Invited Paper for CJC COVID Issue

The impact of COVID-19 on the social determinants of cardiovascular health

Short Title: COVID-19 and cardiovascular health

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Abstract:

Cardiovascular disease (CVD) is the leading non-communicable disease and cause of premature mortality globally. Despite well-established evidence of a cause-effect relationship between modifiable lifestyle behaviours and the onset of risk of chronic disease, preventative approaches to curtail increasing prevalence have been ineffective. This has undoubtedly been exacerbated by the coronavirus disease 2019 (COVID-19) pandemic, which saw widespread national lockdowns implemented to reduce transmission and alleviate pressure on strained healthcare systems. An unintended consequence of these approaches was a well-documented negative impact on population health in the context of both physical and mental well-being. Whilst the true extent of the impact of the COVID-19 pandemic on global health has yet to be fully realised or understood, it seems prudent to review effective preventative and management strategies that have yielded positive outcomes across the spectrum (i.e., individual to society). There is also a clear need to heed lessons learnt from the COVID-19 pandemic in the power of collaboration and how this can be used in the design, development, and implementation of future approaches to address the longstanding burden of CVD.

Introduction

Cardiovascular (CV) disease (CVD) is a prominent non-communicable disease (NCD) phenotype that may be characterized as a group of interacting disorders that includes coronary heart disease, cerebrovascular disease, and stroke. Collectively, CVD is the leading cause of morbidity and premature mortality on a global scale,[1], currently responsible for 18 million deaths and 366 million disability-adjusted life years lost each year [2]. Decades of research have established a cause-effect relationship that exists between modifiable lifestyle behaviours and the onset of risk of premature chronic disease [3,4]. Modifiable lifestyle behaviours are behaviours that can be changed and have a profound impact on physical and mental health [5]. Physical inactivity and a poor diet are two of the most pertinent unhealthy lifestyle risk factors for CVD[6], which are both preventable and reversible [7]. Arguably, the most effective public health strategy is primary prevention where modifying lifestyle choices can reduce the risk of developing CVD by up to 80%[8] [9]. Despite a plethora of evidence to support the relationship between lifestyle behaviours and chronic disease, previous and universal approaches to counter increasing prevalence and the subsequent impact on healthcare providers are confounded by the complex and interactive nature of chronic disease [10]. Previous attempts by international governments and health agencies to influence healthy lifestyle choices have been confounded by poor adherence, accessibility, and scalability[11]. In addition, the broad nature of interacting factors is often neglected and considered in the design, development and implementation of prevention and optimal management efforts to achieve population-level effectiveness. To add further complexity, the coronavirus disease 2019 (COVID-19) pandemic precipitated an unprecedented global healthcare challenge [12]. During this time, unhealthy lifestyle behaviours were exacerbated and have been once again thrust into the forefront of public attention. Unhealthy lifestyle behaviours (e.g., poor quality diet, lack of physical inactivity, and tobacco/alcohol use) are major contributors to the global burden of disease [13].

Whilst the longstanding impact of the COVID-19 pandemic on lifestyle behaviours and chronic disease is yet to be realised, it has almost certainly contributed to a worsening in trends of population-level cardiometabolic risk factors[14,15]. Although empirical methodologies lack consistency, reports clearly demonstrate important changes in lifestyle behaviours and well-being due to imposed social distancing measures and other preventative restrictions to curtail transmission [16]. Of significant interest is the impact of a persisting symptom profile beyond an acute infection, now referred to as post-COVID syndrome or Long COVID. This presents a rapidly evolving global health crisis [17] that significantly limits functional capacity and exists with a broad array of clinical presentations that is inclusive of CVD complications [18]. As the world begins its recovery following the COVID-19 pandemic, there is a significant opportunity to improve public health and well-being that should not be squandered; this opportunity is inclusive of combating the long-standing NCD crisis. Accordingly in this review, we provide a summary of effective

prevention and management strategies that can be implemented to address the growing burden that is and will continue to impact global health and well-being.

The Role of Health and Fitness as a Primary Marker of CV Health

Cardiorespiratory fitness (CRF) is a primary marker of health, resiliency and longevity [19,20]. It is established that individuals that are genetically predisposed to developing chronic diseases but maintain a healthy lifestyle and have a preserved CRF across the lifespan have a lower level of risk for developing CVD [21,22]. **Figure 1** highlights the roles and importance of CRF and other key behavioural characteristics that can be targeted in those individuals that lead unhealthy lifestyles and are subsequently diagnosed with a chronic disease, but then make dramatic changes that emulate a healthy lifestyle can reverse and limit the longstanding implications associated with chronic disease [23]. In a community-based cohort study of 387,109 UK adults, Hamer *et al.* demonstrated that those individuals with positive lifestyle behaviours (defined as those that promote improved health outcomes) and characteristics had a lower incidence of hospitalization due to COVID-19 infection after adjustment for chronic conditions (i.e., CVD and hypertension), supporting the assertion that healthy lifestyle behaviours provide a protective mechanism despite a previous chronic disease diagnosis[24]. In addition, Sallis *et al.* reported an increased risk of adverse outcomes when infected with COVID-19 in those who were physically inactive [25]. Whilst data during the acute stages highlight the protective benefits of healthy lifestyle behaviours, more surveillance research into the effects this has on the development of Long COVID, and chronic disease is needed. Whilst more research is needed to scale up this finding and to stratify it relative to co-morbidities and other healthy living behaviours, initial findings indicate a further complexity in the global response to chronic disease.

****Figure 1 around here****

Effective Strategies to Maintain and Improve CV Health

The primary prevention strategy for improving CV health is through modifying lifestyle behaviours; higher CV health is also associated with being less susceptible to a COVID-19 infection and a reduction in severe outcomes and symptomology [26,27]. These lifestyle behaviours primarily consist of following good nutritional behaviours and being physically active, as these two modifiable factors can nourish the immune system and reduce the inflammatory response following infection [28,29]. This is important due to an elevated inflammatory response that comes to light during COVID-19, characterized as a 'cytokine storm' (i.e., a cascade of cytokine (and chemokine) production which results in leukocyte infiltration and activation that can cause tissue damage and organ dysfunction) [30]. Reducing the incidence of this phenomenon is therefore vital to protect CV health and reduce the chances of severe outcomes for patients with COVID-19.

Adequate and balanced nutrition is imperative to optimise immune system function and our body's response to infections [29]. Observational studies demonstrate that individuals with a 'normal' body mass are less likely to experience COVID-19 hospitalisations and reduced symptomology [31]. Equally, Harrison *et al.* recently observed obesity to have an association with mortality from COVID-19 (Odds ratio (OR): 2.18, 95% CI: 1.10-4.34)[28]. This could be linked to low chronic low-grade inflammation and higher anti-inflammatory cytokines from poor nutrition. Contrastingly, a healthy diet may offer protective effects for CV health and thus, the severity of COVID-19. Moreover, the nutritional status of individuals has also been associated with vaccination effectiveness, whereby low intake of micronutrients (particularly malnourishment) seemed to impair the protection gained from vaccines [32]. Given that both a lack of nutrients and being obese will negatively impact CV health leading potentially to metabolic syndrome, it is clear from this evidence that nutrition is a modifiable factor that could help sustain CV health and reduce the severe consequences of COVID-19. This is an area of great concern given the sharp increase in the rates of obesity, particularly in the western world [3], which may yet be magnified by reduced access to recreational facilities and an increase in sedentary behaviour (SB) throughout the pandemic. The lasting impacts the COVID-19 pandemic will have on lifestyle behaviours and the influence of CV risk factors have yet to be established; initial trends are not certainly troubling for the future. As such, the promotion of healthy lifestyle behaviours is a critical area of consideration for the development of strategies to improve CV outcomes, from both the primary and secondary prevention perspective.

A healthy diet can work synergistically with appropriate levels of PA to improve CV health and reduce negative COVID-19 outcomes. Participating in exercise improves mitochondrial function by initially increasing the acute levels of reactive oxygen species that upregulates mitochondrial biogenesis, as well as super oxygen dismutase, catalase, and glutathione peroxidase [33]. These effects reinforce our antioxidant defence systems and improve immunity, which is critical to a cell's ability to respond to viral infections such as COVID-19 [34]. Accordingly, Tavakol *et al.* demonstrated that those demonstrating low PA levels ($p=0.05$) or low metabolic equivalent (MET).min/week ($p=0.03$) were more likely to experience increased disease severity [35]. It is well established that avoiding SB or conversely engaging in regular PA is a key factor of CV health [36], outlined in more detail below. It is important to note that the intensity of exercise is a modifiable factor and moderate exercise is preferable to intense exercise, whereby the latter can lead to immunosuppression of anti-inflammatory cytokines and thus, greater susceptibility to infection [37]. Further strategies to improve CV health and COVID-19 complications are to avoid behaviours, such as those that can damage the liver (e.g., alcohol) or the respiratory system (e.g., smoking), as these have also been associated with a higher risk of mortality (liver disease OR: 2.81, 95% CI: 1.31-6.01, smoking OR: 1.46, 95% CI: 0.83-2.60) and severity of symptoms (liver disease OR: 0.81, 95% CI: 0.47,1.4, smoking OR: 1.80,

95% CI: 1.14-2.85) [28]. Several modifiable factors can function as preventative tools to help individuals protect their CV health and susceptibility to a severe or life-threatening response to a COVID-19 infection. Equally, behavioural changes could reduce the impact of the cytokine storm that is apparent with a COVID-19 infection through improved immunity. Adhering to healthy lifestyle behaviours which include healthy nutrition and PA is critical in the response moving forward to weaken the grip the virus has on the global population.

Key Points

- The response to a COVID-19 infection is malleable and individuals should attempt via adherence to change the subsequent risk of serious symptoms by reducing the impact of the cytokine storm
- The response to infection is influenced by behaviour changes in nutrition and exercise that help promote improved immunity
- Avoiding unhealthy lifestyle behaviours such as smoking, and sedentary behaviours reduces the severity of a COVID-19 infection.

Strategies to Manage or Mitigate the Implications of Reduced CV Health

Prior to the COVID-19 pandemic, the protective effects of PA in the management of chronic conditions were well established[38]. Whilst the mechanisms of action are multifactorial, they include improved or normalized vascular function, blood pressure, weight loss, glycemic regulation, lipid profile, mitochondrial function, stress reduction and quality of life [39]. The association between PA and CV health has determined a minimum volume of activity to produce a clinically meaningful reduction in the risk of CV events alongside strategies to maximise health benefits. The benefits of accumulating 150-300 minutes of moderate-intensity PA and performing two days of muscle-strengthening activities and the benefits for sleep quality are associated with reduced anxiety, improving cognition and improving insulin sensitivity [39]. Previous recommendations highlight that bouts of at least 10 minutes of aerobic PA were needed to count towards the weekly allotment of PA, however, bouts <10 minutes also provide positive health benefits and reduce mortality risk [40]. This is meaningful when promoting PA to individuals living sedentary and/or physically inactive lives that may perceive planning for structured activities lasting 10 or more minutes as untenable. Alternatively, high-volume, high-intensity exercise emerged as a key strategy for improving CRF in all participants completing 1,800 and 3,000 kcal/week for men and women respectively. High-intensity interval training along with time-efficient forms of training has gained traction. Interventions such as vigorously climbing three flights of stairs, three times per day, separated by a four-hour recovery period, three days/week for at least six weeks contributed to improved CRF and presented potential real-world application in the workplace [41], where sedentary behaviours are prominent[42]. Even more efficient was

performing five, four-second all-out sprints with 45-second rest periods every hour over eight hours on a cycle ergometer that decreased postprandial plasma triglyceride metabolism and increased whole-body fat oxidation[43].

Despite recognition of the health-related benefits of physically activity, only a quarter of adults reported meeting the aerobic and strengthening components of the PA guidelines prior to the COVID-19 pandemic [39]. It is clear that national lockdowns contributed to further reductions in PA,[44] increases in SB and all-round disturbance to positive health behaviours [45,46]. Reduced recreational activities, active travel time and daily activities were significantly associated with lower PA levels. While PA levels were reduced across all age groups, the already low levels of PA in older adults before the pandemic were exacerbated during the lockdown. Browne and colleagues reported PA and SB data in a group of hypertensive older adults before and during the pandemic[47]. On average, participants took 5,809 steps/day, accumulated 303 minutes/day of light PA, 15.5 minutes/day of moderate-vigorous PA and 653 minutes of sedentary time. When measured during the pandemic, there was a decrease of nine hundred steps/per day, 2.8 minutes/per day of moderate to vigorous PA, 26.6 minutes of light activity and a 30-minute increase in sedentary time[47]. This data is sobering when considering that SBs significantly increases the risk of developing CVD. In a previous investigation, sedentary time in healthy older adults was associated with a 22% and 27% better likelihood of having a cluster of traditional CVD risk factors in women and men, respectively[48]. It is important to recognise that those with an established management plan during the pandemic, likely lost contact with physicians due to a reprioritisation of clinical staff to address the challenges of COVID-19 [49]. Contact with care providers is an effective strategy to maintain engagement with lifestyle interventions but a reduction in contact/access during the pandemic may have led to attrition and a worsening of patient outcomes [50]. Whilst challenging and representing a big step change, one positive response was to move the delivery of effective cardiac rehabilitation (CR) services to a virtual platform[51]. Assisted with bespoke guidance and recommendations [52], the role of virtual care made use of available technologies and platforms to increase accessibility[53]. This resulted in the development and implementation of safe, translational, effective, and adaptable CR services for patients [54]. Early data demonstrates that remote, synchronous [(live virtual CR monitoring or hybrid (virtual CR and in-person CR sessions)] models of CR delivery are potential ways to improve access and increase capacity for underserved patients who could benefit from CR participation [55,56].

The impact of lockdowns on PA is not disputed, favourable trends began to emerge once it became clear that a quick resolution to the pandemic was not plausible. With enrollment and membership to health/fitness centres reduced due to limited capacity and/or member hesitancy, individuals turned to spending more time being physically active outside, finding creative ways of increasing PA indoors and/or investing in home

fitness equipment. The development of fitness phone applications outpaced previous years' rates [57] along with increases in self-powered or electronic bicycle sales [58]. Though there are many contributing reasons, it is likely that those that were able to work remotely effectively eliminated or decreased weekly automotive commutes to and from work.

Key point:

- A substantial proportion of the population does not meet minimal activity levels which has been exacerbated by the COVID-19 pandemic. Many forms of exercise can improve CRF and risk of CVD and the use of virtual platforms and synchronous contact might help improve access and capacity to assist with getting individuals to be active.

A Global Call to Action

Notwithstanding the well-documented benefits of healthy living behaviours, availability of knowledge and advancements in medicine, technology, and an array of global initiatives over several decades, there has been little change in public health outcomes. Despite a plethora of initiative-taking models' and global strategies to promote healthy living behaviours, these approaches have been ineffective as CVD prevalence data does not show any signs of improvement and will burden healthcare settings for decades to come[59]. Whilst proactive and preventive approaches are most impactful[60], these approaches have been hindered by a lack of integration, differentiation, acceptability, and scalability above a local or national level. Given the urgency, it is appropriate to establish global health policies that are enriched with behavioural, implementation and system science approaches to coordinate a holistic approach to addressing the current and future global health threats[8]. Whilst the health threats of the ever-evolving circumstances are an immediate concern to global health and well-being, the ongoing and widespread prevalence of CV health issues seen globally is a pre-existing pandemic by its very own nature. Exercise and PA that is effective and accessible via consistent and equitable approaches across nations will seek to address CV health issues. Therefore, international policymakers and decision-makers should prioritise and instil an 'exercise/healthy living is medicine' message across the lifespan and including education on PA and literacy to embed habitual exercise into the global population [61,62].

Initiatives by leading organisations such as the World Health Organisation and the National Institute of Health to address public health challenges have raised awareness of CVD and the associated risk factors. However, their attempts to address global health suffer from a lack of compelling evidence of the effectiveness in thwarting the trajectory and prevalence of CVD and chronic disease more broadly. Indeed, recent reports from the United Kingdom House of Commons Report on Grassroots participation in sports

and physical activity identified that despite a mission statement and promised legacy to increase the number of adults participating in recreational and competitive sports and an £8.8 billion investment, the 2012 Olympic Games in London failed to influence participation levels entirely [63]. It is conceivable that all interested parties share the ambition to improve population health but there is a lack of global representation and widespread opportunity to engage with such agencies to inform decision-making, implementation, and reporting processes. What is most evident is a lack of consideration and global thinking from established health agencies to adopt and implement unified health agendas that could be effective in improving global public health.

In the wake of COVID-19, unhealthy lifestyle behaviours and chronic disease have been amongst society throughout history but what was a pre-existing and sizeable challenge to public health has undoubtedly been accelerated and even synergized[64]. The key to successfully addressing the chronic disease burden can be firstly achieved via formal recognition from international governments and non-government agencies. Global attempts can then be implemented within health authorities, international governments and academic researchers working collaboratively with deep interdisciplinary practice. Under the remit of healthy living medicine, holistic approaches to improving access and widespread adoption of healthy living behaviours should be devised in a manner that will benefit the population's health and well-being for years to come.

Conclusion

With rising prevalence and the impact upon healthcare settings, there is a need to develop cohesive interventions that are accessible and can be implemented at scale to instil healthy living behaviours at a global level. This might appear idealistic but there is a need for a global health infrastructure that is supported with appropriate investment. This could also include data modernization and improved surveillance mechanisms that are transient and reflected by mass media coverage is needed to make this panacea a reality. COVID-19 has served those with an interest in public health a stark reminder that adopting reactive approaches to public health challenges may not be in the public's best interests. We must therefore work collaboratively to establish effective, scalable, and sustainable approaches and increase the recognition and implementation of precision public health.

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Figure Captions:

Figure 1: Modifiable lifestyle behaviours that impact the prevalence of cardiovascular disease which has been impacted by COVID-19.

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