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Spatial disparities in mortality by causes of death in the Republic of Moldova

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Abstract

Background: Previous studies have shown long-term unfavourable changes in mortality in the Republic of Moldova accompanied by recent improvements. Little is known about the regional mortality differentiation which is an important tool for evidence-based public health policy. The aim of the study is to assess the current geographical disparities of all-cause and cause-specific mortality in Moldova and to identify evidence-based modalities to reduce them.
Material and methods: This cross-sectional study is based on the corrected results of the 2014 census and individual death records for the 2012-2016 period provided by the National Agency for Public Health. Global Moran's index and local indicators of spatial autocorrelation were computed based on contiguity matrix.
Results: All-cause mortality gradient between the northern and central regions was found for males (Moran's index=0.47, p<0.001) and females (Moran's index=0.44, p<0.001). Digestive and cardiovascular diseases for both sexes and external causes of death for males had a statistically significant influence on the inter-regional mortality differentiation. Liver cirrhosis contributed the most to the geographical difference between the North and the Centre (Moran's index=0.59, p<0.001), especially for females.
Conclusions: The results of this study point to the existence of different drinking habits of the Moldovan population between the northern and central regions. The central regions that form the cluster of "high-high" mortality from liver cirrhosis should be considered as primarily targets for antialcohol policies.
Key words: mortality, causes of death, spatial autocorrelation.

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Introduction

The problem of high mortality in the countries of the former Soviet Union (FSU), especially in its European part, is largely discussed in the literature. Studies have shown that an increase in adult mortality in these countries that began from the mid-60s of the last century left them far behind the western countries where life expectancy progress has accelerated since the 1970s due to a massive decline in cardiovascular mortality [1]. At the level of causes of death, the main contributors to this long-term health crisis in Russia [2], Ukraine [3] or the Baltic countries [4] are cardiovascular mortality and external causes of death, a category that includes accidental poisoning, traffic accidents, suicides, homicides. Moreover, it was shown that a harmful alcohol consumption behaviour in these traditionally spirits drinking countries was considered as a major factor of population health deterioration [5]. After several decades of rising mortality and short-term fluctuations, considerable recent improvements in life expectancy were achieved in Estonia from the mid-90s, Russia from 2005 or Ukraine from 2009, which points to the beginning of the convergence trend in life expectancies between the FSU countries and the western countries [6]. Although data quality for Moldova is somewhat more questionable as compared to Russia or Ukraine [7], the long-term overall mortality trends are very similar in these countries. The high level of cardiovascular mortality plays a crucial role for low life expectancy of the Moldovan population disregarding its recent improvements [8]. Further, in Moldova, which is a wine drinking country, the role of chronic alcoholism due to a high consumption of unregistered home-made wine is a particular health issue, especially for female population [9].

Along with mortality studies at the national level, researchers pay more and more attention to the regional mortality trends and patterns in the FSU countries. Thus, several studies have been conducted for Ukraine, Russia, Belarus. Poniakina S. demonstrated the geographical diversity of mortality patterns in Ukraine between the western regions that have lower cardiovascular and external mortality and the eastern (for males) and south-eastern regions (for females) whose population face more serious health problems for these two leading causes of death [10]. Timonin S., Danilova I. et al. showed that the recent life expectancy growth in Russia unfold differently across regions, and the two major cities, Moscow and Saint Petersburg, contribute the most to inter-regional divergence [11]. Grigoriev P. et al.

demonstrated that an increasing inter-regional mortality inequality in Belarus is associated with diverging trends from external causes of death [12]. The availability of cause-specific mortality data at the regional level for more and more countries allows researchers to move from international mortality comparison between countries to large-scale studies on cross-country differences in mortality taking into account the significant disparities within countries. Thus, using spatial autocorrelation technics, it was found that the districts located along the Belarusian–Lithuanian border, especially those on the Belarusian part, suffer enormously from conditions associated with an increased alcohol consumption such as liver cirrhosis and alcohol poisoning [13].

Although there are studies of long-term trends in cause-specific mortality in Moldova, little is known about its regional patterns. The study reported in this paper addresses to the regional mortality differences by causes of death in Moldova. The aim of the study is to assess current geographical disparities of overall and cause-specific mortality in Moldova and to identify evidence-based modalities to reduce them.

Material and methods

Present study relied on the 2014 usual resident population according to the 2014 Census adjusted by the Natural Bureau of Statistics (NBS) based on the post-census survey. As for mortality data, were used the individual death records for the period 2012-2016 codified according to the detailed (4-digit level) 10th revision of the International Classification of Diseases and Causes of Death (ICD-10) provided by the National Agency for Public Health (NAPH), which is responsible for the centralized codification of causes of death. To ensure better robustness of death rates at the regional level, was used the average for the given five-year period. Ill-defined causes of death (R00-R99) that constitute less than 1% for the analyzed period were redistributed proportionally among all causes of death. After that the data were aggregated by causes of death according to two lists: a short list that includes seven broad groups of causes of death and an extended one that consists of 20 items.

The mortality data were aggregated by 35 administrative units, including 2 municipalities (Chisinau, the capital of the country, and Balti). The mean population size of regions is 81 thousand (with Chisinau) and 63 thousand (without Chisinau). The minimum population size is 19 thousand (Basarabeasca) and the maximum one is 676 thousand (Chisinau). In 22 out of 35 regions, the population size is 40-80 thousand; in 8 regions, it is 80 thousand and over; in 5 regions – less than 40 thousand. The official statistical data have not been covering Transnistria and the municipality Bender since 1998.

Life expectancy and 95% confidence limits across 35 administrative units were calculated based, respectively, on Chiang C. L. method [14] and Silcocks et al. method [15]. Contributions by age and cause of death to the difference between life expectancy at birth in Moldova and its every region were estimated by E. M. Andreev's method [16, 17]. Mortality rates by sex and seven broad groups of causes of death were standardized by indirect method. Cause-specific death rates calculated for Moldova for the years 2012-2016, both sexes, were used as reference rates. Confidence limits were calculated based on Byar's or exact CI method [15]. To produce mortality maps, we used shape files from DIVA-GIS [18]. The "Jenks" optimization method of classification was used to produce life expectancy maps that maximize the differences between the categories of observations [19].

To carry out spatial analysis, global Moran's index and local indicators of spatial autocorrelation (LISA) [20] were calculated based on contiguity matrix. To construct the contiguity matrix that defines the spatial neighbourhood structure, was used the first-order queen structure. The LISA were presented using the LISA cluster maps that have five categories according to the type of spatial autocorrelation. The "*high-high*" cluster (*"hot" spots*) belongs to the regions that have high level of mortality and are surrounded by other regions that have above the average level of mortality. The "*low-low*" clusters (*"cold" spots*) belong to the regions with low mortality level surrounded by the regions with below average levels of mortality. Other two categories of spatial autocorrelation represent "high-low" and "low-high" spatial outliers (these two categories were not identified in the study). Finally, the fifth category represents statistically non-significant spatial autocorrelation labeled as *non-significant*. The significance level was estimated using Monte Carlo approach (number of simulations = 9999). Data were analysed in R.

Results

Life expectancy at birth (e_0) at the national level in 2012-16 is 68.4±0.2 in males and 76.4±0.2 in females. Across regions, it varies between 65.2±2.2 in Soldonesti and 71.5±0.5 in Chisinau among males and between 72.2±2.1 in Cimislia and 79.2±0.5 in Chisinau among females. Depending on the population size, confidence limits for e_0 varies from ±0.5 year for both sexes from Chisinau to ±3.2 years in males from Basarabeasca. Life expectancy at birth is higher than that at the national level only in six regions out of 35 for males and in 12 regions for females.

Figure 1 shows the maps of life expectancy at birth by sex. Life expectancy values are categorized into five categories by the "Jenks" optimization method. For both sexes, the highest and high values of life expectancy are observed in some northern regions and in Chisinau that are defined as the leading regions. In males, high values of e_0 are also observed in Anenii Noi. The regions with the lowest and low life expectancy defined as the lagging regions are located mainly in the central part of the country. A few southern regions that are adjacent to the Centre (Leova, Cimislia, Basarabeasca and Cantemir) also belong to the lagging regions. The nearest to the capital regions (first-order neighbours) have low values of life expectancy with two exceptions (Anenii Noi for both sexes and Ialoveni in males), while those of the second order have the lowest values of life expectancy. The regions with the lowest values of life expectancy, the most lagging regions, form *the belt of high mortality*. As one moves to the

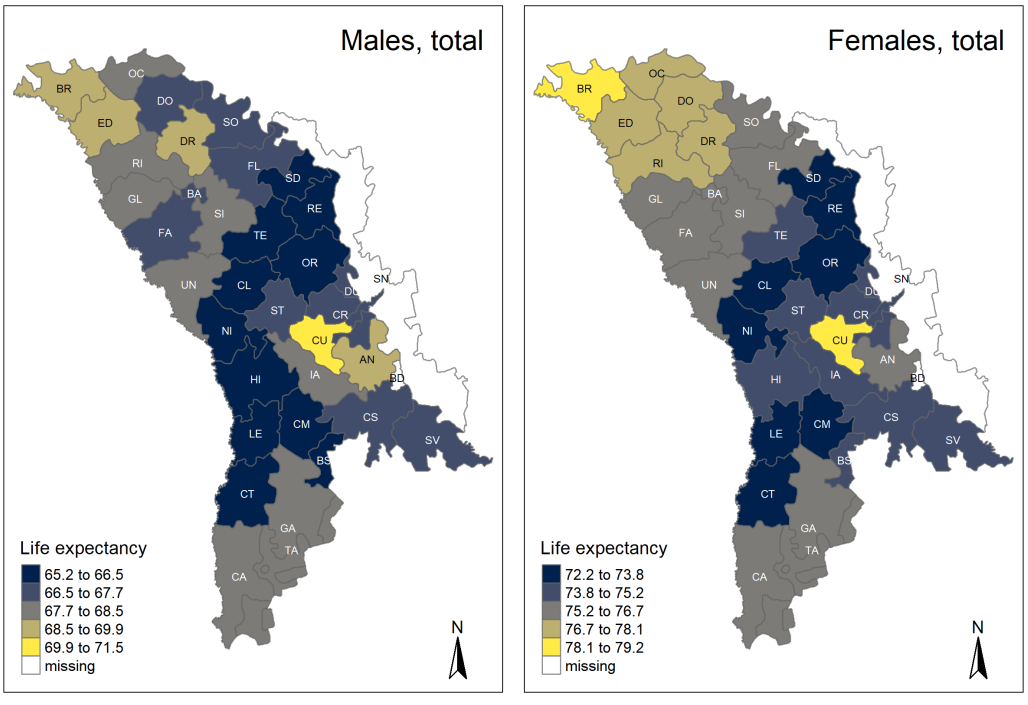

Fig. 1. Life expectancy at birth by regions in the Republic of Moldova, 2012-2016, by sex

Source: author's calculations based on NAPH and NBS data.

Note: "Jenks" optimization method of classification was used.

North or to the South of the country, the situation ameliorates gradually (stagnating regions), and in the most remote northern regions, life expectancy even approaches the level observed in the capital, especially in females. This division of regions into leading (North, capital) and lagging (Centre) can be traced and across age groups, although for older ages (65+) the belt of high mortality becomes less marked (fig. 1).

Contribution of mortality by age groups (less than 1, 1-19, 20-44, 45-64 and 65+) to the differences between e_0 in Moldova and its each region varies by sex. In males from the first three leading regions (Chisinau, Briceni and Edinet), low mortality among young (20-44) and mature (45-64 years old) adults accounts for 60-80% of life expectancy gains. The opposite situation is observed in the lagging regions where high mortality at these two age groups explains the lion's share of life expectancy losses (up to 90% in Cimislia). At the same time, the impact of older age groups among males is of less importance. On the contrary, among females, mortality at mature and older adult age groups contributes the most to the regional mortality differentiation.

At the level of main groups of causes of death (fig. 2), life expectancy differentiation in Moldova is largely explained by diseases of the circulatory system, diseases of the digestive system and external causes of death (in males). More than half of male life expectancy gains in Chisinau as compared to the national level is explained by cardiovascular diseases and external causes of death (1.9 out of 3.2 years). It is interesting to note that the positive contribution of external causes of death is registered only in the capital of the country, while in other regions, even with high life expectancy, it is either close to zero or negative. In females, the positive / negative impact of cardiovascular mortality is more pronounced across leading / lagging regions as compared to males. Females living in the capital gain 2.9 years as compared to the national level mostly due to lower mortality from cardiovascular diseases (60% of the total gain) and digestive diseases (20%). The similar situation for females, even in a lesser extent, is observed in the northern regions like Briceni or Edinet. On the contrary, females from the most lagging regions suffer much more from cardiovascular diseases and diseases of the digestive system. The impact of other main groups of causes of death, including neoplasms that occupy the second place in cause-specific mortality structure at the national level, is of minor importance. The municipality Balti seems to be the only exception concerning neoplasms with an unusually big as compared to other regions negative contribution for both sexes.

Decomposition of the difference in life expectancy at birth between the most lagging regions and the most leading regions by age and causes of death can help to better clarify the most affected population subgroups. The municipality Chisinau was selected as the most leading region where 24% of female and 23% of male population live (e_0 in males is 71.6 years and e_0 in females is 79.2 years). Since the belt of high mortality is more extended for life expectancy at age 25 or 45 than that at birth, the selection of the most lagging regions was based on the maps produced for e_{25}. In eleven regions with the lowest male e_{25} (less than 42.9 years), 21% of male population live. 16% of female population live in nine regions with the lowest female e_{25} (less than 50.2 years).

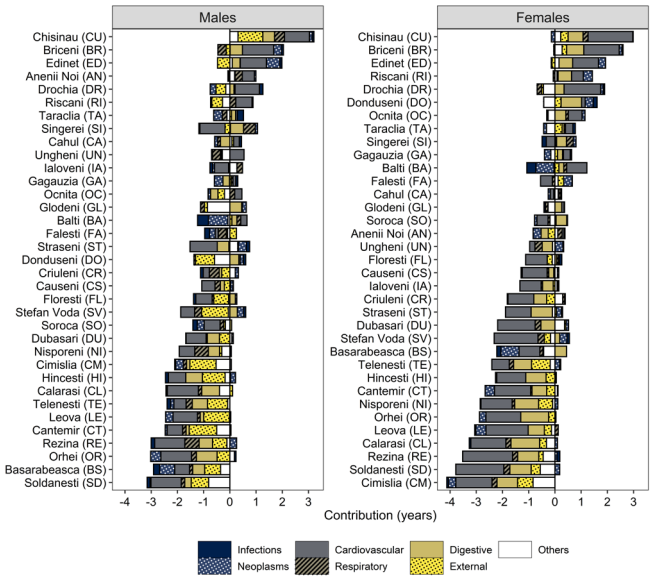

Fig. 2. Contributions by seven causes of death to the differences between life expectancy at birth in Moldova and its 35 administrative units, 2012-2016, by sex

Source: author's calculations based on NAPH and NBS data

Figure 3 shows the contribution by age groups and seven main causes of death to the difference in e_0 between the most lagging regions and the municipality Chisinau. The total difference in life expectancy at birth between these two extreme population subgroups constitutes -5.6 years in males and -5.7 years in females. The biggest losses are registered in mature male adults and older female adults. High mortality from diseases of the circulatory system in the most lagging regions reduced e_0 there by 1.8 years in males and by 3.1 years in females. In males, external causes of death (-1.6 year) and diseases of the digestive system (-0.9 year) are the next two main causes of death that deteriorate population health. In females, diseases of the digestive system constitute the second large group of causes of death that substantially increase the gap between the most lagging regions and Chisinau. It is interesting to note that this category of causes of death in females have almost the same negative impact as external causes of death in males (-1.4 years and -1.6 years, respectfully).

The contribution of mortality among children (0-14 years old) is -0.4 years for both sexes with the highest impact of "Other causes of deaths" mostly presented by perinatal causes of death. The young males (15-39 years old) from the most lagging regions lose 1.3 years (23%) of life expectancy at birth as compared to their counterparts from Chisinau. These losses are explained largely by external causes of death (-0.72 year). Among young female adults, the losses are much less pronounced (-0.6 years or 11%), but like in males they are mostly attributable to external causes of death. In males, the most affected age groups are mature adults (40-64 years old) whose high mortality accounts for 2.5 years or 45% of the overall losses. Although the negative contributions are registered for all causes of death in mature male adults, external causes of death and diseases of the digestive system explain more than half of all the losses. Moldovan females aged 40-64 years old from the most lagging regions lose on average 2.2 years of life expectancy compared to females from Chisinau. The negative impact of diseases of the digestive system for this age and sex group (-1.0 year or 44%) is even larger than that of diseases of the circulatory system (-0.73 year or 32%). At older ages, diseases of the circulatory system play the leading role for both sexes. In females, this age and cause of death group constitutes -2.3 years, which accounts for 90% of the overall losses at older ages (-2.5 years) and for 40% of the overall losses (-5.7 years).

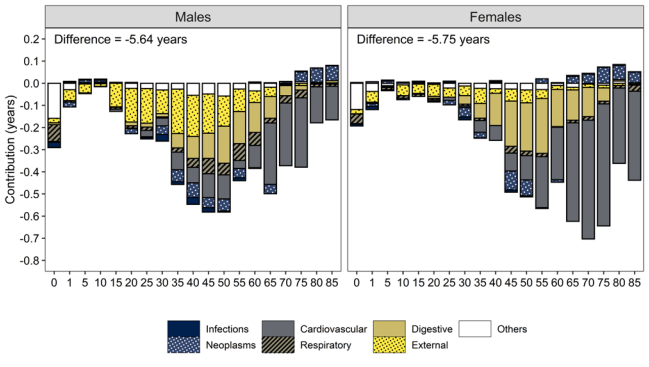

Fig. 3. Contributions by age and seven causes of death to the difference between life expectancy at birth in the most lagging regions and the municipality Chisinau, 2012-2016, by sex

Source: author's calculations based on NAPH and NBS data.

Note: the most lagging regions have life expectancy at age 25 less than 42.9 years in males (11 regions) and less than 50.2 years in females (nine regions)

The results of the global spatial autocorrelation for all-cause and cause-specific mortality are presented in table 1. The Global Moran's index is positive and statistically significant for overall mortality, diseases of the circulatory system,

Table 1. Global Moran's index and significance level for indirectly standardized death rates from seven major causes, by sex, Moldova

No	Cause of death	ICD-10 code	Males	Females
1.	Infections	A00-B99	0.148 (>0.05)	0.081 (>0.05)
2.	Neoplasms	C00-D48	0.037 (>0.05)	0.128 (>0.05)
3.	Diseases of the circulatory system	I00-I99, G45	0.309 (<0.01)	0.308 (<0.01)
4.	Diseases of the respiratory system	J00-J98, U04	0.041 (>0.05)	0.235 (>0.05)
5.	Diseases of the digestive system	K00-K93	0.438 (<0.001)	0.597 (<0.001)
6.	External causes of death	V01-Y98,	0.204 (<0.05)	0.126 (>0.05)
7.	Other causes	D50-G44, G47-H95, L00-Q99	0.05 (>0.05)	0.00 (>0.05)
8.	All causes	A00-Y98	0.473 (<0.001)	0.438 (<0.001)

Source: author's calculations based on NAPH and NBS data

diseases of the digestive system and external causes of death (only in males). It means that in Moldova, there are clusters of regions with the similar mortality patterns, i.e., regions with high mortality are surrounded by regions with high mortality ("hot" spots), while regions with low mortality are surrounded by regions with low mortality ("cold" spots). Diseases of the digestive system mostly presented by liver cirrhosis at the national level have the highest values of the global spatial autocorrelation, especially for females. At the same time, diseases of the circulatory system for both sexes and external causes of death for males have a less strong impact on the inter-regional mortality differentiati.

Figure 4 shows the location of the "high-high" and "low-low" clusters for selected causes of death on the map for both sexes. Depending on the cause of death, the location of these "hot" and "cold" spots on the map may differ. The division between the leading North and the lagging Centre is particularly impressive for liver diseases (Moran's index = 0.59, p<0.001). For diseases of the circulatory system, "low-low" clusters were depicted in the North of the country (Briceni, Ocnita, Edinet and Riscani), while "high-high" clusters were found for a few central regions (Soldanesti, Rezina, Orhei). The similar division remains and for heart diseases (Moran's index=0.29, p<0.05). However, for cerebrovascular diseases the most affected regions are situated in the South rather than in the Centre (Moran's index=0.3, p<0.001). Furthermore, the Moldovan population from the South of the republic seems to suffer much more from "Endocrine, nutritional and metabolic diseases" (Moran's index=0.24, p<0.05) mostly presented by diabetes mellitus as compared to the rest of the country. "Hot" spots for external causes of death were depicted for Hancesti, Leova, Cimislia and Soldonesti and a "cold" spot for the municipality Chisinau. Then, the municipality Chisinau and its first-order neighbours form the cluster of "low-low" mortality for certain conditions originating in the perinatal period, while in Soldanesti and Rezina, the situation is opposite (Moran's index=0.22, p<0.05).

Although the global Moran's index is not statistically significant for the whole category of neoplasms, the spatial autocorrelation analysis at the level of more detailed causes revealed certain specific geographical patterns. Thus, in the South of the country (Basarabeasca, Gagauzia, Cahul, Cantemir, Cimislia, Taraclia), the clusters of "high-high" mortality were detected for malignant neoplasms of stomach (Moran's index=0.19, p<0.05) and urinary organs (Moran's index=0.18, p<0.05). Another interesting finding is that cluster of "high-high" mortality from HIV infection was depicted for the municipality Balti and its first-order neighbours (Riscani, Glodeni, Singerei) (Moran's index=0.26, p<0.001).

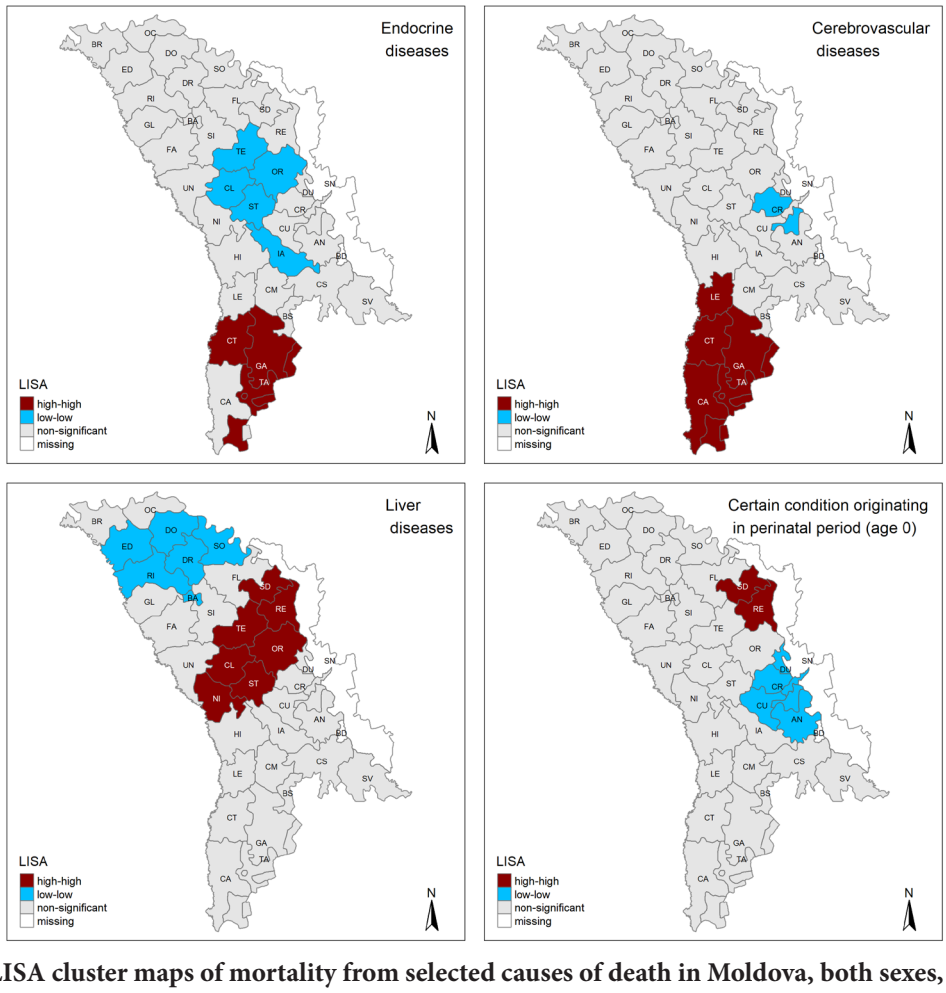

Fig. 4. LISA cluster maps of mortality from selected causes of death in Moldova, both sexes, 2012-2016
Source: author's calculations based on NAPH and NBS data

Discussion

Before discussing the main finding of this study, it is necessary to consider its data quality issues and limitations. Studies on regional data analysis may be complicated by the variation in regional coding practices of causes of death. It is of particular importance for those countries where the system of codification of causes of death is decentralized. Since in Moldova the codification of causes of death is centralized, this problem can be omitted. Then, the statistical continuity of death time series is complicated by periodic revisions of the classification of causes of death and by the changes in coding practices between two classifications. In this study, were used the average mortality data under the 10th revision of ICD-10 for the years 2012-2016. The analysis was performed at the level of the broad groups of causes of death, which is a common measure to avoid discontinuities in time series. The small proportion of ill-defined causes of death (less than 1%) for this period does not affect the results of the study.

The main limitation of the study is the selected time period (2012-2016). To avoid a possible systematic bias that can be induced by intensive internal and international migration flows, was opted the period around the last census conducted in May, 2014. The results of the 2014 census were adjusted by the National Bureau of Statistics due to the incomplete coverage of the population in the municipality Chisinau where it was only 59% [21]. However, since the overall and cause-specific mortality trends in Moldova at the national level have not changed drastically over the last decade, apart from the year 2020 affected by COVID-19 pandemic, it can be assumed that the presented regional mortality patterns correspond and to the period until 2020. The comparative analysis of regional mortality patterns around 2014 census to the period around 2004 census is a future research direction of the study.

In this study, were explored the current regional patterns of all-cause and cause-specific mortality in Moldova. The analysis of all-cause mortality suggests that the inter-regional differences exist between the municipality Chisinau and the North of the country on the one hand and the central regions on the other hand. The regions with the lowest life expectancy values form the belt of high mortality which stretches from Soldanesti to Cantemir. It is interesting to note that most of these regions are the second-order neighbours to the capital of the country. It was surprising to see that in some regions that are the first-order neighbours to Chisinau, the population health is much worse as compared to the capital. Even for such a small country like Moldova, with the total population of 2.6 million, the proximity to the capital does not ameliorate the population's health, but, on the contrary, worsens the situation. On the other hand, the studies on the regional mortality differentiation in the FSU countries have similar results. For example, in Belarus, the inter-regional overall mortality disparities are defined by the differences between the capital and the rest of the country [12].

The spatial analysis of cause-specific mortality patterns revealed that only three broad groups of causes of death play a statistically significant role in the inter-regional mortality differentiation: diseases of the digestive system, diseases of the circulatory system and external causes of death in males. The north-centre gradient in all-cause mortality is largely explained by diseases of the digestive system, liver cirrhosis in particular, both in males and females. The regions involved in the cluster of "high-high" mortality from liver cirrhosis (Soldanesti, Rezina, Telenesti, Orhei, Calarasi, Straseni and Nisporeni) experience serious health problems related to an excessive alcohol consumption. Previous studies showed that chronic consequences of alcohol consumption such as liver cirrhosis had an enormous influence on the Moldovan population's health, especially for females [9]. Unrecorded alcohol consumption dominated by home-made wine plays an important role here. Thus, in Moldova, the consumption of home-made wine constitutes about 30% of the total alcohol consumed, without any significant difference by sex (it is even slightly higher for females). Furthermore, home-made wine consumption is especially popular among Moldovan females aged 45-69 years old, for whom it accounts for about 45% of the total alcohol consumed as compared to 35% for males in the corresponding age group [22].

The results of the spatial analysis suggest that diseases of the circulatory system also contribute to the formation of the north-centre mortality gradient, although to a much less extent as compared to diseases of the digestive system. We explain it by the fact that "high-high" mortality clusters for cerebrovascular diseases were detected in the South of the country, while for heart diseases – in the Centre. Finally, external causes of death account for mortality differentiation between the municipality Chisinau and some central regions.

Conclusions

A statistically significant gradient in all-cause mortality between the northern and central regions was found. At the level of causes of death, liver cirrhosis plays the most crucial role in this inter-regional mortality pattern, especially for female population. The results of the present study point to the existence of different drinking habits of the Moldovan population between the North and the Centre of the country. The central regions that form the cluster of "high-high" mortality from liver cirrhosis should be considered as primary targets for antialcohol policies.

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Author's contribution
OP conceptualized the idea, conducted literature review, collected the data, interpreted the data, and wrote the manuscript.

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No approval was required for this study.

Conflict of Interests
There is no known conflict of interests to declare.