

# COMPARISON OF TEMPORAL TRENDS IN THE GLOBAL BURDEN OF TRACHEA, BRONCHIAL, AND LUNG CANCER <sup>1</sup>

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Trake, Bronş ve Akciğer Kanserinin Küresel Yükünün Zamansal Trendlerinin Karşılaştırılması



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## ARTICLE INFORMATION

Submission Date : xx/xx/xxxx  
Accepted Date : xx/xx/xxxx

**Keywords:** Trachea  
Bronchial and Lung Cancer,  
Mortality-Incidence Ratio,  
Joinpoint Regression  
Analysis

## ABSTRACT

Trachea, bronchial, and lung (TBL) cancers are significant public health problems among the leading causes of death in Turkey and the world. This study aimed to determine and evaluate the temporal trends of incidence, mortality, and Disability Adjusted Life Years (DALY) rates of TBL cancers between 1990 and 2019. Mortality-Incidence Ratio (MIR) and Joinpoint Regression Analysis (JRA) methods were used in this study. Incidence, mortality, and DALYs were utilized as variables in the study. The temporal trends of TBL cancers were compared among the global, Turkey, and Socio-Demographic Index (SDI) groups. This study determined that the age-standardized global burden of TBL cancers tended to decrease between 1990 and 2019. The burden of TBL cancers tended to decline in high-SDI countries during this period, but it went up in low-SDI countries. In Turkey, while the TBL cancer burden decreased until 2005, it increased after 2006. While the global cancer burden of TBL tended to decline in men, it is inclined to increase in women during this period. According to the data obtained from the research findings, the burden of TBL cancers tends to decrease globally. However, it tends to increase in low and low-middle SDI group countries. It is recommended that health policies be developed in both Turkey and international health systems for fair access to cancer treatment to reduce the TBL global cancer burden.

## MAKALE BİLGİSİ

## ÖZ

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Makale Geliş Tarihi : xx/xx/xxxx  
Makale Kabul Tarihi : xx/xx/xxxx

**Anahtar Kelimeler:**

Trakea Bronş ve Akciğer  
Kanseri, Mortalite-İnsidans  
Oranı, Joinpoint Regresyon  
Analizi.

Trakea, bronş ve akciğer (TBA) kanserleri hem Türkiye'de hem de dünyada önde gelen ölüm nedenleri arasında yer alan önemli bir halk sağlığı sorunudur. Bu çalışmada, 1990-2019 yılları arasında trake, bronş ve akciğer (TBA) kanserlerinin insidans, mortalite ve DALY oranlarının zamansal eğilimlerinin belirlenmesi ve değerlendirilmesi amaçlanmıştır. Çalışmada Mortality-Insidans Ratio (MIR) ve Joinpoint Regresyon Analiz (JRA) yöntemi kullanılmıştır. Değişken olarak insidans, mortalite ve engelliliğe göre ayarlanmış yaşam yılları tercih edilmiştir. TBA kanserlerinin zamansal eğilimleri küresel, Türkiye ve Sosyo-Demografik İndeks (SDI) grupları arasında karşılaştırmıştır. Araştırma bulgularında TBA kanserlerinin yaşa göre standardize edilmiş küresel yükü azalma eğiliminde olduğu tespit edilmiştir. TBA kanseri yükü, bu dönem içinde yüksek SDI ülkelerde düşme eğiliminde iken, düşük SDI ülkelerde artma eğilimindedir. Türkiye'de ise TBA kanser yükü 2005 yılına kadar azalma eğilimi gösterirken, 2006 yılından sonra artma eğiliminde olduğu tespit edilmiştir. TBA küresel kanser yükü bu dönem içinde erkeklerde azalma eğiliminde iken kadınlarda artma eğilimindedir. Sonuç olarak, TBA kanser yükünün küresel olarak düşme eğiliminde iken, düşük ve düşük-orta SDI grup ülkelerinde artma eğiliminde olduğu belirlenmiştir. TBA küresel kanser yükünü düşürme noktasında kanser tedavisine adil erişim için hem Türkiye hem de uluslararası sağlık sistemlerinde sağlık politikalarının geliştirilmesi önerilmektedir.

## 1. Introduction

Cancer is the leading cause of death in almost every country worldwide and is a significant barrier to increased life expectancy (Bray et al., 2018: 394; Fitzmaurice et al., 2019: 2). It was estimated that there were 19.3 million new cancer cases and 10 million deaths from cancer in 2020 (Ferlay et al., 2019: 1). Trachea, bronchial, and lung (TBL) cancers are among the leading causes of cancer deaths worldwide, and lung cancer ranks second after breast cancer among all cancer-related cases worldwide (Bray et al., 2018:394). It is estimated that the incidence of lung cancer will increase by approximately 64%, and its mortality will increase by 67% by 2040 (Sung et al., 2021: 240). Lung cancer is among the most frequently diagnosed and deadly cancer types in Turkey and all over the world, and it has the highest incidence rate in men among other countries (Türk et al., 2016: 264). Among all cancer types, 21.8% of men and 4.9% of women have been diagnosed with lung cancer. Its incidence in men has been reported as 60.4 per 100.000 people and 9.3 in women. It was determined that the incidence of lung cancer in Turkey was higher in western regions compared to other areas. Notably, this situation is proportional to urbanization and industrialization (Türk Toraks Derneği, 2016: 6).

Global, regional, and national health indicator statistics are important for assessing the current state of health care and development and prioritizing resource allocation (WHO, 2020: 51; Ahmad et al., 2001: 6). Comparing the global lung cancer burden of different demographic groups contributes to the assessment of primary health care levels. However, although countries' incidence and mortality rates are essential criteria to

understand the prevalence and importance of disease on populations, they are not considered sufficient measures to define fully, measure, and compare health status. In addition, parameters such as incidence and mortality rates may not have a comparable data standard and do not provide sufficient information on non-fatal health outcomes (Chen et al., 2015: 3).

For this reason, many researchers have tried to define a methodology that combines incidence and mortality rates in a single parameter (Glaziou et al., 2016; Murray & Acharya, 1997). Disability Adjusted Life Years (DALYs) reflect both fatal and non-fatal health outcomes with the summary measure that provides comparable information about the health levels of population groups (Abbfati et al., 2020). DALY is a concept that combines mortality and morbidity in a single parameter and consists of the sum of years lost due to disability (YLD) and years of life lost (YLL). For a certain period, the Global Burden of Disease (GBD) project is a systematic, scientific effort to quantify the comparative magnitude of health loss from diseases, injuries, and risk factors by age, gender, and geography (Murray & Lopez, 1996: 23).

This study aimed to determine and evaluate the temporal trends of incidence, mortality, and DALY rates of TBL cancers between 1990 and 2019.

## 2. Materials and Methods

### 2.1. Data Collection

In this study, incidence, mortality, and DALY variables of TBL cancers between 1990 and 2019 were analyzed by Mortality-Incidence Ratio (MIR) and Joinpoint Regression Analysis (JRA) methods. Research data were obtained from the Institute for Health Metrics and Evaluation (IHME) database (IHME, 2022). C33, C34–C34.92, Z12.2, Z80.1–Z80.2, and Z85.1–Z85.20 codes included in the International Classification of Diseases (ICD-10) were used as references in the determination of TBL cancers data (WHO, 2016). The research design separately analyzed the sum of both genders, female and male. In addition, standard age groups per 100.000 inhabitants (WHO Standard Population) were adopted to compare data.

### 2.2. Statistical Analysis

In this study, Joinpoint Regression Software 4.9.0. TBL was utilized to determine temporal trends of cancer data, R statistics software was used to calculate descriptive statistical data, and MIR was used. JRA and MIR, based on standardized age groups and

using rates per 100.000 population, were calculated for global, SDI groups and Turkey. These calculations were applied for the sum of both genders and separately for each of them. When implementing the JRA, the Grid Search method was adopted to estimate the waypoints, and the Monte-Carlo Permutation was used to test the breakpoints.  $P < 0.05$  was accepted as a statistical significance level.

JRA is a piecewise regression model that identifies trends, breakpoints, and significant changes in characteristic structure in a time series (Kim et al., 2000). This analysis technique allows for the examination of the statistical significance level of the changes in the trends of the data based on a particular time (Cayuela et al., 2004). Also known as broken-line regression and multistage regression analysis, this analysis model was developed by Kim et al. (Kim et al., 2000). This method, frequently applied in time series of cancer types, has been made into a standard software by the American National Cancer Institute (National Cancer Institute, 2020).

Starting with the minimum number of connections, JRA tests whether one or more change points are statistically significant depending on the length and structure of the time series. Although there are various tools for determining the number of change points, the Monte-Carlo Permutation test is widely used (Kim et al., 2000). Statistical interpretation of the change points is made using the annual percent change (APC) and the average annual percent change (AAPC). The APC and AAPC values are standard measures to summarize the trend structure occurring in the trend. Common breakpoints usually take matters from 0-5, and the maximum connection point is determined based on the number of observations. In the graphs obtained from the JRA analysis findings, the x-axis shows years as the independent variable, and the y-axis shows the dependent variable (DALY, incidence, mortality, etc.) (Choi et al., 2017). In this type of study, as the data was more than 27, a maximum of 5 junction points were preferred (National Cancer Institute, 2020; Kim et al., 2000: 337).

Cancer incidence and mortality are metrics that summarize the number of new diagnoses and deaths in a given year per population. MIR is a measure that demonstrates the relationship between incidence and mortality rates. It is often used as a comparative parameter to identify disparities in cancer outcomes. In addition, MIR provides a rough estimate of relative survival and quality of care in studies of cancer types. This method is frequently preferred because of its easy applicability (calculated by dividing the number of deaths by the incidence in a given year). In addition, it compares the survival level between countries (Hébert et al., 2009).

The age factor is an essential element in the assessment of cancer incidence. Cancer risk increases with age (White et al., 2014). Age-standardized ratios have been

developed to compare age-specific epidemiological and demographic clusters among populations of different age groups and to eliminate the effects of age groups (Ahmad et al., 2001; Robson et al., 2007). Therefore, an age-standardized ratio was used in this study to make a comparison. In this part of the study, according to the globally standardized age groups of TBL cancers, for global, SDI groups and Turkey, multiple index changes, MIR, and JRA findings are presented.

### **2.3. Ethics Committee Permission**

In order to carry out this study, the ethics approval certificate from the Social and Human Sciences Ethics Committee of Suleyman Demirel University was received on 27.01.2021 with the file number E-87432956-050.99-11426.

### **3. Results**

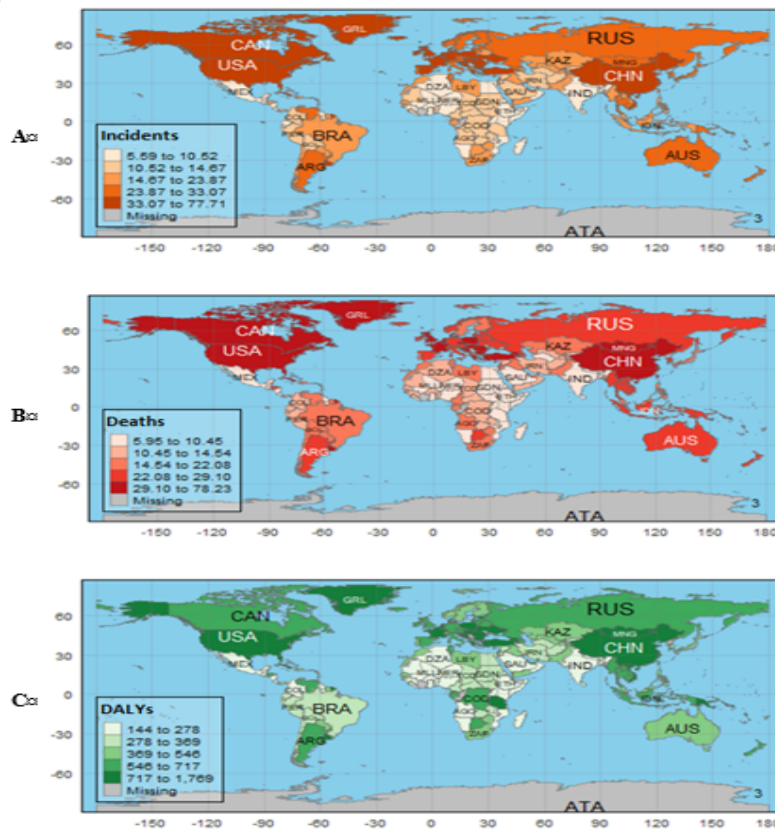
This section of the study presents multiple index changes, MIR, and JRA findings for global, SDI groups, and Turkey based on the globally standardized age groups of TBL cancers.

The multi-index variation of TBL cancers is presented in Table 1. There was a decrease in TBL cancers incidence, mortality, and DALY rates between 1990 and 2019 globally and Turkey. However, despite this decrease, all index values within the scope of research in Turkey are above the world average. Therefore, when the percentages of change between 1990 and 2019 are analyzed, it has been concluded that Turkey has higher negative change rates than the rest of the world.

**Table 1.** Multi-index changes of TBL cancers between 1990-2019 (per 100.000)

	Global			Turkey		
	1990	2019	Percentage of Change	1990	2019	Percentage of Change
<b>Incidents</b>	28.388 (29.666-27.182)	27.660 (29.988-25.280)	-2.564	37.913 (46.820-29.952)	33.081 (41.110-26.245)	-12.744
<b>Mortalities</b>	27.302 (28.587-26.025)	25.181 (27.011-23.164)	-7.768	39.252 (48.159-31.212)	33.765 (41.799-26.893)	-13.978
<b>DALYs</b>	657.979 (690.833-628.279)	551.577 (593.124-508.973)	-16.171	1009.449 (1260.220-782.790)	814.581 (1017.001-643.767)	-19.304

Figure 1 presents the distribution of TBL cancers incidence (A), mortality (B), and DALY (C) rates per 100.000 people worldwide in 2019. It was apparent in these maps that the incidence, mortality, and DALY rates of TBL cancers were concentrated in similar countries and regions in all three maps.



**Figure 1.** Distribution of TBL cancers incidence, mortality, and DALY rates per 100.000 people in 2019 worldwide

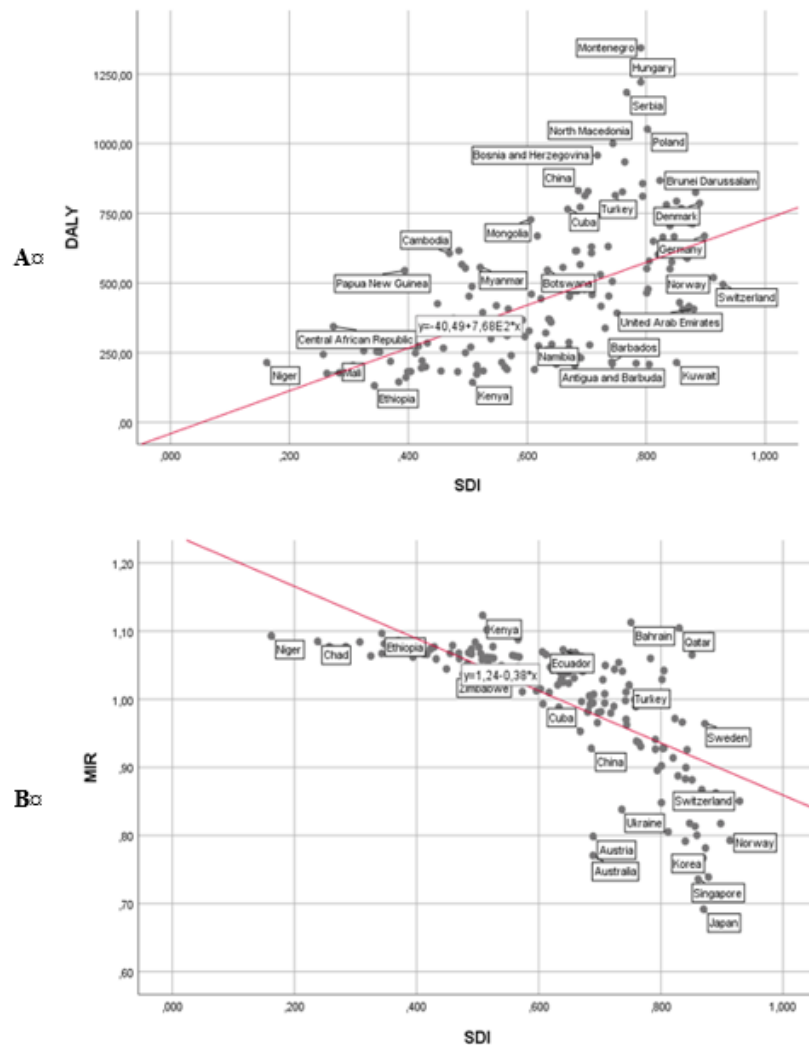
According to 2019 data, the countries with the highest age-standardized DALY rates of TBL cancers are; Greenland (1769), Monaco (1483.26), Montenegro (1343.58), and Hungary (1183.5). Conversely, the countries with the lowest DALY rates are; Sudan (182.48), Ethiopia (146.18) and Nigeria (172.68), and Uganda (182.48). In the graphs showing the distribution of incidence (A), mortality (B), and DALY (C) rates of TBL cancers, the regions with the highest incidence, mortality, and DALY rates of TBL cancers are Micronesia, Polynesia, Eastern, and Southern Europe, China and America are various regions. Turkey is among the countries with the highest burden of TBL cancers globally, with a rate of 814.581 DALYs.

TBL cancers; incidence, mortality rates, and MIR calculations are detailed in Table 2. Low scores are desired when MIR scores are associated with the survival time of TBL cancers. The global MIR score was close to the High-Middle SDI group for both genders (0.910), men (0.924), and women (0.890). The calculated MIR values for both genders (0.797), men (0.817), and women (0.770) of the High SDI group yielded lower results than the global MIR values. It was highlighted that Turkey's MIR value for both genders (1.020), men (1.034), and women (0.978) was higher than the global MIR scores of many SDI groups. In summary, according to MIR findings, countries in the High SDI group may have higher TBL cancer survival rates than other groups. It was reported that Turkey might have a lower survival level as it has MIR scores between Low SDI and Low-Middle SDI groups and has a higher score than global MIR scores.

**Table 2.** Distribution of TBL Cancers by MIR and SDI Scores (2019) (per 100,000)

	Both Genders			Male			Female		
	Incidents	Mortality	MIR	Incidents	Mortality	MIR	Incidents	Mortality	MIR
<b>Global</b>	27,660	25,181	0,910	40,440	37,378	0,924	16,836	14,985	0,890
<b>High SDI</b>	37,359	29,778	0,797	49,650	40,598	0,817	27,328	21,055	0,770
<b>High-Middle SDI</b>	32,651	29,901	0,91	52,039	48,342	0,92	17,132	15,439	0,901
<b>Middle SDI</b>	27,004	26,302	0,974	39,542	38,704	0,978	15,893	15,460	0,972
<b>Low-Middle SDI</b>	12,676	13,179	1,039	18,507	19,332	1,04	7,387	7,654	1,036
<b>Low SDI</b>	8,818	9,413	1,067	13,672	14,669	1,07	4,213	4,475	1,062
<b>Turkey</b>	33,0816	33,765	1,020	57,702	59,686	1,034	13,832	13,529	0,978

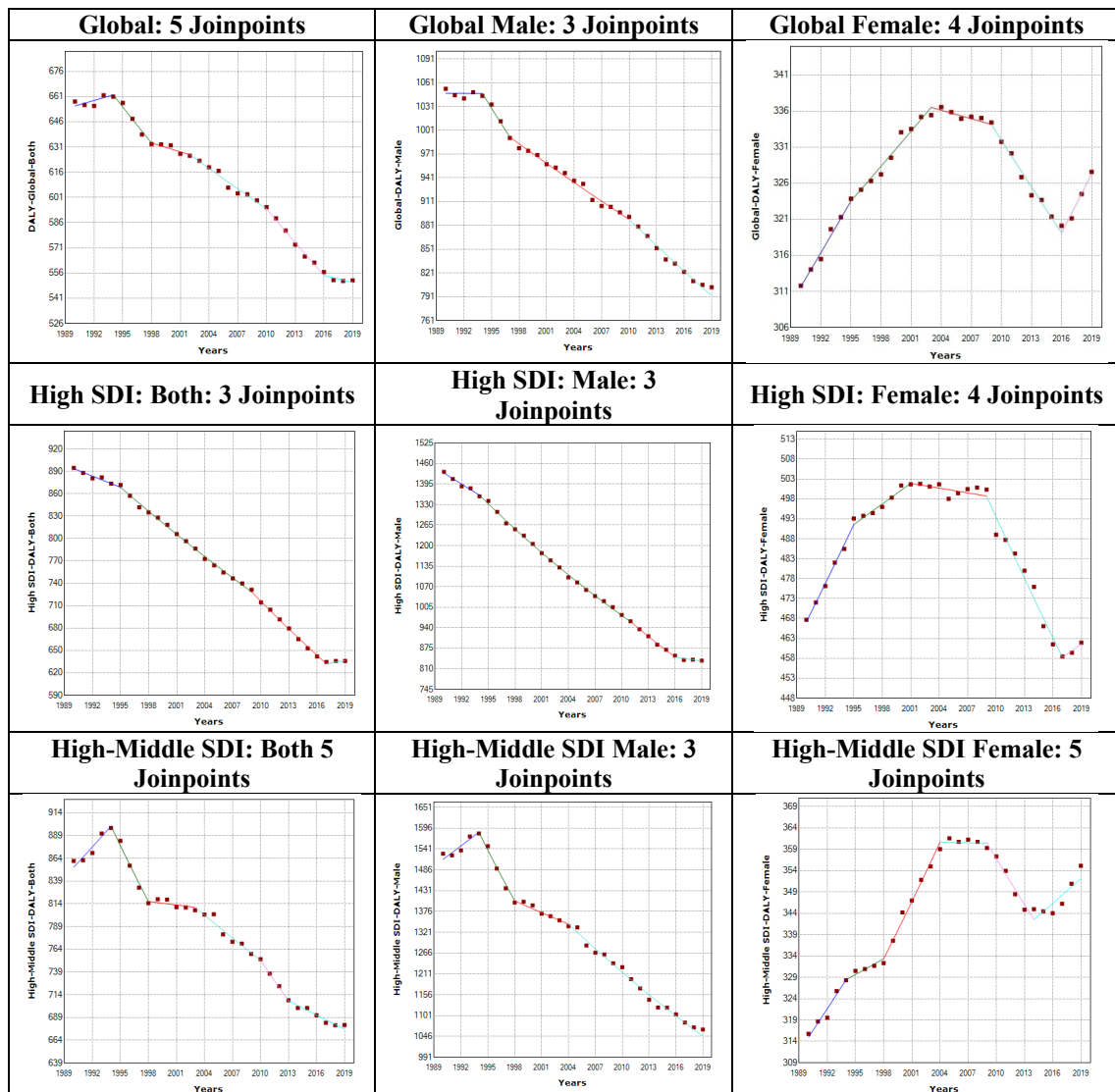
Figure 2. (A) demonstrates the MIR distribution of TBL cancers by the country burden of TBL cancers; Far Eastern countries such as Japan, Singapore, and Korea have the lowest MIR scores, while some African and Arab countries have the highest scores. Turkey is among the countries with the highest MIR scores worldwide. Figure 2. (B) presents the distribution of the burden of TBL cancers by country. It shows that African countries have lower scores for TBL cancer burden. It has been observed that some Eastern European countries differ from other countries with their high DALY rates. Turkey, along with Eastern European countries, is among the countries with the highest TBL cancer burden. A significant proportion of sub-Saharan African countries have been found to have a lower burden of TBL cancers globally.



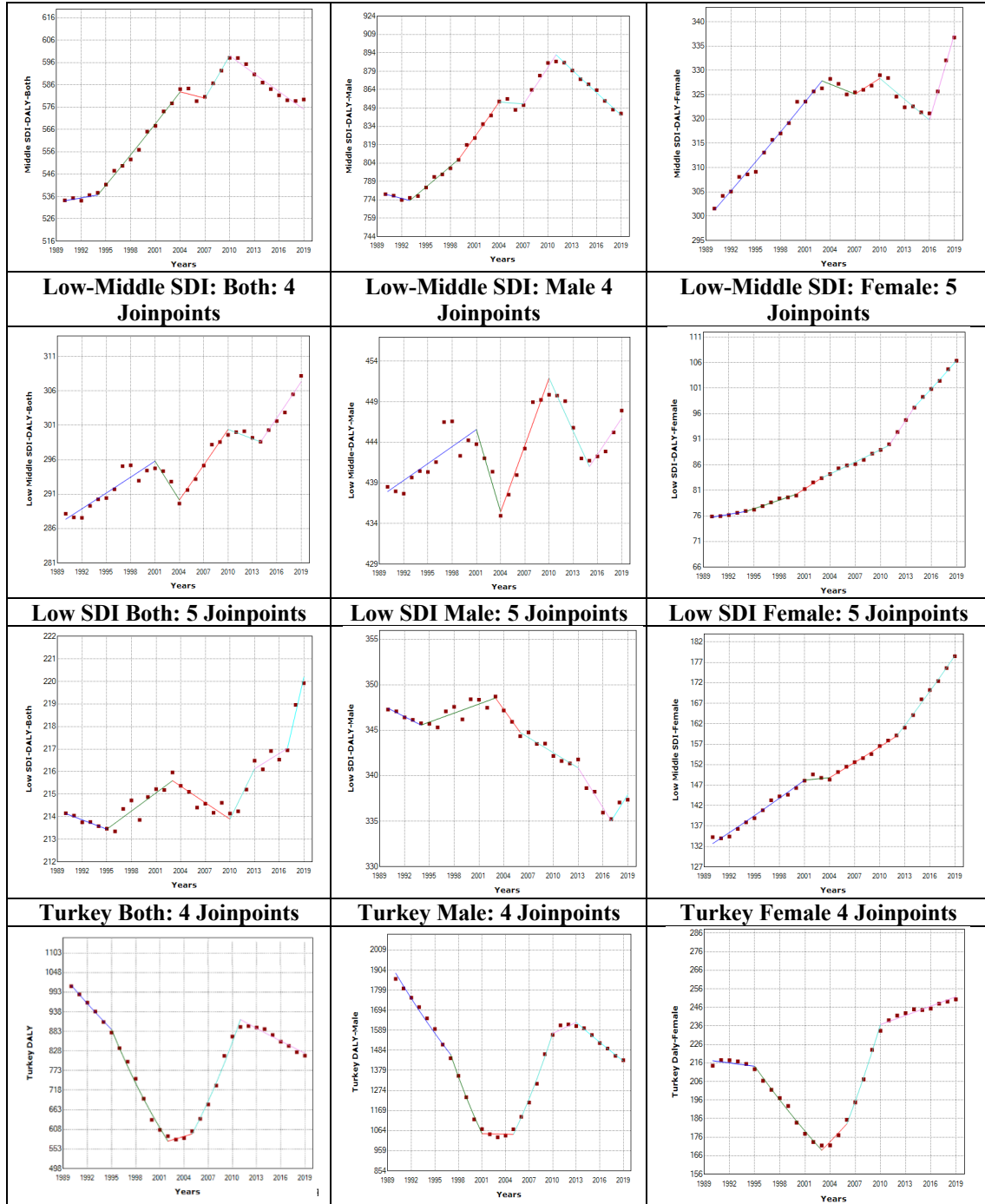
**Figure 2.** MIR and DALY distributions according to the SDI scores of the countries (2019)



Figure 3 depicts the graphs of the JRA analysis outputs of TBL cancers. When both the number of fractures and the trend structures in the graphs were examined, it was seen that men had a higher TBL cancer burden than women. In this 28-year trend, it was revealed that the global TBL cancer burden showed a steady decline, and the burden of TBL cancers shifted from the upper groups to the lower groups according to the SDI groups. Regarding gender, the male tendency structure showed a decreasing trend in the high SDI groups, while the trend for female TBL cancer burden increased. Therefore, it was determined that Turkey's TBL cancers tendency characteristics differed from the global average and SDI groups and had a decreasing trend until 2005, and then increased.



**Figure 3.** JRA Charts of TBL cancers DALYs for the globe, SDI groups, and Turkey



**Figure 3.** JRA Charts of TBL cancers DALYs for the globe, SDI groups, and Turkey (Continued)

Figure 4 shows AAPC values, one of the JRA findings of TBL cancers between 1990-2019. Tables on the analysis findings are presented in the study's appendix. According to the findings of the JRA analysis performed using age-standardized incidence rates, the AAPC values obtained for all genders were statistically significant

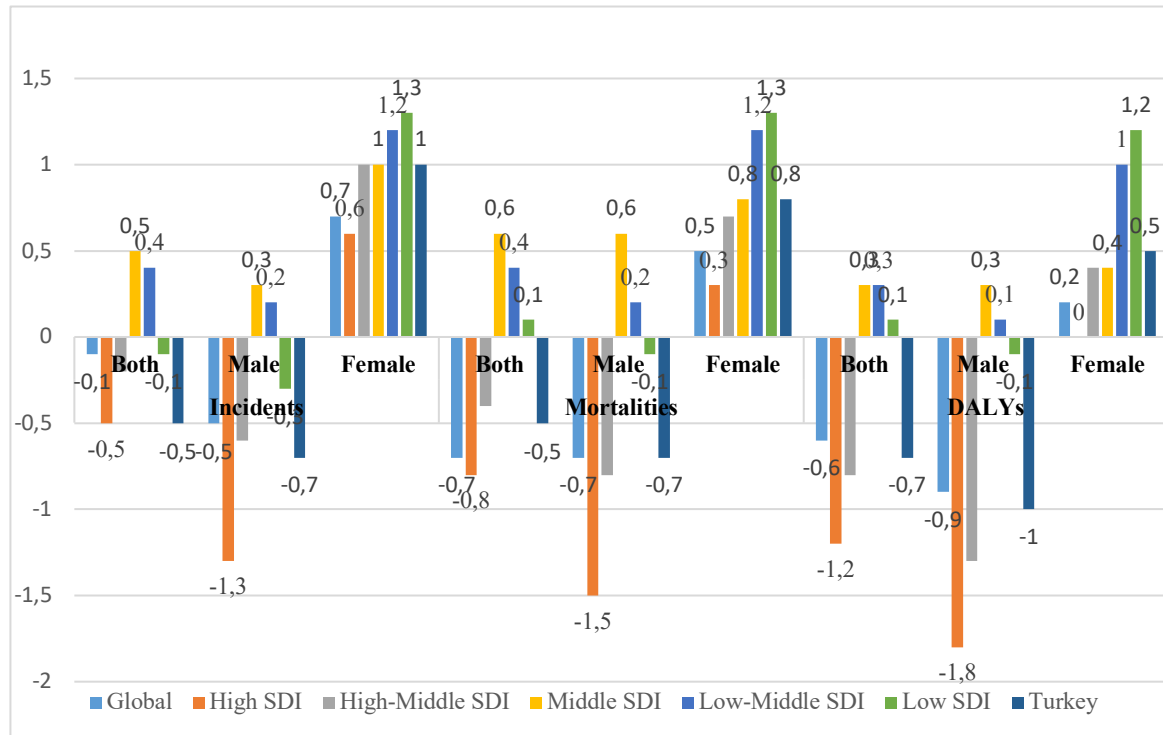
( $p < 0.05$ ), except for the ratio of males in the High-Middle and Low SDI groups and the ratio of females in the Middle SDI group. For the Global, High, and High-Middle SDI groups, the percentages of change of incidence rates for men tended to decrease for the current time series, whereas it is inclined to increase for women. According to the incidence rates of TBL cancers, the highest percentage of negative change was found in the data of men in the High SDI group (AAPC=-1.3,  $p < 0.05$ ), while a significant positive change (AAPC=0.5,  $p < 0.05$ ) was detected in women. The highest rate of change in the incidence data of women was reported in the Low SDI group (AAPC=1.3,  $p < 0.05$ -Appendix 1).

The percentage of change (AAPC=1.2,  $p < 0.05$ ) in the incidence data of women in the Low-Middle SDI group was also quite high within the available data. While the percentage of change in TBL cancer incidence rates in Turkey tended to drop in male data (AAPC=-0.5,  $p < 0.05$ ), it tended to increase in female data (AAPC=-1.0,  $p < 0.05$ ), similar to the global average data.

AAPC values for all genders were statistically significant ( $p < 0.05$ ), according to JRA findings that used mortality rates for TBL cancers. One of the most striking findings is that all female mortality rates have positive AAPC values. Mortality rates were increasing for the current time series of women with TBL cancers. It was reported that the highest percentage of negative change was in the data of men belonging to the High SDI group (AAPC=-1.5,  $p < 0.05$ ), and the highest percentage of positive change was in the data of women belonging to the Low SDI group (AAPC=-1.3,  $p < 0.05$ ). For the mortality rates of TBL cancers in Turkey, a positive change rate was observed not only in the male data (-0.7,  $p < 0.05$ ) but also in the female data (AAPC=0.8,  $p < 0.05$ ), similar to the global average percentage of change (Appendix 2).

As a result of the JRA applied by using the DALY ratios of TBL cancers, the AAPC value was found to be zero in the data of the women in the High SDI group. However, this finding was statistically insignificant ( $p > 0.05$ ). The AAPC values of the global, High, and High-Middle SDI groups for both genders and males were negative. For women, the AAPC values of the DALY ratio of TBL cancers were found to be positive. The lowest percentage of change for DALY rates of TBL cancers was seen in the data of men in the High SDI group (AAPC=-1.8,  $p < 0.05$ ), and the highest percentage of change were seen in the data of women in the Low-SDI group (AAPC=1.2,  $p < 0.05$ ). The temporal trends of the DALY ratio of TBL cancers for Turkey were negative in male data (AAPC=0.7,  $p < 0.05$ ) and positive in female data (AAPC=0.5,  $p < 0.05$ ). Therefore, it was determined that the findings of incidence and mortality and DALY rates of TBL cancers supported each other (Appendix 3).

The common part of the JRA analysis findings made according to the incidence, mortality, and DALY rates of TBL cancers is that a significant portion of the incidence, mortality, and DALY rates for men are negative for AAPC values and these rates for women are positive. Also, in the proportions of men in the High SDI group, the AAPC value had the highest negative value, while women in the Low SDI group had the highest positive AAPC value.



\*Barplots represent the AAPC values of incidence, mortality, and DALY rates of TBL cancers.

**Figure 4.** AAPC values of incidence, mortality, and DALY rates in the applied JRA analysis

#### 4. Discussion

Earlier studies on the temporal trends of TBL cancers are generally based on analyzes using secondary data obtained from TBL cancers. In addition, although there are studies on various types of cancer, studies examining TBL cancers considering the DALY parameter are quite limited. It has been determined that studies focusing on GBD generally make comparisons using SDI groups (Deng et al., 2021; Wong et al., 2017; Wang et al., 2020). Studies focusing on temporal trends in TBL cancer indicators have addressed this issue; globally (Zhou et al., 2022), USA (Zhong et al., 2019), USA and Europe (Jani et al., 2021b), China (Ni et al., 2020), China and USA (Deng et al., 2021), Brazil (Fernandes et al., 2020), Belgium (Vanthomme et al., 2021) and, Iran (Almasi et

al., 2016). When TBL cancers were studied with other types of cancer in Turkey (Doğan et al., 2020), it was observed that the focus was on incidence and mortality.

The findings of this study indicated that the temporal trends of incidence, mortality and DALY rates of global TBL cancers tended to decrease for men, whereas they tended to increase for women. Significant differences in temporal trends and structure of TBL cancers were identified among the global mean, SDI groups, and Turkey. The higher SDI groups had a greater burden of TBL cancers than the lower groups. Men in the High-SDI group had the lowest average percentage change, while females achieved the highest increase in average percentage change in the Low SDI group. Wang et al. (2020)'s findings are in line with the findings of this study. The most common regions of TBL cancers in all countries are Northern Europe, Turkey, China, and parts of North America. In this study, as highlighted in Graph 1 and Graph 2, Turkey was found to be among the regions with the highest TBL cancer burden. The tendency for TBL cancers, which had surged in developed countries before 1990, declined in the following years. According to a different study, this tendency was related to the ability to treat this disease before symptoms appear or with early diagnosis, made possible by sophisticated diagnostic techniques (Jani et al., 2021: 6). Men had a significantly higher cancer burden than women when the gender trends of TBL cancers were analyzed according to the standardized age group., while the burden of TBL cancers tends to decrease in men, incidence, mortality, and DALY rates increase in women.

## 5. Conclusion

In conclusion, the findings of this study indicated that the global burden of TBL cancers tends to decrease, with the highest average percentage of the decrease occurring in men in the High SDI group. The highest average percentage of change occurred in women in the Low and Low-Middle SDI groups. TBL cancers in Turkey between 1990-2019; incidence, mortality, and DALY rates were found to be well above the global average and had a temporal trend structure that decreased until 2005 and then increased. In summary, the incidence, mortality, and DALY rates of TBL cancers were higher in the higher SDI groups, and the temporal trend of TBL cancers tended to decrease in men and increase in women, both globally and for most SDI groups. The TBL cancer burden in Turkey had a decreasing temporal trend up until 2005, after which it began to increase. As a result of MIR calculations, the MIR for both genders at the global level is between 0.89-0.91 for males and females, with High SDI group countries having values below this as an indicator of worse relative survival per unit incidence in a given population. It is reported that Turkey's rates are between Low SDI and Low-Medium SDI group country

scores. It is recommended to develop health policies in Turkey and international health systems for fair access to cancer treatment to reduce the TBL global cancer burden.

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## Appendix Tables

**Appendix 1. JRA Findings of Incidence rates in Global, SDI Groups, and Turkey**

Location	Both			Male			Female		
	Segments	APC	AAPC	Segments	APC	AAPC	Segments	APC	AAPC
Global	1990-1994	0.7*		1990-1994	0.3		1990-1993	1.5*	
	1994-1997	-0.5		1994-1997	-1.3*		1993-2003	1.1*	
	1997-2010	0.1*	-0.1*	1997-2010	-0.2*	-0.5*	2003-2009	0.6*	0.7*
	2010-2019	-0.7*		2010-2019	-0.9*		2009-2016	-0.3*	
							2016-2019	0.9*	
High SDI	1990-1995	0.4*		1990-1994	-0.4		1990-1995	2.2*	
	1995-2009	-0.4*	-0.5*	1994-2006	-1.3*	-1.3*	1995-2001	1.2*	0.6*
	2009-2019	-1.2*		2006-2009	-0.7		2001-2009	0.6*	
				2009-2019	-1.9*		2009-2019	-0.6*	
High-Middle SDI	1990-1994	1.4*		1990-1994	1.2*		1990-1998	0.9*	
	1994-1998	-1.5*		1994-1998	-2.0*		1998-2004	2.1*	
	1998-2003	0.5*	-0.2	1998-2005	-0.1	-0.6*	2004-2010	0.9*	1.0*
	2003-2010	-0.1		2005-2019	-0.9*		2010-2013	-0.7	
	2010-2013	-1.3					2013-2016	0.5	
	2013-2019	-0.2					2016-2019	1.6*	
Middle SDI	1990-1992	-3.7	0.5*	1990-1992	-5.5*	0.3	1990-1995	0.7*	1.0*

	1992-2010	1.2*		1992-2011	1.2*		1995-2004	1.4*	
	2010-2019	-0.0		2011-2019	-0.4*		2004-2007	0.6	
							2007-2010	1.5*	
							2010-2016	0.0	
							2016-2019	2.5*	
<b>Low-Middle SDI</b>	1990-2001	0.4*		1990-2001	0.3*				
	2001-2004	-0.3		2001-2004	-0.4				
	2004-2009	0.8*	0.4*	2004-2009	0.7*	0.2*	1990-2013	1.0*	1.2*
	2009-2015	0.2		2009-2016	-0.2*		2013-2019	1.9*	
	2015-2019	0.9*		2016-2019	0.6*				
<b>Low SDI</b>	1990-1992	-4.5*		1990-1992	-5.2*		1990-1994	0.3	
	1992-2007	0.1*	-0.1	1992-2019	0.0*	-0.3*	1994-2000	0.8*	
	2007-2019	0.4*					2000-2003	1.6*	1.3*
							2003-2011	1.0*	
							2011-2014	2.7*	
						2014-2019	1.9*		
<b>Turkey</b>	1990-1997	-3.3*		1990-1997	-3.5*		1990-1994	0.3	
	1997-2001	-7.0*		1997-2001	-7.4*		1994-2003	-2.4*	
	2001-2005	0.3	-0.5*	2001-2005	0.2	-0.7*	2003-2006	3.6*	1.0*
	2005-2011	8.0*		2005-2010	8.6*		2006-2010	7.9*	
	2011-2019	-1.1*		2010-2013	1.7		2010-2019	1.1*	
				2013-2019	-2.0*				

#### Appendix 2. JRA Findings of Mortalities rates in Global, SDI Groups, and Turkey

Location	Both Segments			Male			Female		
	Segments	APC	AAPC	Segments	APC	AAPC	Segments	APC	AAPC
Global	1990-1994	0.1		1990-1994	0.1		1990-1994	1.1*	
	1994-1997	-1.2*		1994-1997	-1.2*		1994-1998	0.8*	
	1997-2010	-0.5*	-0.7*	1997-2010	-0.5*	-0.7*	1998-2003	1.0*	0.5*
	2010-2019	-1.1*		2010-2019	-1.1*		2003-2009	0.3*	
							2009-2016	-0.4*	
High SDI	1990-1995	-0.1		1990-1995	-1.0*		2016-2019	0.8*	
	1995-2009	-0.8*		1995-2011	-1.7*		1990-1995	1.5*	
	2009-2017	-1.5*	-0.8*	2011-2017	-2.1*	-1.5*	1995-2000	0.8*	
	2017-2019	0.3		2017-2019	0.3		2000-2009	0.2*	0.3*
							2009-2017	-0.8*	
High-Middle SDI	1990-1994	1.3*		1990-1994	1.1*		2017-2019	0.2	
	1994-1998	-1.6*		1994-1998	-2.1*		1990-1994	1.0*	
	1998-2003	0.3	-0.4*	1998-2004	-0.2	-0.8*	1994-1998	0.4	
	2003-2010	-0.6*		2004-2019	-1.2*		1998-2004	1.8*	0.7*
	2010-2013	-1.5					2004-2009	0.3*	
Middle SDI	2013-2019	-0.5*					2009-2015	-0.5*	
	1990-1994	0.5*		1990-1994	0.3*		2015-2019	1.2*	
	1994-1999	1.1*		1994-1999	1.2*		1990-1995	0.7*	
	1999-2004	1.6*	0.6*	1999-2004	1.7*	0.6*	1995-2004	1.4*	
	2004-2007	0.2		2004-2007	0.3		2004-2007	0.3	0.8*
Low-Middle SDI	2007-2010	1.7*		2007-2010	2.2*		2007-2010	1.0*	
	2010-2019	-0.3*		2010-2019	-0.4*		2010-2016	-0.3*	
	1990-2001	0.4*		1990-2001	0.3*		2016-2019	1.9*	
	2001-2004	-0.3		2001-2004	-0.4				
	2004-2008	0.8*	0.4*	2004-2009	0.7*	0.2*	1990-2013	1.0*	1.2*
Low SDI	2008-2015	0.1*		2009-2016	-0.2*		2013-2019	1.7*	
	2015-2019	0.8*		2016-2019	0.6*				
	1990-1996	-0.1		1990-1996	-0.1*		1990-1995	0.5*	
	1996-2003	0.2*	0.1*	1996-2003	0.1*	-0.1*	1995-2000	0.9*	1.3*
	2003-2010	-0.0		2003-2013	-0.1*		2000-2003	1.6*	
	2010-2013	0.3		2013-2017	-0.5*		2003-2011	1.0*	

	2013-2017	0.1		2017-2019	0.5*		2011-2014	2.6*	
	2017-2019	0.9*					2014-2019	1.9*	
	1990-1997	-3.3*		1990-1997	-3.3*		1990-1995	-0.2	
	1997-2001	-6.8*		1997-2000	-8.6*		1995-2002	-3.0*	
Turkey	2001-2005	0.2	-0.5*	2000-2005	-0.6	-0.7*	2002-2005	0.6	0.8*
	2005-2011	7.8*		2005-2010	8.5*		2005-2010	7.5*	
	2011-2019	-1.1*		2010-2013	1.7		2010-2019	0.8*	
				2013-2019	-2.1*				

### Appendix 3 JRA Findings of DALY rates in Global, SDI Groups, and Turkey

Location	Both			Male			Female		
	Segments	APC	AAPC	Segments	APC	AAPC	Segments	APC	AAPC
Global	1990-1994	0.3					1990-1994	0.8*	
	1994-1998	-1.1*		1990-1994	0.1		1994-2003	0.5*	
	1998-2002	-0.3	-0.6*	1994-1997	-1.8	-0.9*	2003-2009	-0.1*	0.2*
	2002-2010	-0.7*		1997-2010	-0.8*		2009-2016	-0.7*	
	2010-2016	-1.1*		2010-2019	-1.2*		2016-2019	0.9*	
High SDI	2016-2019	-0.2							
	1990-1995	-0.6*		1990-1994	-1.3*		1990-1995	1.0*	
	1995-2009	-1.2*	-1.2*	1994-2011	-2.0*	-1.8*	1995-2001	0.3*	
	2009-2017	-1.8*		2011-2016	-2.5*		2001-2009	-0.1	0.0
	2017-2019	0.3		2016-2019	-0.5		2009-2017	-1.1*	
High-Middle SDI							2017-2019	0.4	
	1990-1994	1.3*		1990-1994	1.2*		1990-1994	1.0*	
	1994-1998	-2.4*		1994-1998	-3.0*	-1.3*	1994-1998	0.4	
	1998-2003	-0.2	-0.8*	1998-2004	-0.7*		1998-2004	1.3*	0.4*
	2003-2010	-1.1*		2004-2019	-1.6*		2004-2009	-0.0	
Middle SDI	2010-2013	-2.0*					2009-2014	-1.0*	
	2013-2019	-0.8*					2014-2019	0.5*	
	1990-1994	0.1		1990-1993	-0.2		1990-2003	0.7*	
	1994-2004	0.8*		1993-1999	0.7*		2003-2007	-0.2	
	2004-2007	-0.2	0.3*	1999-2004	1.1*	0.3*	2007-2010	0.3	0.4*
Low-Middle SDI	2007-2010	1.1*		2004-2007	-0.1		2010-2016	-0.4*	
	2010-2019	-0.5*		2007-2011	1.2*		2016-2019	1.8*	
				2011-2019	-0.7*				
	1990-1994	0.1		1990-2001	0.2*		1990-2001	1.0*	
	1994-2004	0.8*		2001-2004	-0.8		2001-2004	0.1	1.0*
Low SDI	2004-2007	-0.2	0.3*	2004-2010	0.6*	0.1	2004-2012	0.8*	
	2007-2010	1.1*		2010-2015	-0.5*		2012-2019	1.7*	
	2010-2019	-0.5*		2015-2019	0.3*				
	1990-1995	-0.1		1990-1994	-0.1		1990-1996	0.4*	
	1995-2003	0.1*		1994-2003	0.1*		1996-2011	1.0*	1.2*
Turkey	2003-2010	-0.1*	0.1*	2003-2006	-0.4	-0.1*	2011-2014	2.7*	
	2010-2013	0.3		2006-2013	-0.2*		2014-2019	1.8*	
	2013-2017	0.1		2013-2017	-0.4*				
	2017-2019	0.7*		2017-2019	0.4				
	1990-1995	-2.6*		1990-1997	-3.6*		1990-1995	-0.3	
Turkey	1995-2002	-6.0*		1997-2001	-8.0*		1995-2003	-2.9*	
	2002-2005	1.2	-0.7*	2001-2005	-0.1	-1.0*	2003-2006	2.7*	0.5*
	2005-2011	7.5*		2005-2010	8.5*		2006-2010	6.6*	
	2011-2019	-1.4*		2010-2013	1.2		2010-2019	0.7*	
				2013-2019	-2.2*				