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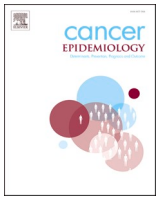

Half a century of cancer transition in Hungary: A visualization and assessment of mortality dynamics in the Lexis diagram, 1970–2020

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ABSTRACT

Objectives: Hungary is among the countries with the highest cancer mortality burden in Europe, consequently there is a crucial need to monitor changes in death rates in the population using appropriate surveillance tools. The Lexis diagram provides a means to depict age, period and cohort influences on long-term cancer mortality trends.

Methods: Age-specific mortality rates for six cancer localizations were constructed based on the Deaths Register of the Hungarian Central Statistical Office and the Human Mortality Database, then smoothed (p-splines) within the cells of the Lexis diagram assuming Poisson distribution. After calculating the annual percentage change in mortality rates, the results were visualized using heat maps.

Results: Substantial reduction in mortality was observable from the mid-1990s in both sexes as a strong period effect, depicting two distinct epidemiological eras in Hungary. Since 2010, breast cancer mortality in women among ages 70–90 (those born between 1930 and 1950) has been rising. Women born between 1940 and 50 experienced two plateaus in lung cancer mortality, unlike men, emphasizing the delayed nature of the smoking epidemic.

Conclusions: The results align with cancer transition patterns observed in similarly developed countries and emphasize a critical need to expand the implementation of effective primary and secondary prevention measures. This includes sustaining organized screening and anti-smoking programs, as well as introducing lung cancer screening with low-dose CT.

1. Introduction

Cancer will become the leading cause of premature death in most countries over the course of this century [1]. As a result, there are major productivity losses in the labor market at a time of spiraling costs of treatment, leading to serious deficits in state budgets. Cancer morbidity and mortality additionally takes a toll on the financial status and mental health of patients and their families, often causing financial and emotional hardship [2]. Primary and secondary methods of cancer prevention have proven to be effective tools in reducing the prevalence of modifiable risk factors or ensuring early diagnosis and curative treatment, respectively, thus making certain common malignancies avoidable, including lung, breast and colorectal cancer. With Hungary among the countries with the highest cancer mortality burden in Europe [3], the aim of this paper is to represent the dynamics of national cancer mortality rates over a half-century using the Lexis diagram. Assessing the cancer-specific mortality trends by sex enables a detailed picture of age-period-cohort effects, assisting in the identification of areas where

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progress has been, or can be achieved, in reducing cancer deaths.

2. Methods

Death counts were extracted from the Deaths Register of the Hungarian Central Statistical Office by calendar year (1970–2020), sex and single year of age (ages 0–100 years). During the half century, three revisions of International Classification of Diseases (ICD) were in use in Hungary: ICD-8 (1970–1978), ICD-9 (1979–1995) and ICD-10 (from 1996). Based on these revisions, we selected the specific subcodes for breast (ICD-10: C50), cervix uteri (ICD-10: C53), colorectal (ICD-10: C18–21), lung (ICD-10: C33–34), myeloid (ICD-10: C92–95) and prostate (ICD-10: C61) malignant neoplasms. The corresponding population exposures were extracted from the Human Mortality Database, and mortality rates were constructed and smoothed within the cells of the Lexis diagram assuming a Poisson distribution. Subsequently, a regression analysis was conducted utilizing penalized splines (p-splines). After calculating the annual percentage change in mortality rates, the results were visualized using heat maps. The changes in the mortality ratio were represented through color gradients, mapped onto a surface defined by the vertical (age), horizontal (calendar year), and diagonal (cohort birth year) axes. We used the 'MortalitySmooth' and 'ROMIplot' packages of R [4–6]. In addition, we compared cancer mortality in the year 2020 vs. previous years to measure the effect of COVID-19, though the impact on mortality was negligible.

3. Results

From a public health perspective, the number of deaths is also a fundamental indicator. Among men, lung cancer deaths largely increased until the millennium, after which it began to decline slightly; nevertheless, in the past decade alone, Hungary lost approximately 55,000 men to this malignancy. In contrast, female lung cancer deaths have increased rapidly by well over 30 % in each decade over the past half a century. Consequently, by 2020 the number of female lung cancer deaths had quadrupled compared to the 1970s, reaching approximately 33,000, similar to the level observed in men in the 1970s. For colorectal cancer, male and female mortality was balanced at about 20,000 deaths in the 1980s. Since then, male deaths shown a continuous, though slowing, increase over the past 50 years, leading to a more than 25 % higher number of deaths among men compared with women in the 2010s (28,000 vs 22,000). Prostate cancer deaths rose slightly during the 1980s and 1990s but have since the millennium stabilized at 12,000–13,000 per decade. Number of female breast cancer deaths largely increased up to the 2000s, then modestly declined, resulting in a rise from 16,000 to 21,000 deaths per decade over the last half a century. More favorably, male myeloid and cervical cancers have lost relevance in terms of number of deaths, with reductions of 12.5 % and 23 %, respectively, compared to 50 years ago. Overall, the cancer burden, if we express it in terms of the number of deaths, has multiplied for both sexes over the past half century, driven primarily by pre-millennium trends (Table 1).

Looking at the Lexis diagrams substantial reduction in mortality was observable from the mid-1990s in both sexes as a strong period effect, depicting two distinct epidemiological eras in Hungary. Women born between 1940 and 50 experienced two plateaus in lung cancer mortality, unlike men, emphasizing the delayed nature of the smoking epidemic (Fig. 1 A, B). Prior to the mid-1990s, females were much less affected by colon cancer mortality at younger ages relative to males, while mortality was also more favorable subsequently, especially in among those aged over 70. This indicates that other causes of death have come to the forefront among the elderly, replacing colon cancer. (Fig. 1 C, D). Since 2010, breast cancer mortality in women among ages 70–90 (those born between 1930 and 1950) has been rising (Fig. 1 E). Half a century of cervical cancer transition commenced with strong period-related increases in mortality between 1970 and 1980 among women aged 20–40 and 60–80. These formed the basis for three subsequent cohort effects which began in the 1990s. The first occurred among those born between 1910 and 1940, who experienced declines in mortality, notably in the calendar period 1990–2000. The second are those born between 1940 and 1960, for whom the slight increase in mortality lasted until the very latest times. Finally, the third cohort represent those born after 1980, for whom mortality rates have been in decline subsequently (Fig. 1 F). Prostate cancer mortality increased markedly among men aged over 40, up to around the start of the millennium, notably among men aged 80 years and over. Subsequently, between 2000 and 2010, there were clear mortality declines at ages 70–90 (cohorts born 1910–1930), followed by an uptick in mortality after 2010 at younger ages (cohorts born in 1930–1950). Since 2000 among younger ages (up to the age of 60) prostate cancer mortality rates have been in minor decline (Fig. 1 G). Finally, myeloid malignancies among men depicts an almost horizontal pattern and a clear age effect, perhaps with some mortality declines among men aged over 70 years from 1990, implying a strong biological determination at play with a relative independence of the disease from modifiable risk factors over time (Fig. 1 H).

Table 1
Number of deaths and their periodical changes by decades, sex and cancer localizations in Hungary, 1970–2020.

Male								
	Lung		**Colorectal**		**Prostate**		**Myeloid**	
	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade
1970–1979	33,875	-	14,047	-	11,350	-	3235	-
1980–1989	47,720	40,9	18,948	34,9	12,354	8,8	2644	− 18,3
1990–1999	57,229	19,9	23,730	25,2	13,155	6,5	2736	3,5
2000–2009	56,431	− 1,4	26,177	10,3	12,442	− 5,4	2731	− 0,2
2010–2019	54,565	− 3,3	28,221	7,8	12,604	1,3	2831	3,7
2020	4818	-	2771	-	1354	-	251	-
Female								
	Lung		**Colorectal**		**Breast**		**Cervix uteri**	
	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade	Number of deaths	% change compared to the previous decade
1970–1979	7828	-	15,183	-	15,737	-	5282	-
1980–1989	11,525	47,2	19,546	28,7	19,519	24,0	6429	21,7
1990–1999	17,863	55,0	22,139	13,3	22,795	16,8	5379	− 16,3
2000–2009	23,925	33,9	22,158	0,1	21,914	− 3,9	4565	− 15,1
2010–2019	32,475	35,7	22,058	− 0,5	21,386	− 2,4	4087	− 10,5
2020	3341	-	2139	-	2195	-	382	-

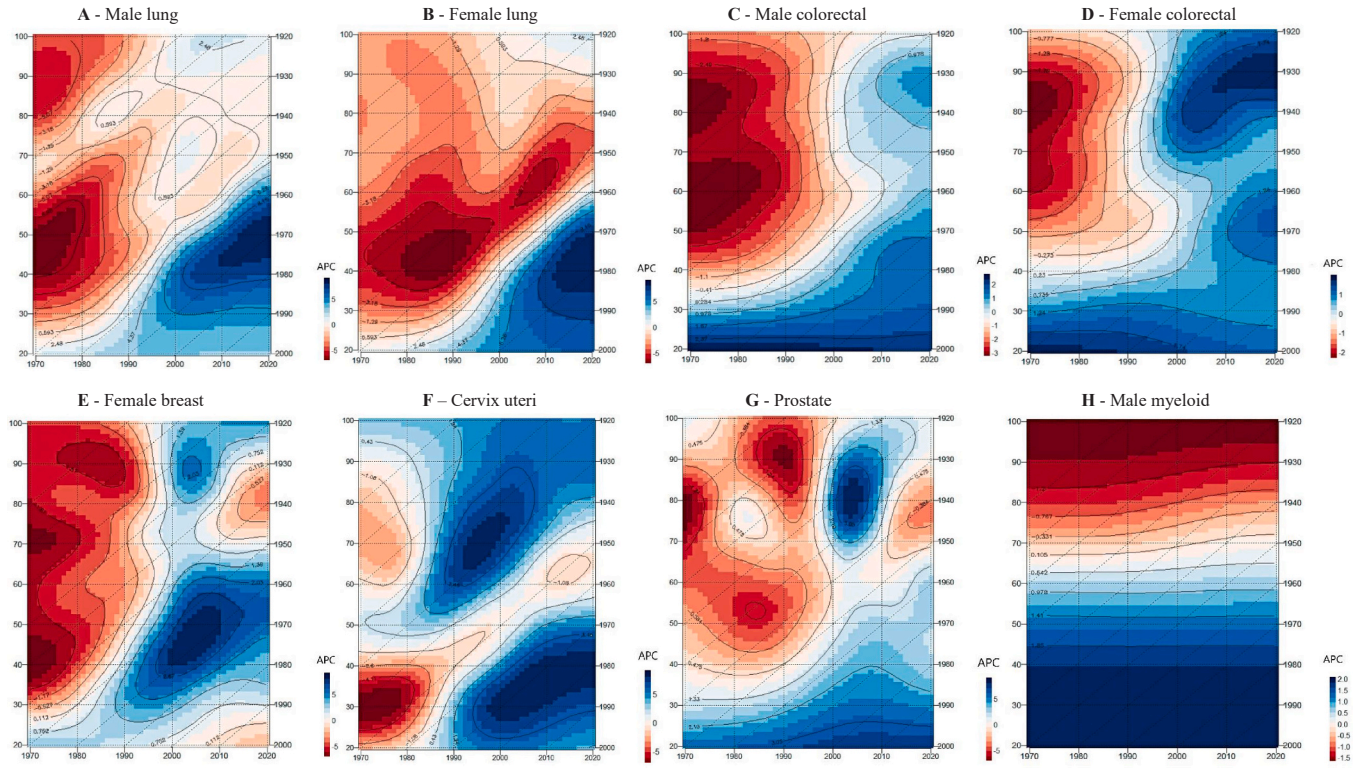

Fig. 1. Mortality trends for selected cancers in Hungary, 1970–2020 and ages 20–100. Abbreviation: APC – Annual Percentage Change, Note: red color scales – increasing cancer mortality, blue color scales – decreasing cancer mortality.
Source: Hungarian Central Statistical Office.

4. Discussion

The Lexis diagram offers a way to represent epidemiological transitions partitioned by cause of death. In Hungary the cancer transition is evident and the visualization sheds light on different epidemiologic aspects, such as the so-called state socialist mortality syndrome, which plays out as an increase in mortality rates due to chronic diseases such as cancer observed in several Eastern European countries between the 1960s and 1990s, and according to the different phases of the smoking epidemic [7–9]. Post-socialist countries appear to be in a recovery phase from this epidemiologic crisis, which was made possible by regime change. From the mid-1990s progress in cancer was confined to lung and stomach cancer through tobacco control and "unplanned triumphs" of primary prevention, respectively [10]. However today, an advanced (late) stage of the cancer transition is becoming increasingly apparent in post-socialist countries like Hungary, with a shift away from cancers triggered by unhealthy lifestyles (e.g.: smoking and drinking) and infection (H Pylori, HPV, HBV), towards a cancer profile more associated with affluence (obesity and physical inactivity) and non-infectious causes (breast and prostate tumors) [11].

Our comparative analysis also identified areas where the greatest progress can be made in reducing the cancer burden. Since smoking prevalence is still high in international context, maintaining anti-smoking measures and introducing lung cancer screening program with low-dose lung CT could be beneficial in targeting the high-risk ever-smoker population, in which significant progress has already been made in Hungary [12]. Besides this, increasing the currently very low participation rates of breast, colorectal and cervical cancer screening would positively affect the mortality across a spectrum of the ages. At the same time, from a public health perspective, population-based PSA screening is not recommended due to the risk of overdiagnosis and overtreatment, however, individualized screening in countries with high mortality rates may be beneficial [13]. With respect to myeloid malignancies, there have been no breakthroughs to report [14].

Given spiraling treatment costs, the focus should be on primary prevention strategies such as the information and provision of vaccination of HPV-unaware girls, with a view to eliminating cervical cancer as a public health problem. In parallel promoting physical activity through changes in the built environment and policies that seek the population-level reduction of the prevalence of key modifiable risk factors, particularly, tobacco smoking, alcohol consumption and obesity, are critical.

We acknowledge important limitations of our research, including uncertainties of in determining underlying causes of death, and the presence of competing risks, particularly at older ages where multimorbidities are common [15].

The Lexis diagram is an indispensable tool for health decision-makers worldwide seeking to identify the current status of national cancer transition, but also the effects of changes in risk factor exposures, health awareness within the population, and the impact of cancer policies across the cancer continuum, including early detection and screening, treatment, and broader health care reforms.

CRediT authorship contribution statement

Freddie Bray: Writing – review & editing, Conceptualization. **Weber Andras:** Writing – original draft, Supervision, Formal analysis, Conceptualization. **Péter Nagy:** Writing – review, editing & funding. **Dávid Kelemen:** Data curation. **Lászlóné Hilbert:** Data curation. **Mátyás Árvai:** Visualization. **Polgár Csaba:** Writing – review & editing. **István Kenessey:** Writing – review & editing.

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Disclosure

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article, and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer/World Health Organization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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