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ORIGINAL ARTICLE

The Anomaly of Cancer Incidence in Denmark: The Fuzzy Line between Gender-disaggregated GDP per Capita, Inflation, and Cancer Incidence

Gülgün ÇİĞDEM

Department of International Trade and Business, İstanbul Gelişim University, İstanbul-*Türkiye*

OBJECTIVE

The increasing incidence of cancer in a highly affluent and developed country like Denmark raises a remarkable problem. This research deeply examines the complex relationships between cancer incidence, GDP (Gross Domestic Product) per capita, and inflation in Denmark.

METHODS

Augmented Dickey-Fuller (ADF) and Phillips-Perron (PP) Unit Root Tests, Toda-Yamamoto Causality Test have been used.

RESULTS

Analyses of data on male and female cancer incidence, GDP per capita growth (annual %), and inflation yield striking results. For instance, the unidirectional causal relationship from male cancer incidence to female cancer incidence is striking. At the same time, the bidirectional causality between GDP per capita and male cancer incidence is also an interesting finding. The finding of a unidirectional causality from female cancer incidence to GDP per capita and unidirectional causal relationship from inflation to female cancer incidence is also important emphasis.

CONCLUSION

This study is a continuation of the tests of the Crisis-Cancer Cycle (CCC) hypothesis proposed by Çiğdem and is an important step towards understanding the complexity behind the cancer surge, concretizing the potential effects of monetary policies on health and informing policymakers.

Keywords: Cancer incidence; crisis-cancer cycle; GDP per capita; gender in cancer incidence; inflation; Toda-Yamamoto.

INTRODUCTION

Cancer is a result of cell growth[1] where cells lose the ability to respond to normal signals and become independent of controls.[2] By becoming independent of the controls that regulate their behavior, these cells gain the ability to invade nearby tissues and spread to distant regions.[3] This condition, defined as excessive proliferation of abnormal cells, indicates that cancer is a complex disease associated with the inability of initially differentiated cells to perform certain functions of other organs or systems and the acquisition of different cell functions.[4] Cancer includes more than 200 different forms and hundreds of approved chemother-

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Assoc. Prof. Gülgün ÇİĞDEM
İstanbul Gelişim Üniversitesi,
Uluslararası Ticaret ve İşletmecilik Bölümü,
İstanbul, Türkiye
E-mail: gulguncigdem@gmail.com

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apeutic agents,[5] and can have an impact on the social, economic and psychological lives of patients and their families.[6,7] It is recognized as a global problem due to high mortality rates and limited healthcare access, especially in developing countries.[8]

In 2020, 10 million people will die from this disease, and the debate on the factors that play a role in its occurrence continues. Various lifestyle factors such as environmental factors, radiation, chemicals, food, air, water, nutrient pollution,[9] tobacco use, red meat consumption, lack of physical activity, obesity, and diet have been found to be effective. In addition, psycho-social processes such as social status, working conditions, life events (depression, hopelessness, loss of a loved one, etc.) have also been found to play a triggering role in the development and progression of certain types of cancer[10] and that socio-economic conditions have a significant impact on the occurrence and treatment of cancers.[10–13]

Poor individuals have less access to preventive, early diagnosis and treatment services within the scope of the fight against cancer,[14] Individuals with low socioeconomic status have low rates of participation in cancer screening programs due to cost, which increases the risk of late diagnosis.[15] Because of these factors, poor cancer patients have short life expectancy and low quality of life.[14] Studies show that lower socio-economic status is associated with higher mortality rates for various types of cancer.[16] People with lower socioeconomic status have been found to be more likely to develop stomach, lung or cervical cancer.[15] Socioeconomic inequalities in cancer morbidity and mortality have been observed with higher rates among disadvantaged groups[13] and socioeconomic factors such as education and income level have been found to be strongly associated with cancer incidence rates.[17,18] It is argued that the differences in cancer incidence and mortality rates between racial and ethnic groups are mostly related to socioeconomic status.[18]

In 2019, I empirically tested the relationship between crises and cancer incidence with a multidisciplinary approach and obtained evidence of this cycle in a study I called "Crisis-Cancer Cycle", which deals with the fact that anxiety disorder, anxiety and depression seen in individuals who descend from socio-economic rungs due to economic crises cause telomere shortening, which in turn causes cancer. The findings reveal that there is a bidirectional relationship between cancer incidence and poverty; accordingly, poverty is a cause of cancer incidence, and cancer incidence is a cause of poverty.[19] Similarly, in another study I conducted in 2021, I found a unidirectional causality between unemployment and cancer incidence in the short run from unemployment to cancer incidence, suggesting that unemployment is a cause of cancer incidence. In this context, my study suggests that implementing policies to prevent unemployment can reduce cancer costs and stress-related incidence.[20] Some studies support these findings, showing that increasing levels of economic wealth can affect changes in cancer incidence rates.[21] However, they emphasize both regional and gender disparities and the need for corrective public policy measures.

Gender differences have significant impacts on cancer incidence rates[22–24] and treatment outcomes. Inequalities have been found between men and women in the prevalence, incidence and severity of various diseases, not only cancer.[22] Sex-specific differences in cancer incidence and mortality are regulated by genetic, molecular and hormonal factors.[24] In multiple non-reproductive cancers, men are more likely to develop cancer and experience worse clinical outcomes compared to women.[25] Sex differences in cancer phenotypes should be considered when developing sensitive cancer treatment plans.[26] Gender-based disparities in treatment allocation and overall survival have been observed in advanced gastroesophageal cancer.[27] Sex differences in colorectal cancer affect disease incidence, clinicopathologic characteristics, therapeutic outcomes and tolerability to treatments. Understanding and addressing these sex differences is crucial to improve cancer diagnosis, treatment and outcomes.

The primary objective of this research is to explore the correlation between cancer incidence rates, GDP per capita, and inflation rate. The focus is on Denmark, which holds the top position in global cancer incidence rates, serving as a case study to comprehend the dynamics in a developed nation with a high standard of living. Gender differences are also integrated into the empirical examination of these variables. The methodology involves initiating the study with a literature review, followed by in-depth analyses. Aligning with the findings from the Crisis-Cancer Cycle research conducted by,[19,20] this study adopts a multidisciplinary approach, encompassing socio-economic factors, sex dynamics, and cancer incidence.

Literature Review

This section will review the findings of previous research by examining the key variables relevant to the analyses to be conducted. First, the literature will be reviewed where there are few studies, such as the gender factor on cancer incidence.

Gross Domestic Product (GDP) Per Capita and Cancer Incidence

GDP per capita is acknowledged as a crucial economic factor influencing cancer incidence.[13,28,21] Within this context, a study conducted by Luzzati et al.[29] identified a direct correlation between GDP per capita and cancer incidence. The researchs indicates that individuals with lower personal income may exhibit higher incidence rates for specific types of cancer.[30] Furthermore, insights from other studies underline a significant correlation between cancer occurrence and the middle-income group. It is emphasized that individuals with higher education and income are less susceptible to developing cancer, with the disease often diagnosed at earlier stages.[31] Additionally, studies have revealed a notable connection between income level and oral cancer rates. Particularly in the United States of America (USA), Italy, Hong Kong, and Singapore, there is evidence suggesting that the rise in real Gross Domestic Product is inversely associated with the incidence of oral cancer in men.[32] These findings underscore the necessity for a comprehensive evaluation of the impact of economic factors on cancer incidence.

Inflation and Cancer Incidence

Although there are studies discussing the effect of economic variables such as poverty,[33] national income per capita, growth,[28] economic development[34] on cancer incidence, there is no study in the literature on the effect of inflation on cancer incidence. Therefore, this study is a contribution to the literature. Further research is needed to fully understand the underlying mechanisms.

Gender Factor in Cancer Incidence

Gender-specific disparities in the incidence and mortality of certain malignancies have been reported, with differences in cancer incidence between the sexes regulated by genetic and molecular factors as well as sex hormones.[30] Gender plays an important role in the incidence, prognosis and mortality of cancers.[35] This means that the likelihood of developing cancer, the severity of the disease and the chances of survival may differ between men and women. However, despite this knowledge, gender is often neglected in the treatment of cancer patients. This may be due to a lack of understanding of the differences between male and female biology or a lack of recognition of the importance of gender in cancer research and treatment. A study conducted by Dong et al.[35] emphasizes that gender differences in cancer incidence and survival should not be ignored, as these differences may offer insights into cancer biology and help personalize treatments for men and women. Therefore, health professionals and researchers should consider gender as an important variable in cancer diagnosis, treatment and prevention.

Research shows that the incidence of cancer is higher in men.[36] Men have a 20% higher likelihood of developing cancer in their lifetime compared to women,[24] and men are less likely to survive a cancer diagnosis.[37–40] Men in China have a significantly higher incidence than women worldwide.[41]

Men are at higher risk than women for non-sex-specific cancers, but research examining these differences is limited. The higher incidence rates seen in men suggest that known risk factors and factors beyond female sex hormones may contribute to these differences. For example, kidney cancer has a male to female incidence rate of 2:1, which is fixed by age, year and region. This suggests that factors other than sociocultural habits and health behaviors are responsible for this gender disparity.[42] Specifically for lung cancer, smoking is significantly associated with increased risk in both men and women, but incidence is higher in men than in women.[24] According to the findings of the study by Huang et al.,[43] the mortality and incidence of PM2.5-related lung cancer is higher in men than in women. The incidence of colorectal cancer is also influenced by gender and is higher in men than in women.[44] Additionally, specific cancers with higher incidence in men (such as Kaposi's sarcoma) and specific cancers with higher incidence in women (such as thyroid cancers) have been identified.[35] Studies have also reported higher rates of non-reproductive cancers in men compared to women, and these differences may be influenced by biological factors or environmental exposures.[23] Age-specific incidence rates show that although men have lower cancer rates at younger ages, they increase with age, leading to a higher incidence in men after the sixth decade of life.[45]

These results demonstrate the critical importance of gender-based variations in cancer incidence in shaping cancer prevention and treatment strategies. These findings suggest that gender is a complex factor influencing cancer incidence, course and outcomes and should not be ignored. Understanding the role of sex differences in cancer incidence is important to advance diagnostic and treatment strategies.[46] In this context, gender-sensitive approaches need to be more embedded in cancer research and clinical practice, and cancer-fighting strategies need to be designed to take gender differences into account.

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Table 1 Variables

Variables	Abbreviation	Souce	Period
Incidence (female)	Female	Nordic statistics	1961–2020
Incidence (male)	Male	Nordic statistics	1961–2020
GDP per capita growth (annual %)	GDP	Worldbank	1961–2020
Inflation	INF	Worldbank	1961–2020

GDP: Gross Domestic Product; INF: Inflation

The impact of gender differences on cancer diagnosis and treatment can positively influence the course of the disease, emphasizing the importance of early detection. Therefore, understanding gender-based differences can form the basis of a patient-centred and personalized health approach. Furthermore, reducing gender-based health inequalities and identifying effective strategies to cope with the disease is also crucial to ensure equity across society in the fight against cancer. In addition to biological and genetic factors that influence gender's risk of cancer, social factors such as lifestyle choices, environmental factors and access to health services, and even economic factors need to be examined.

In conclusion, the relationships between cancer incidence and personal income, gender, and other socio-economic factors are complex and multifaceted. The impact of these factors on cancer risk may differ for different types of the disease and may vary across regions. It is important to understand the role of these factors in the fight against cancer worldwide. Therefore, future studies will help us better understand the causes and incidence of cancer and may help to develop more effective prevention and treatment approaches against cancer. With this approach, the next section will begin the analysis of Denmark, which ranks first in cancer incidence.

MATERIALS AND METHODS

The examination will investigate the intricate connections among cancer incidence, GDP per capita growth (annual %), and inflation in Denmark, which ranks at the top of the ranking. To accomplish this, data on male and female cancer incidence spanning the years 1961–2020 will be sourced from the Association of the Nordic Cancer Registries (NORDCAN). Additionally, inflation and GDP per capita growth (annual %) data will be acquired from the World Bank (Table 1). This approach ensures a comprehensive investigation into the nuanced dynamics shaping the relationships between health indicators and economic variables in Denmark.

Figures 1, 2, and 3 illustrate the dynamics of the data spanning the period 1961–2020. Furthermore, the graphical exploration underscores the absence of a trend structure in GDP per capita. Consequently, in the unit root tests, a trendless structure will be selected to accurately reflect the inherent characteristics of the data. Figure 1 visually depicts that male incidence rates surpass those of females, and both exhibit a parallel trend. The graphical representation employs years on the horizontal axis and cancer incidence rates (%) on the vertical axis, providing a comprehensive visualization of the temporal patterns in the dataset.

An intriguing observation arises when scrutinizing the GDP per capita trends in Denmark, particularly during significant global crises. Specifically, a notable downturn in GDP per capita is discerned in the years 1974–75 (1st Oil Crisis), 1980–81 (2nd Oil Crisis, World Debt Crisis), 2009 (2008 Global Financial Crisis), and 2020 (COVID-19 Crisis). These periods align with pivotal moments of global upheaval. The temporal alignment of these economic downturns with global crises is visually represented in the graph, where the horizontal axis delineates the years and the vertical axis illustrates the percentage change in GDP per capita. This visual representation provides a compelling insight into the interplay

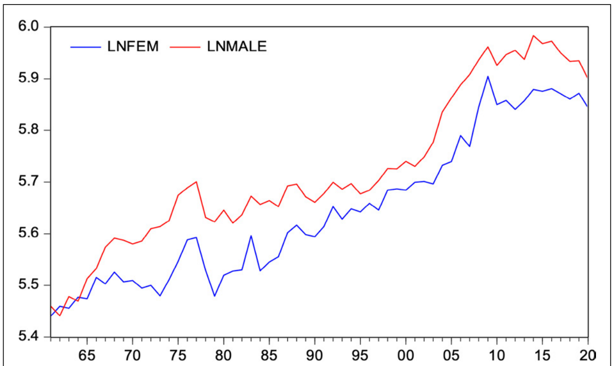

Fig. 1. Female and male incidence, Denmark (1961–2020). LNFEM: Incidence (female)-logarithmically transformed; LNMALE: Incidence (male)-logarithmically transformed.

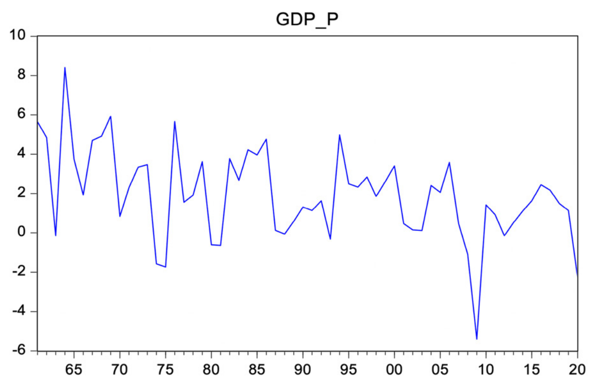

Fig. 2. GDP per capita growth, Denmark (1961–2020).
GDP: Gross Domestic Product.

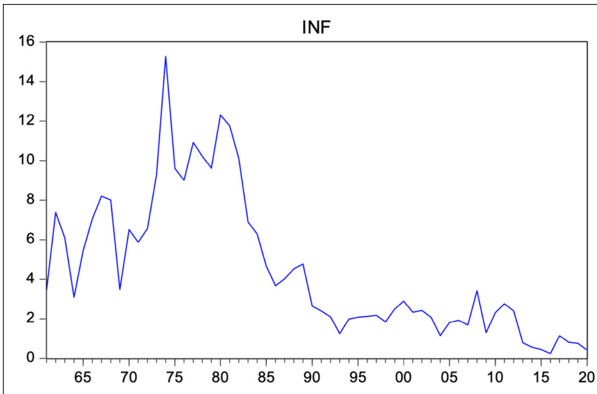

Fig. 3. Inflation, Denmark (1961–2020).
INF: Inflation.

between Denmark's economic performance and the overarching global economic landscape during these crisis-ridden periods.

After reaching its second peak in 1980 and plunging steeply until 1986, when it was brought under control, the inflation rate had its highest point of 15.3% in 1974 (Fig. 3). The number of years is displayed on the horizontal axis of the graph, while the inflation rate (%) is displayed on the vertical.

Following a detailed examination of tables and graphs, the initiation of these analyses allows for a deeper understanding of the data and a more robust drawing of conclusions. By clarifying the relationships between gender, GDP per capita, and inflation variables, the analyses will provide more information on how cancer incidence is affected.

In time series analysis, unit root tests represent a first and necessary step. Unit root tests provide critical information about the stationarity of data series. In this study, The unit root properties of the data were initially examined using the Augmented Dickey Fuller (ADF) and Philips and Perron (PP) unit root tests. The test outcomes are shown in Table 2.

Observing different degrees of stationarity in the series, the Toda-Yamamoto Causality Test will be used to examine causal relationships comprehensively. This test provides a flexible methodology applicable to series with different degrees of stationarity. Both the de-

Table 2 Unit root test results

Variables	**ADF**			
	Test statistics	**1%**	**5%**	**10%**
LNFEM, level	-2.876993	-4.121303	-3.487845	-3.172314
LNFEM, 1st difference	-8.895207	-4.124265	-3.489228	-3.173114
LNMALE, level	-1.715881	-4.121303	-3.487845	-3.172314
LNMALE, 1st difference	-7.394469	-4.124265	-3.489228	-3.173114
GDP_P, level	-6.001736	-3.546099	-2.911730	-2.593551
INF, level	-4.718093	-4.152511	-3.502373	-3.180699
	PP			
LNFEM, level	-2.836473	-4.121303	-3.487845	-3.172314
LNFEM, 1st difference	-9.878270	-4.124265	-3.489228	-3.173114
LNMALE, level	-1.843027	-4.121303	-3.487845	-3.172314
LNMALE, 1st difference	-7.410104	-4.124265	-3.489228	-3.173114
GDP_P, level	-5.971778	-3.546099	-2.911730	-2.593551
INF, level	-3.386716	-4.121303	-3.487845	-3.172314

ADF: Augmented Dickey-Fuller; LNFEM: Incidence (female)-logarithmically transformed; LNMALE: Incidence (male)-logarithmically transformed; GDP: Gross Domestic Product; INF: Inflation; PP: Phillips-Perron

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Table 3 Results of Toda-Yamamoto causality analysis

Chi-Square test statistic	Result	Direction of causality
0.000894	H_0 rejected, causal relationship exists	LNMALE→LNFEM
0.047931	H_0 rejected, causal relationship exists	INF→LNFEM
0.318139	H_0 cannot be rejected, no causal relationship	GDP≠LNFEM
0.620856	H_0 cannot be rejected, no causal relationship	LNFEM≠LNMALE
0.100739	H_0 cannot be rejected, no causal relationship	INF≠LNMALE
0.026045	H_0 rejected, causal relationship exists	GDP→LNMALE
0.10982	H_0 cannot be rejected, no causal relationship	LNMALE≠INF
0.306906	H_0 cannot be rejected, no causal relationship	GDP≠INF
0.01883	H_0 rejected, causal relationship exists	LNFEM→GDP
0.00897	H_0 rejected, causal relationship exists	LNMALE→GDP
0.000298	H_0 rejected, causal relationship exists	INF→GDP

$K+D_{max}=2$. LNFEM: Incidence (female)-logarithmically transformed; LNMALE: Incidence (male)-logarithmically transformed; INF: Inflation; GDP: Gross Domestic Product

gree of integration and the existence of a cointegration relationship are not prerequisites for the Toda-Yamamoto[47] technique,[48] making it an effective tool for analyzing complex relationships and data series with varying stationarity properties.

The Toda-Yamamoto causality analysis, based on the Vector Autoregression (VAR) model, estimates the causality relationship between variables using the WALD test, regardless of the level of stationarity and cointegration relationship between the series.[47–50] This method can be applied whether a series is I(0), I(1), or I(2), cointegrated or not.[51]

RESULTS

The results of the Toda-Yamamoto causality analysis are presented in Table 3 and visualized in Figure 4 for a clearer understanding of the results of the analysis.
As a result of the analysis;

- Bidirectional causality between LNMALE and GDP,
- Unidirectional causality from LNMALE to LNFEM,
- Unidirectional causality from LNFEM to GDP,
- Unidirectional causality from INF to LNFEM, has been detected.

The outcomes of the intricate analysis reveal a reciprocal causation connection between male cancer incidence and per capita income. The influence of per capita income on cancer incidence in men is evident, as male cancer incidence concurrently impacts per capita income. Furthermore, per capita income is subject to the influence of both female and male incidence as well as inflation. Notably, the findings underscore that female cancer incidence is influenced by both male incidence and inflation, whereas male incidence is solely influenced by per capita income. These results highlight the intricate nature of the impacts of economic factors, particularly per capita income and inflation, on gender-specific cancer incidence.

DISCUSSION

The global distribution of cancer presents an intricate and complex scenario. Despite the conventional notion that cancer prevails more prominently in developing or underdeveloped nations, it is paradoxical that Denmark, a country marked by high affluence, holds the top position in cancer incidence. This anomaly underscores the necessity for a comprehensive examination of cancer patterns on a global scale.

In addressing the challenge of cancer, it is imperative to undertake a thorough investigation encompass-

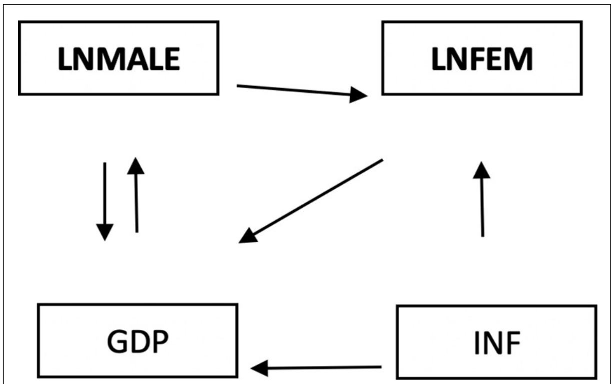

Fig. 4. Results of Toda-Yamamoto causality analysis.
LNFEM: Incidence (female)-logarithmically transformed; LNMALE: Incidence (male)-logarithmically transformed; GDP: Gross Domestic Product; INF: Inflation.

ing all countries worldwide. However, a significant impediment lies in the dearth of accessible data, hindering a comprehensive understanding of the impact of cancer as a global health concern.

The ramifications of this global health burden extend beyond direct costs, encompassing expenses related to diagnosis, treatment, care, and the losses of organs or lives. Furthermore, there are economic losses stemming from factors that disrupt economic stability. It is indisputable that diseases compel individuals to disengage from productive activities, thereby detrimentally affecting national economies. Consequently, a nuanced comprehension of how monetary policy decisions influence human life becomes paramount in averting a disease triggered, in part, by economic factors.

In conclusion, combatting cancer transcends the realm of mere medical intervention; it evolves into a multifaceted matter involving economic and social dimensions. Hence, the formulation of effective strategies to combat cancer necessitates a holistic consideration of the intricate interplay between health, economy, and the overall well-being of society.

CONCLUSION

Cancer is a leading global health issue with rising incidence and mortality rates. It is crucial to monitor changes in cancer registration, incidence, and survival to develop strategies for reducing the cancer burden and improving patient outcomes. Contrary to popular belief, rich countries exhibit higher cancer rates than poorer countries, with Denmark having the highest incidence.

This study examines the relationship between cancer incidence rates, GDP per capita, and inflation, offering a perspective that significantly diverges from existing literature. In this context, I adopt a different approach from previous studies such as Yang et al.[52] on socio-economic status, Luzzati et al.[29] on personal income, Bandyopadhyay[31] on GDP per capita and Chen et al.[32] on the relationship between real GDP and cancer incidence. The study investigated gender-based causal relationships and reached remarkable results. The study investigated gender-based causal relationships and reached remarkable results found a unidirectional causality from GDP per capita to male cancer incidence, indicating that a decline in income affects male cancer incidence.

Additionally, it was revealed that inflation influences female cancer incidence, suggesting that economic factors beyond GDP per capita impact cancer rates. In addition to these revelations, the research underscores another unidirectional causality, this time from inflation to female cancer incidence. This result suggests that inflation, a previously ignored factor, affects female cancer incidence. Although there are studies investigating the relationship between income and cancer, there is no study investigating the relationship between inflation, which reduces the purchasing power of individuals and impoverishes them, and cancer. This suggests that economic factors extending beyond GDP per capita play a role in influencing cancer incidence rates, inviting nuanced discussions on the broader economic context.

In accordance with the Crisis-Cancer Cycle (CCC),[19,20,53,54] this study shows that individual impoverishment affects cancer incidence differently based on gender: decreasing personal income affects male incidence rates, while declining purchasing power impacts female rates. It is surprising that biological differences emerge at this point. In addition, causality was found from both male and female incidence rates to GDP per capita. Together with this finding, the bidirectional causality between male cancer incidence rates and GDP per capita points to a vicious circle. Cancer incidence reduces GDP per capita. Individuals who are diagnosed with cancer and withdraw from the labor force experience a decline in their income. Decline in income also affects the incidence of cancer. Individuals who are worried about life and treatment withdraw from the work/production process. This means that despite the heavy costs of the disease, it causes financial losses at national and global level. This intricate bidirectional relationship between male cancer incidence rates and GDP per capita underscores the need to explore the underlying mechanisms. Does higher income contribute to better healthcare access and, subsequently, earlier cancer detection, or does it indicate that wealthier individuals engage in behaviors that elevate cancer risk? These questions necessitate further investigation. In addition to the few studies in the literature that emphasize gender differences and find an interaction between cancer incidence rates, a surprising finding was obtained in this study; unidirectional causality was found from male incidence rates to female incidence rates. This discovery challenges conventional assumptions and raises intriguing questions about the potential shared risk factors and environmental exposures that transcend gender boundaries. Further studies are needed to explain this finding. Kreiter et al.[55] and Ly et al.[33] found that breast cancer incidence rates were related between genders, but no explanation was provided regarding the direction of causality in this relationship. This study fills this gap.

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This study provides important findings that support the Crisis-Cancer Cycle (CCC) hypothesis proposed by Çiğdem[19,20,53,54] and contribute to existing research on gender differences in cancer. It also makes a valuable contribution to the literature by providing a new perspective on the causes of cancer incidence from an economic perspective. The study highlights the complexity of the impact of economic stability on cancer epidemiology. It also points to the need for greater consideration of gender and economic factors in the design of anti-cancer strategies. In particular, given that periods of economic crisis contribute significantly to the incidence of cancer and place a heavy burden on both the national and global economy, and that the loss of income and productivity experienced by cancer patients has serious consequences at both the individual and societal levels, it is important to raise awareness on this issue and to emphasize economic stability. In conclusion, this study will pave the way for further research on the relationship between cancer and the economy and contribute to understanding the epidemiology of cancer from an economic perspective. It is clear that such studies will help to develop more effective strategies in the fight against cancer.

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