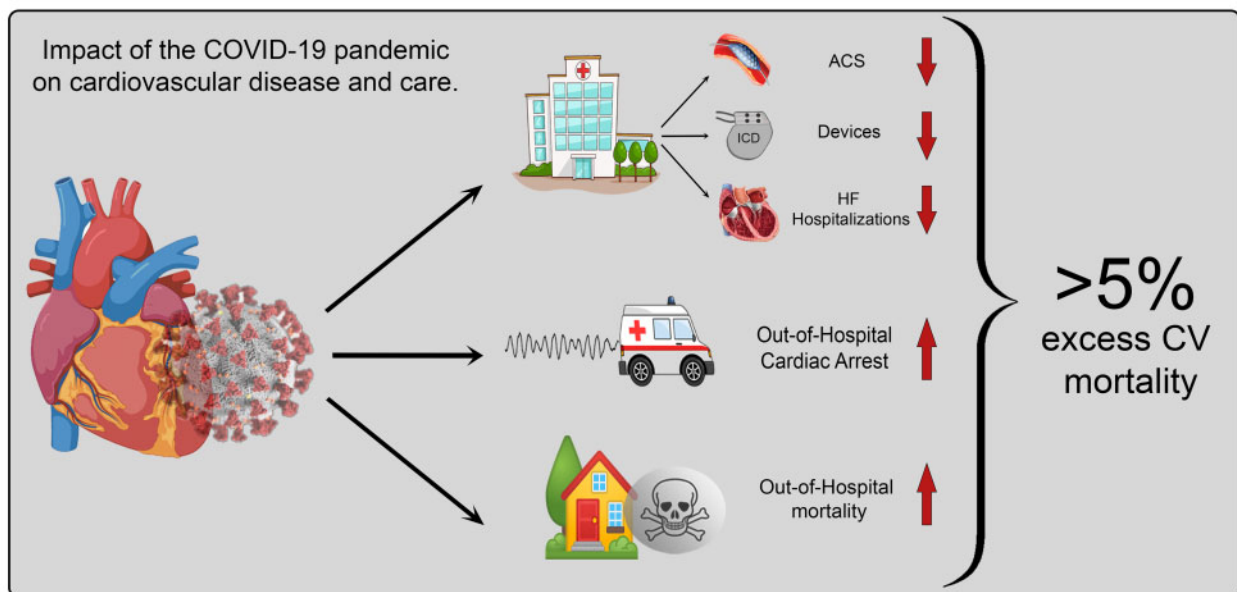


# The collateral cardiovascular damage of COVID-19: only history will reveal the depth of the iceberg

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This editorial refers to 'All-cause mortality and location of death in patients with established cardiovascular disease before, during, and after the COVID-19 lockdown: a Danish nationwide cohort study', by J. Butt *et al.*, doi:10.1093/eurheartj/ehab028.



**Graphical abstract** Impact of the COVID-19 pandemic on patients with cardiovascular disease worldwide. ACS, acute coronary syndrome; CV, cardiovascular; HF, heart failure; ICD, implantable cardioverter-defibrillator.

The coronavirus disease 2019 (COVID-19) pandemic is an unprecedented global public health emergency that has dramatically changed all aspects of our lives. To date, the novel severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) has infected almost 100 million people and directly caused >2 million deaths.<sup>1</sup> To prevent the spread of the virus and relieve pressure on healthcare services,

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**Table 1** Effect of the COVID-19 pandemic on hospitalizations for cardiovascular conditions, mortality rates, and excess cardiovascular mortality worldwide, regardless of infection rates

Study	COVID-19 impact	Country	Admission rate	In-hospital mortality	Out-of-hospital mortality	Overall CV mortality	Excess CV mortality
<b>All CV conditions</b>							
Butt <i>et al.</i> <sup>3</sup>	Low	Denmark	–	↓	↑	↔	0%
Brant <i>et al.</i> <sup>4</sup>	High	Brazil	–	–	–	↑	4%
Konig <i>et al.</i> <sup>5</sup>	Moderate	Germany	↓	↑	–	–	1%
Del Pinto <i>et al.</i> <sup>6</sup>	Low <sup>a</sup>	Italy	↓	↔	–	–	–1%
Wu <i>et al.</i> <sup>7</sup>	High	UK	–	↔	↑	↑	8%
Bhatt <i>et al.</i> <sup>8</sup>	High	USA	↓	↔	–	–	2%
<b>Acute coronary syndrome</b>							
Mesnier <i>et al.</i> <sup>9</sup>	High	France	↓	↔	–	–	2%
Popovic <i>et al.</i> <sup>10</sup>	High	France	↓	↑	–	–	22%
Nef <i>et al.</i> <sup>11</sup>	Moderate	Germany	↓	–	–	↑	12%
Primessnig <i>et al.</i> <sup>12</sup>	Moderate	Germany	↓	↑	–	–	13%
Tam <i>et al.</i> <sup>13</sup>	High	Hong Kong	↓	↑	–	–	7%
De Rosa <i>et al.</i> <sup>14</sup>	High	Italy	↓	↑	–	–	7%
Wilson <i>et al.</i> <sup>15</sup>	High	UK	↓	↔	–	–	3%
Gluckman <i>et al.</i> <sup>16</sup>	High	USA	↓	↔	–	–	0%
<b>Heart failure</b>							
Andersson <i>et al.</i> <sup>17</sup>	Low	Denmark	↓	↔	–	↔	0%
Bollmann <i>et al.</i> <sup>18</sup>	Moderate	Germany	↓	↑	–	–	2%
Cannata <i>et al.</i> <sup>19</sup>	High	UK	↓	↑	–	–	3%
Doolub <i>et al.</i> <sup>20</sup>	High	UK	↓	↑	–	–	10%
<b>Out-of-hospital cardiac arrest</b>							
Marijon <i>et al.</i> <sup>21</sup>	High	France	↑	↑	↑	↑	2%
Baldi <i>et al.</i> <sup>22</sup>	High	Italy	↑	↑	↑	↑	6%

CV, cardiovascular.

<sup>a</sup>Relatively low impact region for COVID cases at the time of the analysis.

governments enforced lockdown measures. At the same time, healthcare systems rapidly repurposed by redeploying resources and staff to tackle this unique challenge. These strategies limited the impact of the first wave of COVID-19 but disrupted usual care pathways for non-COVID-19 conditions.

The prevalence of cardiovascular diseases has consistently increased over time as effective interventions have prolonged survival. Despite this, they are still the leading cause of morbidity and mortality worldwide, mandating ongoing efforts to provide prompt diagnosis, complex interventions, structured follow-up, and uninterrupted care.<sup>2</sup> The advent of the COVID-19 pandemic has abruptly discontinued this continuum of care for all cardiovascular conditions, with potentially devastating consequences.

In this issue of the *European Heart Journal*, Butt *et al.* provide an interesting analysis of the impact of the COVID-19 pandemic on patients with cardiovascular disease in Denmark.<sup>3</sup> Using the Danish nationwide registry, the authors did not find a difference in overall mortality for patients with established cardiovascular disease compared with the same period in 2019, despite lockdown measures and healthcare reconfiguration. They found lower in-hospital mortality that was, unfortunately, counter-balanced by higher out-of-hospital mortality. This important contribution adds to a growing literature on outcomes for patients admitted to hospital with cardiovascular

disease during the COVID-19 pandemic. Furthermore, this report is one of the first to describe parallel changes in out-of-hospital mortality of patients with cardiovascular conditions and the temporal association with lockdown measures.

The COVID-19 pandemic has affected countries differently for several reasons, including the timing and extent of lockdown measures, which have ranged from almost none to severe draconian approaches. These measures were typically accompanied by public health messages urging the public to stay at home whenever possible. Most countries have struggled to manage the dramatic increase in demand for healthcare during the COVID-19 pandemic, and many systems have been stretched significantly, to the verge of collapse. The reconfiguration of both primary and secondary care has included the redeployment of medical staff, sudden cessation of routine face-to-face appointments, interruption of established care pathways, and reduced availability of medical facilities. Together with the public's hesitancy to present to primary or secondary care, for new and established cardiovascular diseases, this has resulted in important changes in hospital admissions for cardiovascular conditions (Table 1).<sup>3–22</sup> Most reports have consequently described a significant reduction in admission rates, including for acute coronary syndromes and acute heart failure.<sup>3,8,14,16,17,23</sup> Patients often presented later, sicker, and with a higher prevalence of comorbidities.<sup>5,17,23</sup>

Moreover, in-hospital management changed: patients with cardiovascular conditions requiring admission were more frequently admitted to general medical wards, and had shorter lengths of stay and increased complication rates for invasive procedures.<sup>7,8,14,16,19</sup> In this situation, despite lower absolute admission numbers, the resilience of healthcare systems to accommodate patients with more advanced disease was limited, ultimately leading to higher in-hospital mortality rates.<sup>5,7,13–15,19</sup>

Denmark promptly implemented local restrictions and experienced a relatively low burden of COVID-19 compared with some other countries.<sup>3</sup> This might have resulted in the preservation of specialist hospital care that, despite the reconfiguration of medical services, contributed to avoid the excess in-hospital mortality compared with non-pandemic periods.<sup>3</sup> Nonetheless, the implications for countries that have been more aggressively affected have been more unfavourable,<sup>5,7,13–15,17,19,23–25</sup> and the findings of Butt *et al.*<sup>3</sup> should be interpreted in the context of the wider sequelae of COVID-19.

On the other hand, less is known about out-of-hospital mortality due to cardiovascular disease during the COVID-19 pandemic. To date, this is one of the few reports addressing this important topic. As reported by Butt *et al.*, out-of-hospital mortality was significantly higher in Denmark during the lockdown, although it had a limited impact on overall mortality.<sup>3</sup> The higher out-of-hospital mortality also reported in other countries has been attributed to lockdown restrictions and reluctance to seek medical care.<sup>3,7,24</sup> Furthermore, delayed provision of medical help resulted in higher rates of out-of-hospital cardiac arrest during the COVID-19 pandemic, which was associated with increased response times and a significant reduction in advanced life support for these patients.<sup>25</sup> Together with increased in-hospital mortality, these factors have combined to worsen overall outcomes and result in significant excess mortality for patients with cardiovascular diseases<sup>7,24</sup> (*Graphical abstract*).

To date, while we continue to experience further waves of the COVID-19 pandemic, exacerbated by the advent of new strains of the virus, we can only as yet hypothesize about a detailed and comprehensive evaluation of the global collateral damage. The potential global implications for patients with cardiac disease relate to missed or delayed diagnosis, reduced availability of routine testing, interrupted referral pathways, lack of proper and timely optimization of medical treatment, prevention of exacerbations, postponed or cancelled follow-ups, and reduced specialist care. Similarly, disruption in research, education, teaching, training, and personal growth for healthcare professionals will compound these insults. Furthermore, several hitherto uncharacterized features of the pandemic are likely to have affected cardiovascular health, including lifestyle changes, reduction in physical exercise, home working, disrupted education for pupils, reduced social interactions, more perilous mental health, and socioeconomic hardship. These may play a substantial role, in both the short and long term, in how history views the interplay between the COVID-19 pandemic and cardiovascular disease. These and other, as yet undetermined, social and medical factors will undeniably contribute to the longstanding impact of the COVID-19 pandemic. Therefore, the available reports of short-term out-of-hospital mortality are certain to be only the tip of the iceberg.

While it appears crucial to continue specialist and uninterrupted medical care for at-risk groups, including those with cardiovascular conditions, further research is needed to better understand the full

scope of contributory factors to cardiovascular mortality during the COVID-19 pandemic, beyond infection rates. This information is essential to determine the best approaches to caring for patients, improving outcomes in extreme conditions, and minimizing collateral damage in future outbreaks. Novel analyses, like the elegant one published in this issue of the journal,<sup>3</sup> are needed and welcome to address direct and indirect consequences of the pandemic. However, while comprehensive research will help us better understand the implications for patients with cardiovascular disease, for now, the full effect of the COVID-19 pandemic on cardiovascular disease cannot yet be seen. Only history will reveal the depth of the iceberg.

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