TEMPORAL TRENDS AND PATTERNS IN COVID-19 MORTALITY IN THE REPUBLIC OF MOLDOVA

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ABSTRACT

The Republic of Moldova Ministry of Health releases individual death records of COVID-19 patients on a daily basis since March 18, 2020. It is important to understand the quality of this data and to compare them to medical death certificate data available for 2020 where COVID-19 infection was indicated as an underlying cause of death. Aim: To analyse the temporal trends and age and sex pattern of mortality from COVID-19 infection and to assess the impact of the pandemic on the overall mortality in Moldova. Materials and methods: individual death records published by the Ministry of Health between March 18, 2020 and October, 10 2021 and medical death certificates for 2017-2020. Demographic methods of mortality analysis, descriptive and inferential statistics were used. Results: In Moldova, mortality from COVID-19 infection is limited to laboratory-confirmed cases, which does not meet the WHO recommended definition. The weekly dynamics of COVID-19-related deaths published by the Ministry of Health are mainly consistent with the death certificate data for 2020. Three waves of mortality were identified with their peaks in the middle of December 2020, March 2021 and October 2021. Excess mortality among the elderly in late 2020 (wave 1) is attributed in part to cardiovascular disease. The male-to-female ratio for mortality from COVID-19 infection is higher in older age and much less so in middle age. The COVID-19 pandemic has had quite a sizable effect on mortality trends and cause-of-death patterns in 2020.

Keywords: mortality, COVID-19, data quality, excess mortality, Republic of Moldova.

Ministerul Sănătății al Republicii Moldova publică zilnic înregistrările individuale ale deceselor pacienților cu COVID-19 începând cu 18 martie 2020. Este important să înțelegem calitatea acestor date și să le comparăm cu datele privind certificatele medicale de deces disponibile pentru 2020, unde infecția cu COVID-19 a fost indicată ca o cauză principală a decesului. Scop: Să analizeze tendințele temporale și structura pe vârstă și sex a mortalității prin infecția cu COVID-19 și să evalueze impactul pandemiei asupra mortalității generale în Moldova. Materiale și metode: înregistrările individuale de deces publicate de Ministerul Sănătății în perioada 18 martie 2020 – 10 octombrie 2021, precum și certificate medicale de deces pentru anii 2017-2020. Au fost utilizate metode demografice de analiză a mortalității, statistici descriptive și inferențiale. Rezultate: În Moldova, mortalitatea prin infecția cu COVID-19 este limitată la cazurile confirmate de laborator, ceea ce nu corespunde definiției recomandate de OMS. Dinamica săptămânală a deceselor COVID-19 publicată de Ministerul Sănătății este în concordanță, în principal, cu datele certificatelor de deces pentru 2020. Au fost identificate trei valuri de mortalitate, cu vârfuri la mijlocul lunii decembrie 2020, martie 2021 și octombrie 2021. Mortalitatea excesivă în rândul persoanelor în vârstă la sfârșitul anului 2020 (valul 1) este atribuită parțial bolilor cardiovasculare. Raportul dintre bărbați și femei pentru mortalitatea cauzată de COVID-19 este mai mare la vârsta înaintată și mult mai puțin la vârsta mijlocie. Pandemia de COVID-19 a avut un efect destul de considerabil asupra tendințelor și structurii mortalității pe cauze de deces în 2020.

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Cuvinte cheie: mortalitate, COVID-19, calitatea datelor, mortalitatea excesivă, Republica Moldova.

Министерство здравоохранения Республики Молдова публикует ежедневно индивидуальные записи о смерти пациентов с подтверждённой инфекцией COVID-19, начиная с 18 марта 2020 года. Важно понимать качество этих данных, а также произвести их сравнение с данными медицинских свидетельств о смерти, доступными за 2020 год, в которых инфекция COVID-19 была указана в качестве основной причины смерти. Цель: проанализировать временные тенденции и возрастно-половые особенности структуры смертности от инфекции COVID-19, а также оценить влияние пандемии на общую смертность в Республике Молдова. Материал и методы: собраны индивидуальные записи о смерти пациентов с COVID-19 инфекцией, которые были опубликованы Министерством здравоохранения в период с 18 марта 2020 по 10 октября 2021, а также медицинские свидетельства о смерти за 2017-2020 годы. Были использованы демографические методы анализа смертности, методы описательной и инференциальной статистики. Результаты: В Республике Молдова смертность от инфекции COVID-19 ограничивается лабораторно подтвержденными случаями, что не соответствует определению, рекомендованному ВОЗ. Еженедельная динамика смертей от COVID-19, публикуемых ежедневно Министерством здравоохранения, главным образом согласуется с данными медицинских свидетельств о смерти за 2020 год. Были определены три волны смертности с пиками в середине декабря 2020 года, в марте и октябре 2021 года. Избыточная смертность среди пожилых людей в конце 2020 года (волна 1) частично может быть объяснена заболеваниями сердечно-сосудистой системы. Соотношение мужчин и женщин по смертности от инфекции COVID-19 в пожилом возрасте значительно выше, чем в трудоспособном возрасте. Пандемия COVID-19 оказала значительное влияние на тенденции и структуру смертности по причинам смерти в 2020 году.

Ключевые слова: смертность, COVID-19, качество данных, избыточная смертность, Республика Молдова.

INTRODUCTION

The COVID-19 outbreak began in late 2019 and spread rapidly around the world, with significant health impacts. National and international authorities have established several indicators to track the pandemic. Analysis of mortality by sex and age is a useful tool for better understanding pandemic evolution and monitoring the effect of health policy measures. If the number of positive cases of COVID-19 or hospitalizations is directly dependent on the country's resources, the death counts are less dependent. Furthermore, various data collection systems exist and the differences between them influence the comparative analysis between the countries(Garcia et al. 2021).

According to the definition of what constitutes a COVID-19 death recommended by the World Health Organization, "a death due to COVID-19 is defined for surveillance purposes as a death resulting from a clinically compatible illness, in a suspected or confirmed COVID-19 case unless there is a clear alternative cause of death that cannot be related to COVID disease (e.g., trauma). There should be no period of complete recovery from COVID-19 between illness and death". This definition was approved by the Ministry of Health (MH) of the Republic of Moldova with the following ICD-10 codes:

U07.1 – COVID-19, virus identified

U07.2 – COVID-19, virus unidentified

However, in reality, only laboratory-confirmed cases of death due to COVID-19 (U07.1) are registered in the country. Hospitals, if a patient with confirmed COVID-19 infection died in hospital, or primary health care institutions, if a patient with confirmed COVID-19 infection died at home, notify the National Agency for Public Health daily about the confirmed COVID-19 deaths. These data are transferred to the MH to be published on their website.

This paper addresses the comparability of different data sources on COVID-19 and changes in temporal mortality trends and patterns in Moldova between March 18, 2020 and October 10, 2021. The research questions are as follows:
1. Are individual COVID-19 death records published daily by MH comparable to medical death certificate data in 2020?
2. What are the weekly mortality trends and mortality patterns by sex and age for COVID-19 infection?
3. What impact did the COVID-19 infection have on overall mortality in 2020?

LITERATURE REVIEW

A growing number of publications on COVID-19 mortality, including international comparative analyses, have appeared in recent times. Many countries, including the Republic of Moldova, publish COVID-19 death counts on a regular basis. However, before analysing such data, it is essential to understand the principles behind the registration of COVID-19-related deaths in a given country. From this perspective, the "Demography of COVID-19 deaths" database (https://dc-covid.site.ined.fr/en/) produced by the French Institute for Demographic Studies (INED) gathers deaths by age and sex across 21 countries, including the Republic of Moldova, and provides metadata for each country (INED 2021c). According to Garcia et al., some countries report numbers of deaths attributable to COVID-19, according to different sources and definitions (Garcia et al. 2021). For example, in England and Wales, the Office for National Statistics (ONS) provide COVID-19 death data that include "COVID-19 or suspected COVID-19 mentioned anywhere on the death certificate, including in combination with other health conditions" (INED 2020). Garcia et al. consider this type of data as "comprehensive". At the same time, the National Health Service provides data on COVID-19-related deaths in England that occurred in hospitals among people who tested positive for COVID-19. This type of data is considered "restrictive" by the same author. Moreover, the definition of COVID-19 death can vary within one country over time. For example, in Belgium, only PCR-confirmed death counts were reported initially, while probable or presumed cases began to be included as the pandemic progressed (Garcia et al. 2021). In Belgium, in the first wave, only 68.8% of the COVID-19-related deaths were laboratory-confirmed, while in the second wave, due to improved testing capacity, this share reached 95.3% (Peeters et al. 2021). In Romania, COVID-19 death statistics refer to laboratory-confirmed deaths reported by medical facilities, but deaths among suspected cases need to be laboratory-confirmed post-mortem. Of the 1 360 individual death records published by the Romanian Ministry of Health between March 22, 2020 and June 10, 2020, 2.5% were diagnosed with COVID-19 infection post-mortem. However, these figures may be underestimated as the daily publication of death records reduces the accuracy of the data (since June 11, 2020, Romania has released aggregate death data related to COVID-19). Analysis of COVID-19 mortality time series should also be interpreted with caution and based on metadata released by the responsible authorities. For example, in Romania, since May 28, 2021, daily data on COVID-19 deaths also include deaths that occurred before the reference date which coincides with the date of reporting. As a result, of the 46430 COVID-19-related deaths reported on October 28, 2021, nearly 8% occurred prior to the reference date.

Garcia et al. demonstrate that in the group of countries with comprehensive death counts, such as England and Wales (ONS data), the distribution of COVID-19-related deaths by age and gender is characterized by the highest proportion at age 90 and older. In these countries, the distribution of COVID-19 deaths by gender and age is primarily similar to that of death from all causes. Countries that provide the restricted data sources on COVID-19 deaths, such as Italy or Ukraine, have younger age distribution.

DATA SOURCES AND USED METHODS

In the study, we use two data sources regarding COVID-19 deaths:

1. Daily death records published by the Ministry of Health on the website https://msmps.gov.md since March 18, 2020 up to now;
2. Death certificates with the underlying cause of death U07.1 provided by the National Agency for Public Health for 2017-2020.

The Ministry of Health publishes daily death records notified to the National Agency for Public Health during the last 24 hours with the indication of the serial death number, age in complete years, sex, district, name of the medical institution where the case of death was registered and concomitant diseases. If a deceased person belonged to medical personnel, his/her name, age, and place of work are usually indicated. Prior to November 11, 2020, the MH also published the date of hospitalization or transfer to another hospital. On October 14, 2021, 96% of deaths from COVID-19 were registered as occurred in hospitals, while 0.4% of deaths were registered at home due to the patient's refusal of hospitalization as indicated in the daily MH report. For the remaining deaths (3.6%), the place of death was not indicated. Further, for reasons of simplicity, we will refer to this data source as "hospital death records". The MH also publishes data on deaths registered in the Transnistrian region (8% as of October 14, 2021 or 600 out of 7137 deaths). However, in our analysis, deaths from COVID-19 in Transnistria were excluded from the analysis because of the lack of data on the corresponding population. In Moldovan official statistics, death counts registered in this region are not included since 1998. To calculate weekly probabilities of death, we used population counts referring to the usually resident population (without Transnistria) as of January 1, 2020 and January 1, 2021.

In the analysis, we used weekly probabilities of death, life tables, the method of decomposition (Andreev and Shkolnikov 2012), standardised death rates (direct method, the 2013 European standard population), descriptive and inferential statistics. Since data on the age of death are skewed (Shapiro-Wilk test, $p<0.05$ and data visualization based on Q-Q plot), we used median and interquartile range (IQR) as descriptive statistics and Wilcoxon rank sum test as inferential statistics. To analyse weekly excess mortality in 2020, we used the 2017-19 average as a baseline to ensure better robustness of data over time. Data were analysed in R.

THE RESULTS OF RESEARCH AND DISCUSSIONS

Figure 1 presents weekly changes in COVID-19 deaths in Moldova based on two data sources: hospital death records of laboratory-confirmed COVID-19 cases from March 18, 2020 to October 7, 2021 and death certificate records with the underlying cause U07.1 from March 18, 2020 to December 31, 2020.

Death certificates, n = 2819

Hospital records, n = 2790

Period: from 2020-03-18 to 2020-12-31, without Transnistria

Figure 1. **Hospital death records (laboratory-confirmed deaths)** *versus* **death certificate records (underlying cause = U07.1), Moldova, both sexes**
Source: Hospital death records – Ministry of Health (https://msmps.gov.md); death certificate records – National Agency for Public Health

Following a relatively steady increase in COVID-19-related deaths since March 18, 2020, the first wave occurred between late November and late December, with the highest weekly deaths in mid-December 2020. The second wave occurred shortly after the first one, from early March to late April, and the intensity was much higher. Finally, after a certain relief in May and summer, the new wave started in the fall of 2021.

At least before early November 2020, in other words, before the first wave, the two curves coincide nearly exactly. The intensity of the first peak in mortality in November and December 2020 is underestimated and somewhat delayed over time, based on hospital death records, compared to certificate death records. The explanation for this is simple. During this period over-burdened medical facilities have sent information to the National Agency for Public Health on a daily basis with some delay. On the other hand, weekly deaths, according to death certificates, fall sharply at the very end of 2020, while those according to hospital death records decrease smoothly until mid-January 2021. This situation for the temporal evolution of death certificate records is quite typical since some deaths that occurred at the end of December will be registered at the beginning of the next year. Nonetheless, the cumulative number of deaths on December 31, 2020 is very close according to two sources.

Figure 2 shows the weekly probabilities of COVID-19 deaths by gender for the pre- and post-60 age groups. Data for the whole period are based on hospital death records.
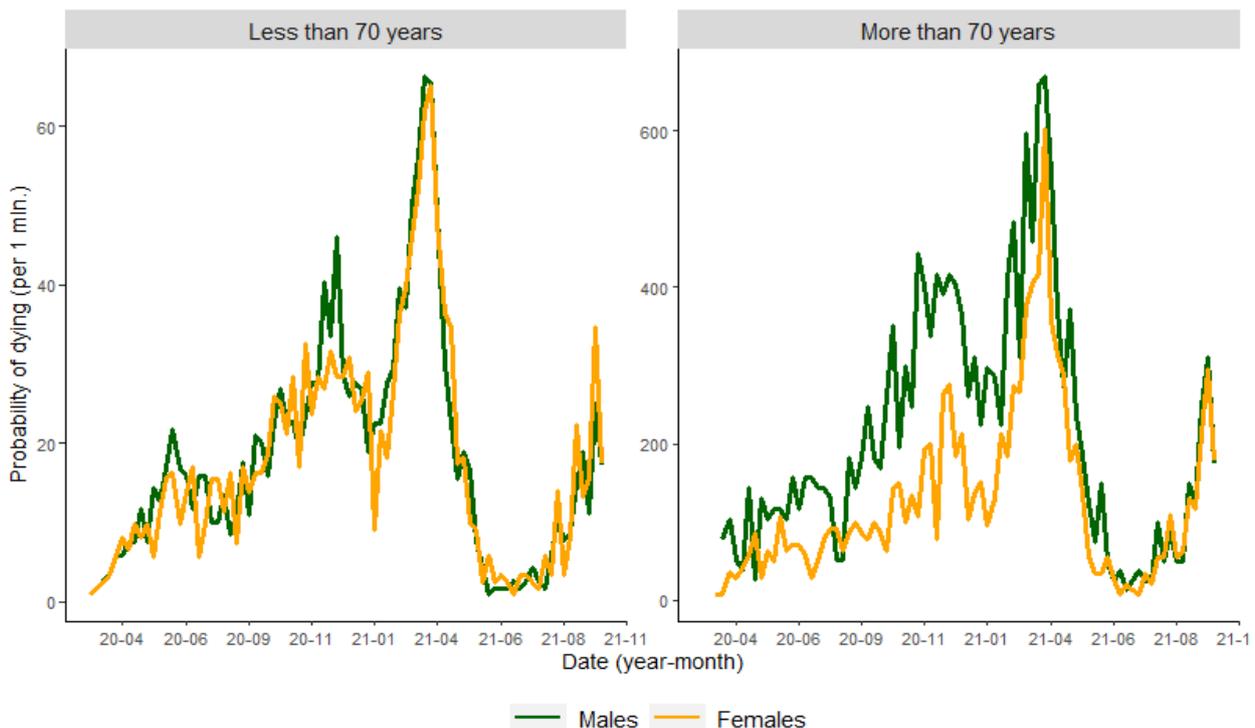

Figure 2. **Weekly probability of dying from COVID-19, hospital death records (laboratory-confirmed cases), Moldova, by sex and age**
*Source: Hospital death records – Ministry of Health (https://msmps.gov.md)*
Note: without Transnistria

It is interesting to note that in the pre-70 age group, the crude probabilities of death do not differ by gender. At the same time, mortality is higher among males than females in the post-70 age group prior to the start of the second wave. During the second and third waves, the intensity of COVID-19-related mortality does not appear to differ by gender, whether in middle-aged or elderly individuals. For both genders and all ages, the second wave referring to the warm season (spring) proved much stronger than the first wave referring to the cold season (late autumn – beginning of winter). The situation improved substantially in the months when the lowest (January, February) or highest (late spring,

summer) temperatures were observed. Certainly, these improvements are in part a result of restrictive measures against COVID-19. In Moldova, vaccination for COVID-19 started in early March 2021, and as of October 23, 2021, 849435 individuals had received two doses of the COVID-19 vaccine (Government of the Republic of Moldova 2021), representing 33% of the usually resident population. The impact of the vaccination campaign will be particularly important for the current third wave.

The distribution of cumulative COVID-19 deaths by gender and age as of December 31, 2020 and October 7, 2021 is shown in Figure 3. On December 31, 2020, the maximum number of deaths was recorded in the 65-69 age group for both males and females. The median age at death was 67.0 years in males and 67.5 years in females at that time, with no statistically significant difference (p>0.05, Wilcoxon rank sum test). On October 7, 2021, the maximum cumulative number of deaths attributable to COVID-19 occurred in the same age group (65-69). However, this time, the distribution of deaths has shifted according to gender. The proportion of deaths among older men, particularly those aged 70 to 74 and 85 and over, has increased considerably. Among women, as of October 7, 2021, the distribution of deaths remained essentially the same as at the end of 2020, although the impact of the oldest age group increased as it also did among men. These changes are most likely due to a better diagnosis of COVID-19 in the elderly. As a result, the median age at death has increased in men (68.0 years, IQR=61-74) and women (69.0 years, IQR=62-75). The difference in the median age at death among men and women on October 7, 2021 is statistically significant (p<0.05, Wilcoxon rank sum test). The same applies to the difference between the two points in time, for both men and women.
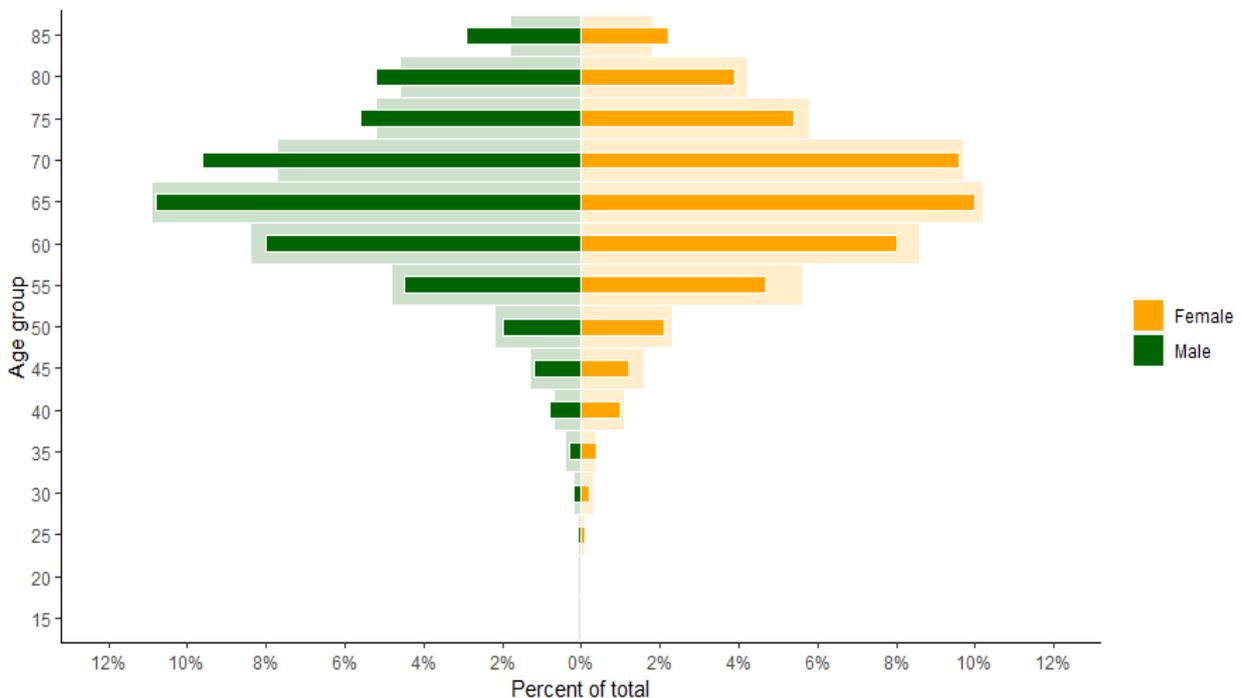
07 Oct. 2021 shown on the top of 31 Dec. 2020 (without Transnstria)

07 Oct. 2021, n = 6370 (age or sex missing for 52 deaths)

31 Dec. 2020, n = 2749 (age or sex missing for 14 deaths)

Figure 3. **Age and sex distribution of COVID-19 deaths as of 07 October 2021 as compared to 31 December 2020, Moldova**
Source: *based on hospital death records published by the Ministry of Health*
(*https://msmps.gov.md*)

Another important aspect in the analysis of time series is excess mortality that can be defined as the ratio of weekly probabilities of dying in 2020 to the average in 2017-19. This ratio calculated for all ages and causes of death has the highest values (2.5-3.0) at the end of 2020 when the first wave was recorded. Figure 4 presents weekly excess mortality in 2020 by main age groups for all causes of death and diseases of the circulatory system. Excessive all-cause mortality for those over the age of 40 in November and December 2020 makes perfect sense. However, it is not quite usual to see excess mortality from diseases of the circulatory system among the elderly in late 2020. This is most likely the result of misdiagnosis and attribution of undiagnosed COVID-19 deaths to cardiovascular disease.
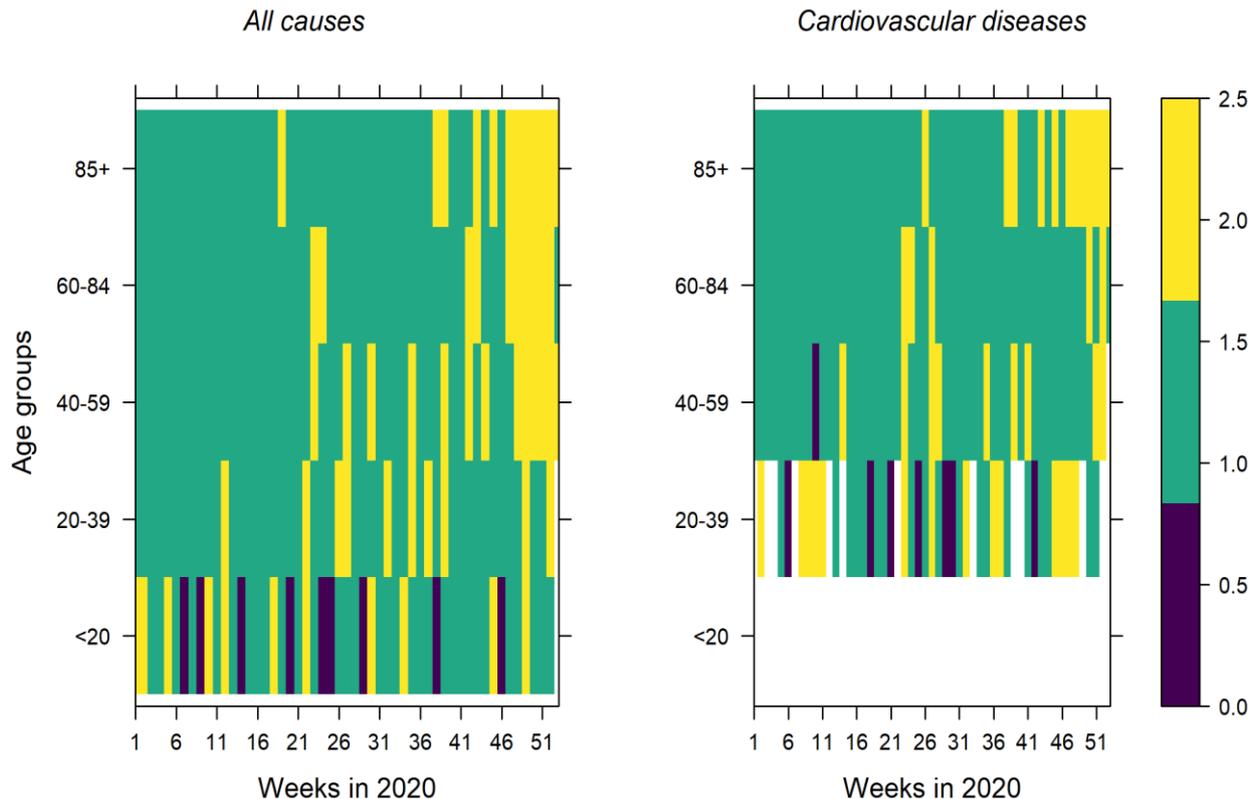

Figure 4. **Ratio of weekly probabilities of dying from all causes and cardiovascular diseases in 2020 to average in 2017-2019, by main age groups, both sexes, Moldova**
Source: *based on death certificate records provided by the National Agency for Public Health*

To understand the impact of COVID-19 infection on life expectancy at birth (e_0), it is possible to decompose the changes in e_0 between 2019 and 2020 by age and cause of death (Fig. 5). In Moldova, life expectancy at birth decreased by 0.8 years in males and 1.1 years in females in 2020 (65.8 in males and 73.9 in females) compared to 2019 (66.6 in males and 75 in females). In men, this drop in life expectancy is explained by the increase in mortality from infectious diseases (-0.6 years) and diseases of the circulatory system (-0.2 years). In women, the increase in mortality from infectious diseases is also the main cause of the decrease in life expectancy (-0.8 years), while the impact of cardiovascular diseases is noticeable (-0.2 years). The increase in infectious disease-related mortality in 2020 was between 50 and 79 for males and between 45 and 79 for females. Cardiovascular mortality has increased in 2020 compared to 2019 in some older age groups (65-74 in men and 70-74 and 85+ in women). In Moldova, positive annual trends in old-age mortality from cardiovascular diseases, especially among women, have been observed since at least 2005. The reversal in 2020 is very likely the result of excessive cardiovascular mortality among older adults in late 2020. The lack of mortality growth in the oldest age group can be attributed to positive trends in cardiovascular mortality that also continued in 2020 up to the first wave of COVID-19.
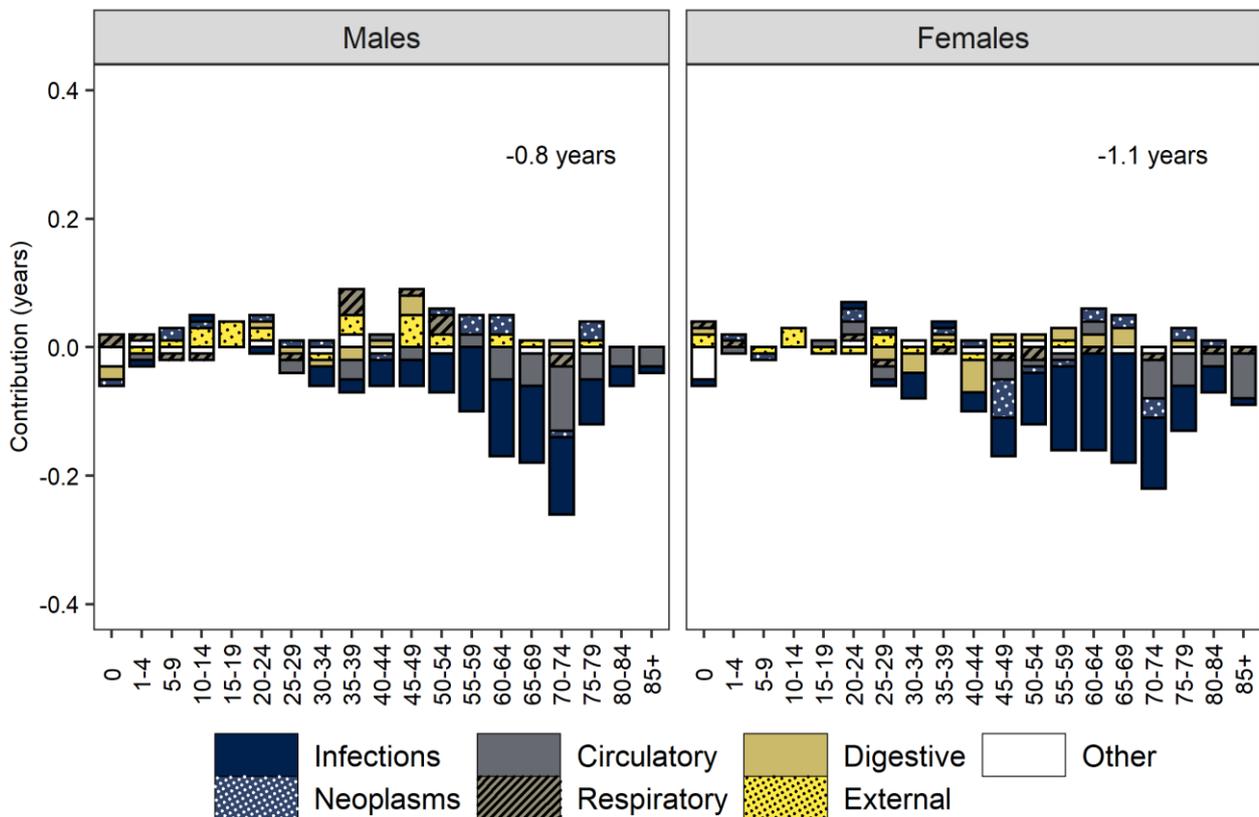
Figure 5. **Decomposition of changes in life expectancy at birth in 2020 compared to 2019 by age and causes of death in Moldova, by sex**
Source: *based on death certificate records provided by the National Agency for Public Health*

In terms of the standardised death rates, the COVID-19 pandemic resulted in a 10-fold increase in infectious disease mortality in 2020 compared to the previous year for both men and women. As a result of this enormous increase, the risk of dying from infectious diseases in 2020 was even higher than that from injury and poisoning in males or identical to that from diseases of the digestive system in females.

CONCLUSIONS

The COVID-19 deaths registration system in Moldova is limited to laboratory-confirmed cases recorded in hospitals or at home when a patient refuses to be hospitalized. In 2020, hospital records statistics are more or less consistent with death certificate information where COVID-19 is reported as an underlying cause of death. In 2020, deaths from COVID-19 infection were under-registered, especially among older adults. Excess mortality among the elderly in late 2020 (wave 1) is attributed in part to cardiovascular disease. In 2021, the registration of COVID-19 deaths has improved compared to 2020, especially among the elderly, due to better testing capacities. The male-to-female ratio for COVID-19 mortality is higher in older age and much less so in middle age. The gender difference among older adults is larger for the first wave and smaller for the second wave and the start of the current third wave. An important aspect of the research is the gender difference in COVID-19 mortality from an international perspective. Disregarding the under-registration of COVID-19 deaths in 2020, the pandemic has had a quite sizable effect on life expectancy at birth for both genders. Considering the intensity of the second wave and the current third wave, the impact of infections seems to increase in 2021. Vaccination is the only solution to overcome the crisis.

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