Balkan Med J 2024;41:298-307



# Modifiable Risk Factors for Breast Cancer Mortality in Türkiye from 1990 to 2019: A Temporal Analysis of Global Burden of Disease Data

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**Background:** Breast cancer is the leading cause of cancer-related mortality in women in Türkiye.

**Aims:** Explore the trends in female breast cancer mortality rates and the associated modifiable factors in Türkiye between 1990 and 2019.

**Study Design:** Epidemiological descriptive analysis.

**Methods:** The database of the Global Burden of Disease study was used to obtain data regarding breast cancer-related mortality and modifiable (behavioral and metabolic) risk factors among women in Türkiye from 1990 to 2019. The average annual percentage change (AAPC) for female breast cancer mortality rates was computed using the Joinpoint regression method.

**Results:** From 1990 to 2009, the breast cancer mortality rates in Türkiye tended to increase [from 12.26/105 in 1990 to 12.65/105 in 2019; AAPC=0.1 "95% confidence interval (CI): 0.1-0.1"]. In terms of breast cancer mortality attributed to modifiable factors, a 3% increase was observed from 1990 (20.4%) to 2019 (23.1%), the highest contributor being high body mass index (3.19% in 1990 to 5.87% in 2019; AAPC=1.5; 95% CI: 1.3-1.5), followed by high fasting plasma glucose (5.01% in 1990 to 7.72% in 2019; AAPC=1.4; 95% CI: 1.3-1.5).

**Conclusion:** The proportion of breast cancer-related deaths attributed to metabolic factors has been increasing in Türkiye from 1990 to 2019. Therefore, health policies aimed at managing metabolic factors in women are warranted to reduce breast cancer-related mortality in Türkiye.

## INTRODUCTION

Breast cancer is the most common type of cancer diagnosed in women in Türkiye and has the highest mortality rates among all cancer types. As per the data estimated by the Global Cancer Observatory, in 2020, an annual incidence of 24,175 new cases and 7,161 deaths were attributed to breast cancer.[1] The CONCORD-3 research data states that global cancer survival rates vary notably among countries and regions, which is true in the case of breast cancer as well. The 5-year survival rates (2010-2014) for women diagnosed with breast cancer were reported as 90.2% in the United States, 89.5% in Australia, and 84.8% in Türkiye.[2]

As per the literature, the risk factors for breast cancer can be categorized as unmodifiable (sex, age, genetic mutations, family history, and hormone exposure) and modifiable factors (behaviors like smoking, alcohol intake, obesity, and metabolic conditions).[3,4] Studies show that active and secondhand smoke, alcohol consumption, obesity, and high glucose levels increase the risk of breast cancer.[5] Even light alcohol consumption (≤ 1 drink/day) increases the risk of breast cancer by 4-15%.[6] In contrast, regular physical activity can reduce the risk of developing breast cancer.[7] A previous meta-analysis reported a ~30% higher risk of cancer recurrence or death in women diagnosed with breast cancer who are obese compared to those with normal weight.[8] Mammography screening is vital for early detection and reducing mortality rates. In Türkiye, cancer was classified as a notifiable disease in 1982, and screening programs were started after 2004; cancer screening follows national guidelines aimed at enhancing early diagnosis and treatment access to prioritize public health and well-being.[9-11]

This study aimed to identify behavioral and metabolic risk factors associated with breast cancer mortality in Türkiye from 1990 to 2019 and use these factors to guide the development of preventive public health policies for breast cancer in the country.

## MATERIALS AND METHODS

### *Data sources and search parameters*

We used an epidemiological and descriptive design to examine the data from the Global Burden of Disease (GBD) study of 2019.

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**Received:** April 24, 2024 **Accepted:** June 16, 2024 **Available Online Date:** 04.07.2024 • **DOI:** 10.4274/balkanmedj.galenos.2024.2024-4-91

Available at www.balkanmedicaljournal.org

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**Cite this article as:** Yekdeş AC, Han Yekdeş D, Çelikkalp Ü, Ekuklu G. Modifiable Risk Factors for Breast Cancer Mortality in Türkiye from 1990 to 2019: A Temporal Analysis of Global Burden of Disease Data. Balkan Med J.; 2024; 41(4):298-307.

The GBD database assembled various input sources to estimate mortality, causes of death, and risk factors for each country. The data sources used in creating estimations for Türkiye are explained in detail in the GBD study.[12] This study centered on female patients in Türkiye diagnosed with breast cancer between 1990 and 2019. We gathered secondary data attributed to risk factors mentioned in the GBD study regarding case numbers, mortality rates, rates, age-standardized rates (adjusted to the World Health Organization's standard population), and percentages of breast cancer deaths;[13] these data are freely available at the Global Health Data Exchange (GHDx; https://vizhub.healthdata.org/gbd-results/) and can be extracted using the GBD Results Tools repository. The search parameters were "breast cancer" and specific cancer types attributable to seven estimated risk factors for cause ["alcohol use," "diet high in red meat," "high fasting plasma glucose," "low physical activity," "secondhand smoke," "smoking," and "high body mass index" (HBMI)] and risk, "deaths" for measurements, "1990-2019" for time in years, "Türkiye" for location, and "number, rate, and percent" for metrics. We followed the Guidelines for Accurate and Transparent Health Estimates Reporting guidelines for this study.

### Global Burden of Disease estimation framework

The cause of death (COD) database mentioned in the GBD study is a compilation of data gathered from various primary source documents, including vital registration, sample vital registration, and verbal autopsy records. The incidence and mortality data are subjected to a multi-step process that involves adjustments based on age groups and the aggregation of implausible and unspecified COD codes. Due to the limited availability of mortality data from many countries, the cancer registry incidence data were converted into mortality data by modeling the mortality-to-incidence ratio. For breast cancer estimates, the International Classification of Diseases-10 (ICD-10) edition codes C50-C50.9, D05-D05.9, D24-D24.9, D48.6, and D49.3 were used.[14]

### Ethical considerations

Ethical approval and institutional permissions were not required for this study as the secondary data were collected from online open-access databases. Informed consent was not applicable as we only used disease-specific mortality data in the study.

### Statistical analysis

Detailed methodologies for incorporating data on risk factors and estimating mortality have been documented in prior studies conducted by GBD collaborators.[15] For this study, we conducted a descriptive analysis of the proportion data [death counts, Age-Standardized Mortality Rates (ASMR), and percentage] for breast cancer mortality, categorizing them by age, age intervals, and annual variations; we also examined the change in trends over the 30-year period from 1990 to 2019. To assess mortality trends, we used Joinpoint software (version 5.0.2.0; https://surveillance.cancer.gov/joinpoint/); this software facilitates the fitting of consecutive straight lines to age-standardized rates and percentage trends. In the analysis, we specified options for including the logarithmic transformation of rates and percentages, ensuring constant variance (homoscedasticity), and applying the weighted Bayesian Information Criterion. To assess the scale and trajectory of recent trends, we conducted calculations for the average annual percentage change (AAPC) and its associated 95% confidence intervals (CI) over the last 30 years. The AAPC serves as a geometrically weighted average of the various annual percentage changes obtained from the Joinpoint trend analysis, with each segment's length during the specified time interval serving as the weight.[16] A CI containing zero indicated that there is no evidence to reject the null hypothesis that the true AAPC is zero at a significance level $p<0.05$. Otherwise, we rejected the null hypothesis in favor of the alternative hypothesis that the true AAPC is different from zero.[17]

## RESULTS

In 1990, a total of 4,046 (95% CI: 3,201-5,151) cases of breast cancer were observed in Türkiye; this number increased to 17,129 (95% CI: 13,439-21,566) in 2019. Regarding ASMRs (per $10^5$ people) there was an annual percentage change of 0.86 (95% CI: 0.31; 1.59) over the 30 years. In terms of mortality, in 1990, 2,450 (95% CI: 1,949-3,125) breast cancer-related deaths were reported in Türkiye which accounted for 1.45% (95% CI: 1.21; 1.81) all-cause mortality. By the year 2019, this number had risen to 5,926 deaths (95% CI: 4,728-7,337), making up for 2.84% (95% CI: 2.57; 3.17) of all-cause mortality in Türkiye. However, when age-standardized rates were evaluated, only a slight increase in proportions was observed from 1990 to 2019 [from 12.26 in 1990 to 12.65 in 2019; AAPC=0.1 (95% CI: 0.1-0.1); Table 1].

For further analysis, the data were categorized into five age groups: 15-39 years, 40-44 years, 45-49 years, 50-69 years, and ≥ 70 years. Both the number of breast cancer-related deaths and the proportion of these deaths among all-cause mortality increased for all five age groups between 1990 and 2019. However, increases in ASMR were particularly noteworthy for the 15-39 years and the ≥ 70 years age groups. In contrast, the ASMRs decreased for the other three age groups (Table 1). In terms of mortality parameters attributed to risk factors for breast cancer, the number of breast cancer-related deaths attributed to all risk factors (calculated risk factors in GBD) increased from 479 (95% CI: 293-704) in 1990 to 1,361 (95% CI: 783-2113) in 2019. Among the risk factors, high fasting plasma glucose was associated with the highest number of deaths, ASMR, and mortality proportions in both 1990 and 2019. While active- and passive-smoking-related ASMRs showed a decline over 30 years, an increase was observed in other risk factors, with the greatest increment for HBMI (AAPC=1.5, 95% CI: 1.4-1.5).

Figure 1 illustrates the trends for the number of deaths and ASMRs attributed to all risk factors and three significant risk factors from 1990 to 2019. The number of deaths attributed to all risk factors showed a slight decrease from 1998 to 2003; subsequently, there was a trend of increasing death counts and the associated ASMR, followed by a parallel trajectory up to the years 2009-2010, a slight plateau, and a decline thereafter (Figure 1a). Similar trends were observed for high fasting plasma glucose, which had the highest proportion of risk-factor-associated deaths in both 1990 and 2019 (Figure 1b). In contrast, a decline in ASMRs was observed for both

active and secondhand smoke, with a more obvious decrease between 1994 and 2003, and a less pronounced increase from 2003 to 2009. Although the number of deaths has continued to increase, a declining trend has become more pronounced since 2009-2010 (Figure 1c, d).

The temporal distribution of the percentage of deaths attributed to risk factors in breast cancer mortality is presented in Figure 2. Over the years, the amount of deaths attributable to risk factors has been increasing, with a noticeable increase in the percentages attributed to high plasma glucose, especially after 2005.

When ASMRs were examined by the Joinpoint regression program, five breakpoints were identified in the mortality rates attributed to all risk factors (in order - 1995, 2002, 2005, 2009, 2013). Between 1990 and 1995, there was a slight increase (AAPC=0.05), followed by a significant decrease between 1995 and 2002 (AAPC=-2.31), an increase between 2002 and 2005 (AAPC=2.75), and a substantial

**TABLE 1.** Breast cancer-related mortality in women in Türkiye from 1990 to 2019: death counts, age-standardized mortality rates, and percentages along with the average annual percentage change in age-standardized mortality rates (Generated from data available at http://ghdx.healthdata.org/gbd-results-tool).

| | Breast Cancer Mortality Data in Females in Türkiye | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1990 | | | 2019 | | | AAPC (95% CI) |
| | Count | ASMR (/$10^5$) | Percent (%) | Count | ASMR (/$10^5$) | Percent (%) | |
| Total (female) | 2450.43 (1949.38 to 3125.94) | 12.26 (9.80 to 15.63) | 1.45 (1.21 to 1.81) (in all deaths) | 5926.21 (4728.61 to 7337.49) | 12.65 (10.07 to 15.67) | 2.84 (2.57 to 3.17) (in all deaths) | 0.1 (0.1 to 0.1) |
| Age (years) | | | | | | | |
| 15-39 | 238.80 (170.86 to 326.77) | 1.97 (1.41 to 2.70) | 2.63 (1.95 to 3.53) | 393.16 (291.17 to 521.24) | 2.39 (1.77 to 3.17) | 7.12 (5.98 to 8.23) | 0.7 (0.6 to 0.8) |
| 40-44 | 208.11 (141.36 to 293.61) | 14.68 (9.97 to 11.12) | 8.07 (5.56 to 11.12) | 414.81 (293.10 to 549.43) | 13.26 (9.37 to 17.56) | 14.80 (11.87 to 17.91) | -0.3 (-0.4 to -0.2) |
| 45-49 | 289.01 (193.77 to 416.77) | 24.88 (16.68 to 35.88) | 8.11 (5.66 to 11.44) | 473.09 (340.52 to 627.15) | 18.21 (13.10 to 24.13) | 13.12 (10.81 to 15.76) | -1.1 (-1.1 to -1.0) |
| 50-69 | 1235.54 (952.52 to 1631.75) | 36.69 (28.29 to 48.46) | 3.51 (2.79 to 4.55) | 2479.73 (1900.14 to 3178.91) | 32.02 (24.53 to 41.05) | 5.92 (5.18 to 6.82) | -0.5 (-0.6 to -0.5) |
| ≥ 70 | 478.96 (372.17 to 609.36) | 54.55 (42.39 to 69.41) | 0.79 (0.64 to 0.98) | 2165.42 (1712.82 to 2679.16) | 81.82 (64.72 to 101.24) | 1.48 (1.26 to 1.70) | 1.4 (1.4 to 1.5) |
| Risk factors | | | | | | | |
| All risk factors | 479.17 (293.67 to 704.38) | 2.50 (1.56 to 3.69) | 20.40 (13.40 to 28.12) (in all breast cancer deaths) | 1361.12 (783.24 to 2113.58) | 2.92 ( 1.68 to 4.54) | 23.10 (14.95 to 33.07) (in all breast cancer deaths) | 0.5 (0.5 to 0.6) |
| Alcohol use | 55.70 (38.85 to 78.14) | 0.26 (0.18 to 0.37) | 2.27 (1.70 to 2.91) | 126.50 (83.05 to 178.75) | 0.27 (0.17 to 0.37) | 2.13 (1.56 to 2.79) | -0.3 (-0.3 to 0.3) |
| Active smoking | 91.63 (57.79 to 140.88) | 0.45 (0.28 to 0.68) | 3.74 (2.48 to 5.33) | 196.42 (123.91 to 274.05) | 0.41 (0.26 to 0.57) | 3.32 (2.24 to 4.45) | -0.08 (-0.38 to 0.37) |
| Secondhand smoking | 100.31 (21.86 to 186.59) | 0.50 (0.11 to 0.92) | 4.09 (1.00 to 6.99) | 174.34 (39.60 to 315.26) | 0.37 (0.08 to 0.67) | 2.95 (0.72 to 5.10) | -1.0 (-1.1 to -1.1) |
| Low physical activity | 31.93 (14.26 to 60.03) | 0.17 (0.08 to 0.32) | 1.30 (0.57 to 2.36) | 108.74 (44.16 to 196.79) | 0.24 (0.10 to 0.43) | 1.83 (0.75 to 3.13) | 1.0 (0.9 to 1.2) |
| High body mass index | 78.11 (21.26 to 192.45) | 0.49 (to0.04 to 1.12) | 3.19 (0.92 to 7.65) | 348.70 (30.55 to 750.24) | 0.76 (0.08 to 1.63) | 5.87 (0.54 to 12.41) | 1.5 (1.4 to 1.6) |
| High fasting plasma glucose | 122.74 (22.76 to 293.41) | 0.66 (0.12 to 1.57) | 5.01 (0.92 to 11.39) | 457.55 (1073.96 to 85.73) | 0.99 (0.19 to 2.32) | 7.72 (1.51 to 16.88) | 1.4 (1.3 to 1.5) |
| Diet high in red meat | 48.50 (9.65 to 73.93) | 0.24 (0.05 to 0.36) | 1.98 (0.39 to 2.59) | 113.12 (23.41 to 173.26) | 0.24 (0.05 to 0.37) | 1.91 (0.38 to 2.59) | 0.0 (-0.0 to 0.0) |

ASMR, Age Standardized Mortality Rate; AAPC, Estimated Annual Percentage Change for ASMR's; CI, confidence interval; All data are presented along with 95% confidence intervals

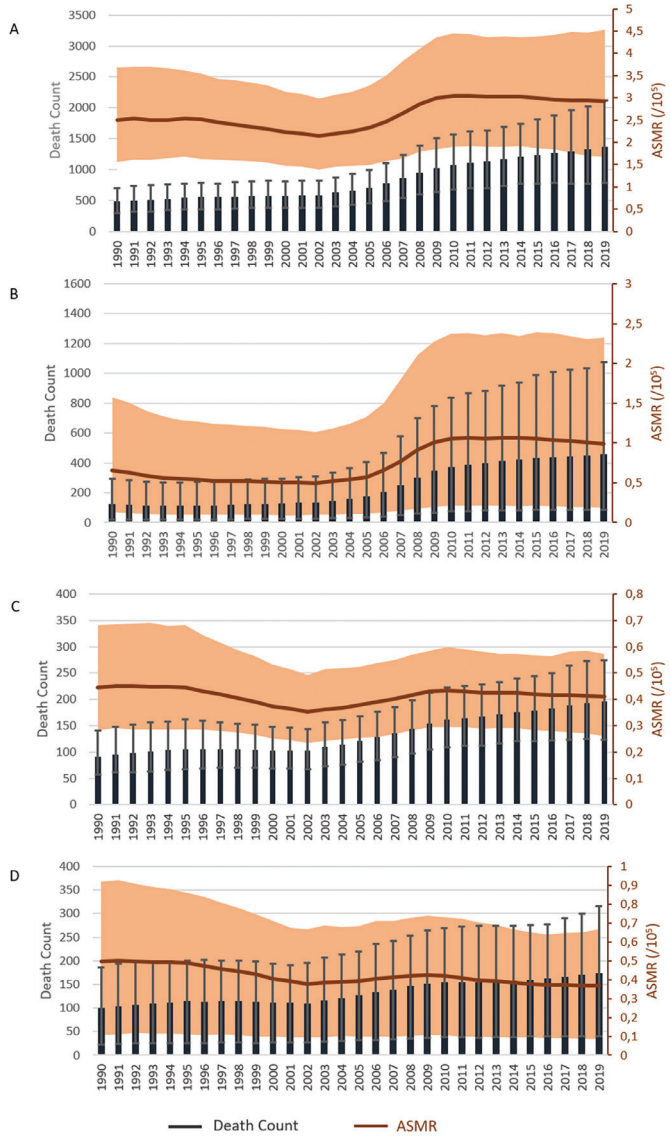


**FIG. 1.** Trends of the total death counts and age-standardized mortality rates of breast cancer attributed to various risk factors: (a) Mortality data attributed to all evaluated risk factors; (b) Mortality data attributed to high fasting plasma glucose levels; (c) Mortality data attributed to smoking; (d) Mortality data attributed to secondhand smoking (the data was obtained from the website *http://ghdx.healthdata.org/gbd-results-tool).*

uptrend from 2005 to 2009 (APC=6.87). From 2009 to 2013, the ASMRs plateaued (AAPC=0.08) and declined again between 2013 and 2019 (AAPC=-0.67) (Figure 3). The calculated breakpoints for the amounts attributed to other risk factors differed slightly from those calculated for all risk factors. Furthermore, in the pairwise comparison, we did not observe a statistically significant parallelism between the ASMR trend attributed to all risk factors versus each risk factor. Five breakpoints were calculated for high fasting plasma glucose; although there was a similar trend in the ASMRs attributed to each risk factor between 2005 and 2009, the increase in trends for

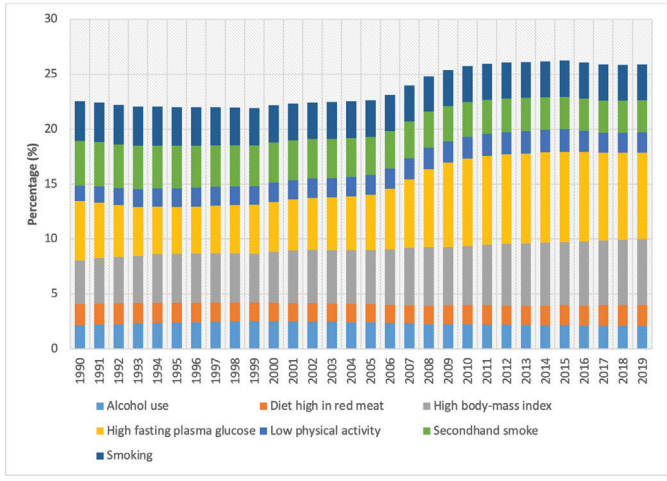


**FIG. 2.** Proportional distribution trends for breast cancer deaths attributable to calculated risk factors (data be obtained from the website *http://ghdx.healthdata.org/gbd-results-tool).*

high fasting plasma glucose (AAPC=16.19) was particularly notable compared to other risk factors (Figure 3).

Among the trends of percentages attributed to risk factors for breast cancer mortality, HBMI and high fasting plasma glucose, were identified as significant risk factors. HBMI had the highest AAPC with overall increasing trends; five breakpoints were identified for HBMI which occasionally showed decreases in this trend, but a significantly declining trend was never observed. In contrast, there have been instances of decreasing trends in the percentages attributed to other risk factors at certain time intervals. Similar to the ASMR analysis, high fasting plasma glucose also showed five breakpoints in the trends of percentages attributed to risk factors; although there was a difference in the first two breakpoints, they were similar in terms of trends. Until 1996, it exhibited a decreasing trend in percentages, which increased till 2014, reaching the highest AAPC between 2005 and 2009; from 2014 onward, the trend in percentages began to decline. The percentages attributed to alcohol use, smoking, and secondhand smoking had generally decreasing trends; notably, increasing trends were observed for alcohol use before 1999, for active smoking between 2008 and 2011, and for secondhand smoking after 2017 (Figure 4).

Figure 5 presents the distribution of AAPC values for ASMRs of breast cancer attributed to all causes and risk factors by age groups (five-year intervals) from 1990-2019. For the age groups < 20 years and 20-24 years, the ASMR values attributed to each risk factor, except for alcohol use and HBMI, were not available in the dataset, which is why AAPC calculations were not performed or added to the graph. Between the ages of 30 and 70 years, there was a decreasing trend (negative AAPC values) in the ASMRs for breast cancer attributed to all causes; however, the 20-24 years and ≥ 70 years age groups showed increasing trends. While no decrease was observed in the ASMRs attributed to risk factors in individuals aged ≥ 75 years, similar to ASMRs for all causes of breast cancer, the ASMRs decreased between the ages of 30 and 70, with declining trends for risk factors such as smoking, secondhand smoking, and alcohol use. In contrast, the

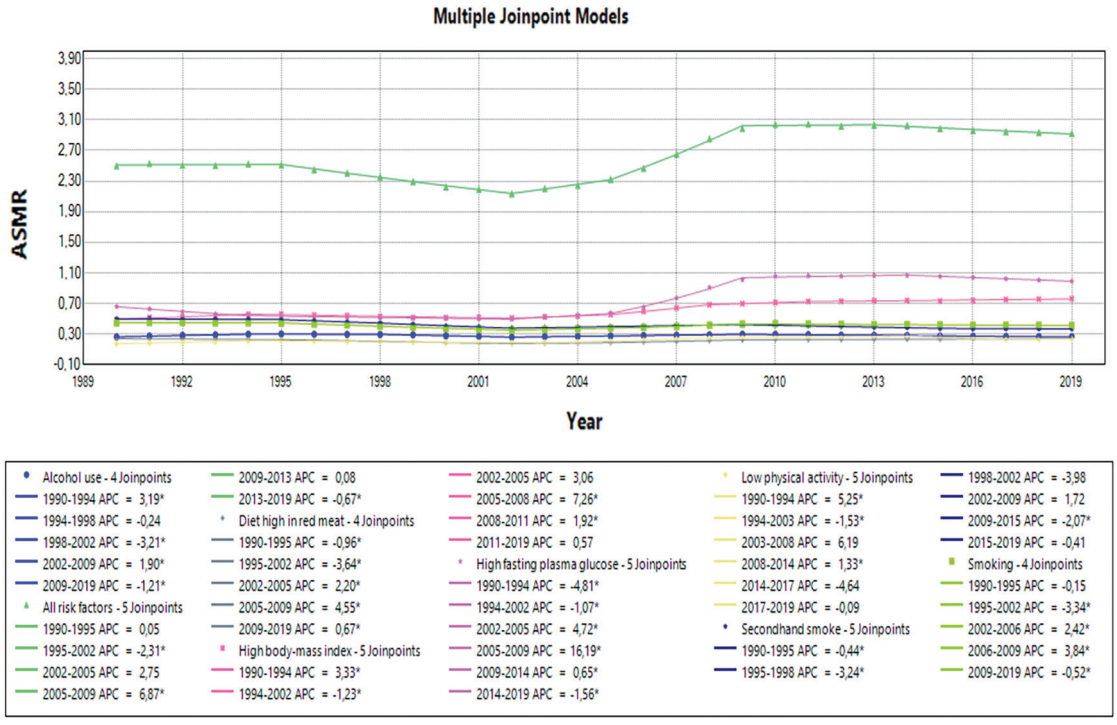


**FIG. 3.** Temporal changes and turning points in age-standardized mortality rates for breast cancer attributed to risk factors examined using Joinpoint regression (data obtained from the website *http://ghdx.healthdata.org/gbd-results-tool)* values signed * represent a p value of < 0.05.

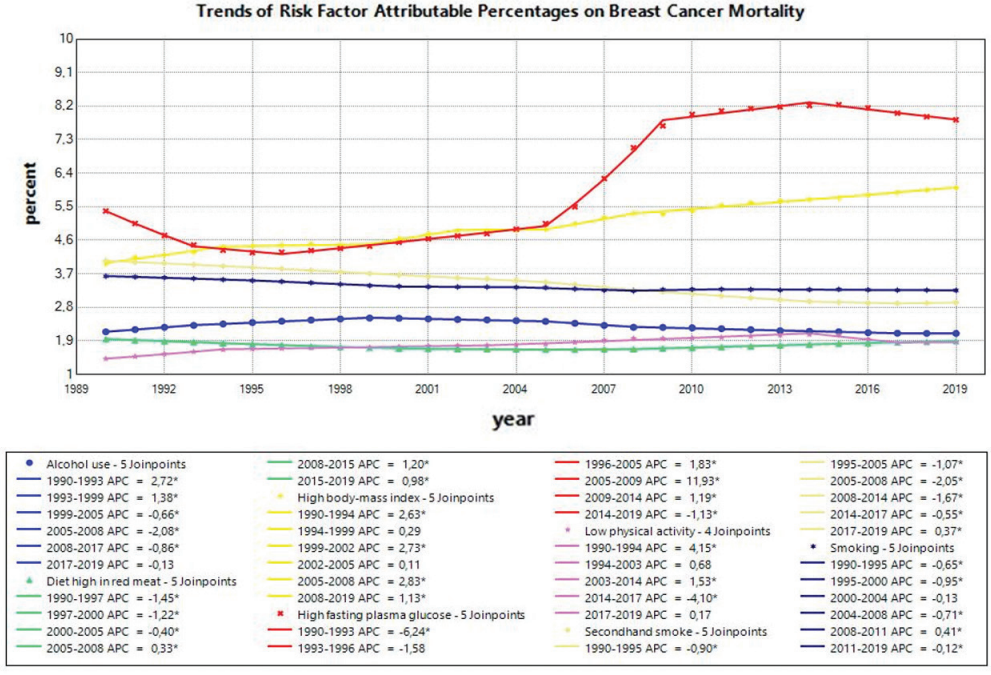


**FIG. 4.** Temporal changes and turning points in percentages (%) of breast cancer mortality attributed to risk factors using Joinpoint regression (data obtained from the website *http://ghdx.healthdata.org/gbd-results-tool)* values signed * represent a p value of < 0.05.

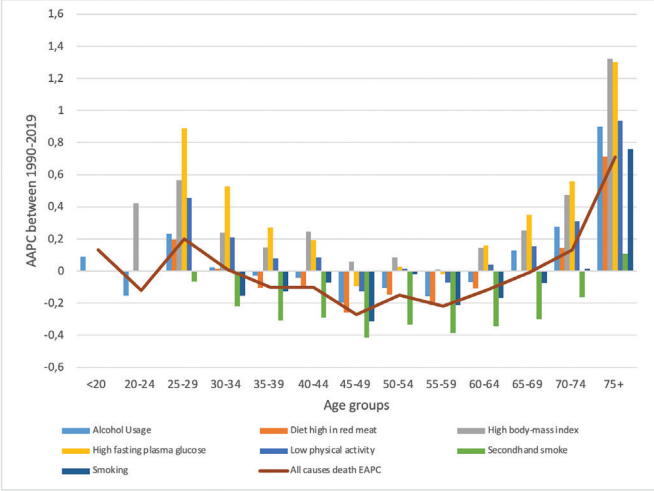


**FIG. 5.** Distribution of the average annual percentage change in breast cancer mortality rates from 1990-2019 attributed to various risk factors for different age groups (data obtained from the website *http://ghdx.healthdata.org/gbd-results-tools)*.
AAPC, average annual percentage change.

ASMRs attributed to high fasting plasma glucose showed consistently increasing trends in all age groups except for women aged 45-49 years and 55-59 years. Similarly, except for the 50-54-year-olds, the ASMRs attributed to HBMI increased consistently for all age groups.

## DISCUSSION

This study examines the trends in behavioral and metabolic risk factors associated with breast cancer mortality in women in Türkiye from 1990 to 2019. The research revealed somewhat increasing trends in the ASMRs related to breast cancer in Turkish women, rising from 12.26 to 12.65 per 100,000 people over these 30 years. Notably, the most significant increase was observed in women aged 70 years and above. When examining the data from 1990, the ASMR was particularly higher in women aged 50-69 years and ≥ 70 years. By 2019, the increasing trends in ASMR were observed in both the younger (15-49 years) and older women (≥ 70 years), while a decreasing trend was noted in the 50-69 years age group.

Our research findings are consistent with a previous study examining the global breast cancer-related mortality trends from 1990 to 2015, supporting an overall increase in breast cancer-related mortality rates across the world.[18] However, another study analyzing the GBD data and classifying countries based on social development reported a decreasing trend in breast cancer-related mortality in high and middle-income countries, while an increasing trend was found in low-income countries.[19] Although Türkiye is classified as a high-middle-income country[20] there has been a slight increase in breast cancer-related mortality over the last three decades, with the increase being more pronounced between 2000 and 2013, followed by a small decline from 2013 to 2019. According to the findings of this study, the ASMRs due to breast cancer have increased in Türkiye between 1990 and 2019, as have the age-specific incidence rates (from 35 to 44 per 100,000 as per the GLOBOCAN data).[21] While the incidence of breast cancer is considerably high in developed countries, the mortality rates are relatively low[22] presumably because of more frequent mammography screenings. Screening enables early diagnosis, increases the rate of breast-conserving surgical treatment, reduces mortality, and is ultimately, more cost-effective.[23] In Türkiye, since 2004, mammography screenings have been recommended every two years for women aged 50-69 years.[24] However, considering the younger average age of the Turkish female population and the increasing incidence of breast cancer in the premenopausal period, the screenings were adjusted in 2014 to include all women aged 40-69 years in a population-based screening program.[25] Nevertheless, the coverage of mammography screenings in Türkiye was reported to be only around 20-30% by opportunistic screening practices.[26] One of the barriers to ensuring effective screening practices at the primary care level could be the changes in the healthcare system.[27] A Turkish study from 2020 reported that only 11.8%, of women performed breast self-examination, 8.9% obtained clinical breast examinations, and 11.3% underwent mammography.[28] The study also found that perceived sensitivity, severity, self-efficacy, benefits, health motivation, and perceived barriers had strong associations with breast screening. Therefore, individual factors, such as fear of cancer, and social factors, such as spousal and family support, are also relevant apart from organizational factors in breast cancer screenings.[29]

The increase in breast cancer rates observed between 2000 and 2013 in Türkiye may also be attributed to the development of a population-based cancer registry system and improvements in data quality. In Türkiye, cancer surveillance was carried out through passive reporting after 1983, leading to low data quality; subsequently, a community-based cancer registry system was developed which led to improvements in the frequency data of cancer occurrences.[30,31]

In this study, we focused on behavioral and metabolic risk factors associated with breast cancer-related mortality, including physical inactivity, HBMI, high fasting plasma glucose, smoking, and alcohol use, rather than individual factors causing breast cancer. We found that the proportion attributed to modifiable risk factors has increased from around 20% to about 23% over the last three decades. The prevalence of obesity, characterized as the pandemic of our time, has increased in both Türkiye and Europe.[32,33] The TURDEP-1 and TURDEP-2 studies also indicated an increasing prevalence of diabetes in Türkiye.[34,35] In our study, metabolic factors were the most significant contributors to modifiable causes of breast cancer deaths. In general, a significant portion of chronic diseases occur due to metabolic (such as high fasting plasma glucose and obesity) and behavioral reasons (such as an inactive lifestyle).[36] A recent large cohort study with participants from 10 European countries reported that diabetic predisposition and elevation of C-peptide were linked to breast cancer in obese and postmenopausal women, especially those over the age of 50.[37] Despite the implementation of health projects, such as the Healthy Living Centers organized by the Ministry of Health in Türkiye for the management of chronic diseases and risk factors, the inadequacy of specialized centers and personnel makes problem management difficult.[38] Moreover, the current demand-driven healthcare delivery model in Türkiye complicates

the management process related to early diagnosis, screening, and treatment of chronic diseases.[39] Performance payments to physicians in Türkiye were introduced in 2004 for working in public secondary and tertiary care hospitals and in 2010 for academic tertiary care hospitals.[40] Eventually, therapeutic services gained importance and preventive health services remained in the background. A system with a dominant primary healthcare model, an established referral chain, community-based health services, and an adequate number of healthcare workers, including physicians and support staff, is required to ensure adequate screening and management of breast cancer in Türkiye.

A notable finding of this study was that the breast cancer mortality attributed to alcohol and smoking in Türkiye remained almost constant over the 30-year period (Figure 2). Smoking behaviors have increased from 25% to 28% in the last two decades; conversely, alcohol use has remained relatively stable (around 12%).[33] Our findings are consistent with the overall trend of smoking and alcohol consumption observed in the country. Another study based on the GBD data examining breast cancer mortality trends on a global scale between 1990 and 2017 noted that the proportion of deaths attributed to alcohol use has remained significant despite a decreasing trend in alcohol consumption over the years.[41] In our study, the proportion attributed to alcohol use did not increase over the years which may be attributed to the general societal structure and religious beliefs in Türkiye and the relatively low per capita annual alcohol consumption.[42] This may be one of the reasons for the low cause-specific mortality rate. Furthermore, the lack of increase in breast cancer mortality attributed to smoking observed in this study may be associated with the tobacco control policies implemented in our country. Türkiye ratified the "Framework Convention on Tobacco Control" in 2004 and implemented preventive initiatives and measures like a ban on smoking in enclosed areas.[43]

The study has some limitations. The primary data source for Türkiye extensively utilized by the GBD study is the data from the Turkish Statistical Institute (Turkstat); multiple studies have highlighted inadequacies in the accuracy and completeness of these data.[44-46] The calculated death rates may have been underestimated due to the possibility of inappropriate diagnoses being entered into the death notification system and the existence of deaths without a diagnosis. The use of ICD-8 as the international coding system before 2009, followed by the transition to the ICD-10 system after 2009 might have introduced additional breaks in the 30-year trends we analyzed.[47] Moreover, potential improvements in the death notification system in Türkiye in recent years could have influenced the mortality trend.[45] We used the homoscedasticity method for estimating AAPCs due to the lack of availability of standard errors for ASMRs, potentially leading to biases in AAPC calculations. Despite these limitations, our study is the first to examine trends in breast cancer mortality in Türkiye over a 30-year-long period. While previous studies with different methodologies for breast cancer risk factors focused on different risk factors, the present study particularly focused on modifiable behavioral and metabolic risk factors.[48]

In conclusion, there has been an increase in breast cancer mortality rates in Türkiye between 1990 and 2019, with modifiable behavioral risk factors contributing to a quarter of these deaths and showing increasing trends. The most significant increases are attributed to HBMI, followed by elevated fasting plasma glucose levels and low physical activity. Therefore, substantial measures are required to improve the effectiveness of screening programs in the country by implementing them on a population basis. Management of obesity, low physical activity, and high fasting plasma glucose levels are critical for preventing one out of every four deaths related to breast cancer in Türkiye.

**Ethics Committee Approval:** Ethical approval and institutional permissions were not required for this study as the secondary data were collected from online open-access databases. Informed consent was not applicable as we only used disease-specific mortality data in the study.

**Data Sharing Statement:** Raw data is publicly available from the GBD website (GHDx; https://vizhub.healthdata.org/gbd-results).

**Authorship Contributions:** Concept- A.C.Y.; Design- A.C.Y.; Data Collection or Processing- A.C.Y., D.H.Y.; Literature Search- D.H.Y., Ü.Ç., G.E.; Writing- A.C.Y., D.H.Y.; Critical Review- A.C.Y., D.H.Y., Ü.Ç., G.E.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Funding:** The authors declared that this study received no financial support.

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