Rural/urban disparities in cancer mortality: a case-study from northeast Greece
Diferenças na mortalidade por câncer rural/urbana: um estudo de caso do nordeste da Grécia

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Abstract
A descriptive epidemiological approach was undertaken in order to address the issue of rural/urban disparities in cancer mortality at northeast Greece. The direct standardization method was used to control for differences in the age-group distribution between the two regions. Region A was highly urbanized (>90%) and region B, predominantly agricultural. Registering of cases was carried out according to the World Health Organization ICD-10 protocol. Statistically significant findings emerged for prostate cancer mortality, which was 86% higher in rural as opposed to urban males (RR=1.86, 95%CI 1.10–3.14). In other cancer types (e.g. stomach cancer) a cohort effect may be present, thus necessitating further research into the hypothesis. Socioeconomic inequalities, such as access to health care and education are key factors for the eradication of rural/urban disparities in cancer mortality. Interventions should focus in health promotion and awareness, especially addressing the importance of early cancer screening and diagnosis.

Keywords: neoplasms; Greece; survival.

Resumo
Uma abordagem epidemiológica descritiva foi realizada a fim de abordar a questão das disparidades rural/urbana da mortalidade por câncer no nordeste da Grécia. O método de normalização direta foi usado para controlar as diferenças na distribuição da faixa etária entre as duas regiões. A região A era altamente urbanizada (>90%) e a região B, predominantemente, agrícola. O registro dos casos foi realizado de acordo com o protocolo da CID10 da Organização Mundial de Saúde. Foram observados resultados estatisticamente significativos para mortalidade por câncer de próstata, que foi 86% maior na área rural em oposição aos indivíduos de áreas urbanas (RR=1,86, IC95% 1,10–3,14). Em outros tipos de câncer (por exemplo, câncer de estômago) um efeito coorte pode estar presente, necessitando assim mais investigações sobre a hipótese. Desigualdades socioeconômicas, tais como acesso a cuidados de saúde e educação, são fatores fundamentais para a erradicação das disparidades rural/urbana na mortalidade por câncer. As intervenções devem centrar-se na promoção da saúde e conscientização, especialmente abordando a importância do rastreamento precoce e diagnóstico de câncer.

Palavras-chave: neoplasias; Grécia; sobrevida.

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INTRODUCTION

Differential patterns of cancer incidence and mortality have been observed between rural and urban communities around the world. Social, cultural, economic, occupational, environmental and demographic factors have been suggested as major driving forces behind these disparities. Although there are significant differences from one region (country or even continent) to another, certain principles do apply at the global scale. The process of economic development leads to advances in medical technologies and improved access to healthcare, which tend to reduce the impact of infectious diseases, especially that of infant and childhood mortality. This transition is typically followed by lower fertility rates, increased life-expectancy and an overall change in the structure of population. Demographic ageing brings forward a prominent modification of epidemiological indices, namely an increase in chronic and degenerative diseases, such as cancer.

These processes also occur at the interregional (within country) level and may become evident across the rural/urban axis. Social and economic deprivation, on the hand, which is commonly observed among poor and underdeveloped rural communities further exacerbates this effect. Rural populations tend to be less well-educated and with lower economic means, thus suffer significant inequalities in terms of access to medical care and health awareness. Moreover, the ecology of rural populations differs markedly from that of urban dwellers as regards environmental and occupational hazards. The use of agrochemicals, impact of ultraviolet radiation (sunlight) and poorer hygienic conditions tend to aggravate physical threats in rural areas. Conversely, social discriminations, noise, stress, and air pollution are more widespread in the urban environment.

Several studies have investigated the relationship between rurality and cancer. One of the most important findings is that rural residents are generally diagnosed at a later stage and have decreased survival rates as opposed to their urban counterparts. This has been shown for many types of cancer in both developed and developing countries, including colorectal, breast and prostate adenocarcinomas. At least, for these type of cancers it is known that secondary prevention (i.e. colonoscopy, mammography and PSA screening, respectively) plays an important role. It could be, thus, speculated that the time of referral is detrimental to final cancer outcome and patient prognosis. Moreover, it suggests that interventions should focus selectively on early screening and diagnosis.

Prostate cancer, in particular, is the most common cancer in males in developed countries and third in terms of mortality. In developing countries prostate cancer is only sixth in both incidence and mortality, although this discrepancy is probably due to differences in the efficiency of diagnostic methods. In 2008 Southern Europe and Southern America had identical age-standardized incidence rates equal to 50.2 per 100,000 males, albeit mortality in the latter was slightly higher (16.2 versus 10.5 per 100,000). Age, race and family history are the only well-established risk factors for prostate cancer. Diet, physical activity and obesity have been suggested as modifiable ones, although with weaker evidence of association.

Here we describe a descriptive epidemiological study concerning cancer mortality in northeast Greece. The aim was to compare age-standardized rates in a rural and an urban community, in order to derive specific epidemiological information and establish a working hypothesis based on local findings. This approach has allowed the characterization of health inequalities across the rural/urban axis and gave the opportunity for dynamic health policy formulation targeted at: (A) improved health care access and (B) health promotion and education among agricultural populations.

MATERIAL AND METHODS

Mortality data were collected for the period 1999–2000 from the death registries of two regions: region A (n=3,879 records) with 92.7% urbanization and region B (n=2,237 records), where the majority (14 out 15 communities) are rural. The case definition involved male and female deaths with permanent residence in either of the two regions registered according to the International Classification of Disease (ICD-10) of World Health Organization (WHO). Standardization for age was performed by the direct method using the Standard European Population as reference and confidence intervals for rate ratios were calculated by the Poisson approximation method.

RESULTS

Standardization for age alleviated the imbalances in crude mortality that are produced by demographic differences in the two regions. Rate ratios in Table 1 suggest that all cause mortality is 63% higher in region B (rural) as opposed to region A (urban), albeit this difference is diminished to 5% after controlling for population structure.

Table 1. General all cause mortality per 100,000 person years (both genders)

<table>
<thead>
<tr>
<th></th>
<th>Region B (rural)</th>
<th>Region A (urban)</th>
<th>Rate ratio</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR</td>
<td>1181.2</td>
<td>725.59</td>
<td>1.63</td>
<td>1.32–1.76</td>
</tr>
<tr>
<td>SMR</td>
<td>750.72</td>
<td>711.67</td>
<td>1.05</td>
<td>0.89–1.14</td>
</tr>
</tbody>
</table>

CMR: Crude mortality ratio; SMR: age-standardized mortality ratio; 95%CI: 95% confidence interval
Table 2 shows the age-standardized cancer mortality per 100,000 person-years for both genders in region A and region B. Rate ratios and 95% confidence interval (95%CI) are used to compare rural/urban differences in mortality over several types of cancers. Mortality from stomach, colorectal, bladder, brain and lymphatic/hematopoietic cancers is generally higher in rural areas, whereas mortality from liver, kidney and lung cancer is lower, although not statistically significant. As regards gender-specific cancers, prostate cancer mortality in males is 86% higher in rural as opposed to urban areas and the confidence interval for the rate ratio is 1.10–3.14. Hence, it can be concluded that there is a burden of prostate cancer among rural males versus their urban counterparts. For the female population on the other hand, breast and ovarian cancer mortality is higher in rural areas, whereas endometrial cancer mortality is lower, albeit of no statistical value.

Figure 1 shows age-standardized rates of prostate cancer in the two regions across age-strata in a semi-logarithmic scale. Clearly, prostate cancer mortality is higher in rural areas across age groups. Rates of stomach cancer are also depicted (Figure 1B) for comparison. In this case, mortality in rural areas is lower in younger age groups (35–64) but higher in older ones (65 and more). Hence, if truncated rates were considered it could possible that these differences would become

<table>
<thead>
<tr>
<th>Type of cancer (ICD-10)</th>
<th>Region B (rural)</th>
<th>Region A (urban)</th>
<th>Rate ratio</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All types (C00-97)</td>
<td>183.4</td>
<td>174.2</td>
<td>1.05</td>
<td>0.91–1.18</td>
</tr>
<tr>
<td>Stomach (C16)</td>
<td>18.3</td>
<td>13.3</td>
<td>1.38</td>
<td>0.95–2.00</td>
</tr>
<tr>
<td>Colorectal (C18-20)</td>
<td>21.2</td>
<td>16.4</td>
<td>1.31</td>
<td>0.92–1.81</td>
</tr>
<tr>
<td>Pancreatic (C25)</td>
<td>10.6</td>
<td>7.8</td>
<td>1.36</td>
<td>0.82–2.26</td>
</tr>
<tr>
<td>Liver (C22)</td>
<td>7.0</td>
<td>9.4</td>
<td>0.78</td>
<td>0.47–1.19</td>
</tr>
<tr>
<td>Bladder (C67)</td>
<td>6.6</td>
<td>5.9</td>
<td>1.17</td>
<td>0.63–2.00</td>
</tr>
<tr>
<td>Kidney (C64)</td>
<td>2.0</td>
<td>3.8</td>
<td>0.50</td>
<td>0.22–1.24</td>
</tr>
<tr>
<td>Lung (C34)</td>
<td>42.4</td>
<td>44.3</td>
<td>0.95</td>
<td>0.84–1.09</td>
</tr>
<tr>
<td>Brain (C71)</td>
<td>8.1</td>
<td>6.3</td>
<td>1.27</td>
<td>0.93–1.74</td>
</tr>
<tr>
<td>Lymphatic/hematopoietic (C81-96)</td>
<td>12.4</td>
<td>10.4</td>
<td>1.20</td>
<td>0.95–1.52</td>
</tr>
<tr>
<td>Prostate (C61) ♂</td>
<td>28.1</td>
<td>15.1</td>
<td>1.86</td>
<td>1.10–3.14*</td>
</tr>
<tr>
<td>Breast (C50) ♀</td>
<td>22.6</td>
<td>21.3</td>
<td>1.10</td>
<td>0.67–1.68</td>
</tr>
<tr>
<td>Endometrial (C54) ♀</td>
<td>4.1</td>
<td>8.1</td>
<td>0.50</td>
<td>0.21–1.18</td>
</tr>
<tr>
<td>Ovary (C56) ♀</td>
<td>11.8</td>
<td>10.2</td>
<td>1.16</td>
<td>0.60–2.23</td>
</tr>
</tbody>
</table>

ICD-10: International Classification of Disease-10; 95%CI: 95% confidence interval; ♂: male; ♀: female; *statistically significant at the 5% level (p<0.05)
statistically significant in certain cohorts. This finding raises certain aspects of descriptive epidemiology that are typical of small areas and necessitates further research into the hypo-
thesis. These data could for example reveal a pattern of early-life exposure, such as that for stomach cancer in rural areas.

**DISCUSSION**

Health disparities have been observed between rural and urban regions around the world. Several risk factors have been described as potential drivers of this epidemiological polarization. Access to health care, including distance from medical facilities, physician-to-population ratio, availability of cancer detection technologies and screening methods constitute some of the most important aspects of social deprivation and rural-
ity. Limited financial resources and economic factors tend to augment these disparities even further. The availability of public versus private medical centers and public health insurance coverage of medical costs is also detrimental.

Moreover, health promotion and education is usually minimal in rural populations. Limited disease control and pre-
vention (primary or secondary) is predisposing for increased incidence and mortality from chronic diseases. Behavioral factors, such as smoking, diet and alcohol consumption may alter individual outcomes, albeit cultural or religious beliefs may be equally important. For example, higher levels of stoicism and fatalism have been observed among rural populations due to the denial of presenting symptoms and the fear of stigmatization, which results in delayed screening and, thus, diagnosis. Increased time to diagnosis, on the other hand, ultimately leads to heavier tumor burden and worse treatment compliance.

This is best exemplified in the case of prostate cancer. Prostate cancer typically develops slowly and the cancer may be preceded by dysplastic lesions for many years, or even decades. Thus, small, localized prostate neoplasias can remain unrecognized for many years before progressing to a clinically significant disease. For many oncologists, prostate hyperplasia is an inevitable feature of male physiology that comes with advanced age. In fact, in many autopsies prostate cancers are found incidentally, suggesting that they have been asymptomatic and not a cause of death. In 2008 there were 903,500 estimated new cases of prostate cancer worldwide and 258,400 deaths. The use of PSA testing to detect prostate cancer in an early phase has shifted the spectrum of diagnosed cancers toward an increased diagnosis of moderately differen-
tiated tumors (Gleason sum scores 5–7). PSA screening has altered the age distribution of prostate cancer cases as well. In Germany for example the mean age at diagnosis has declined from 73 years of age in 1980 to 69 years in 2006. Thus, ef-
fective screening is the key to combating this type of cancer. This can be best realized in the 5-year survival rates, which are almost 100% for local or regional tumors. However, when distant (stage IV, M1) tumors are considered, 5-year survival rates drop to less than 30%.

In this study, the comparison between rural and urban regions has indicated a clear distinction as regards prostate cancer mortality. In rural residents the mortality from this type of malignancy was 86% higher, when compared to their urban counterparts. This discrepancy was observed across all age-groups indicating an effect that is independent of age. Moreover, is suggests that the potential modifying factors are probably resilient to population characteristics and thus not crudely determined. A possible explanation for this phe-
nomenon could be the socioeconomic and educational status of agricultural populations. Lack of health attitude towards preventive (early) screening and diagnosis in combination with limited medical resources, including the absence of a specialist urologist/andrologist and diagnostic facilities in the area may predispose for higher morbidity and mortality.

On the other hand, a different picture emerges when it comes to cancers of the digestive tract, especially that of stom-
ach cancer. Here, a clear cohort effect is observed. Mortality from this type of malignancy in rural areas is higher in the older age groups. The semiology of this finding is very im-
portant because it addresses diachronic aspects of cancer epidemiology. Global trends of stomach cancer have been declining since the 1950s. This is an intrinsic feature of the dietary transition brought about by the advances in food pres-
ervation, the introduction of refrigerators and the overall im-
provement in the quality of nutrition. This development has led to a decrease in the consumption of salt-preserved food and cured meat, such as pickled or smoked products and the increase in the availability of fresh substitutes. The cohort of 65 and more years involved in this study was born between 1934 and 1943 and earlier. This suggests that they have been exposed to risk factors that probably persisted in rural areas for a longer period than in the urbanized environment.

Overall, a distinction is drawn as regards cancer mortality in northeast Greece. Although this study focuses only in two regions that represent a small portion of the total population, it may well serve as a global paradigm. More research is required in order to establish a clear picture of the epidemiological map and assess temporal trends that will confirm the hypothesis of rural/urban disparities in cancer mortality to a wider scale. It is also important to extend the findings to other nosological types, including both chronic and communicable diseases, as well as external causes and infant mortality. This will then enable
intervention studies to be conducted in order to mitigate the effects of morbidity and mortality in the local populations. The reasons behind increased incidence (or prevalence) of disease must be analyzed and fully explained, in order to establish efficient public health policies. Health promotion and education of agricultural populations towards preventive measures — including the benefits of early screening — must be pursuit, along with improving their access to medical and diagnostic centers. Finally, reversing socioeconomic inequalities is the ultimate goal for supporting the health status of rural populations and this goal should be in line with central government policies for fair distribution of funds and resources.

### REFERÊNCIAS