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Anticipating and curtailing the cardiometabolic toxicity of social isolation and emotional stress in the time of COVID-19

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Coronavirus disease 2019 (COVID-19) is a formidable global health challenge and is projected to result in as many as 20 million deaths globally.¹ To address the pandemic, intensive scientific and clinical efforts have been directed at deciphering the molecular mechanisms of disease, the implementation of large-scale containment measures, and the development of effective preventive and treatment therapies. And yet, much less attention has been given to anticipating and mitigating the potential health consequences of the only currently proven intervention to inhibit its spread – isolation, quarantine, and social distancing.

The abrupt and severe restrictions to the physical mobility of millions of individuals worldwide, coupled with the associated psychological stress, may lead to a surge of cardiometabolic risk factors and potentially an eventual increase in cardiovascular disease, depending in part on the duration of restrictions. Ignoring these factors may add insult to injury by precipitating an acute on chronic exacerbation of the cardiovascular disease epidemic and warrants attention to the implementation of a cardiovascular health containment plan.

Physical isolation and cardiovascular disease are strongly associated. Prospective longitudinal studies demonstrate that poor social relationships are associated with a 29% higher risk of coronary heart disease and a 32% increased risk of stroke.² Individuals in social isolation and those who report loneliness are also at elevated risk of developing obesity, hypertension, dyslipidemia, and diabetes mellitus.³ The pathways through which social isolation influences cardiovascular health are complex and involve lifestyle factors (i.e. unhealthy diet, physical inactivity, smoking), emotional stress, treatment nonadherence, direct effects on surrogate biomarkers (i.e.

inflammation) and possibly epigenetic changes and immune dysregulation.⁴

With wide-reaching lockdowns imposed on entire cities and states with the goal of flattening the COVID-19 curve, it is incumbent upon us to identify and address the potential contributors to cardiometabolic disease in individuals who are placed in physical isolation. Frameworks, such as proposed below, should recognize social isolation as a major cardiovascular risk factor and devise novel preventive strategies, based on the understanding that multiple steps along the social isolation-cardiovascular disease sequence could be targeted to diminish the deleterious health effects of inter-personal distancing. However, untangling the effects of social isolation and social support from other socioeconomic factors that have complex interaction with disease stage and complications will be challenging.

In individuals with or without known cardiovascular disease, a structured preventive approach, analogous to the Prevention checklist of the American College of Cardiology and American Heart Association⁵ but modified to settings of social isolation or poor social support, would be important. First, clinicians should assess the individual cardiovascular risk, weighing conventional factors and sociodemographic aggravators. This will require a paradigm shift in which social structures are systemically integrated into the risk assessment calculus, acknowledging aspects of people's lives outside medical care that are contributory to their illnesses and barriers to care.⁶ For example, not being able to afford medications, being uninsured, or not being convinced that certain medications should be taken, are critical determinants of failure to obtain adequate care and require fundamental community- and team-based interventions.⁶

Overweight individuals and those who follow a sedentary lifestyle are clearly at heightened risk of cardiovascular disease, but so are those who are single and with limited social networks, both in regard to size and the quality of relationships. Individuals experiencing sustained deficiencies in social interaction attributable to quarantine or physical distancing should be considered at higher risk of cardiovascular disease. Clearly, the duration of social isolation that is needed to result in disease development or exacerbation is multi-factorial and

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individual-specific and cannot be predicted, as are the magnitude of the excess cardiovascular risk conferred by social isolation and the potential ameliorating effect of digital social interactions.

Estimation of cardiovascular risk should incorporate validated atherosclerotic risk markers as well as a social integration evaluation, considering the capacity and quality of persons' objective and subjective relationships. Factors such as the absence of social support, poor satisfaction with life, and lack of purpose, are important to consider as they predict self-perception of loneliness. In addition, the elderly are a particularly vulnerable group given that physical restrictions commonly prohibit their interactions with their children and grandchildren, and many are less facile in the use of the internet to facilitate social interactions.

Second, social isolation is a risk factor for elevated *blood pressure*. Mediators of hypertension in these settings include lower physical activity levels, weight gain, high dietary sodium intake and emotional stress, although alcohol and substance use also play a role. In the special circumstances of social isolation, periodic blood pressure measurements, even in healthy individuals, should be considered, given that persistently high values would trigger an investigation to delineate its cause (i.e. emotional stress, inability to fill prescriptions, excess alcohol consumption) and allow for a targeted intervention. Availability of home blood pressure monitors and the competence associated with obtaining accurate self-measurements should eventually be disseminated in the community ideally with full coverage by health insurance companies.

For some individuals, the knowledge that hypertension appears to be associated with worse outcomes in patients with COVID-19 may serve as a motivating factor to optimize blood pressure even though we have little hard evidence for a mechanistic explanation for this association (direct effect from elevated blood pressure, medication-mediated cellular changes, influence of age, confounders, etc).⁷ Guideline-endorsed recommendations for blood pressure control should be emphasized, with particular attention to medication adequacy, low-sodium diet, and regular brisk physical activity. Precautions should also be taken to decrease caffeine, nicotine, alcohol, and decongestant use. The use of meditation, yoga, Pilates and stress-reduction health apps may help reduce sympathetic activation and improve blood pressure.

Third, stressful periods and physical isolation may aggravate *cigarette* use in active smokers and lead former smokers to relapse. Adults at high risk of smoking or smoking complications (i.e. lower education levels, lower income, psychiatric illness), should be identified and provided education regarding the importance of limiting nicotine use. They should also be counseled that nicotine use is associated with higher COVID-19 severity. The underlying trigger for nicotine use (ie, depression, anxiety, loneliness) should be pinpointed and addressed. Active smokers should be offered nicotine replacement

therapies. Digital smoking cessation and app-delivered platforms are particularly valuable in individuals under social mobility constraints.

Fourth, physical isolation has the potential to worsen *dietary* habits due to lower access to healthy ingredients and lack of social engagement. Living alone has been associated with lower vegetable and fruit consumption and higher intake of sugar-sweetened beverages. Emotional stress has the potential to magnify these behaviors. Dietary enhancement opportunities for individuals in social isolation include preparation and delivery of home-cooked products, moderation in dietary sodium and cholesterol consumption, and avoidance of excessive portions.

The use of health apps to trend calorie count, body weight, and waist circumference could help individuals monitor their overall nutritional status. Telehealth services could support virtual encounters with internists, endocrinologists, and dietitians. Manufacturers and governments could consider introducing discounts on healthy foods, food stamps, or free nutritionist consultations, during periods requiring prolonged social isolation.

Fifth, social isolation and stress often serve as an obstacle to aerobic *exercise*. The importance of physical activity stems from its favorable influence on blood pressure and weight, glucose control, and equanimity, and should be encouraged for all individuals. Regular aerobic activity may be technically challenging in settings of social isolation. Possible solutions include the use of home-made gym equipment and fitness workouts, stairs, and the outdoors. Online exercise classes could also help preserve cardiorespiratory fitness. A tailor-made exercise protocol that maximizes the use of a person's home space and local environment could be designed by a clinician, taking into account the individual's baseline health and cardiopulmonary status.

Targeting social isolation and psychological stress in the time of COVID-19 is paramount in order to prevent a rise of cardiometabolic disease in the months and years to come. The challenges of social isolation are driven and compounded by inequalities in socioeconomic status and to fully tackle the health hazards of physical isolation, we will have to restore social justice by supporting the under-privileged and lessening wealth and resource disparities. Understanding social isolation and its public health consequences is key to minimizing the late cardiometabolic burden of COVID-19 but is also fundamental to optimizing cardiovascular health outside the context of COVID-19 going into the future. Furthermore, the ramifications of inter-personal distancing, social isolation, and quarantine on short- and long-term non-Covid-19 disease exacerbations, hospital utilization, and health care costs, will require dedicated study which will provide important learning points. In the meantime, an approach utilizing home-adapted exercise regimes, promotion of healthy dietary habits, medication adherence, and stress-reduction, leveraging telehealth technologies and health apps, could be the cornerstone of cardiovascular health containment during these testing times.

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