

COVID-19-related excess mortality – an overview of the current evidence

Nadmierna śmiertelność związana z COVID-19 – przegląd aktualnych informacji

Aleksander Zińczuk, Marta Rorat, Tomasz Jurek

Department of Forensic Medicine, Wroclaw Medical University

Abstract

Analysis of excess deaths, defined as the difference in the total number of deaths in an emergency compared to the number of deaths expected under normal conditions, allows a more reliable assessment of the impact on health systems caused by the global threat of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2). So far, data for the two years of the pandemic (2020-2021) indicates the occurrence of 14.9 million excess deaths according to WHO (World Health Organization) estimates. The purpose of the analysis conducted was to define the concept and identify the causes of excess mortality during the COVID-19 pandemic. Inconsistent and unreliable death registration systems; overburdened health systems in low- and middle-income countries; reduced access to medical services for patients with health problems other than COVID-19; the introduction of social distancing and lockdown rules, which translated into increased deaths from psychiatric illnesses and addictions; political considerations and media messages that interfered with vaccination acceptance and adherence; and the additional impact of other natural disasters (hurricanes, floods, drought) were identified as the most important reasons for excess deaths occurrence. The correct identification of country-specific factors and the correct response and countermeasures taken appear crucial in terms of limiting the negative impact of the current pandemic, but also of future threats of a similar nature, in order to reduce excess deaths.

Keywords

SARS-CoV-2, death, global mortality, pandemic

Streszczenie

Analiza zgonów nadmiarowych definiowanych jako różnica w całkowitej liczbie zgonów w sytuacji kryzysowej w porównaniu do liczby zgonów oczekiwanych w normalnych warunkach, pozwala bardziej wiarygodnie ocenić wpływ globalnego zagrożenia jakim okazał się nowy koronawirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronaviruse-2) na systemy opieki zdrowotnej. Dotychczasowe dane dotyczące dwóch lat pandemii (2020-2021) wskazują na wystąpienie 14.9 miliona zgonów nadmiarowych według szacunków WHO (World Health Organization). Celem przeprowadzonej analizy było zdefiniowanie pojęcia oraz wskazanie przyczyn występowania nadmiarowych zgonów w trakcie pandemii COVID-19. Jako najważniejsze przyczyny ich pojawienia się należy uznać: niespójne i mało wiarygodne systemy rejestracji zgonów; przeciążenie systemów opieki zdrowotnej w krajach o niskich i średnich dochodach; ograniczenie dostępu do świadczeń medycznych dla pacjentów z innymi niż COVID-19 problemami zdrowotnymi; wprowadzenie zasad dystansu społecznego oraz lockdownu, co przełożyło się na zwiększenie liczby zgonów z powodu chorób psychiatrycznych i uzależnień; względy polityczne i przekaz medialny, które ingerowały w akceptację szczepień i stosowanie się do zaleceń; dodatkowy wpływ innych klęsk żywiołowych (huraganów, powodzi, suszy). Właściwa identyfikacja czynników występujących w danym kraju oraz prawidłowa reakcja i podjęte środki zaradcze wydają się kluczowe w aspekcie ograniczenia negatywnych skutków aktualnej pandemii, ale także przyszłych zagrożeń o podobnym charakterze, w celu ograniczenia liczby nadmiarowych zgonów.

Słowa kluczowe

SARS-CoV-2, zgon, globalna śmiertelność, pandemia

Introduction

Infections with the new Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), initially referred to as pneumonia of unknown cause, were first reported on 31 December 2019 by the China Country WHO Office. As early as on 5 January 2020, WHO officially announced the detection of a cluster of infections with an unknown biological agent [1]. Initial observations of the mechanism of spread of the infection and the clinical picture of the disease it causes indicated similarities with SARS-CoV-1 (Severe Acute Respiratory Syndrome Coronavirus-1) and MERS-CoV (Middle East Respiratory Syndrome Coronavirus). The increasing number of infections, confirmation of human-to-human transmission and emergence of new cases in other countries prompted WHO to declare a Public Health Emergency of International Concern (PHEIC) on 30 January 2020, while on 11 March 2020, due to the lack of control of the disease, COVID-19 (Coronavirus disease 2019) was classified as a pandemic [2], [3].

Analyzing the impact of a pandemic on public health is crucial for any national health system to identify links that are not functioning properly. Proper evaluation of the causes of death and their circumstances in the context of preventable deaths is a task that unites epidemiologists, clinicians and pathologists (including forensic pathologists) who determine the pathogenesis of death. All over the world, the first cases of COVID-19 deaths were subjected to post-mortem diagnosis [4], and further studies allowed rapid understanding of the etiopathogenesis and course of the disease, refining ways to diagnose and treat it [5], [6]. During the pandemic, there was a tendency for COVID-19 deaths to be diagnosed in almost every case of positive antigen or PCR (Polymerase Chain Reaction) test, significantly affecting epidemiology and mortality statistics. Inferring the cause of death is based on establishing causation. Not every abnormality is necessarily important in the pathogenesis of death, not every positive test result means active infection, much less disease. Lack of diagnostic insight leads to a false assessment of the mortality structure with omission of its important elements not directly related to coronavirus disease incidence. This could be very important for learning from the effects of the pandemic and, in the event of further global threats, for increasing the number of deaths that could have been avoided. For this reason, in the authors' opinion, it is necessary to present many different aspects of mortality during the COVID-19 pandemic.

The rapidly increasing number of cases of respiratory failure in the course of SARS-CoV-2 infection, which required hospitalization and specialized treatment, significantly limited the capacity of the health care system to provide services to other patients in need. Initially, only selected centers, particularly infectious diseases wards/hospitals, provided care for patients with COVID-19. Lack of knowledge about the mechanisms of virus transmission and action; organizational chaos due to lack of recommendations, limited access to personal protective equipment, and unpreparedness of medical entities for an epidemiological disaster; coupled with fear of the medical personnel, resulted in greatly impaired access to



many procedures and specialists. All this had an obvious impact on the number of deaths, because in addition to the cases caused by SARS-CoV-2, there were also deaths that were an indirect effect of the pandemic (so-called non-COVID victims of the pandemic). This is an issue that is difficult to assess, as it also involves a critical assessment of the correctness of medical personnel's conduct and systemic errors made by health care managers.

The analysis of the available data on excess mortality related to the COVID-19 pandemic aims to define the issue, identify the causes of their occurrence, and establish common areas to create a coherent strategy for responding to future pandemic biological threats. The literature review was performed on 11 May 2023 in the Pubmed database using the keywords: COVID-19, SARS-COV-2, excess deaths, excess mortality.

Excess Deaths

Excess deaths are considered to be "the difference in the total number of deaths in a crisis compared to those expected under normal conditions" [7], [8]. This is a concept used to assess the impact of a threat on the number of deaths during a crisis, taking into account intermediate elements such as the restrictions implemented or the overloading of the health care system, which more reliably reflects the true scale of the problem [9], [10]. Assessing excess deaths is also an indicator to show how prepared a country's health system is for a mass event. and to indicate social inequalities, such as those related to gender, age, wealth, ethnicity [11]. It should be noted that excess death rates report aggregate numbers of deaths due to various causes, such as an increase as a result of lack of access to health care, but also a decrease due to a reduction in traffic accidents after the introduction of movement restrictions due to the pandemic [10]. The COVID-19 pandemic is not the first global event to use this parameter. The impact of the so-called "Spanish flu" pandemic in 1918 and other mass disaster-type events (Hurricane Maria in Puerto Rico) was previously evaluated in this way [12], [13]. In practice, excess deaths are the difference between observed deaths and those expected based on the averages from previous years.

Excess Mortality

Excess mortality is the ratio of the number of observed deaths to expected mortality in percentage terms. The higher it is, the higher the number of all additional deaths above the expected ones, a negative value means mortality lower than average. Rates of excess mortality caused by COVID-19, in addition to the infection itself, are related to overall mortality rates in a country and to the age structure of the population - especially the number of >65 year olds, the group most at risk of death [14], [15]. For this reason, the COVID-19 pandemic is referred to as a syndemic, or synergistic epidemic, during which the virus causes deaths primarily in key populations (the elderly and people with concomitant diseases) [16]. It is emphasized that the impact of COVID-19 on the number of excess deaths related to the mechanisms of health systems under the impact of the pandemic may be spread over time and also occur in subsequent years, not only during the period of death registration [17].

In order to comprehensively assess deaths during the pandemic, a WHO Technical Advisory Group on COVID-19 Mortality Assessment was established in February 2021. Based on its analysis, WHO states the number of victims of the 2020 pandemic to be at least 3 million, about 1.2 million more than the reported number of COVID-19-related deaths in that period. However, the data came from only two areas - European and American, while the others lacked sufficient data for calculations [7]. In contrast, the latest available report covering the period from 1 January 2020 to 31 December 2021 found that the number of excess deaths was 14.9 million (13.3-16.6), 84% of which occurred in middle-income countries [18]. A higher figure for this time frame was reported by the authors of an analysis published in The Lancet, according to which the number of excess deaths by 31 December 2021 reached 18.2 million globally [95% uncertainty interval (UI) 17.1-19.6], and the excess mortality rate reached 120.30 [95% UI 113.1-129.3] per 100,000, with the highest rates per 100,000 population in Andean Latin America (511.9), Central (315.7) and Eastern (345.2) Europe, Southern Sub-Saharan Africa (308.6) and Central America (274.4)[17]. The country that accounted for 22.3% of the globally analyzed excess deaths is India with 4.07 million (95% UI 3.71-4.36) [17]. In contrast, a meta-analysis by Shang et al. covering data available from 1 January 2020 to 21 May 2022 indicates 104.84 [95% confidence interval (CI) 85.56-124.13] excess deaths per 100,000 globally. The highest rates were achieved in South America (134.02) and North America (124.63), and in Europe (122.16), as well as among people over 60 (781.74) and among men (130.10) [9]. More recent data is available for the European area. According to the information provided by Eurostat, February 2023 was the first month since the start of the pandemic in which there were no excess deaths for the entire European Union (EU) area - the excess mortality rate dropped to -2.3%. In contrast, analysis of the entire EU pandemic period to date indicates that there have been 4 peaks of excess mortality the highest one in November 2020 (40.0%, in Eastern European countries reaching over 90.0%), in November 2021 (26.5%), in April 2020 (25.2%) and in April 2021 (20.9%) [19].

Causes

The gap between the recorded number of COVID-19 deaths and the actual number of pandemic victims is filled by excess deaths, the number of which reflects the actual impact of the pandemic on public health. When discussing the causes of the occurrence of these deaths, it is important to note the strongly varying background of this issue.

Diagnosis and Registration of Deaths

Since their inception, COVID-19 death registration systems have been based on a positive test result for SARS-CoV-2. Later on, with the possibility of diagnosis based on symptoms and results of additional laboratory and imaging tests, but laboratory confirmation was usually required anyway [10]. It should also be noted that testing policies varied from country to country and from pandemic stage to pandemic stage [10]. This has obvious implications. Where access to diagnostics is limited and the number of symptomatic patients is high, there is a significant overload on the system and an underestimation of the number of COVID-19 cases identified, which translates into underestimating deaths from this cause and showing more excess deaths [20]. Such a relationship was described especially at the beginning of the pandemic in China. Based on a mathematical model, the authors of one publication showed that up to 86% of COVID-19 cases were unrecognized prior to the implementation of travel restrictions within Wuhan on 23 January 2020, translating into a rapid global spread of the infection [21]. Similar observations have been found in other countries around the world, while emphasizing the importance of early isolation in the absence of access to widespread and efficient diagnostics [22]-[25].

An additional diagnostic concern is the sensitivity and specificity of PCR tests, which depends, among others, on the type of test, the timing of the test, and where and how the biological material is collected for testing [26]. False-negative PCR test results were obtained at the beginning of the pandemic in up to 29% of cases [27]. It is emphasized that a single negative result of such a test in a situation of high probability of disease (e.g., based on the clinical picture) is not sufficient to exclude the disease, especially when the test was developed in a population with a large number of cases, and is used in conditions where there are fewer cases, which translates into a higher number of false-negative results [10], [14], [28]. Incorrect test results affect death registries based on the need for a positive result, especially if a negative test result was obtained before the patient died [29].

Overburdening the health system may have led to COVID-19 deaths being attributed to iatrogenic causes - such as the use of harmful pharmacotherapy, as in the case of hydroxychloroquine, or inappropriate oxygen therapy [30]–[33]. The issue of iatrogenic harm associated with the use of therapies with no proven efficacy in the treatment of COVID-19 was addressed in the course of establishing the respective WHO recommendations. The current guidelines, dated 13 January 2023, include summaries of studies arguing against the use of hydroxychloroquine (30 randomized clinical trials), lopinavir-ritonavir (7 randomized clinical trials) and ivermectin (16 randomized clinical trials), detailing the adverse effects caused by these therapies [34]. However, there was no clear effect on increased mortality in the groups taking the drugs analyzed.

It should be emphasized that the difference between the actual and laboratory-confirmed number of COVID-19 deaths is only a fraction of the total number of excess deaths, although the difference indicates the quality of national health systems' preparation for the pandemic [35]. Post-mortem diagnosis of COVID-19-related deaths has not been routinely conducted on a large scale. The time of the COVID-19 pandemic, especially its beginning, was a period when the number of autopsies performed dropped dramatically. In April 2020, when some 150,000 deaths from SARS-CoV-2 were reported, only 16 autopsy descriptions were published in the literature, with more than half of the autopsies incomplete [36]. This is a disadvantageous situation due, among others, to uncertainty about the proper classification of the cause of death, as well as the lack of key information about the pathological changes caused by the virus [37]. As a rule, a full post-mortem diagnosis includes not only an autopsy with histopathological, toxicological or microbiological examinations, but also a detailed analysis of the patient's medical history, medical data or history from witnesses to the last days of the patient's life - which often allows verification of the causes of death assumed by clinicians. In the case of COVID-19, patient autopsies were limited to single or serial case studies to clarify the etiopathogenesis and nature of the pathologies caused by the disease, with occasional indications for forensic medical autopsies [38]-[40]. For this reason, the most thorough investigations into the causes and circumstances of death by pathologists and forensic pathologists have little impact on epidemiological determinations of the causes of excess mortality.

Looking at the issue from the other side - during successive periods of pandemics, further effective methods of fighting the infection, such as targeted therapies and vaccines, were acquired, which are particularly important in protecting key populations [14]. Access to reliable, rapid diagnostic tests has improved, with most patients having tests performed in primary care, which has significantly improved the detection of infections, including those asymptomatic or with few symptoms. Deaths of people with a history of positive results, often due to lack of proper case analysis, were routinely classified as caused by infection, which translated into overestimation of the total number of COVID-19 deaths [14], [41].

The term "death with SARS-CoV-2 infection" has appeared in the literature [10], [42]. This described, inter alia, situations in which the death was a result of a crime, suicide or road traffic accident, and a post-mortem test positive for SARS-CoV-2 was obtained [43]. In 2020, WHO issued a document with instructions for recognizing COVID-19 as a direct cause of death. According to the proposed definition, it is "a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID disease" [44]. Currently, in the dominant phase of the Omicron variant, this issue is particularly relevant, due to the decidedly milder nature of the infection [45], [46]. This requires a meticulous analysis of the case before classifying it as a COVID-19 death [10], [47].

An additional motive for improper reporting of the cause of death may have been the funding of benefits depending on



Underestimation of the number of deaths	Overestimation of the number of deaths
Lack of testing at the start of the pandemic.	Attribution of death due to COVID-19 in those with a positive test result and no signs of infection or respiratory failure.
The use of low-sensitivity tests.	latrogenic deaths (use of incorrect therapy) attributed to COVID-19.
Lack of adequate technical facilities and infrastructure for diagnostics.	Lack of post-mortem diagnosis and verification of causes of death.
Lack of reliable death registers.	Better funding of COVID-19 diagnosis by healthcare funding authorities.

 Table 1. Summary of factors affecting the reliability of COVID-19 death rate data

 Tabela 1. Podsumowanie czynników wpływających na wiarygodność danych dotyczących współczynnika zgonów z powodu Covid-19

the diagnosis code. In some health systems, temporarily including Poland, making a COVID-19 diagnosis according to the ICD-10 (International Classification of Diseases, Tenth Revision) classification has been associated with better valuation of services, in others - even with compensation payments to families, including India [48].

Reliability and consistent maintenance of medical records is a very important factor in determining the reliability of statistical data. The shortcomings of electronic medical records were highlighted - an analysis of electronic data, and data in paper form, of 516 patients of a London hospital, showed differences of 40% of cases. This also translates into the veracity of the conclusions drawn from the interpretation of these documents [49]. WHO notes that the reliability of the data is influenced by a well-functioning statistical system that allows for efficient recording and evaluation of population demographics. For the African region, the lowest death registration rates in the world are found (about 10%), resulting in underestimation of deaths and lack of reliable epidemiological data from the area [7], [50]. In contrast, an analysis of death certificates from the US shows a high correspondence between the actual number of deaths and the reports according to the ICD-10 classification [51].

In sum, with successive periods of the pandemic, diagnostic advances and changes in the dominant variants, there was a downward trend in the number of underestimated deaths and an increase in the overdiagnosis of COVID-19 as the cause of death, which obviously translated into a global assessment of excess mortality – these factors are summarized in Table 1.

Political Considerations Affecting Reporting

Pandemic in some countries has also proven to be a tool of political gamesmanship to keep voters with a particular party. The applied narrative of the authorities, in which there was no clear message about the positive effects of vaccination or the actual number of deaths, and the failure to admit their own mistakes in preparing and organizing the health system to deal with the pandemic, caused a false sense of security among the public, which resulted, among others, in challenging vaccinations and translated into a large number of excess deaths in the subsequent waves of the pandemic in Poland [52]. In the US and South Korea, political views were related to perceptions of the risk of viral infection being significantly higher, which the US researchers found to be reflected in the use of masks, frequency of vaccinations, number of COVID-19 cases and SARS-CoV-2 deaths [53]-[56]. The use of political disinformation, the undermining of the authority of the health ministry, and the promotion of pseudoscience by the Brazilian president at the beginning of the COVID-19 pandemic, were important underpinnings of the country's subsequent health crisis, as highlighted in various studies [57]–[59]. A study from Italy revealed a significant influence of politics and the media on the perception of scientific messages and scientific authorities during the pandemic [60]. This shows the importance of properly conducted political leadership based on clear principles and in cooperation with authorities, in order to make sound decisions that will translate into later success in the fight against the pandemic. The effectiveness of such measures has been confirmed in Asian countries [61].

Impact of Lockdown and Other Restrictions on the Occurrence of Certain Medical Events

From the very beginning of the pandemic, non-pharmaceutical interventions (NPIs), such as social distance, lockdown and movement restrictions, were undertaken to reduce the number of COVID-19 cases and deaths [62], [63]. However, it transpired that these restrictions also had a direct impact on the number of excess deaths, as a result of the occurrence of (mostly incorrect) non-COVID-19 events related to the provision of medical services. The impact on the number of excess deaths was greater the longer and more intensive the restrictions applied, as found in an analysis of countermeasures taken in 22 European countries [64]. As a consequence of lockdown, the number of hospital emergency department admissions and patient hospitalizations for general causes and cardiovascular events decreased, as studies from Germany, England and Greece have shown [65]–[69]. In the US, it has been estimated that the pandemic affected a 12% decrease in emergency care reporting for adult patients and more than 30% for elective reasons [70]. There has also been a catastrophic decline in the number of detected and treated cases

of tuberculosis, which had been previously the most common infectious cause of death worldwide [71]. According to WHO reports, this has translated into an increase in tuberculosis-related deaths and an increase in cases of drug-resistant tuberculosis [72]. A significant decline in cancer diagnoses has been found in numerous countries as a result of a decrease in the number of screening tests performed and restrictions on cancer treatment, such as the choice of systemic treatment regimens that are less effective but carry a lower risk of patient hospitalization [73]–[76]. In particular, there was a significant decrease in the number of surgical procedures performed compared to other therapies (-33.9% vs. -12.6%) [77]. A reduction in vaccination rates has also been shown globally for the number of vaccinations with the third dose of DTP (diphtheria-tetanus-pertussis) and the first MCV (measles-containing vaccine) [78]. In India and Namibia, a decline in hospital births of about 50% has been reported [79], [80]. The use of existing resources (personnel and medical infrastructure) to combat COVID-19 has resulted in restrictions on access to medical assistance for patients with other disorders. This has been shown to have been responsible for about 20% of excess deaths in Italy and England and up to 62% in Greece during the early stages of the pandemic [9], [69], [81], [82]. The main reason was lack of access to outpatient care and surgical procedures [69]. Similar reasons for the high number of deaths during the pandemic were found in Poland [83].

Isolation and restrictions on movement have also translated into mental health problems - an increase in depressive disorders, suicide and drug overdose deaths [84], [85]. According to the data published by the Centers for Disease Control and Prevention (CDC), by the end of May 2020 alone, there were more than 80,000 drug overdose deaths in the US, the highest recorded so far in analyzed 12-month periods [86]. In addition to social distancing requirements, the factors underlying suicides were financial stressors related to reduced or no income, more frequent alcohol abuse and lack of access to existing psychiatric care [87]. This is a phenomenon also observed during other pandemics, including the Spanish flu in 1918 in the US and SARS in Hong Kong in 2003 [88]–[90].

One of the positive effects of the reduction in population movement, the global use of personal protective equipment and hand hygiene, has proven to be a decrease in the number of deaths caused by exposure to certain risk factors, such as a reduction in traffic accidents [91]–[93]. Another effect of the pandemic was a significant reduction of up to 80% in cases of influenza or RSV infection, including deaths caused by these viruses [94]–[100].

Other Natural Disasters During the Period of the COVID-19 Pandemic

The vast majority of excess deaths during the pandemic were related to COVID-19. The co-occurrence of other natural disaster events affecting higher death rates added to the catastrophic nature of the pandemic [17]. Of particular importance were events that occurred before the peaks of COVID-19 incidence, which translated into an accumulation of negative factors, such as the need to evacuate the population, the inability to maintain a safe distance and isolate sick people, limited access to medical infrastructure and pharmaceuticals [101], [102]. Such events have occurred in many areas of the world, including: tropical cyclone Yasa in Fiji, Vanuatu, Tonga and the Solomon Islands: Hurricane Laura in the southern US; floods in South Africa; Cyclone Amphan in Bangladesh and West Bengal; heat waves and droughts in Zimbabwe, the US and Europe [101], [103]. According to the data reported by Eurostat, excess mortality in August 2022 reached 13.9%, almost double that of the same period in 2020 (7.6%). A heat wave that covered Europe at the time is believed to be the cause of that condition [19]. The authors of a theoretical mathematical model showed that the eruption of Vesuvius in Campania, Italy, during the COVID-19 outbreak, would cause up to 8-fold higher mortality in the area compared to the situation without such an event [101]. These results show that there are also numerous independent factors occurring during a pandemic that can dynamically affect the overall number of deaths.

Systems with Poor Health Care Quality

Even before the pandemic, low- and middle-income countries (LMICs) showed some 15.6 million excess deaths, 5 million of which were related to access to a low-quality health system [104]. The COVID-19 pandemic highlighted gaps in access to Intensive Care Units (ICUs), shortages of trained medical personnel, insufficient diagnostic facilities, and limited access to pharmaceuticals, personal protective equipment and vaccines in developing countries [105], [106]. The authors of an analysis of the impact of the pandemic on excess mortality published in The Lancet emphasize that the high death rates for such countries can probably be attributed at least in part to diagnostic deficiencies, limited access to certain medical practices, and ambiguous guidelines for recording COVID-19 deaths [17]. Analyses from the respective countries confirm these reports. In Peru, the total number of deaths during the pandemic period consisted, among others, of those related to the limited availability of ICU beds and qualified personnel to work in such units, oxygen shortages, lack of testing, and lack of clear guidelines and support from medical authorities [93]. The data from Mexico indicates an increased exposure to COVID-19-related adverse events, but also an underestimation of the number of deaths due to it and a higher rate of excess deaths in socially marginalized populations, which additionally have poorer access to medical care as a result of transport restrictions [107], [108]. In comparison, the number of excess deaths due to the COVID-19 pandemic in some high-income countries (Belgium, Sweden), which conduct meticulous death reporting, was little related to the impact of COVID-19 on deaths from other causes, such as chronic diseases [17]. Oceania was the least affected area in Shang et al.'s meta-analysis in terms of the magnitude of excess deaths, as it had a lower-than-expected number of deaths from any cause (a rate of -32.15 per 100,000) [9]. Among the reasons cited for this in Australia and New Zealand are a well-functioning medical surveillance system and strict rules for detecting and monitoring COVID-19 cases, as well as the substantial support provided to at-risk groups [109], [110].

Analysis of the location of deaths (home, hospital, long-term care center) also provides important data. It has been noted that more deaths attributed to COVID-19 were found in high-income countries, where hospital and elderly care is provided at a higher level, mainly among patients in terminal conditions residing in long-term care facilities [14]. This has been influenced by a number of factors, primarily better diagnostics, but also a higher number of infections in clusters of susceptible people [111]–[113]. It is also known that the elderly population (aged >60) is particularly susceptible to the occurrence of excess deaths, as shown in the meta-analysis by Shang et al. and reports from various countries [9], [10], [114], [115]. In contrast, an analysis of causes of death in one hospital in Spain at the start of the pandemic found that 15% of 128 patients with a positive test for SARS-CoV-2 died from causes other than Acute Respiratory Distress Syndrome (ARDS) or complications of infection ("death with SARS-CoV-2 infection"). Among the reasons for this are the susceptibility of an older group of patients to decompensation of their chronic conditions and the inability to use supportive therapies (such as systemic rehabilitation) during hospitalization in isolation [116]. In this group, more deaths are attributed to COVID-19, although the recognition of SARS-CoV-2 infection as a cause of death among the elderly, and especially those in the terminal condition, without a thorough analysis of each case, is a matter of debate, as partially discussed above. Hence, the high number of excess deaths in this group, especially in low-income countries. Inferior diagnostic capabilities, marginalization of their health problems and reduced access to existing medical ser-



vices during a pandemic particularly hit populations burdened by other health problems that come with age [9].

Summary

The full impact of the COVID-19 pandemic on the world population cannot be measured by the incidence and deaths from the infection alone. One additional parameter, which depends on many different factors, is excess mortality. Proactively searching for the causes of excess mortality is extremely important for any country to detect weaknesses in the organization of the health care system and, at the same time, implement adequate safety mechanisms. Without knowing, analyzing and significantly eliminating risk factors for excess mortality during the current pandemic, we will not avoid increased mortality during other emergencies. Currently, after three years of COVID-19, despite a decrease in the severity of the infection and countries adapting to the new situation, some of them are still recording excess mortality. This may indicate a delayed effect of the pandemic in these countries.

Analysis of excess mortality carries certain limitations, including those related to the quality of the data used to assess them. Death registration systems that function in a limited way do not allow to obtain certain data. In addition to epidemiological data derived from collections of death certificates or statistical codes of disease entities, post-mortem investigations based on analysis of baseline medical data, circumstances of death and post-mortem diagnostic results should be considered on a larger scale. The assessment of excess mortality in the context of the global impact of the COVID-19 pandemic is only an estimate, but nonetheless, the lack of a coherent and consistent epidemiological and clinical strategy; limitations in access to health care and organizational errors; as well as lack of intensive support for groups at high risk of death, can be considered as the main reasons for its occurrence.

date of submission | data nadesłania: 02.07.2023 acceptance date | data akceptacji: 11.07.2023

Corresponding author: Aleksander Zinczuk Department of Forensic Medicine, Wrocław Medical University ul. J. Mikulicza-Radeckiego 4, 50-372 Wrocław, Poland e-mail: aleksander.zinczuk@student.umw.edu.pl

References

- "Pneumonia of unknown cause China." https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON229 (accessed May 11, 2023).
- [2] "Archived: WHO Timeline COVID-19." https://www.who.int/news/item/27-04-2020-who-timeline---covid-19 (accessed May 11, 2023).
- [3] "Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV)." https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov) (accessed May 11, 2023).
- [4] X. W. Bian, "Autopsy of COVID-19 patients in China," Natl Sci Rev, vol. 7, no. 9, pp. 1414–1418, Sep. 2020, doi: 10.1093/NSR/NWAA123.
- [5] R. G. Menezes, T. Rizwan, S. S. Ali, W.Hassan et al., "Postmortem findings in COVID-19 fatalities: A systematic review of current evidence," *Leg Med (Tokyo)*, vol. 54, p. 102001, Feb. 2022, doi: 10.1016/J.LEGALMED.2021.102001.
- [6] D. Wichmann, J. P. Sperhake, M. Lutgehetmann, S. Steurer et al., "Autopsy Findings and Venous Thromboembolism in Patients With COVID-19," https://doi.org/10.7326/M20-2003, vol. 173, no. 4, pp. 268–277, May 2020, doi: 10.7326/M20-2003.
- [7] "The true death toll of COVID-19: estimating global excess mortality." https://www.who.int/data/stories/the-true-death-toll-ofcovid-19-estimating-global-excess-mortality (accessed May 09, 2023).
- [8] F. Checchi and L. Roberts, "Interpreting and Using Humanitarian Mortality Data in Humanitarian Emergencies. A primer for non-epidemiologists," 2005, Accessed: May 11, 2023. [Online]. Available: www.ennonline.net/mortalitydataprimer
- [9] W. Shang, Y. Wang, J. Yuan, Z. Guo et al., "Global Excess Mortality during COVID-19 Pandemic: A Systematic Review and Meta-Analysis," *Vaccines* (*Basel*), vol. 10, no. 10, Oct. 2022, doi: 10.3390/VACCINES10101702.
- [10] M. Karanikolos and M. Mckee, "HOW COMPARABLE IS COVID-19 MORTALITY ACROSS COUNTRIES?," *Eurohealth (Lond)*, vol. 26, no. 2, 2020.
- [11] N. Islam, "Excess deaths' is the best metric for tracking the pandemic," BMJ, vol. 376, 2022.
- [12] R. Cruz-Cano and E. L. Mead, "Excess Deaths After Hurricane Maria in Puerto Rico," JAMA, vol. 321, no. 10, p. 1005, Mar. 2019, doi: 10. 1001/JAMA.2018.20861.
- [13] S. Dahal, M. Jenner, L. Dinh, K. Mizumoto et al., "Excess mortality patterns during 1918-1921 influenza pandemic in the state of Arizona, USA," Ann Epidemiol, vol. 28, no. 5, pp. 273–280, May 2018, doi: 10.1016/J.ANNEPIDEM.2017.12.005.
- [14] J. P. A. Ioannidis, "Over- and under-estimation of COVID-19 deaths," Eur J Epidemiol, vol. 36, no. 6, p. 581, Jun. 2021, doi: 10.1007/ S10654-021-00787-9.
- [15] M. O'Driscoll, G. R. dos Santos, L. Wang, D. A. T. Cummings et al., "Age-specific mortality and immunity patterns of SARS-CoV-2," Nature, vol. 590, no. 7844, pp. 140–145, Feb. 2021, doi: 10.1038/S41586-020-2918-0.
- [16] R. Horton, "Offline: COVID-19 is not a pandemic," Lancet, vol. 396, no. 10255, p. 874, Sep. 2020, doi: 10.1016/S0140-6736(20)32000-6.
- "Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21," *Lancet*, vol. 399, no. 10334, pp. 1513–1536, Apr. 2022, doi: 10.1016/S0140-6736(21)02796-3.
- [18] "14.9 million excess deaths associated with the COVID-19 pandemic in 2020 and 2021." https://www.who.int/news/item/05-05-2022-14.9-million-excess-deaths-were-associated-with-the-covid-19-pandemic-in-2020-and-2021 (accessed May 12, 2023).
- [19] "Excess mortality statistics Statistics Explained." https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Excess_ mortality_-_statistics#Excess_mortality_in_the_EU_between_January_2020_and_February_2023 (accessed May 12, 2023).
- [20] S. Achilleos, A. Quattrocchi, J. Gabel, A. Heraclides *et al.*, "Excess all-cause mortality and COVID-19-related mortality: a temporal analysis in 22 countries, from January until August 2020," *Int J Epidemiol*, vol. 51, no. 1, pp. 35–53, 2022, doi: 10.1093/IJE/DYAB123.
- [21] R. Li, S. Pei, B. Chen, Y. Song *et al.*, "Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2)," *Science*, vol. 368, no. 6490, p. 489, May 2020, doi: 10.1126/SCIENCE.ABB3221.
- [22] C. Rothe, M. Schunk, P. Sothmann, G. Bretzel *et al.*, "Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany," *New England Journal of Medicine*, vol. 382, no. 10, pp. 970–971, Mar. 2020, doi: 10.1056/NEJMC2001468.
- [23] I. C. Álvarez, L. Orea, and A. Wall, "Estimating the propagation of both reported and undocumented COVID-19 cases in Spain: a panel data frontier approximation of epidemiological models," *Journal of Productivity Analysis*, vol. 59, no. 3, p. 259, Jun. 2023, doi: 10.1007/S11123-023-00664-5.
- [24] R. K. Biswas, A. Afiaz, and S. Huq, "Underreporting COVID-19: the curious case of the Indian subcontinent," *Epidemiol Infect*, vol. 148, 2020, doi: 10.1017/S0950268820002095.
- [25] E. Kupek, "How many more? Under-reporting of the COVID-19 deaths in Brazil in 2020," *Trop Med Int Health*, vol. 26, no. 9, pp. 1019–1028, Sep. 2021, doi: 10.1111/TMI.13628.



- [26] N. N. Y. Tsang, H. C. So, K. Y. Ng, B. J. Cowling et al., "Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis," *Lancet Infect Dis*, vol. 21, no. 9, pp. 1233–1245, Sep. 2021, doi: 10.1016/S1473-3099(21)00146-8.
- [27] I. Arevalo-Rodriguez, D. Buitrago-Garcia, D. Simancas-Racines, P. Zambrano-Achig *et al.*, "False-negative results of initial RT-PCR assays for COVID-19: A systematic review," *PLoS One*, vol. 15, no. 12, p. e0242958, Dec. 2020, doi: 10.1371/JOURNAL.PONE.0242958.
- [28] J. Watson, P. F. Whiting, and J. E. Brush, "Interpreting a covid-19 test result," BMJ, vol. 369, May 2020, doi: 10.1136/BMJ.M1808.
- [29] J. R. Gill and M. E. Dejoseph, "The Importance of Proper Death Certification during the COVID-19 Pandemic," JAMA Journal of the American Medical Association, vol. 324, no. 1, pp. 27–28, Jul. 2020, doi: 10.1001/jama.2020.9536.
- [30] Y. Prkachin, "The Reign of the Ventilator: Acute Respiratory Distress Syndrome, COVID-19, and Technological Imperatives in Intensive Care," *Ann Intern Med*, vol. 174, no. 8, pp. 1145–1150, Aug. 2021, doi: 10.7326/M21-0270.
- [31] L. Gattinoni, D. Chiumello, P. Caironi, M. Bussana *et al.*, "COVID-19 pneumonia: different respiratory treatments for different phenotypes?," *Intensive Care Med*, vol. 46, no. 6, pp. 1099–1102, Jun. 2020, doi: 10.1007/s00134-020-06033-2.
- [32] C. Axfors, A. M. SchmitT, P. Janiaud, J. van't Hooft *et al.*, "Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19 from an international collaborative meta-analysis of randomized trials," *Nat Commun*, vol. 12, no. 1, Dec. 2021, doi: 10.1038/S41467-021-22446-Z.
- [33] N. Maggialetti, S. Piemonte, E. Sperti, F. Inchingolo *et al.*, "Iatrogenic Barotrauma in COVID-19-Positive Patients: Is It Related to the Pneumonia Severity? Prevalence and Trends of This Complication Over Time," *Biomedicines*, vol. 10, no. 10, Oct. 2022, doi: 10.3390/ BIOMEDICINES10102493.
- [34] "Therapeutics and COVID-19: Living guideline, 13 January 2023." https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1 (accessed Jul. 02, 2023).
- [35] F. Sanmarchi, D. Golinelli, J. Lenzi, F. Esposito *et al.*, "Exploring the Gap Between Excess Mortality and COVID-19 Deaths in 67 Countries," JAMA Netw Open, vol. 4, no. 7, pp. e2117359, Jul. 2021, doi: 10.1001/JAMANETWORKOPEN.2021.17359.
- [36] A. Tzankov and D. Jonigk, "Unlocking the lockdown of science and demystifying COVID-19: how autopsies contribute to our understanding of a deadly pandemic," *Virchows Archiv*, vol. 477, no. 3, p. 331, Sep. 2020, doi: 10.1007/S00428-020-02887-5.
- [37] M. Salerno, F. Sessa, A. Piscopo, A. Montana *et al.*, "No Autopsies on COVID-19 Deaths: A Missed Opportunity and the Lockdown of Science," *J Clin Med*, vol. 9, no. 5, May 2020, doi: 10.3390/JCM9051472.
- [38] L. A. Mucheleng'anga, V. Telendiy, A. Hamukale, A. L. Shibemba, et al., "COVID-19 and Sudden Unexpected Community Deaths in Lusaka, Zambia, Africa – A Medico-Legal Whole-Body Autopsy Case Series," Int J Infect Dis, vol. 109, pp. 160–167, Aug. 2021, doi: 10.1016/J.IJID.2021.07.001.
- [39] R. L. Geller, J. N. Aungst, A. Newtion-Levinson, G. P. Smith *et al.*, "Is it COVID-19? The value of medicolegal autopsies during the first year of the COVID-19 pandemic," *Forensic Sci Int*, vol. 330, Jan. 2022, doi: 10.1016/J.FORSCIINT.2021.111106.
- [40] C. V. Siserman, I. I. Jeican, D. Gheban, V. Anton *et al.*, "Fatal Form of COVID-19 in a Young Male Bodybuilder Anabolic Steroid Using: The First Autopsied Case," *Medicina (B Aires)*, vol. 58, no. 10, Oct. 2022, doi: 10.3390/MEDICINA58101373.
- [41] B. I. B. Lindahl, "COVID-19 and the selection problem in national cause-of-death statistics," *Hist Philos Life Sci*, vol. 43, no. 2, Jun. 2021, doi: 10.1007/S40656-021-00420-8.
- [42] T. A. Slater, S. Straw, M. Drozd, S. Kamalathasan et al., "Dying 'due to' or 'with' COVID-19: a cause of death analysis in hospitalised patients," *Clinical Medicine*, vol. 20, no. 5, p. e189, 2020, doi: 10.7861/CLINMED.2020-0440.
- [43] M. Bogdanović, T. Atanasijević, V. Popović, Z.Mihailović *et al.*, "Proper death certification in the time of the COVID-19 pandemic: Forensic perspective," *J Infect Dev Ctries*, vol. 16, no. 6, pp. 966–968, Jun. 2022, doi: 10.3855/jidc.16556.
- [44] C. Rao, "Medical certification of cause of death for COVID-19," *Bull World Health Organ*, vol. 98, no. 5, May 2020, doi: 10.2471/ BLT.20.257600.
- [45] T. Nyberg, N. M. Ferguson, S. G. Nash, H. H. Webster *et al.*, "Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study," *Lancet*, vol. 399, no. 10332, pp. 1303–1312, Apr. 2022, doi: 10.1016/S0140-6736(22)00462-7.
- [46] L. A. Post and R. Lorenzo-Redondo, "Omicron: fewer adverse outcomes come with new dangers," *The Lancet*, vol. 399, no. 10332, pp. 1280–1281, Apr. 2022, doi: 10.1016/S0140-6736(22)00514-1.
- [47] C. Yek, S. Warner, A. Mancera, and S. S. Kadri, "Misclassification bias in estimating clinical severity of SARS-CoV-2 variants," *The Lancet*, vol. 400, no. 10355, p. 809, Sep. 2022, doi: 10.1016/S0140-6736(22)01469-6.
- [48] D. Juyal, A. Kumar, S. Pal, S. Thaledi et al., "Medical certification of cause of death during COVID-19 pandemic a challenging scenario," J Family Med Prim Care, vol. 9, no. 12, p. 5896, 2020, doi: 10.4103/JFMPC.JFMPC_1435_20.
- [49] J. Poulos, L. Zhu, and A. D. Shah, "Data gaps in electronic health record (EHR) systems: An audit of problem list completeness during the COVID-19 pandemic," *Int J Med Inform*, vol. 150, p. 104452, Jun. 2021, doi: 10.1016/J.IJMEDINF.2021.104452.

- [50] L. Mwananyanda, C. J. Gill, W. MacLeod, G. Kwenda *et al.,* "Covid-19 deaths in Africa: prospective systematic postmortem surveillance study," *BMJ*, vol. 372, Feb. 2021, doi: 10.1136/BMJ.N334.
- [51] A. V. Gundlapalli, A. M. Lavery, T. G. Boehmer, M.J. Beach *et al.*, "Death Certificate–Based ICD-10 Diagnosis Codes for COVID-19 Mortality Surveillance — United States, January–December 2020," *MMWR Morb Mortal Wkly Rep*, vol. 70, no. 14, pp. 523–527, 2021, doi: 10.15585/MMWR.MM7014E2.
- [52] M. P. Walkowiak and D. Walkowiak, "Underestimation in Reporting Excess COVID-19 Death Data in Poland during the First Three Pandemic Waves," *Int J Environ Res Public Health*, vol. 19, no. 6, Mar. 2022, doi: 10.3390/IJERPH19063692.
- [53] Y. Ju and M. You, "It's Politics, Isn't It? Investigating Direct and Indirect Influences of Political Orientation on Risk Perception of COVID-19," Risk Anal, vol. 42, no. 1, pp. 56–68, Jan. 2022, doi: 10.1111/RISA.13801.
- [54] K. T. Paul, J. M. Eberl, and J. Partheymüller, "Policy-Relevant Attitudes Toward COVID-19 Vaccination: Associations With Demography, Health Risk, and Social and Political Factors," *Front Public Health*, vol. 9, Jul. 2021, doi: 10.3389/fpubh.2021.671896.
- [55] D. Albrecht, "Vaccination, politics and COVID-19 impacts," BMC Public Health, vol. 22, no. 1, Dec. 2022, doi: 10.1186/S12889-021-12432-X.
- [56] J. Kerr, C. Panagopoulos, and S. van der Linden, "Political polarization on COVID-19 pandemic response in the United States," *Pers Individ Dif*, vol. 179, Sep. 2021, doi: 10.1016/J.PAID.2021.110892.
- [57] R. Parker and D. Ferraz, "Politics and pandemics," https://doi.org/10.1080/17441692.2021.1947601, vol. 16, no. 8–9, pp. 1131–1140, 2021, doi: 10.1080/17441692.2021.1947601.
- [58] E. M. da Fonseca, N. Nattrass, L. L. B. Lazaro, and F. I. Bastos, "Political discourse, denialism and leadership failure in Brazil's response to COVID-19," https://doi.org/10.1080/17441692.2021.1945123, vol. 16, no. 8–9, pp. 1251–1266, 2021, doi: 10.1080/17441692.2021. 1945123.
- [59] F. Ortega and M. Orsini, "Governing COVID-19 without government in Brazil: Ignorance, neoliberal authoritarianism, and the collapse of public health leadership," *Glob Public Health*, pp. 1257–1277, 2020, doi: 10.1080/17441692.2020.1795223.
- [60] S. Crabu, P. Giardullo, A. Sciandra, and F. Neresini, "Politics overwhelms science in the Covid-19 pandemic: Evidence from the whole coverage of the Italian quality newspapers," *PLoS One*, vol. 16, no. 5, May 2021, doi: 10.1371/JOURNAL.PONE.0252034.
- [61] F. Sazzad, V. P. Rajan, and M. A. Demircioglu, "The Role of Leadership in Public Sector Innovation: A Systematic Review and Meta-Analysis of the Management of COVID-19 in Asian Countries," Front Public Health, vol. 9, p. 743748, Dec. 2021, doi: 10.3389/ FPUBH.2021.743748.
- [62] S. Talic, S. Shah, H. Wild, D.Gasevic *et al.*, "Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: Systematic review and meta-analysis," *The BMJ*, vol. 375, Nov. 2021, doi: 10.1136/BMJ-2021-068302.
- [63] S. Flaxman, S. Mishra, A. Gandy, H. J. T. Unwin *et al.*, "Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe," *Nature*, vol. 584, no. 7820, pp. 257–261, Aug. 2020, doi: 10.1038/S41586-020-2405-7.
- [64] F. Zhou, T. J. Hu, X. Y. Zhang, K. Lai et al., "The association of intensity and duration of non-pharmacological interventions and implementation of vaccination with COVID-19 infection, death, and excess mortality: Natural experiment in 22 European countries," J Infect Public Health, vol. 15, no. 5, pp. 499–507, May 2022, doi: 10.1016/J.JIPH.2022.03.011.
- [65] V. Schwarz, F. Mahfoud, L. Lauder, W. Reith *et al.*, "Decline of emergency admissions for cardiovascular and cerebrovascular events after the outbreak of COVID-19," *Clin Res Cardiol*, vol. 109, no. 12, pp. 1500–1506, Dec. 2020, doi: 10.1007/S00392-020-01688-9.
- [66] M. Seiffert, F. J. Brunner, M. Remmel, G. Thomalla *et al.*, "Temporal trends in the presentation of cardiovascular and cerebrovascular emergencies during the COVID-19 pandemic in Germany: an analysis of health insurance claims," *Clinical Research in Cardiology*, vol. 109, no. 12, pp. 1540–1548, Dec. 2020, doi: 10.1007/s00392-020-01723-9.
- [67] A. K. Gitt, A. K. Karcher, R. Zahn, and U. Zeymer, "Collateral damage of COVID-19-lockdown in Germany: decline of NSTE-ACS admissions," *Clinical Research in Cardiology*, vol. 109, no. 12, pp. 1585–1587, Dec. 2020, doi: 10.1007/s00392-020-01705-x.
- [68] J. Thornton, "Covid-19: A& E visits in England fall by 25% in week after lockdown," BMJ, vol. 369, p. m1401, Apr. 2020, doi: 10.1136/ BMJ.M1401.
- [69] E. Kondilis, F. Tarantilis, and A. Benos, "Essential public healthcare services utilization and excess non-COVID-19 mortality in Greece," *Public Health*, vol. 198, pp. 85–88, Sep. 2021, doi: 10.1016/J.PUHE.2021.06.025.
- [70] M. É. Czeisler, K. Marynak, K. E.N. Clarke, Z.Salah *et al.*, "Delay or Avoidance of Medical Care Because of COVID-19-Related Concerns – United States, June 2020," *MMWR Morb Mortal Wkly Rep*, vol. 69, no. 36, pp. 1250–1257, Sep. 2020, doi: 10.15585/MMWR.MM6936A4.
- [71] A. Zumla, J. Chakaya, M. Khan, R.Fatima et al., "World Tuberculosis Day 2021 Theme 'The Clock is Ticking' and the world is running out of time to deliver the United Nations General Assembly commitments to End TB due to the COVID-19 pandemic," International Journal of Infectious Diseases, vol. 113, pp. S1–S6, Dec. 2021, doi: 10.1016/j.ijid.2021.03.046.
- [72] World Health Organization, "Annual Report of Tuberculosis," *Annual Global TB Report of WHO*, vol. 8, no. 1, pp. 1–68, 2022, Accessed: May 15, 2023. [Online]. Available: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-re-



port-2022%0Ahttps://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022#:~:text=context of global..-,Download,-Read More%0Ahtt

- [73] A. G. Dinmohamed, O. Visser, R. H. A. Verhoeven, M. V. J. Louwman *et al.*, "Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands," *Lancet Oncol*, vol. 21, no. 6, pp. 750–751, Jun. 2020, doi: 10.1016/S1470-2045(20)30265-5.
- [74] D. Schrag, D. L. Hershman, and E. Basch, "Oncology Practice during the COVID-19 Pandemic," JAMA Journal of the American Medical Association, vol. 323, no. 20, pp. 2005–2006, May 2020, doi: 10.1001/JAMA.2020.6236.
- [75] D. Bu, "The impact of COVID-19 on Australian cancer screening and strategies to mitigate ongoing disruption of screening services," *Aust J Gen Pract*, vol. 50, pp. 1–2, 2021, doi: 10.31128/AJGP-COVID-50.
- [76] F. Teglia, M. Angelini, L. Astolfi, G. Casolari et al., "Global Association of COVID-19 Pandemic Measures With Cancer Screening: A Systematic Review and Meta-analysis," JAMA Oncol, vol. 8, no. 9, pp. 1287–1293, Sep. 2022, doi: 10.1001/JAMAONCOL.2022.2617.
- [77] F. Teglia, M. Angelini, G. Casolari, L. Astolfi et al., "Global Association of COVID-19 Pandemic Measures with Cancer Treatment: A Systematic Review and Meta-Analysis.," *Cancers (Basel)*, vol. 14, no. 22, Nov. 2022, doi: 10.3390/cancers14225490.
- [78] K. Causey, N. Fullman, R. J. D. Sorensen, N. C. Galles *et al.*, "Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modelling study," *The Lancet*, vol. 398, no. 10299, pp. 522–534, Aug. 2021, doi: 10.1016/S0140-6736(21)01337-4.
- [79] V. Kumari, K. Mehta, and R. Choudhary, "COVID-19 outbreak and decreased hospitalisation of pregnant women in labour," *Lancet Glob Health*, vol. 8, no. 9, pp. e1116–e1117, Sep. 2020, doi: 10.1016/S2214-109X(20)30319-3.
- [80] B. N. Ezenwa, I. B. Fajolu, H. Nabwera, D. Wang, et al., "Impact of COVID-19 lockdown measures on institutional delivery, neonatal admissions and prematurity: a reflection from Lagos, Nigeria," *BMJ Paediatr Open*, vol. 5, no. 1, Apr. 2021, doi: 10.1136/BMJPO-2021-001029.
- [81] G. Alicandro, G. Remuzzi, and C. La Vecchia, "Italy's first wave of the COVID-19 pandemic has ended: no excess mortality in May, 2020," *Lancet*, vol. 396, no. 10253, p. e27, Sep. 2020, doi: 10.1016/S0140-6736(20)31865-1.
- [82] E. Kontopantelis, M. A. Mamas, J. Deanfield, M. Asaria et al., "Excess mortality in England and Wales during the first wave of the COVID-19 pandemic," *J Epidemiol Community Health* (1978), vol. 75, no. 3, pp. 213–223, Mar. 2021, doi: 10.1136/JECH-2020-214764.
- [83] K. Barański, G. Brożek, M. Kowalska, A. Kaleta-Pilarska et al., "Impact of COVID-19 Pandemic on Total Mortality in Poland," *Int J Environ Res Public Health*, vol. 18, no. 8, Apr. 2021, doi: 10.3390/IJERPH18084388.
- [84] A. John, J. Pirkis, D. Gunnell, L. Appleby et al., "Trends in suicide during the covid-19 pandemic," *BMJ*, vol. 371, Nov. 2020, doi: 10.1136/ BMJ.M4352.
- [85] M. Rezaeiahari and B. J. Fairman, "Impact of COVID-19 on the characteristics of opioid overdose deaths in Arkansas," Int J Drug Policy, vol. 109, p. 103836, Nov. 2022, doi: 10.1016/J.DRUGP0.2022.103836.
- [86] "Overdose Deaths Accelerating During COVID-19 | CDC Online Newsroom | CDC." https://www.cdc.gov/media/releases/2020/p1218 -overdose-deaths-covid-19.html (accessed May 15, 2023).
- [87] D. Gunnell, L. Appleby, E. Arensman, K. Hawton *et al.*, "Suicide risk and prevention during the COVID-19 pandemic," *Lancet Psychiatry*, vol. 7, no. 6, pp. 468–471, Jun. 2020, doi: 10.1016/S2215-0366(20)30171-1.
- [88] I. M. Wasserman, "The Impact of Epidemic, War, Prohibition and Media on Suicide: United States, 1910–1920," *Suicide Life Threat Behav*, vol. 22, no. 2, pp. 240–254, Jun. 1992, doi: 10.1111/J.1943-278X.1992.TB00231.X.
- [89] Y. T. Cheung, P. H. Chau, and P. S. F. Yip, "A revisit on older adults suicides and Severe Acute Respiratory Syndrome (SARS) epidemic in Hong Kong," Int J Geriatr Psychiatry, vol. 23, no. 12, pp. 1231–1238, 2008, doi: 10.1002/GPS.2056.
- [90] S. M. S. Chan, F. K. H. Chiu, C. W. L. Lam, P. Y. V. Leung et al., "Elderly suicide and the 2003 SARS epidemic in Hong Kong," *Int J Geriatr Psychiatry*, vol. 21, no. 2, pp. 113–118, Feb. 2006, doi: 10.1002/gps.1432.
- [91] Y. J. Yasin, M. Grivna, and F. M. Abu-Zidan, "Global impact of COVID-19 pandemic on road traffic collisions," *World Journal of Emergency Surgery*, vol. 16, no. 1, pp. 1–14, Dec. 2021, doi: 10.1186/S13017-021-00395-8/TABLES/2.
- [92] S. Parr, B. Wolshon, J. Renne, P. Murray-Tuite, et al., "Traffic impacts of the COVID-19 pandemic: statewide analysis of social separation and activity restriction," *Nat Hazards Rev*, vol. 21, no. 3, p. 04020025, Aug. 2020, doi: 10.1061/(asce)nh.1527-6996.0000409.
- [93] M. C. Ramírez-Soto and G. Ortega-Cáceres, "Analysis of Excess All-Cause Mortality and COVID-19 Mortality in Peru: Observational Study," *Trop Med Infect Dis*, vol. 7, no. 3, Mar. 2022, doi: 10.3390/TROPICALMED7030044.
- [94] S. Tempia, S. Walaza, J. N. Bhiman, M. L. McMorrow *et al.*, "Decline of influenza and respiratory syncytial virus detection in facility-based surveillance during the COVID-19 pandemic, South Africa, January to October 2020," *Euro Surveill*, vol. 26, no. 29, Jul. 2021, doi: 10.2807/1560-7917.ES.2021.26.29.2001600.
- [95] J. H. Kim, Y. H. Roh, J. G. Ahn, M. Y. K. RN *et al.*, "Respiratory syncytial virus and influenza epidemics disappearance in Korea during the 2020-2021 season of COVID-19," *Int J Infect Dis*, vol. 110, pp. 29–35, Sep. 2021, doi: 10.1016/J.IJID.2021.07.005.
- [96] N. Spantideas, A. M. Bougea, E. G. Drosou, N. Khanderia et al., "COVID-19 and Seasonal Influenza: No Room for Two," *Cureus*, vol. 13, no. 9, Sep. 2021, doi: 10.7759/CUREUS.18007.

- [97] H. Mirza, M. Mirza "Lessons Learned From the COVID-19 Pandemic: Factors Affecting Decreased Incidence of Influenza PubMed." https://pubmed.ncbi.nlm.nih.gov/36940124/ (accessed May 14, 2023).
- [98] V. Rana, M. William, A. Kewalramani, J. Daloya *et al.*, "COVID-19 Mask Mandates in NY and Their Effect on the Incidence of Flu," *J Community Hosp Intern Med Perspect*, vol. 13, no. 1, Jan. 2023, doi: 10.55729/2000-9666.1140.
- [99] F. W. S. Ko, L. H. S. Lau, S. S. Ng, T. Ch. F. Yip *et al.*, "Respiratory admissions before and during the COVID-19 pandemic with mediation analysis of air pollutants, mask-wearing and influenza rates," *Respirology*, vol. 28, no. 1, pp. 47–55, Jan. 2023, doi: 10.1111/RESP.14345.
- [100] N. Horita and T. Fukumoto, "Two years of the pandemic suppressed deaths from non-COVID-19 respiratory infections: A nationwide surveillance in Japan," *Respirology*, vol. 28, no. 1, pp. 82–83, Jan. 2023, doi: 10.1111/resp.14392.
- [101] M. V. W. de Vries and L. Rambabu, "The impact of natural disasters on the spread of COVID-19: a geospatial, agent-based epidemiology model," Theor Biol Med Model, vol. 18, no. 1, pp. 1–9, Dec. 2021, doi: 10.1186/S12976-021-00151-0/FIGURES/4.
- [102] M. C. Quigley, J. Attanayake, A. King, and F. Prideaux, "A multi-hazards earth science perspective on the COVID-19 pandemic: the potential for concurrent and cascading crises," *Environ Syst Decis*, vol. 40, no. 2, p. 199, Jun. 2020, doi: 10.1007/S10669-020-09772-1.
- [103] C. A. Phillips, A. Caldas, R. Cleetus, K. A. Dahl *et al.*, "Compound climate risks in the COVID-19 pandemic," *Nature Climate Change* 2020 10:7, vol. 10, no. 7, pp. 586–588, May 2020, doi: 10.1038/s41558-020-0804-2.
- [104] M. E. Kruk, A. D. Gage, N. T. Joseph, G. Danaei et al., "Mortality due to low-quality health systems in the universal health coverage era: a systematic analysis of amenable deaths in 137 countries," *The Lancet*, vol. 392, no. 10160, pp. 2203–2212, Nov. 2018, doi: 10.1016/S0140-6736(18)31668-4.
- [105] C. R. Wells and A. P. Galvani, "The global impact of disproportionate vaccination coverage on COVID-19 mortality," *Lancet Infect Dis*, vol. 22, no. 9, pp. 1254–1255, Sep. 2022, doi: 10.1016/S1473-3099(22)00417-0.
- [106] P. G. T. Walker, Ch. Whittaker, O. J. Watson, M. Baguelin *et al.*, "The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries," *Science*, vol. 369, no. 6502, pp. 413–422, Jul. 2020, doi: 10.1126/SCIENCE.ABC0035.
- [107] V. Rios, E. Denova-Gutierrez, and S. Barquera, "Association between living in municipalities with high crowding conditions and poverty and mortality from COVID-19 in Mexico," *PLoS One*, vol. 17, no. 2 Febuary, Feb. 2022, doi: 10.1371/journal.pone.0264137.
- [108] N. E. Antonio-Villa, L. Fernandez-Chirino, J. Pisanty-Alatorre, J. Mancilla-Galindo *et al.*, "Comprehensive Evaluation of the Impact of Sociodemographic Inequalities on Adverse Outcomes and Excess Mortality During the Coronavirus Disease 2019 (COVID-19) Pandemic in Mexico City," *Clin Infect Dis*, vol. 74, no. 5, pp. 785–792, Mar. 2022, doi: 10.1093/CID/CIAB577.
- [109] S. Jefferies, N. French, Ch. Gilkison, G. Graham *et al.*, "COVID-19 in New Zealand and the impact of the national response: a descriptive epidemiological study," *Lancet Public Health*, vol. 5, no. 11, pp. e612–e623, Nov. 2020, doi: 10.1016/S2468-2667(20)30225-5.
- [110] A. Stobart and S. Duckett, "Australia's Response to COVID-19," Health Econ Policy Law, vol. 17, no. 1, pp. 95–106, Jan. 2022, doi: 10.1017/ S1744133121000244.
- [111] T. M. McMichael, S. Clark, S. Pogosjans, M. Kay *et al.*, "COVID-19 in a Long-Term Care Facility King County, Washington, February 27–March 9, 2020," *Morbidity and Mortality Weekly Report*, vol. 69, no. 12, p. 339, Mar. 2020, doi: 10.15585/MMWR.MM6912E1.
- [112] M. He, Y. Li, and F. Fang, "Is There a Link between Nursing Home Reported Quality and COVID-19 Cases? Evidence from California Skilled Nursing Facilities," *J Am Med Dir Assoc*, vol. 21, no. 7, pp. 905–908, Jul. 2020, doi: 10.1016/j.jamda.2020.06.016.
- [113] R. T. Konetzka, E. M. White, A. Pralea, D. C. Grabowski et al., "A systematic review of long-term care facility characteristics associated with COVID-19 outcomes," J Am Geriatr Soc, vol. 69, no. 10, pp. 2766–2777, Oct. 2021, doi: 10.1111/JGS.17434.
- [114] L. Sempé, P. Lloyd-Sherlock, R. Martínez, S. Ebrahim et al., "Estimation of all-cause excess mortality by age-specific mortality patterns for countries with incomplete vital statistics: a population-based study of the case of Peru during the first wave of the COVID-19 pandemic," *The Lancet Regional Health – Americas*, vol. 2, Oct. 2021, doi: 10.1016/j.lana.2021.100039.
- [115] M. A. Sinnathamby, H. Whitaker, L. Coughlan, J. L. Bernal et al., "All-cause excess mortality observed by age group and regions in the first wave of the COVID-19 pandemic in England," *Euro Surveill*, vol. 25, no. 28, Jul. 2020, doi:10.2807/1560-7917.ES.2020.25.28.2001239.
- [116] M. Cobos-Siles, P. Cubero-Morais, I. Arroyo-Jimenez, M. Rey-Hernandez *et al.*, "Cause-specific death in hospitalized individuals infected with SARS-CoV-2: more than just acute respiratory failure or thromboembolic events," *Intern Emerg Med*, vol. 15, no. 8, p. 1533, Nov. 2020, doi: 10.1007/S11739-020-02485-Y.