

# Physical inactivity and cardiovascular disease at the time of coronavirus disease 2019 (COVID-19)

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With an increasing number of governments hardening nationwide quarantine, or considering various forms of lockdown in attempts to hinder the spread of the novel coronavirus disease 2019 (COVID-19),<sup>1</sup> a major problem emerges concerning the potential deleterious effects of physical inactivity due to personal restrictions. According to the regulations recently set by the Italian government, for example, it is mandated that all citizens must remain at home unless required to move for valid reasons, such as work, health or for other unavoidable issues such as assisting those who are sick or disabled, or purchasing groceries and medications. Many companies and organizations have mandated telecommuting. All sporting events and competitions have been suspended or cancelled. However, one important exception has been made to allow people to practise sports and outdoor physical activity, provided that an interpersonal distance of at least 1 m could be maintained. This seems a reasonable compromise between the unfavourable health consequences associated with physical inactivity and the compelling need to contain the COVID-19 outbreak by avoiding social gatherings and other forms of personal contact.

The World Health Organization (WHO) has established clear guidelines on the minimal amount of physical activity necessary to maintain adequate health and fitness. For example, it is recommended that adults aged between 18 and 64 years, the age group most affected by COVID-19 according to recent statistics (i.e. accounting for over 70% of all severe cases),<sup>2</sup> should engage in weekly training of at least 150 min of moderate-intensity physical activity or 75 min of vigorous-intensity physical activity, or a corresponding combination of moderate- and vigorous-intensity activity.<sup>3</sup> Recent evidences also attest to the benefits of regular physical activity on survival.<sup>4–6</sup> Leisure-time physical activity has been negatively correlated with

the risk of cardiovascular mortality independently from age, sex and presence or lack of pre-existing cardiovascular disease.<sup>5</sup> Physical fitness has been independently associated with risk of early cardiovascular death in the population aged 50 years or older, which suggests that physical fitness may not only modulate cardiovascular death risk, but that it may also be improved by practising regular physical exercise.<sup>6</sup>

Limited physical activity or, even more worrisome, inability to take a regular walk out of one's home as a consequence of strict quarantine, may be associated with a kaleidoscope of unfavourable metabolic effects that would dramatically increase the risk of many severe and disabling disorders such as diabetes,<sup>7</sup> cancer,<sup>8</sup> osteoporosis<sup>9</sup> and cardiovascular disease.<sup>10</sup> Reductions in physical activity may also affect one's mental health, which may be experienced as unpleasant emotions such as sadness, anger, frustration and/or irritation. In a review on psychological impact of quarantine recently performed by Brooks et al., the authors stated that experiencing disease outbreaks can trigger symptoms of post-traumatic stress, depression and/or confusion, among others.<sup>11</sup>

A recent meta-analysis of prospective studies, totaling 36 investigations and over three million subjects

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followed up for a median period of 12 years, concluded that achieving the WHO recommended physical activity levels was associated with 17% lower risk of cardiovascular events (relative risk (RR), 0.83; 95% confidence interval (CI), 0.77–0.89), 23% lower risk of cardiovascular mortality (RR, 0.77; 95% CI, 0.71–0.84) and 26% lower incidence of type 2 diabetes (RR, 0.74; 95% CI, 0.72–0.77).<sup>12</sup> These findings were more recently confirmed by Kivimäki and colleagues,<sup>13</sup> who pooled data from 19 prospective observational cohort studies, totalling 404,840 subjects. Overall, physical inactivity was associated with 24% higher risk of coronary heart disease (hazard ratio, 1.24; 95% CI, 1.13–1.36), 16% enhanced risk of stroke (hazard ratio, 1.16; 95% CI, 1.05–1.27) and 42% higher risk of diabetes (hazard ratio, 1.42; 95% CI, 1.25–1.61). Importantly, it should be noted that increased mortality in COVID-19 patients is observed for many of the above-mentioned comorbidities.<sup>14</sup>

Deleterious effects have also been described after acute cessation of physical activity, which may occur after abrupt establishment of quarantines. Sudden exercise cessation has been associated with rapid onset of insulin resistance in muscle tissue and decreased muscle glucose utilization, with consequent muscle atrophy.<sup>15</sup> It is also established that many beneficial metabolic and cardiovascular adaptations in response to physical exercise can be lost with only two weeks of inactivity, impairing aerobic capacity and/or increasing blood pressure. The reduced energy consumption by unused muscles leads to reallocation of metabolic substrates to the liver, where production of atherogenic lipoproteins may be fostered, thus promoting obesity and lipids accumulation within the blood vessels, accelerating atherosclerotic disease.<sup>15</sup> Importantly, abrupt cessation of physical activity may also lead to decreased venous return and reduced coronary perfusion, which can then predispose individuals to collapse upon resuming exercise.<sup>16</sup> Finally, the resting heart rate has been shown to rapidly increase after acute cessation of physical activity, which may further amplify the risk of cardiovascular events and mortality.

During quarantine, staying active and maintaining a physical exercise routine will be essential for mental and physical health. Fortunately, a wide range of exercises, such as video- or app-guided equipment-free aerobics or strength training, can be performed at home and should be encouraged. We hence encourage national, federal and regional governments around the world to include clear exceptions for physical activity in nationwide lockdowns. These should also allow for safe performance of outdoor physical activities (e.g. walking, running or other individual sports, where an adequate interpersonal distance can be maintained),

and thus prevent the COVID-19 pandemic from generating unfavourable cardiovascular consequences due to acute cessation of physical activity.

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