



Global spotlights

Is COVID-19 the deadliest event of the last century?

Riccardo Di Pietro¹, Simone Calcagno¹, Giuseppe Biondi-Zoccai (b^{2,3}*, and Francesco Versaci (b¹)

¹UOC UTIC Emodinamica e Cardiologia, Santa Maria Goretti Hospital, Via Antonio Canova, 04100 Latina, Italy ²Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Corso della Repubblica 79, 04100 Latina, Italy³Mediterranea Cardiocentro, Via Orazio 2, 80122 Napoli, Italy

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Historia vero testis temporum, lux veritatis, vita memoriae, magistra vitae, nuntia vetustatis, qua voce alia nisi oratoris immortalitati commendatur?

By what other voice, too, than that of the orator, is history, the witness of time, the light of truth, the life of memory, the directress of life, the herald of antiquity, committed to immortality?

Cicero, De Oratore

Cicero's quote poignantly embodies history as a life. Despite the passing of more than 2000 years, this statement is still relevant today. Indeed, according to people born in the second half of the 20th century, the most grievous cause of loss of lives was Second World War (World War II,: WWII), with 75 million deaths between 1939 and 1945 (Figure 1).¹ But: this global war was not the worst cause of fatalities of the last century (Table 1). Before WWII, in 1918, the Spanish flu due to the H1N1 virus: was the deadliest pandemic in human history.² Its death toll is typically: estimated to be between 50 and 100 million during only 12 months, divided in four main waves. It is true that there have been other pandemics since 1918, but none of them as disastrous as the Spanish flu. From these: pandemics the world learned several lessons and measures to deal with them, including social distancing, wearing masks, avoiding public gatherings, caring for health care professionals, quarantine, and isolation.³ Luckily, after WWII, there were no more global conflicts, and this time lapse could be due to the awareness of state leaders of the necessity of avoiding a world conflict, especially after the advent of nuclear weapons. Evidently, a current war would express a human madness of even greater magnitude than the ones from the past.

Until 2019, it was thought that the lessons of the H1N1 pandemic had provided us appropriate knowledge for the management of new pandemics, just like what happened in 2003 with severe acute respiratory syndrome (SARS). Yet, 2020 clearly invalidated this theory. On 31 December 2019, the Wuhan Municipal Health Commission in Wuhan City, Hubei Province, China, reported a cluster of pneumonia cases (including seven severe cases) of unknown aetiology, with a common reported link to Wuhan Huanan Seafood Wholesale Market, a wholesale fish and live animal market (*Figure 2*): it was the beginning of a new pandemic.⁴

The International Committee on Taxonomy of Viruses announced severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) to be the name of the new virus on 11 February 2020 and, on the same date, the World Health Organization (WHO) announced that the disease caused by the novel coronavirus would be named COVID-19 (COronaVIrus Disease 19).⁵ It took 3 months, more than 148 000 total cases of COVID-19 and more than 4000 deaths before WHO explicitly stated that COVID-19 should be characterized as a pandemic. From March 2020, governments have decided independently for the use of patient isolation, social distancing, face masks, and local/ regional/national lockdowns in order to contain and mitigate the diffusion of SARS-COV2. In April 2020, the New England Journal of Medicine highlighted the risk of transmission with aerosols and fomites, and WHO provided clear recommendations for masks in healthcare and community settings. Nevertheless, in 12 months of pandemic due to SARS-COV2, the world counts more than 100 million cases and almost 3 million deaths.⁶ It would seem that the most frequent cause of deaths since December 2019 is COVID-19, given its high contagiousness and capability to cause severe disease, especially in the elderly and the frail.

Despite the dreadfulness of infectious diseases, other factors also continue to heavily impact on the global burden of disease. For instance, environmental changes and social conditions have increased the prevalence of what once were relatively obscure ailments, e.g. myocardial infarction and lung cancer, and according to the latest data from WHO, cardiovascular disease (CVD) is still the first cause of death globally, taking an estimated 18 million lives every year: more than any war or pandemic!

*Corresponding author. gbiondizoccai@gmail.com; giuseppe.biondizoccai@uniroma1.it

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K A I AND SAVE YOUR LIFE! The Emergency That New Cosinuin One Cire is Derend the Facilities of the North Organization The RED CROSS has come to the assistance of the Board of Health, Doctors and nurses can not be obtained to take care of the afflicted. You must wear a mask, not only to protect yourself but your children and your neighbor from influenza, pneumonia and death Alber .. A GAUZE MASK IS 99 PROOF AGAINST INFLUENZA m. Thus also do not won' it WEAR MASKS Alameda County Relief Committee Outland Cleaning Har Outland Cleaning of - 10

Figure I The first page of the Charlotte Observer on 15 August 1945 (top panel). A family picture (bottom left panel), and a newspaper page on the use of face masks during the Spanish flu (bottom right panel).

Table I Principal global causes of death in the last 100 years (updated on 7 April 2021)

Massacre	Period/years	Number of deaths
Spanish flu (H1N1 influenza A virus)	1918–19	50–100 million
Asian flu (H2N2 Influenza A virus)	1957–58	1–4 million
Swine flu (H1N1/09 influenza A virus)	2009–10	18 449
AIDS (HIV virus)	1981-present	35 million
Second World War	1939–45	75 million
Vietnam War	1955–75	5 million
Cardiovascular disease	2017	17.8 million
Cancer	2018	9.6 million
Lung cancer	2018	1.76 million
COVID-19 (SARS-CoV-2 virus)	1 January 2020 to 7 April 2021	2 874 372

AIDS, acquired immunodeficiency syndrome; COVID-19, COronaVIrus Disease 19; HIV, human immunodeficiency virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



In the current COVID-19 era, mass media are encouraging 'stay-athome' policies, with healthcare systems reducing elective procedures and surgeries. Collectively, such strategies have resulted in an important decrease in the number of patients admitted for non-COVID-19 conditions. Accordingly, reductions in admissions for acute STelevation myocardial infarction (STEMI) have been evident, together with increases in out-of-hospital cardiac arrests and late presentations of STEMI (including those complicated by cardiogenic shock, apical thrombus, or wall rupture) (*Figure 3*).^{8,9} There are a lot of COVID-19related reasons that may explain the declining incidence of STEMI, both in a positive and negative way. For instance, favourable lifestyle changes may include remote work and education, with lower stress burden. Most importantly, lockdowns have dramatically reduced industrial activities, traffic, and pollution, an established precipitant of STEMI.¹⁰ Lastly, closure of restaurants and non-essential services may possibly have improved diets by controlling salt intake, decreasing consumption of fried foods, and increased uptake of fruits and vegetables. Conversely, patient fear of contracting COVID-19 in hospitals may force individuals to stay at home even when symptomatic, forcibly underestimating their symptoms.

Despite these arguments, to date, there are no conclusive data to definitively explain the reduction in hospital admissions for acute coronary syndromes, and clarifying whether this is expression of prevention or consequence of an indirect increase in deaths from CVD. The latter scenario would unfortunately make the COVID-19 pandemic even

Wuhan Municipal Health Commission notified the outbreak of pneumonia

27 cases of pneumonia found, no human-to-human transmission has been found

Hubei Daily News (Reporter Yu Jinyi) On December 31, 2019, the Wuhan Municipal Health Commission notified the epidemic situation of pneumonia in Wuhan: Recently, some medical institutions in Wuhan received multiple cases of pneumonia patients, all of which were related to South China Seafood City. After receiving the report, the Wuhan Municipal Health Commission immediately carried out case searches and retrospective investigations related to South China Seafood City in the city's medical and health institutions. Twenty-seven cases of pneumonia have been found, of which 7 are in serious condition, while the remaining cases are in stable and controllable condition, and 2 cases have improved and are scheduled to be discharged in the near future. The clinical manifestations of the cases were mainly fever, a few patients had difficulty breathing, and chest radiographs showed infiltrating foci of both lungs. At present, all cases have been treated in isolation, follow-up investigation and medical observation of close contacts are underway.

Wuhan has organized clinical medicine, epidemiology, and virology expert consultations in Tongji Hospital, Provincial Center for Disease Control and Prevention, Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan Infectious Disease Hospital, and Wuhan Center for Disease Control and Prevention. The experts have returned from illness and treatment. , Epidemiological investigations, preliminary laboratory tests and other aspects of the analysis believe that the above cases are viral pneumonia. So far, no obvious human-to-human transmission has been found in the investigation, and no medical personnel have been infected. The detection of the pathogen and the investigation of the cause of the infection are ongoing.

Figure 2 Wuhan Municipal Health Commission notification of the outbreak of pneumonia on 31 December 2019.



Figure 3 Reductions in admissions for acute myocardial infarction (AMI) across Italy between 12 March and 19 March 2019 and between 12 March and 19 March 2020 (reprinted from De Rosa *et al.*⁹). NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

more cruel than we currently know. Similarly, the post-COVID-19 era (hopefully foreseeable given the ongoing vaccination campaign) remains difficult to predict, especially in terms of impact on and of CVD. In conclusion, the winner for the worst massacre award of the last 100 years is not yet known. Only history will reveal it, being the teacher of life for the umpteenth time.

Conflict of interest: G.B.-Z. has consulted for Cardionovum, Bonn, Germany, Innovheart, Milan, Italy, Meditrial, Rome, Italy, and Replycare, Rome, Italy.

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