: Changes in diet and physical activity increase the risk of cardiovascular disease



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#### **KEYWORDS**

Quarantine; COVID-19; Stress; Lifestyle; Gender; Physical activity; Vitamin D **Abstract** Aims: CoV-19/SARS-CoV-2 is a highly pathogenic virus that is causing a global pandemic with a high number of deaths and infected people. To contain the diffusion of infection, several governments have enforced restrictions on outdoor activities or even collective quarantine on the population. The present commentary briefly analyzes the effects of quarantine on lifestyle, including nutrition and physical activity and the impact of new technologies in dealing with this situation.

Data synthesis: Quarantine is associated with stress and depression leading to unhealthy diet and reduced physical activity. A diet poor in fruit and vegetables is frequent during isolation, with a consequent low intake of antioxidants and vitamins. However, vitamins have recently been identified as a principal weapon in the fight against the Cov-19 virus. Some reports suggest that Vitamin D could exert a protective effect on such infection. During quarantine, strategies to further increase home-based physical activity and to encourage adherence to a healthy diet should be implemented. The WHO has just released guidance for people in self-quarantine, those without any symptoms or diagnosis of acute respiratory illness, which provides practical advice on how to stay active and reduce sedentary behavior while at home.

Conclusion: Quarantine carries some long-term effects on cardiovascular disease, mainly related to unhealthy lifestyle and anxiety. Following quarantine, a global action supporting healthy diet and physical activity is mandatory to encourage people to return to a good lifestyle routine. © 2020 The Italian Diabetes Society, the Italian Society for the Study of Atherosclerosis, the Italian Society of Human Nutrition and the Department of Clinical Medicine and Surgery, Federico II University. Published by Elsevier B.V. All rights reserved.

The emergence of novel coronavirus, officially known as Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS- CoV-2), has presented an important challenge for healthcare systems across the world. Rapid transmission is due to

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high infectivity, capacity to be transmitted even during asymptomatic phase and relatively low virulence [1].

On March 12, 2020 the WHO defined the COVID-19 infection as pandemic [2].

Quarantine and isolation are two measures that can prevent, or minimize, the impact of infectious disease outbreaks. In public health practice, "quarantine" refers to the separation of persons (or communities) who have been exposed to an infectious disease. "Isolation", in contrast, applies to the separation of persons who are known to be infected [3].

The word quarantine comes from the Italian quarantena, meaning "forty days", used in the 14th to 15th-century Venetian language and designating the period that all ships were required to be isolated before passengers and crew could go ashore during the Black Death plague epidemic [4].

In the Modern Era, there are several examples of government-imposed quarantine or travel bans, i.e. at least 18 U S. states guarantined people returning from West Africa during the 2014 Ebola outbreak [3]. Recently, the Italian government among others has enforced quarantine on the population to contain the diffusion of the COVID-19 virus. The previous experience of the SARS outbreak showed the efficacy of timely quarantine and isolation measures [5,6]. Singapore and Hong Kong, both of which had severe acute respiratory syndrome (SARS) epidemics in 2002-03, provide hope and many lessons to other countries. Today, quarantine and social distancing reduced transmission of COVID-19 infection by about 60% in China [7]. However, a further peak will likely occur when restrictive measures to avoid major economic impact are relaxed [7]. Nevertheless, quarantine is an unpleasant experience: with loss of freedom, uncertainty over disease status, and boredom it can affect the health status of subjects. Therefore, the potential benefits of mandatory mass quarantine need to be weighed carefully against the possible long-term negative effects on health, i.e. cardiovascular risk burden, and mental disease [8,9].

Quarantine induces anxiety and stress. Western health care systems have been built around the concept of patient-centered care, but such a pandemic requires a change of perspective toward a concept of community-centered care [10]. This increases anxiety in people who have concerns about their own health. Survey studies on subjects who had been quarantined reported a high prevalence of psychological distress and disorder symptoms. These included emotional disturbance, depression, stress, low mood, irritability, insomnia, and post-traumatic stress [11–14].

During outbreaks of infection people are likely to experience fear of falling sick or dying themselves, feelings of helplessness, and stigma [13,14]. During one influenza outbreak, around 10%–30% of the general public were very or fairly worried about the possibility of contracting the virus. With the closure of schools and business, negative emotions experienced by individuals increased [15,16].

The present commentary briefly analyzes the effects of quarantine on lifestyle, including nutrition and physical activity and the impact of new technologies in dealing with this situation.

## Effects of stress and anxiety on lifestyle during quarantine

Sudden catastrophic events i.e. earthquake are associated with an increase in sudden cardiac deaths, and an overall increase in death due to atherosclerotic and ischemic heart disease [17].

The reasons for this increase in cardiac events after catastrophic events include an acute increase in sympathetic nervous activity and catecholamines.

In the case of quarantine people suffered from a chronic increase of sympathetic nervous activity leading to a chronic negative effect on heart and vessels. Social isolation and loneliness are associated with a very high risk of mortality and the development of major chronic disease [18]. Specifically, social isolation is associated with an increased risk of mortality in patients with cardiovascular disease (CVD) [19].

The acute stress response of an integrated cascade of physiological reactions has been well described [20,21] On the contrary, less is known about how chronic stress responses convert to pathological changes over time, contributing to the development and progression of CVD [21].

The great majority of data come from studies evaluating personal stress (i.e. the death of a close person) or categories of persons (i.e. workers during major economic recession). Little is known about outcome after a period of quarantine and outbreaks, even though all agree this corresponds to a period of high stress. Stress-related changes in the sympathetic-parasympathetic balance and the neuroendocrine dysregulation involving the hypothalamus-pituitary- adrenal responses might adversely affect the cardiovascular system both by accelerating the atherosclerotic process and by precipitating the occurrence of a cardiovascular event. Repeated or chronic exposure to stress facilitates the progression of atherosclerosis. Adrenaline and noradrenaline increase the heart rate and decrease heart rate variability, optimize blood flow to muscle tissues, and elevate core body temperature. The sympathetic nervous system has direct cardiostimulatory effects (chronotropy and inotropy via β1adrenergic receptors) and pressor effects (via α1adrenergic receptors) and also affects metabolism (promotes insulin resistance and lipolysis) and the immune system [22-24].

Moreover, unhealthy behaviors and economic crisis contribute to increased health risk, with socially isolated and lonely individuals having less favorable lifestyles [25,26].

An analysis of UK Biobank indicated that health behavior accounted for more than 30% of the excess risk of mortality attributed to social isolation and loneliness over a 6.5 year follow-up period [27].

The main consequence of stress related to quarantine is a change in lifestyle and nutritional habits (Table 1). Changes

**Table 1** What is known about the effects of quarantine and isolation on diet and physical activity.

What is known

- Quarantine and isolation are effective measures to reduce diffusion of infection and to prevent pandemic. However these conditions can induce depression, anxiety, anger, and stress.
- Stress, depression and anxiety induce people to eat sugar-rich food and drink alcohol to feel better.
- During quarantine and isolation people reduce physical activity, and also reduce relaxing activities (i.e. yoga)
- Apps for Smartphone can help to control diet and maintain personal ideal weight.
- After quarantine, economic crisis could maintain or sometimes worsen unhealthy lifestyle, mainly in individuals of a low socio-economic level.

in nutritional habits can be due to: 1. reduced availability of goods, 2. limited access to food caused by restricted store opening hours, and 3. switch to unhealthy food.

Analysis performed following the Ebola outbreak quarantine showed that having inadequate food and water supplies was a source of frustration and emotional stress. The WHO and Liberia's Ministry of Health found that during the outbreak many families in quarantine did not receive food supplies. In some cases even access to water and sanitation facilities could not be guaranteed for people in quarantine. These conditions do not seem compatible with quarantine or isolation being forms of "easy rescue". In addition, Ebola-exposed families who were subject to quarantine measures in West Africa during the 2014–2015 outbreak suffered significantly from stigmatization and loss of livelihoods, as well as possible increased exposure [6,28,29].

Owing to anxiety surrounding future food shortage, people purchase packaged and long-life food rather than fresh food. Foods with long shelf-life shorten the life line owing to their salt, sugar or trans-fat content [30].

This leads to an unhealthy diet poor in antioxidants, i.e. fresh fruit and vegetables that would increase oxidative stress and inflammation [31,33].

The modern diet era began with the primate evolution when primate biology lost its ability to synthesize vitamin C consequent to a healthy consumption of fruits [33].

Over the last 150 years, refining, hydrogenation, salting and frying were adopted as methods of prolonging the shelf life of food substances. Refined sugar with added fat increased the energy density of the food materials by 6 times [34]. These dietary changes generated a major mismatch between the genetic structure of man and what he could metabolize [35]. Over the last 40 years dietary guidelines and population strategies together with good public education and simultaneous efforts directed at other lifestyle issues, such as promoting healthy diet (i.e. the Mediterranean Diet or Dash Diet), improving physical activity and reducing tobacco consumption, have notably reduced cardiovascular mortality [32,35–37].

During quarantine our diet takes a step back from being a healthy diet rich in fresh food to one containing foods with a long shelf-life. In addition, for many people, the typical response to chronic stressful situations is not to avoid food but possibly to seek out and consume energy-dense foods [38–41].

Anxiety, depression, uneasiness, and anger are emotions that commonly accompany chronic stress [42]. The responses to acute or chronic stress also include a number of modifying behaviors such as alcohol consumption, smoking, and eating [40,42].

When individuals respond to stress by eating more, anecdotal evidence suggests the foods selected are typically high in sugar and fat [42]. This desire to consume a specific kind of food is defined as "food craving". Food craving is a multidimensional experience as it includes cognitive (e.g., thinking about food), emotional (e.g., desire to eat or changes in mood), behavioral (e.g., seeking and consuming food), and physiological (e.g., salivation) aspects [43,44].

The craving for carbohydrates encourages the production of serotonin, which has a positive effect on mood. This effect on mood is proportional to the glycemic index of foods [43].

Muscogiuri and colleagues have recently pointed out that quarantine-related stress translates into sleep disturbances that further worsen stress and increase food craving [43].

They reported on the importance of consuming foods containing or promoting the synthesis of serotonin and melatonin at dinner (e.g. roots, leaves, fruits, and seeds such as almonds, bananas, cherries, and oats), In addition, milk and dairy products are the main sources of sleep-inducing tryptophan amino acid, a precursor of serotonin and melatonin.

Tryptophan is involved in the regulation of satiety and calorie intake via serotonin, which mainly reduces carbohydrate and fat intake and inhibits neuropeptide Y [43]. Dairy products such as yogurt could also increase the activity of natural killer cells and reduce the risk of respiratory infections, suggesting a potential function protection against SARS-CoV-2 disease. This unhealthy nutritional habit may contribute to excess energy intakes and weight gain, increasing the risk of developing obesity [45,46]. Obesity is associated with chronic inflammation, and it is a strong risk factor of heart disease, diabetes, and lung disease that have been demonstrated to increase the risk for more serious complications of CoVID-19 [47].

Torres and coworkers identified that people cope with stress by eating and drinking in an attempt to feel better ("stress-related eating"). These stress-driven eaters and drinkers were more likely to consume unhealthy foods such as snacks, hamburgers, soda cola, and chocolate regularly and to drink wine and spirits more frequently. In addition, the lack of emotional support from friends and relatives was predictive of stress driven eating and drinking behaviors [42,48]. During quarantine, stress-driven eaters would easily switch from a healthy diet to an unhealthy one. In addition, the increase in macronutrient intake could also be accompanied by micronutrient deficiency. During quarantine, the diet is poor in fresh fruit

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and vegetables. Fruits and vegetables are rich in micronutrients and antioxidants [49]. Micronutrients include vitamins that act as antioxidants by reducing the inflammatory response and improving the immune response. Anti-oxidants increase the number of T-cell subsets, enhance lymphocyte response to mitogen, increase interleukin-2 production, and potentiate natural killer cell activity. This would affect cardiovascular risk mainly in high-risk patients. Therefore, during this period, it is essential to follow a balanced nutritional diet that includes a high amount of antioxidants and vitamins. In some cases it may be helpful to take vitamin and mineral supplements. However, despite epidemiologic studies have reported that high dietary intake of foods rich in vitamin E, vitamin C, and β-carotene, has been inversely associated with the incidence of CAD, different results are obtained with vitamin and antioxidant supplementations [50].

Several reasons have been proposed to explain this lack of results obtained with antioxidant supplements: define the optimal dosage, use the appropriate vitamin isomer, interference or competition between vitamins, interindividual variation to response to vitamin [50].

The very recent literature focused on the potential beneficial effect of Vit. D supplementation on patients with COVID-19.

#### Vitamin D and COVID-19

From recent journal literature, it is known that COVID-19 infection is associated with the increased production of pro-inflammatory cytokines and C-reactive protein [51,52]. Antioxidants and vitamins exert protective effects against infection and inflammation. Some research suggested the efficacy of vitamin supplements to prevent COVID 19 infections. A letter from Panarese and coworkers suggested that vitamin D deficiency may also contribute to airway/ gastrointestinal infectious illnesses [53]. Vitamin D has immune-modulatory properties, which include downregulation of pro-inflammatory cytokines [54-56]. It is possible that the protective effect of vitamin D against COVID-19 is related to suppression of cytokine response and reduced severity/risk for ARDS. In addition, a metaanalysis shows that regular oral vitamin D2/D3 intake (in doses up to 2000 IU/d without additional bolus), is safe and protective against acute respiratory tract infection, especially in subjects with vitamin D deficiency [56]. The elderly display a very high prevalence of hypovitaminosis D, especially during the winter [53]. It therefore seems plausible that Vitamin D prophylaxis may contribute to reducing the severity of illness caused by SARS-CoV-2, particularly in settings where hypovitaminosis D is frequent, including people currently living in Northern countries [54]. Regardless of age, ethnicity, and latitude, recent data showed that 40% of the Europeans are vitamin D deficient (25(OH)D levels <50 nmol/L) and 13% are severely deficient (25(OH)D < 30 nmol/L). It is known that severe vitamin D deficiency dramatically increases the risk of mortality, infections, and many other diseases [57].

In a retrospective multicenter study of 212 cases with laboratory-confirmed infection of SARS-CoV-2, an increase in serum 25(OH)D level in the body could either improve clinical outcomes or mitigate worst (severe to critical) outcomes, while a decrease in the serum 25(OH)D level in the body could worsen clinical outcomes of COVID-2019 patients.

[58].

In this patient's population, those with 25OHD >75 nmol/l had lower symptoms than those with lower 25OHD.

A recent review suggested using vitamin D loading doses of 200,000–300,000 IU in 50,000-IU capsules to reduce the risk and severity of COVID-19. Grant and coworkers suggested that higher vitamin D doses and 250HD concentrations would be better for prevention and probably reduce the risk of influenza and COVID-19 incidence and death [59]. Several reviews consider the ways in which vitamin D reduces the risk of viral infections [56,59,60]. Vitamin D has many mechanisms by which it reduces the risk of microbial infection and death. Vitamin D helps maintain tight junctions, gap junctions, and adherens junctions (e.g., by E-cadherin) fighting against the action of viruses to disturb junction integrity, increasing infection by the virus and other microorganisms [61].

Vitamin D also enhances cellular immunity by reducing the cytokine storm induced by the innate immune system. The latter generates both pro-inflammatory and antiinflammatory cytokines in response to viral and bacterial infections, as observed in COVID-19 patients [51]. Vitamin D can reduce the production of pro-inflammatory Th1 cytokines, such as tumor necrosis factor  $\alpha$  and interferon  $\gamma$ [62]. Food rich in vitamin D are salmon, sardines, cod liver oil, canned tuna, egg yolks, mushrooms, and meat [63]. Fish are poorly represented in the diet typically consumed by the elderly people living in the North of Italy, leading to a reduced intake of Vitamin D. Magnesium supplementation is recommended when taking vitamin D supplements. Magnesium helps activate vitamin D, which, in turn, helps regulate calcium and phosphate homeostasis to influence the growth and maintenance of bones. All the enzymes that metabolize vitamin D seem to require magnesium, which acts as a cofactor in the enzymatic reactions in the liver and kidneys [64].

Practical tips to avoid vitamin D deficiency during quarantine are: taking short walks, increasing sun exposure, consuming foods rich in vitamin D, and/or taking drug supplementation.

Preliminary observations support the hypothesis that vitamin D supplementation can reduce the risk of influenza and COVID-19. However, the incidence and death should be investigated in trials to determine the appropriate doses of serum 25(OH)D concentrations.

#### Effects of stress and anxiety on physical activity

The "GLOBAL ACTION PLAN ON PHYSICAL ACTIVITY 2018–2030" published by WHO indicated physical activity

as mandatory for prevention of non-communicable disease [65]. Regular physical activity is associated with reduction in cardiovascular risk [65–67].

The "2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease" recommended that "Adults should engage in at least 150 min per week of accumulated moderate-intensity or 75 min per week of vigorousintensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk" (Class I LOE B-NR) or "for adults unable to meet the minimum physical activity recommendations, engaging in some moderate- or vigorous-intensity physical activity, even if less than this recommended amount, can be beneficial to reduce ASCVD risk" (Class IIa LOE B-NR) [68]. Prolonged TV viewing time is associated with an increased risk of type 2 diabetes mellitus, CVD, and allcause mortality [68]. Prolonged sedentary time is independently associated with deleterious health outcomes, regardless of levels of physical activity [67,68] During quarantine governments prohibited the great majority of outdoor exercise and social activities (e.g. going to the gym), resulting in a reduction of physical activity. Inflammation is an underlying pathophysiological process in chronic diseases, such as obesity, T2 diabetes, and CVD. Regular physical activity reduces inflammation, and oxidative stress and helps to maintain normal weight and reduce visceral fat accumulation [65,66]. Limited physical activity and inability to take a regular walk out of one's home as a consequence of collective quarantine, may be associated with several metabolic effects that would increase the cardiovascular risk. It is also established that many beneficial metabolic and cardiovascular adjustment in response to physical exercise can be lost in just two weeks of inactivity, impairing aerobic capacity, and/or increasing blood pressure. Sudden exercise cessation has been associated with rapid onset of insulin resistance in muscle tissue and decreased muscle glucose utilization that worsened muscle performance [69].

During quarantine, staying active and maintaining a physical exercise routine will be essential for mental and physical health [70–72]. The WHO has just released guidance intended for people in self-quarantine without any symptoms or diagnosis of acute respiratory illness, containing practical advice on how to stay active and reduce sedentary behavior while at home. They suggest following on-line exercise classes, and using video- or appguided aerobics training at home. Table 2 summarizes the WHO indication "Stay physically active during self-quarantine" [73]. Little is known about the effects of homebased physical activity on chronic disease [67,74,75]. The Web could prove useful, since today there are many workout videos available that can assist people in exercising on their own. However, trying to execute all steps (body pose alignments) in a workout accurately, in order to avoid long-term muscle and joint injuries, is risk related

In addition, almost all modern smartphones provide step-count and application for nutrition. Today, it is estimated that more than 5 billion people have mobile **Table 2** WHO guide for quarantine: "Stay physically active during self-quarantine" new line for people in self-quarantine without any symptoms or diagnosis of acute respiratory illness. It should not replace medical guidance in case of any health condition. Modify from WHO guide, freely available at <a href="http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/novel-coronavirus-2019-ncov-technical-guidance/stay-physically-active-during-self-quarantine">health-topics/health-emergencies/coronavirus-covid-19/novel-coronavirus-2019-ncov-technical-guidance/stay-physically-active-during-self-quarantine.</a>

- Take short active breaks during the day. Short bouts of physical activity add up to the weekly recommendations. You may use the suggested exercises below as inspiration to be active every day. Dancing, playing with children, and performing domestic chores such as cleaning and gardening are other means to stay active at home.
- Follow an online exercise class. Take advantage of the wealth of online exercise classes. Many of these are free and can be found on YouTube. If you have no experience, be cautious.
- **Walk.** Even in small spaces, walking around or walking on the spot, can help you remain active. If you have a call, stand or walk around your home while you speak, instead of sitting down. If you can go outside to walk or exercise, be sure to maintain at least a 1-m distance from other people.
- **Stand up.** Reduce your sedentary time by standing up whenever possible. Ideally, aim to interrupt sitting and reclining time every 30 min. Consider setting up a standing desk by using a high table or stacking a pile of books or other materials, to continue working while standing. During sedentary leisure time prioritize cognitively stimulating activities, such as reading, board games, and puzzles.
- Relax. Meditation and deep breaths can help you remain calm.
- Eat healthily and stay hydrated. WHO recommends drinking water instead of sugar-sweetened beverages. Limit or avoid alcoholic beverages for adults and strictly avoid these in young people. Ensure plenty of fruits and vegetables, and limit the intake of salt, sugar and fat.

devices, and over half of these connections are smartphones. Therefore, there are higher potential apps to be developed for lifestyle behavior change in the community. Many people to control their diet and maintain their personal ideal weight use mobile applications related to nutrition. The increasing number of health and nutrition applications available on Google Play and the Apple App Store proves the awareness of community regarding adopting a healthy lifestyle. App programs may be more effective when social support is advocated and could be a useful instrument in order to reduce the negative impact of quarantine on lifestyle [76,77].

Telemedicine is an important tool for patient home monitoring and is very useful for nutritional, motor, psychiatric and psychological support in quarantined patients.

#### Sex differences

Sex differences are present in several diseases. Preliminary data suggest that SARS—CO—2 affected more men than women. One reason seems to be that men have higher rates of chronic disease, a risk factor for COVID-19. However, women are less physically active than men. Severe COVID-19 patients had significantly higher levels of Th1

cytokines (IL-6 and TNF- $\alpha$ ) and higher incidence rate of ARDS, compared with non-severe cases, suggesting a more intense inflammatory response [78]. It is known that after ischemic damage, male gender has a significantly higher level of IL-6 [79]. Similarly, exercise-induced muscle damage triggers inflammatory responses that result in elevations of inflammation markers such as C-reactive protein (CRP) and some inflammatory interleukins (IL-1, IL-6) and tumor necrosis factor (TNF- $\alpha$ ) [80]. On the contrary, regular physical activity seems to reduce IL-6 and Creactive protein. Usually women are less physically active than men and the gap increase after menopause [66]. During and after menopause, most women tend to reduce their physical activity levels and together with the reduction in basal metabolic rate, these lead to a loss of skeletal muscle mass as well as loss of bone mineral density [66,81]. During perimenopause period, fat deposition shifts to favor the visceral depot that, in addition to the decreased protective effect of estrogen, contributes to endothelial dysfunction, inflammation, altered fatty acid metabolism, insulin resistance, and all markers of CVDs [66,67]. There is a direct relationship between time spent sitting, physical activity, and the CVD risk in postmenopausal women, independent of leisure-time physical activity. Prolonged sitting time determines many detrimental adaptations, such as increased energy intake and reduction of skeletal muscle lipoprotein lipase activity that might explain its effect on cardiovascular risk factors [66] In addition, the described food craving has a higher prevalence in women than in men [43,44].

Quarantine induced a reduction of physical activity and an increase in the sitting time leading to an increase in cardiovascular risk in women. It is mandatory to promote a call of action for women mostly after 40 years, for a healthy life style during quarantine to reduce, as consequence, cardiovascular risks.

#### Impact of quarantine on people with obesity

During the quarantine, patients suffering from obesity experienced immense stress which made them more vulnerable to over-eating and sedentary lifestyle, thus predisposing them to further weight gain. Moreover, the incoming economic downturn will also lead to more consumption of unhealthy foods as it is cheaper. This will lead to further increase in obesity prevalence especially in weaker sections of the society. Recently, growing scientific evidence has reported an important role of obesity in Covid-19's prognosis. [82]

Obesity is a leading risk factor of CVD, diabetes, and renal disease, and has a detrimental effect on lung function. A pro-inflammatory state coupled with malnutrition may lead to impaired immune response in patients suffering from obesity and increased susceptibility to all influenza viruses including COVID-19 [83,84] Obesity has some detrimental effects on immune system that include alterations in leukocyte development, phenotypes and activity. In particular, obesity has been shown to impair memory CD8+T cell responses to influenza virus infection,

resulting in increased mortality, viral titers in lung, and worsened lung pathology [82]. Two possible mechanisms have been hypothesized to explain the relationship between obesity and more serious disease in patients with Covid-19: lung function disorders and endothelial dysfunction. Both mechanisms have a common pathway: the increase in pro-inflammatory cytokines and the "cytokine storm". SARS-Cov-2 binds the trans-membrane angiotensin converting enzyme-II receptor inducing an acute endothelial injury. The storm of pro-inflammatory cytokines increases the expression of adhesion molecules which promotes endothelial activation and cascade activation of coagulation, leading to a worsening of the microcirculation system and tissue perfusion [85]. The "cytokine storm" can lead to acute respiratory distress syndrome or even multiple organ failure. It represents a phenomenon of immune hyper activation very similar to cytokine-release syndrome (CRS).

Subjects presented with obesity have a proinflammatory status and the exposure to COVID-19 could further exacerbate inflammation exposing them to higher levels of circulating inflammatory molecules [82].

Obese subjects must be carefully informed about the risk of an unhealthy lifestyle during the quarantine due to the increasing risk of disease. These subjects need careful monitoring of their health and strong psychological support to reduce stress and anxiety.

Weight stigma is not uncommon in social media outlets such as Twitter, Facebook, and Instagram and the recent COVID-19 quarantine has sparked social media posts that refer to "quarantine-15". Social media posts that stigmatize obesity and mock or diminish real struggles with weight and eating can be particularly harmful to individuals with obesity who are actively trying to manage their weight [86].

#### **Conclusion**

We need to be prepared to confront the likely increase in cardiovascular risk burden following the pandemic. During quarantine we must promote healthy diet and physical activity at home. After quarantine we need to re-evaluate the cardiovascular risk in patients, assessing biometrical and metabolic parameters. Patients also need to be evaluated by a psychologist to early identify the persistence of anxiety and stress and/or evolution to a post-traumatic syndrome. Global action supporting healthy diet and physical activity is mandatory to encourage people to return to a good lifestyle. This action needs to be stronger for individuals of a low socio economic level that will suffer to a higher degree from the inevitable restrictions and economic crisis following a vast and prolonged quarantine.

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#### **Author contribution**

AVM, SS, SM, and SG conceived the idea at the basis of the article, AVM, CC, and SG developed different parts of the manuscript, and AVM, SS, CC, SM, and SG performed the final supervision. All authors contributed to and approved the final manuscript.

#### **Declaration of Competing Interest**

None Declared.

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#### References

- [1] Li G, Hu R, Gu X. A close-up on COVID-19 and cardiovascular diseases [published online ahead of print, 2020 Apr 8]. Nutr Metab Cardiovasc Dis 2020;30(7):1057–60. https://doi.org/10.1016/j.numecd.2020.04.00.
- [2] WHO announces COVID-19 outbreak a pandemic. 2020. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic.
- [3] Parmet WE, Sinha MS. Covid-19 the law and limits of quarantine. N Engl J Med 2020. https://doi.org/10.1056/NEJMp2004211.
- [4] Mackowiak PA. The origin of quarantine. Clin Infect Dis 2002;35: 1071–2
- [5] WHO. Update 58 first consultation on SARS epidemiology, travel recommendations for Hebei province (China), situation in Singapore. 2003. http://www.who.int/csr/sars/archive/2003\_05\_ 17/en/.
- [6] Giubilini A, Douglas T, Maslen H, Savulescu J. Quarantine, isolation and the duty of easy rescue in public health. Develop World Bioeth 2018 Jun;18(2):182–9. https://doi.org/10.1111/dewb.12165. Epub 2017 Sep. 18.
- [7] Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? Lancet 2020;395(6):931–4.
- [8] Mattioli AV, Ballerini Puviani M. Lifestyle at time of COVID-19, how could quarantine affect cardiovascular risk. Am J lifestyle 2020; 14(3):240–2. https://doi.org/10.1177/1559827620918808. Published 2020 Apr 17.
- [9] Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet 2020;395: 912–20. https://doi.org/10.1016/S0140-6736(20)30460-8.
- [10] Nacoti M, Ciocca A, Giupponi A, Brambillasca P, Lussana F, Pisano M, et al. At the epicenter of the covid-19 pandemic and humanitarian crises in Italy: changing perspectives on preparation and mitigation. N Engl J Med 2020 March 21:2020. https://doi.org/10.1056/CAT.20.0080.
- [11] DiGiovanni C, Conley J, Chiu D, Zaborski J. Factors influencing compliance with quarantine in Toronto during the 2003 SARS outbreak. Biosecur Bioterror 2004;2:265–72.
- [12] Hawryluck L, Gold WL, Robinson S, Pogorski S, Galea S, Styra R. SARS control and psychological effects of quarantine, Toronto, Canada. Emerg Infect Dis 2004;10:1206—12.
- [13] Jeong H, Yim HW, Song Y-J, Ki M, Min JA, Cho J, et al. Mental health status of people isolated due to Middle East respiratory syndrome. Epidemiol Health 2016;38:e2016048.
- [14] Lee S, Chan LY, Chau AM, Kwok KP, Kleinman A. The experience of SARS-related stigma at Amoy Gardens. Soc Sci Med 2005;61: 2038–46.

[15] Hall RCW, Chapman MJ. The 1995 Kikwit Ebola outbreak: lessons hospitals and physicians can apply to future viral epidemics. Gen Hosp Psychiatr 2008;30:446–52.

- [16] Rubin GJ, Potts HWW, Michie S. The impact of communications about swine flu (influenza A H1N1v) on public responses to the outbreak: results from 36 national telephone surveys in the UK. Health Technol Assess 2010;14:183—266.
- [17] Kloner RA, Leor J. Natural disaster plus wake-up time: a deadly combination of triggers. Am Heart J 1999;137:779–81.
- [18] Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress, Lancet 2007;370:1089–100.
- [19] Steptoe A, Kivimäki M. Stress and cardiovascular disease. Nat Rev Cardiol 2012;9:360–70.
- [20] Huang QH, Takaki A, Arimura A. Central noradrenergic system modulates plasma interleukin-6 production by peripheral interleukin-1. Am J Physiol 1997;273;R731–8.
- [21] Goebel MU, Mills PJ, Irwin MR, Ziegler MG. Interleukin-6 and tumor necrosis factor-alpha production after acute psychological stress, exercise, and infused isoproterenol: differential effects and pathways. Psychosom Med 2000;62:591–8. 2000.
- [22] Steptoe A, Shankar A, Demakakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. Proc Natl Acad Sci U S A 2013;110:5797–801.
- [23] Yu B, Steptoe A, Chen LJ, Chen YH, Lin CH, Ku PW. Social isolation, loneliness, and all-cause mortality in patients with cardiovascular disease: a 10-year follow-up study. Psychosom Med 2020;82(2):208–14. https://doi.org/10.1097/PSY.00000000000000000777.
- [24] Cacioppo JT, Cacioppo S, Capitanio JP, Cole SW. The neuroendocrinology of social isolation. Annu Rev Psychol 2015;66:733–67.
- [25] Grippo AJ, Lamb DG, Carter CS, Porges SW. Social isolation disrupts autonomic regulation of the heart and influences negative affective behaviors. Biol Psychiatr 2007;62:1162–70.
- [26] Loucks EB, Berkman LF, Gruenewald TL, Seeman TE. Relation of social integration to inflammatory marker concentrations in men and women 70 to 79 years. Am J Cardiol 2006;97:1010–6.
- [27] Elovainio M, Hakulinen C, Pulkki-Råback L, Virtanen M, Josefsson K, Jokela M, et al. Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK biobank cohort study. Lancet Public Health 2017;2: e260–6.
- [28] Kutalek R, Wang S, Fallah M, Wesseh CS, Gilbert J. Ebola interventions: listen to communities. Lancet 2015;3:e131. https://doi.org/10.1016/S2214-109X(15)70010-0.
- [29] ACAPS. WASH in Guinea, Liberia, and Sierra Leone. The impact of Ebola. 2016. Available at: https://www.acaps.org/special-report/ wash-guinea-liberia-and-sierra-leone-impact-ebola.
- [30] Sivasankaran S. The cardio-protective diet. Indian J Med Res 2010; 132(5):608–16.
- [31] Mattioli AV, Ballerini Puviani M, Nasi M, Farinetti A. COVID-19 pandemic: the effects of quarantine on cardiovascular risk. Eur J Clin Nutr 2020 May 5:1–4. https://doi.org/10.1038/s41430-020-0646-z.
- [32] Mattioli AV, Coppi F, Migaldi M, Scicchitano P, Ciccone MM, Farinetti A. Relationship between Mediterranean diet and asymptomatic peripheral arterial disease in a population of premenopausal women. Nutr Metabol Cardiovasc Dis 2017;27(11): 985–90. https://doi.org/10.1016/j.numecd.2017.09.011.
- [33] Leupker RV. Decline in incident coronary heart disease. Why are the rates falling? Circulation 2008;117:592—3.
- [34] Ford AS, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE. Explaining the decrease in US deaths from Coronary disease: 1980-2000. N Engl J Med 2007;356:2388–98.
- [35] Benzie IFF. Evolution of dietary antioxidants. Comp Biochem Physiol Physiol 2003:136:113–26.
- [36] Kopp W. High-insulinogenic nutrition an etiologic factor for obesity and the metabolic syndrome. Metabolism 2003;52:840–4.
- [37] O'Keefe Jr JH, Cordain L. Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome: how to become a 21st century Hunter-gatherer. Mayo Clin Proc 2004;79: 101–8.
- [38] Johnson RK, Appel LJ, Brands M, Howard BV, Lefevre M, Lustig RH, et al. American heart association nutrition committee of the council on nutrition, physical activity, and metabolism and the council on epidemiology and prevention. Dietary sugars intake

- and cardiovascular health: a scientific statement from the American heart association. Circulation 2009 Sep 15;120(11):1011–20.
- [39] Vreman RA, Goodell AJ, Rodriguez LA, Porco TC, Lustig RH, Kahn JG. Health and economic benefits of reducing sugar intake in the USA, including effects via non-alcoholic fatty liver disease: a microsimulation model. BMJ Open 2017 Aug 3;7(8):e013543, d.
- [40] Schiffman SS, Graham BG, Sattely-Miller EA, Peterson-Dancy M. Elevated and sustained desire for sweet taste in African-Americans: a potential factor in the development of obesity. Nutrition 2000;16:886–93.
- [41] Bracale R, Vaccaro CM. Changes in food choice following restrictive measures due to Covid-19. Nutr Metab Cardiovasc Dis 2020; 30:1423—6. https://doi.org/10.1016/j.numecd.2020.05.027.
- [42] Torres SJ, Nowson CA. Relationship between stress, eating behavior, and obesity. Nutrition 2007;23(11- 12):887–94. https://doi.org/10.1016/j.nut.2007.08.008.
- [43] Muscogiuri G, Barrea L, Savastano S, Colao A. Nutritional recommendations for CoVID-19 quarantine. Eur J Clin Nutr 2020. https://doi.org/10.1038/s41430-020-0635-2 [published online ahead of print, 2020 Apr 14].
- [44] Rodríguez-Martín BC, Meule A. Food craving: new contributions on its assessment, moderators, and consequences. Front Psychol 2015;6:21. https://doi.org/10.3389/fpsyg.2015.00021. Published 2015 Ian 22.
- [45] Walcott-McQuigg JA. The relationship between stress and weight control behavior in African-American women. J Natl Med Assoc 1995:87:427—32.
- [46] Heraclides AM, Chandola T, Witte DR, Brunner EJ. Work stress, obesity and the risk of type 2 diabetes: gender-specific bidirectional effect in the Whitehall II study. Obesity 2012;20(2):428–33. https://doi.org/10.1038/oby.2011.95.
- [47] Wu Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020. https://doi.org/10.1001/jama internmed.2020.0994.
- [48] Laitinen J, Ek E, Sovio U. Stress-related eating and drinking behavior and body mass index and predictors of this behavior. Prev Med 2002;34(1):29—39. https://doi.org/10.1006/pmed.2001.0948.
- [49] Mattioli AV, Coppi F, Migaldi M, Farinetti A. Fruit and vegetables in hypertensive women with asymptomatic peripheral arterial disease. Clinical Nutrition ESPEN 2018;27:110—2.
- [50] Badimon L, Vilahur G, Padro T. Nutraceuticals and atherosclerosis: human trials. Cardiovasc Ther 2010;28(4):202-215. https://doi.org/10.1111/j.1755-5922.2010.00189.x.
- [51] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in wuhan, China. J Am Med Assoc 2020.
- [52] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020.
- [53] Panarese A, Shahini E. Letter: Covid-19, and vitamin D [published online ahead of print, 2020 Apr 12]. Aliment Pharmacol Ther 2020. https://doi.org/10.1111/apt.15752.
- [54] Panarese A, Pesce F, Porcelli P, Riezzo G, Iacovazzi PA, Leone CM, et al. Chronic functional constipation is strongly linked to vitamin D deficiency. World J Gastroenterol 2019;25:1729–40.
- [55] Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. Nutrients 2015;7:4240-70.
- [56] Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ 2017;356:i6583. https: //doi.org/10.1136/bmi.i6583.
- [57] Kara M, Ekiz T, Ricci V, Kara Ö, Chang KV, Özçakar L. Scientific strabismus' or two related pandemics: COVID-19 & vitamin D deficiency [published online ahead of print, 2020 may 12]. Br J Nutr 2020:1-20. https://doi.org/10.1017/S0007114520001749.
- [58] Alipio Mark. Vitamin D supplementation could possibly improve clinical outcomes of patients infected with coronavirus-2019 (COVID-19). Available at: SSRN: https://ssrn.com/ abstract=3571484; 2020.
- [59] Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, et al. Evidence that vitamin D supplementation could

- reduce risk of influenza and COVID-19 infections and deaths. Nutrients 2020;12:988.
- [60] Beard JA, Bearden A, Striker R. Vitamin D and the anti-viral state. J Clin Virol 2011;50:194–200.
- [61] Hewison M. An update on vitamin D and human immunity. Clin Endocrinol 2012:76:315—25.
- [62] Schwalfenberg GK. A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. Mol Nutr Food Res 2011;55:96–108.
- [63] Crowe F, Steur M, Allen N, Appleby P, Travis R, Key T. Plasma concentrations of 25-hydroxyvitamin D in meat eaters, fish eaters, vegetarians and vegans: results from the EPIC—Oxford study. Publ Health Nutr 2011;14(2):340—6. https://doi.org/10.1017/S1368980010002454.
- [64] Uwitonze AM, Razzaque MS. Role of magnesium in vitamin D activation and function. J Am Osteopath Assoc 2018;118:181–9.
- [65] WHO Global action plan on physical activity 2018–2030: more active people for a healthier world. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.
- [66] Mattioli AV, Sciomer S, Moscucci F, Maiello M, Cugusi L, Gallina S, et al. Cardiovascular prevention in women: a narrative review from the Italian Society of Cardiology working groups on 'Cardiovascular Prevention, Hypertension and peripheral circulation' and on 'Women Disease. J Cardiovasc Med 2019;20:575–83. https://doi.org/10.2459/JCM.000000000000831.
- [67] Nasi M, Patrizi G, Pizzi C, Landolfo M, Boriani G, Dei Cas A, et al. The role of physical activity in individuals with cardiovascular risk factors: an opinion paper from Italian Society of Cardiology-Emilia Romagna-Marche and SIC-Sport. J Cardiovasc Med 2019;20: 631–9. https://doi.org/10.2459/JCM.00000000000000855.
- [68] Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. Circulation 2019. https://doi.org/10.1161/-CIR.000000000000000678. 000:eλλλ—eλλλ.
- [69] Womack VY, De Chavez PJ, Albrecht SS, Durant N, Loucks EB, Puterman E, et al. A longitudinal relationship between depressive symptoms and development of metabolic syndrome: the coronary artery risk development in young adults study. Psychosom Med 2016;78:867–73.
- [70] Thompson PD, Franklin BA, Balady GJ, Blair SN, Corrado D, Estes 3rd NA, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American heart association council on nutrition, physical activity, and metabolism and the council on clinical cardiology. Circulation 2007;115:2358–68.
- [71] Ricci F, Izzicupo P, Moscucci F, Sciomer S, Maffei S, Di Baldassarre A, et al. Recommendations for physical inactivity and sedentary behavior during COVID-19. Front. Public Health 2020. https://doi.org/10.3389/fpubh.2020.00199.
- [72] Mattioli AV, Nasi M, Cocchi C, Farinetti A. COVID 19 outbreak: impact of the quarantine-induced stress on cardiovascular disease risk burden. Future Cardiol 2020. https://doi.org/10.2217/fca-2020-0055. Published online: 30 April 2020.
- [73] WHO guideline "Stay physically active during self-quarantine". 2020. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/novel-coronavirus-2019-ncovtechnical-guidance/stay-physically-active-during-self-quarantine.
- [74] Nagarkoti A, Teotia R, Mahale AK, Das PK. Realtime indoor workout analysis using machine learning & computer vision. Conf Proc IEEE Eng Med Biol Soc 2019 Jul;2019:1440—3. https: //doi.org/10.1109/EMBC.2019.8856547.
- [75] Taylor JK, Buchan IE, van der Veer SN. Assessing life-space mobility for a more holistic view on wellbeing in geriatric research and clinical practice. Aging Clin Exp Res 2019;31:439–45. https://doi.org/10.1007/s40520-018-0999-5.
- [76] Paramastri R, Pratama SA, Ho DKN, Purnamsari SD, Mohamed AZ, Galvin CJ, et al. Use of mobile applications to improve nutrition behaviour: a systematic review [published online ahead of print, 2020 Mar 19]. Comput Methods Progr Biomed 2020;192:1054–9. https://doi.org/10.1016/j.cmpb.2020.105459.
- [77] DiFilippo KN, Huang WH, Andreade JE. The use of mobile apps to improve nutrition outcomes: a systematic literature review. J Telemed Telecare 2015;21:243–53.

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[78] Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan [published online ahead of print, 2020 Apr 12]. J Allergy Clin Immunol 2020. https://doi.org/10.1016/j.jaci.2020.04.006. In press.

- [79] Mattioli AV, Bonetti L, Zennaro M, Bertoncelli P, Mattioli G. Acute myocardial infarction in young patients: nutritional status and biochemical factors. Int J Cardiol 2005;101(2):185–90.
- [80] Fatouros IG, Jamurtas AZ. Insights into the molecular etiology of exercise-induced inflammation: opportunities for optimizing performance. J Inflamm Res 2016;9:175–86.
- [81] Mattioli AV, Coppi F, Migaldi M, Farinetti A. Physical activity in premenopausal women with asymptomatic peripheral arterial disease. J Cardiovasc Med 2018 Nov;19(11):677–80. https://doi.org/10.2459/JCM.000000000000014.
- [82] Muscogiuri G, Pugliese G, Barrea L, Savastano S, Colao A. Obesity: the "Achilles heel" for COVID-19? [published online ahead of print,

- 2020 Apr 27]. Metabolism 2020;108:154251. https://doi.org/10.1016/j.metabol.2020.154251.
- [83] Green WD, Beck MA. Obesity impairs the adaptive immune response to influenza virus. Ann Am Thorac Soc 2017;14:S406–9.
- [84] Bhasker AG, Greve JW. Are patients suffering from severe obesity getting a raw deal during COVID-19 pandemic? [published online ahead of print, 2020 may 12]. Obes Surg 2020:1-2. https://doi.org/10.1007/s11695-020-04677-z.
- [85] Tibiriça E, De Lorenzo A. Increased severity of COVID-19 in people with obesity: are we overlooking plausible biological mechanisms?. 2020. https://doi.org/10.1002/oby.22887 [published online ahead of print, 2020 May 13]. Obesity (Silver Spring).
- [86] Pearl RL. Weight stigma and the "Quarantine-15. 2020. https://doi.org/10.1002/oby.22850 [published online ahead of print, 2020 Apr 23]. Obesity (Silver Spring).