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Research Article

METHODS AND ISSUES IN NOSOLOGICAL ANALYSIS OF MORTALITY DURING THE COVID-19 PANDEMIC

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ABSTRACT

The article discusses different approaches to assessing mortality during the COVID-19 pandemic. The analysis of international data shows that different countries use different approaches to assessing mortality from COVID-19 and the increase in mortality from all causes. The most probable reasons for the variability of the increase in mortality rates are the rate of spread of infection, the quality of isolation and quarantine measures, the commitment of the population to their implementation, the resource capacity of the healthcare system and the quality of medical care (both for the treatment of COVID-19 and other diseases), features of living conditions, socio-economic and political processes that are difficult to formalize (and therefore assess the contribution by methods of mathematical statistics). For a correct comparison of excess mortality rates, it will be necessary to calculate standardized indicators and compare data in five-year age groups.

In 2021, serious problems should be expected with the comparison of mortality rates in different countries from individual causes. The methodology for recording deaths from COVID-19 and other causes is not

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uniform at the global level, problems are associated with differences in approaches to determining the primary cause of death, difficulties in determining the cause of death if a patient has multimorbid pathology (especially without postmortem examination). A full-fledged analysis is possible only with transdisciplinary cooperation under the auspices of the WHO of doctors, mathematicians, economists, and information technology specialists.

KEYWORDS

COVID-19 pandemic; mortality; lethality; excess mortality.

INTRODUCTION

Mortality per 100,000 population (mortality) is a population-wide indicator defined as the ratio of the number of deaths (usually per year, from all causes or a specific cause of death) to the average annual population of a country (region, city) × 100,000. The term excess mortality is used to describe the increased (compared with "normal" conditions) number of deaths from all causes during (day, month, year) of public health emergencies. Such situations develop as a result of abrupt changes in socio-economic, environmental conditions, disasters, wars, epidemics, etc. Often health resources are insufficient to deal with their medical consequences In these conditions, the mobilization of the health care system - the process of responding to an emergency situation, including the introduction of additional resources into the system, its restructuring to ensure maximum medical efficiency of the existing medical organizations. "The 'redundancy' of deaths in an emergency is assessed in several ways. 1) Comparing the absolute number of deaths.

The number of deaths during a given period (week, month, year) of the COVID-19 pandemic is compared with the average number of deaths during the same period in previous years. Since the influenza A (H1N1) pandemic, the European Mortality Monitoring Programme aims to detect and measure additional deaths related to

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seasonal influenza, pandemics and other threats to public health by tracking the number of deaths from all causes weekly in 27 European countries, which provide regular weekly mortality data for all ages and by age groups [3]. The results of mortality analysis are part of the regular monitoring of seasonal influenza in Europe, a systematic assessment of mortality within countries and in comparison with other countries [4-6]. Such results are particularly useful in the context of pandemics caused by a new infectious agent, where the true mortality burden from a new infection is difficult to ascertain. Such an estimate permits an approximate estimate of magnitude, as values across countries cannot be compared because of wide variations in population size. In addition, as stated on the web site, operational data may be inaccurate due to delayed death registrations, and should therefore be interpreted with caution [7].

2)Comparison of mortality rates. Definition of excess mortality as the difference between the mortality rate (ratio of the number of deaths from all causes to the average annual population of the country, multiplied by 100 thousand) in the analysed period compared to the same period in previous years. The indicator does not take into account the demographic composition of the population, so countries with a higher proportion of the elderly population with a higher risk of dying from all causes, including from COVID-19, will have higher mortality rates. Therefore, when comparing countries, it is better to estimate rates in comparable age groups. 3)Determination of the P-score (P-score/scale) is the percentage difference between the number of deaths for the period being assessed (e.g. month 2020) and the average number of deaths for the same period (e.g. 2015-2019). If the P-score is 100%, it means that the number of deaths is twice as high as the average number of deaths in the same week during the previous five years. The indicator does not take into account the size and demographic composition of the population [8], so countries with a higher proportion of older people will have a higher P-score. Countries with smaller populations may have a higher P-score than countries with larger populations.

In the USA, for example, the P-score is significantly lower than in Italy, 45% and 150% respectively (April 2020). The Our World In Data website (a project of the Global Change Data Lab, a charity registered in England and Wales) provides such calculations (age groups) online for

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40 countries [9]. 4) Definition of the Z-score, or Z-score, is a measure of the relative dispersion of an observed value that shows how many standard deviations the dispersion of that indicator is relative to the mean baseline value. With a Z-score of 0, the assessed data point is identical to the mean; with 1.0, the value differs from the mean by one standard deviation. A positive value indicates that the value is above the mean, while a negative value is below the mean. Absolute values of deaths, mortality rates, P-score and Z-score vary considerably not only between countries but also between time periods. All these indicators can only be calculated by comparing current data with data from previous years. However, it should be taken into account that operational data on the number of deaths from all causes in all countries are incomplete in the weeks and even months after the death occurs, which depends to a large extent on the registration (accounting) systems of deaths in the country. Thus, the magnitude of excess deaths will depend on approaches to estimating the phenomenon. Preliminary operational data for 2020 are already available on websites in some countries. Throughout 2020, operational data on COVID-19 mortality in different countries and the reasons for the differences (features of isolation and quarantine measures, population adherence to them, features of the functioning of the health care system, mutations of the virus, demographic structure of the population, approaches to determining the cause of death of those who died) were published and actively discussed on individual websites [12-14]. During 2020, indicators reflecting excess mortality varied: China showed a slight increase in mortality only at the beginning of the year, the USA recorded excess mortality throughout most of 2020, and some European countries (Austria, Denmark, Estonia, Finland, Germany, Greece, Hungary, Luxembourg, Norway) showed no or very limited excess mortality. In Germany, the COVID-19 pandemic caused increased mortality only during the first wave, from week 10 to week 23 in 2020, with an estimated excess of 8,071 deaths during this period [15]. A more thorough analysis of international mortality rates is likely to follow once the operational data have been refined. It should be noted that the recording of COVID-19 deaths did not start at the beginning of 2020, the criteria for recording have been revised and there is still no evidence that all countries follow the same criteria for recording deaths from COVID-19 and for COVID-19. The official name of the disease, COVID-19 (virus - SARSr-CoV-2), was

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announced by WHO on 11 February 2020 and only published guidelines for recording COVID-19-related deaths on 25 March 2020 [16]. COVID-19, according to the WHO guidelines, is listed on the death certificate as any other cause of death, and the rules for choosing the initial cause of death are the same as, for example, for influenza. No special instructions are required.

If COVID-19 is considered to be the main cause of death based on the clinical and pathological-anatomical assessment, it must be stated in the last line of Part 1 of the Medical Certificate of Death (MDS). If there is another underlying cause of death and COVID-19 is regarded as contributing to the death, it should be indicated in Part 2 of the MSC. The ICD has codes "B97.2 - Coronavirus disease classified under other headings" and "B34.2 - Coronavirus infection unspecified". There is currently no data on which countries were using these codes before the WHO recommendations were published, or for how long. Difficulties in recording and comparing individual-cause mortality rates across countries have been discussed previously..COVID-19 exacerbated the situation. National health services in different countries accounted for COVID-19 deaths differently (and probably continue to do so). In the United States, for example, a different approach from that proposed by WHO was used in the early stages . Some countries report only deaths from confirmed COVID-19 in hospitals based on both test data and clinical presentation (e.g. in Spain, not including deaths at home and in nursing homes others, only deaths with a positive COVID-19 test [12]. In Italy, for example, those who were not tested for COVID-19 while alive, if it was suspected that the deceased might have been infected with the virus, were tested after death, and if positive, regardless of other data, COVID-19 was given as the cause of death. Belgium includes all suspected COVID-19 deaths. Deaths in nursing homes in Belgium account for about half of all additional deaths, but only 26% of these deaths were confirmed as COVID-19. In the UK, the criteria for recording a COVID-19 death differ within the country [13].

In Russia, pathological and anatomical autopsies of COVID-19 deaths are mandatory1 , and the methodological recommendations of 28 May 2020 fully reflect WHO positions on statistical recording and coding of cases and deaths from and in COVID-19 [5]. It is also worth noting that medical certificates of death are often completed in error in all countries, and the number of such

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errors, possibly due to the pandemic, has increased [6]. In high-income countries, most of the deceased had a chronic illness prior to COVID-19, which has generated controversy about causation and the original cause of death [7].

At the same time, in low- and middle-income countries, causes of death may remain undetected in settings where people have limited access to health services [8]. In the process of recording deaths, it has become apparent that in some cases COVID-19, based on existing approaches to recording causes of death, is the immediate but not the original cause of death. For example, a patient has a terminal chronic illness (cancer or heart failure) or the patient is admitted to hospital with a severe acute illness and already in hospital has COVID-19, in which situation COVID-19 is a contributory cause of death. In some cases there is a combined cause of death, and there is currently no information on how different countries record the cause of death in these and more complicated medical situations. For example, Wadhera R.K. et al. note that determining the exact cause of death during the COVID-19 pandemic remains problematic; some of the deaths coded as circulatory disease deaths in the US may have been due to cardiovascular complications of undiagnosed COVID-19 [9].

Thus, there is still no consensus on whether the deaths of these patients should be counted as COVID-19 or deaths from existing and exacerbated by COVID-19. From our point of view, in a certain proportion of cases it is a combined cause of death (death from several causes, each of which has contributed to some extent). Because of the problems described, there is considerable variation between countries in the relative contribution of deaths due to COVID-19 to the total number of excess deaths, ranging from 70% to 100% [3]. According to Beaney T., in Belgium, Sweden and France, deaths from COVID-19 exceeded excess deaths from all causes (compared for the same periods from 2015 to 2019), while deaths from other causes decreased. In Spain, Italy, USA, the increase in excess mortality was due to both COVID-19 and non-COVID-related causes.

In the UK, for example, until 1 May 2020, 28% of additional deaths were unrelated to COVID-19 (predominantly in care homes, where dementia was reported as one of the most common causes of death). However, according to another study, in the UK, a proportion of COVID-19 deaths in care

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homes went unrecognised because not all residents in these homes were tested for COVID-19 [11]. Advice from politicians and health professionals to "stay at home and do not visit health facilities unless absolutely necessary" has led to a significant reduction in referrals from patients not suffering from COVID-19 [12]. In some countries, some elective surgeries have been cancelled during the period of maximum bed occupancy by patients with COVID-19 and physicians have been encouraged to postpone even surgery and anti-tumour therapy for malignant neoplasms if possible in order to reduce patient interaction with the healthcare system, thereby reducing the risk of infection [4]. As a result, patients are admitted to hospitals in a more severe condition and some patients die at home [5]. Thus, according to WHO, 53 % of countries have problems with medical care; for cancer, 42 %; and for cardiovascular disease, 31 % [6]. In the USA, according to the Chicago Society of Thoracic Surgeons, the volume of all adult cardiac surgery nationwide in 2020 has decreased by 53% compared with 2019. And patients who underwent coronary bypass surgery during the pandemic had an increased risk of complications and death [37]. Many publications reflect projections of the continued impact of COVID-19 on public health and mortality rates. Overloading the health system with patients with acute manifestations of COVID-19, patients' fear of becoming infected when seeking care, and forced changes in approaches to managing prevention and treatment of other diseases have contributed to increased mortality in 2020 and are likely to have an impact on mortality rates in the future [1].

In addition, there is evidence of adverse effects of unemployment, financial crises, depression and social isolation (particularly significant for older people) on morbidity and mortality [10], while social restrictions are likely to result in some reduction in injury mortality rates. Other predictions have been made that excess mortality from social isolation and quarantine measures is likely to be much higher than the number of COVID-19 deaths [43]. Suicide and poisoning deaths are likely to change. On the one hand, it cannot be ruled out that the relatively short-lived spike in COVID-19 deaths may lead to a relative decrease in deaths from other causes in the following weeks and a gradual decrease in overall excess mortality over time. On the other hand, there are reports of a higher risk of death (7-fold) among patients discharged from hospital after

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treatment for COVID-19 than in the general population (the most common causes being multi-organ involvement in existing chronic disease) (14). The table presents a summary of possible causes of excess mortality, with comments. The ability of public health to rapidly adapt to the needs of a population in an emergency of uncertain duration, such as a COVID-19 pandemic comparable to a "wartime" situation, is also importan.

CONCLUSION

Excess mortality is an indicator of the overall impact of the pandemic on mortality but there is currently no single source of data on "excess" mortality for 2021 across the world compared with previous years. The most likely reasons for the variability in excess mortality rates are: the rate of spread of infection, quality of isolation and quarantine measures, population adherence, health system resource capacity and quality of care (for both COVID-19 and other diseases), and characteristics of living conditions. The COVID-19 pandemic has caused significant changes both in social life and in the organisation of health care, which has an impact on mortality not only from COVID-19 but also from other causes not directly related to the viral infection. The global economic downturn, social exclusion, restrictions on mobility, overburdening of health systems and changing priorities in the use of available medical capacity are leading to poorer health outcomes, including fatalities. In order to compare excess mortality rates correctly, it will be necessary to calculate standardised rates or to compare data in five-year age groups. In 2021, major problems with cross-country comparisons of deaths from individual causes are to be expected. The methodology for recording deaths from COVID-19 and other causes during the pandemic is not uniform across the world. Differences between countries in approaches to identifying the primary cause of death and difficulties in determining the cause of death on the medical death certificate (especially without an autopsy) are problems. In-depth clinical and pathological analysis can provide important information for assessing the nosological cause of death and subsequent year-end decisions. A complete analysis is only possible with the transdisciplinary cooperation of doctors, mathematicians, economists and information technology specialists.

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