FRIGID ZONE **MEDICINE**
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"Nothing burns like the cold": Cardiovascular disease in frigid zones

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Cardiovascular disease (CVD) is the leading cause of death globally, with the majority of the adult population exposed to multiple traditional or non-traditional CVD risk factors[1]. Among the latter, both acute and lengthy exposures to low temperatures can increase cardiovascular risk, particularly in individuals with an underlying CVD. The link between CVD and cold weather is reflected in a well-documented peak in cardiovascular deaths during the winter months[2]. For example, investigators in Germany found that a 10°C decrease in 5-day average temperature was associated with a 1.10 relative risk of myocardial infarction[3], while in China each 1°C decrease in temperature during a cold wave increased the mortality risk from myocardial infarction by 1.82%[4].

Interestingly, the increase in coronary events during the winter is smaller in populations residing in overall colder climates[5], such as Frigid Zones, in which the average winter temperature is below 0°C[6]. These observations suggest the existence of various mechanisms to acclimate to the detrimental effects of colder climates. In fact, that protection seems lost in individuals that are either unaccustomed to cold environments[7] or unable to properly adapt to extreme temperatures[8]. Furthermore, the risk of acute coronary events has been recently shown to be exacerbated by both considerable changes in temperature over the course of the day[8] and by an extremely low apparent temperature (that perceived by the combined effects of air temperature, relative humidity, and wind speed)[9]. However, even amongst those acclimated to cold climates, exposure to an extreme cold increases cardiac mortality[10], suggesting a functional limit on cardiovascular adaptation to cold.

The patho-mechanisms underlying the increased mortality in cold weather are multi-factorial. Proposed mechanisms include a rise in cardiac workload and strain, cold-induced vasoconstriction, and activation of the renin–angiotensin–aldosterone system, elevating blood pressure[11]. As cold exposure reduces myocardial oxygen supply, activities that increase cardiac workload and oxygen demand can lead to myocardial ischemia and infarction[9]. This is especially true in the elderly, who have increased arterial stiffness and exaggerated pressor response to cold, which in turn raise myocardial oxygen demand[12]. Cold weather has also been linked to a hypercoagulable state[13] raising the risk of arterial thrombosis, as well as of cold-induced cardiac hypertrophy[11]. These might be aggravated by decreased exposure to sunlight and consequent vitamin D deficiency, reduced regular physical activity[2], and increased exposure to respiratory infections, inducing inflammation and hypercoagulability[14]. While much research has been done, there is a gap in knowledge regarding cold-induced CVD, and further understanding of its pathogenesis would increase our ability to both prevent and treat events to reduce mortality.

The trajectory of cold-induced CVD can be speculated. As global temperatures rise due to climate change, increased climate variability in parallel is predicted to evoke a somewhat paradoxical surge in the frequency of cold extremes, which may contribute to increased mortality during the winter months[15]. Besides the increase in overall temperature, climate change also produces fewer but more intense snowfall events[16]. Pertinently, snow shoveling leads to an average of 100 deaths/year in the United States. In Norway, a 1 cm increase in snowfall is associated with a 44% increase in myocardial infarction risk[17]. Warmer days with heavier snowfall yield wetter snow that is linked to amplified myocardial infarctions[18]. This association is exacerbated by an aging population with diminished adaptability to physiological stressors, and the number of people aged 65 or older is projected to almost triple from 2010 to 2050, mostly in developing countries. Hence, diminished CVD secondary to less overall frigid temperatures might be offset by both altered precipitation patterns and increased frequency of extreme cold events. Cardiovascular risk, however, is not limited to myocardial infarction, as there is a significantly increased risk of hemorrhagic stroke and death

due to both cold temperature and snowfall[19]. Compounding the effects of pollution on the overall weather trends is its direct impact on cardiovascular health specifically during cold weather. For example, increased levels of NO_2 have been recently shown to be associated with a rise in cardiovascular deaths during the winter[20]. As NO_2 levels are a marker for increased climate change, this trend is expected to continue. Finally, rising mental stress levels over cold exposure, climate change, or unpredictable weather patterns may precipitate CVD[21].

Notably, the association between cardiovascular events and climate is not limited to low temperatures. Heatwaves and extreme heat events are associated with an increased risk of myocardial infarction[22], and similar to cold weather, this risk is enhanced in the elderly. As many elderly choose to live in long-term care facilities, various measures to ameliorate the effect of rising global temperatures on the elderly have been proposed, such as improved microclimates in long-term care facilities that blunt extreme temperatures[23]. Besides age, cardiovascular susceptibility to temperature seems to be sex-based as well. Paradoxically, the risk of myocardial infarction during an extreme heat event is greater in females[24], whereas the risk of myocardial infarction in extreme cold is higher in males[25]. Various causes have been proposed, including varying levels of outdoor physical activity in the winter months (such as snow shoveling). Ultimately, however, women show increased mortality from myocardial infarction[26], and women between ages 35-64 years living in normally warm climates exhibit an increased incidence of coronary events during cold compared to men of the same age group[5], possibly related to the underuse of protective attire. Some theories regarding the sex-based vulnerability to the effects of temperature implicated sex hormones, given that the discrepancy between females and males is mitigated in postmenopausal women[9]. However, further studies are needed to elucidate the mechanisms underlying age- dependency and sex-dependency of sensitivity to both cold and warm temperatures.

Therefore, the future impact of Frigid Zones on CVD remains to be unearthed. Additional research is required on the impact of weather fluctuations on vulnerable populations[8], on shaping future policy regarding climate change, and on developing novel strategies for protection from extreme weather patterns. In the meantime, we should consider bundling up.

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Conflicts of interests

The authors declare no conflicts of interests.

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