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Original Article

Quantifying Health-Related Risk Factors Associated with Breast and Prostate Cancer Burden: The Role of Trends and Disparities in Obesity and Cholesterol

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Abstract

Background: We aimed to identify and quantify trends and disparities in the burden of breast and prostate cancer associated with health-related risk factors.

Methods: Cancer outcomes data, such as age-standardized rate of incidence, prevalence, and mortality were retrieved by year and country. The sociodemographic index (SDI) and human development index (HDI) was extracted from Global Burden of Disease (GBD) 2021 study and the Human Development Report. Univariate and linear regression analyses were uded to explore mean differences and correlation between cancer outcomes and independent variables.

Results: During their decades, there was an upward trend in age-standardized rate of incidence and prevalence for breast cancer (EAPC=0.15 and 0.09, respectively) and prostate cancer (EAPC=0.12 and 0.27, respectively), but a downward trend in age-standardized rate of mortality for breast (EAPC=−0.14) and prostate cancer (EAPC=−0.17). Over time, the prevalence of obesity and overweight increased by 54% and 34%, respectively. An upward trend in the non-HDL level was observed among middle-SDI (+3.76%), lower-middle-SDI (+6.92%), and low-SDI (+14.14%) countries, whereas the opposite trend was observed for high-middle-SDI (-10.12%) and high-SDI (-25.07%) regions. Multivariable regression revealed that the HDI was the main factors affecting cancer outcomes, especially for the prevalence (beta=0.73, *P*<0.001) and incidence of prostate cancer (beta=0.59, *P*<0.001).

Conclusion: Disparities in risk factors of cancer outcomes across different regions highlight the need for indispensable actions and policies on the implementation and evaluation of prevention programs among countries to address this problem.

Keywords: Breast cancer; Prostate cancer; Cholesterol; Obesity; Global buden of disease

Introduction

The prevalence and incidence of cancers, especially breast (BC) and prostate (PC) cancers, are increasing worldwide (1, 2). In 2020, an estimation of 19.3 million incidence cases of cancer and almost 10 million cancer-related mortality were reported worldwide, ranking cancer as the second cause of mortality. Breast and prostate cancers had the highest incidence among female and male groups, accounting for 19.0% of all new cancer cases (ranking first and third) and 10.7% of all cancer deaths in 2020 (1). Generally, the burden of cancers is rapidly rising; this trend echoes both population growth and aging as well as variations in the prevalence and distribution of the key modifiable HRRFs for chronic diseases, several of associated with sociodemographic and lifestyle determinants. Previous research has identified lifestyle-related factors, such as body mass index (BMI), smoking status, insufficient physical activity (IPA), and cholesterol level, as risk factors for a set of chronic diseases, including cardiovascular disease and many cancers (2). As international health leaders work to develop prevention strategies and new treatments to address cancer development, timely and precise information about health-related risk factors (HRRFs) and cancer outcomes at the country, region, state, or population level is needed. Although the mortality of cancers has steadily declined worldwide (3), there remains a gap in knowledge regarding the relationship between cancers and lifestyle risk factors using big data (4-6).

In recent decades, increasing unceasing attempts and persuasive policies have been introduced to measure the trends and associations of modifiable risk factors and cancers within and across nations (7). Some projects have quantified the plausible effects of IPA, BMI, smoking status, cholesterol level, and environmental hazards on a variety of different cancer outcomes (2, 4). Previous studies, while useful, have not been consider the disparities of modifiable risk factors among different countries and gender. The inconsistent associations between risk factors, such as BMI, total cholesterol (TC), and cancer mortality, have also been questioned.

Understanding the risk factors related to health consequences is necessary to help policy makers and inform public health policy. To address this less known aspect of cancer research, we explored the trends in the incidence, prevalence, and mortality of BC and PC and some major modifiable HRRFs as well as the distribution of the variables in 204 countries and territories.

Materials and Methods

Overview

The GBD 2021 study offers a comprehensive and scientific assessment of health outcomes due to 371 diseases, injuries, and 88 risk factors related to communicable and non-communicable diseases across 204 countries and territories from 1990 to 2021, leveraging the most recent available epidemiological data. The cancer data and trends presented in this cross-sectional study originated from the GBD 2021 study (https://vizhub.healthdata.org/gbd-results/).

The retrospective data for modifiable HRRFs were also derived from the most recent publicly available datasets of the World Health Organization (WHO) (https://www.who.int/data/gho/legacy?lang=en), United Nations Development Programme (UNDP) (https://hdr.undp.org/), and Non-Communicable Diseases Risk Factor Collaboration (NCD-RisC) (www.ncdrisc.org/). In this section, we mention the main information on the methodological steps for the key variables, while other detailed sources of the main variables will be linked to original studies by the GBD study or health risk factors (2). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cross-sectional studies.

Cancer data sources and definitions

The incidence, prevalence, and mortality rate of BC and PC were extracted from the GBD 2021 study from 1990 to 2019. We used data before 2019 to avoid the effects of COVID-19 pandemic on the burden of other diseases. All cancer data were extracted for groups over 15 yr of age and categorized by sex, age group (15-49, 50-74, and +75 yr), age-standardized rate, and socioeconomic and demographic category. The countries and territories were also categorized by sociodemographic index (SDI), human development index (HDI), World Bank income, and continent for the presentation of certain results. All cancer rates are defined per 100,000 people (with 95% uncertainty intervals (UIs)). The 30-year estimated annual rate change (EARC, %) in all rates, extracted for quantifying the association between dependent and independent variables, is available online in the GBD results tool (https://vizhub.healthdata.org/gbd-results/).

Lifestyle, sociodemographic, and modifiable HRRFs

There are several risk factors affecting cancer outcomes based on epidemiological studies (8). As for the major modifiable HRRFs values, we retrieved the prevalence of daily smoking (%), tobacco use (%), burden of diseases related to smoking (share of age-standardized deaths that are from neoplasms attributed to tobacco (SNDAT) and share of total deaths attributable to smoking (SADAS)), prevalence of IPA (%), mean BMI (kg/M2) and prevalence of obesity (BMI ≥30), overweight (BMI ≥25), and underweight (BMI ≤18.5) among adults over 18, and mean total cholesterol (mmole/L) and its subtypes (HDL and non-HDL cholesterol) from different sources (9, 10). In addition, the SDI and HDI are considered as two socioeconomic and demographic factors, considered as covariates in our study. Countries were divided into five SDI quintiles (High, High-Middle, Middle, lower-Middle, and Low). The previous GBD studies presented additional SDI details along with annual SDI scores attributable to each country and territory. The HDI is introduced to measure the development of countries in accordance with three key dimensions (ranging between 0 and 1): life expectancy at birth, education status, and income (11). We demonstrated the ASIR, ASPR, and ASMR of cancers for HDI categories, including Very High (HDI≥0.800), High (0.700≤HDI<0.800), Medium (0.556≤HDI<0.700), and Low (HDI<0.556). The variables are also evaluated based on the overall HDI cut-off for developed countries (HDI≥0.788) and developing countries (HDI<0.788). Additional explanations are provided in the supplementary file.

Statistical analysis

First, the mean rates (± 95% UI) of incidence, prevalence, and mortality of cancers were reported in tables and figures. All the data were categorized into different subgroups according to HDI, SDI, country, region, or state groups. Next, the temporal trends of the cancers were extracted, both globally and regionally, from 1990 to 2019. Furthermore, stratified analyses were performed to determine the significant differences in the means of the groups via univariate analysis. In addition, rates of change (ROC) were gathered to identify the associations between cancer outcomes and the mean values of different risk factors. Regarding the impact of chronic risk factors, such as BMI, cholesterol, or smoking, we also analysed data from 30 to 40 yr ago (1980 or 1990) to assess the correlation coefficient for cancers outcomes. Finally, multivariable regressions were performed to analyse different risk factors in combination with the cancer outcome ratios. In this section we check the multicollinearity and enter the main variables with the variance inflation factor (VIF) below 5. A 2-sided $P<0.05$ was considered to indicate statistical significance. The RStudio program (version 4.0.2) and GraphPad Prism (version 8.0.2) were used in statistical analyses.

$$\text{Rate of Change (ROC, \%)} = \frac{x_i - x_j}{x_i} \quad \text{Eq. 1}$$

which xi is the value for the base year and xj is the value for the last year.

Ethics approval

An ethics code (IR.KHOMEIN.REC.1402.030) was obtained from the Research Ethics Committees of Khomain University of Medical Sciences.

Results

Global incidence, prevalence and mortality of cancers

In 2019, 2,039,160 (95% UI, 1,922,148–2,149,815) and 1,269,619 (95% UI, 1,172,739–1,334,257) new cases of BC and PC reported globally, respectively, and the global age-standardized incidence rates (ASIR) per 100,000 were 26.33 (95% UI, 24.82–27.76) and 16.39 (95% CU: 15.14–17.23) (Table S1 in the supplementary file- Not published).

Fig. 1 illustrates the distribution of the age-standardized prevalence rate (ASPR) of BC and PC, and the HRRFs at the national level. Globally, the ASPR of BC was 218.44 (203–237.82) and 239.12 (225.59–250.82) per 100,000 people in 1990 and 2019, respectively.

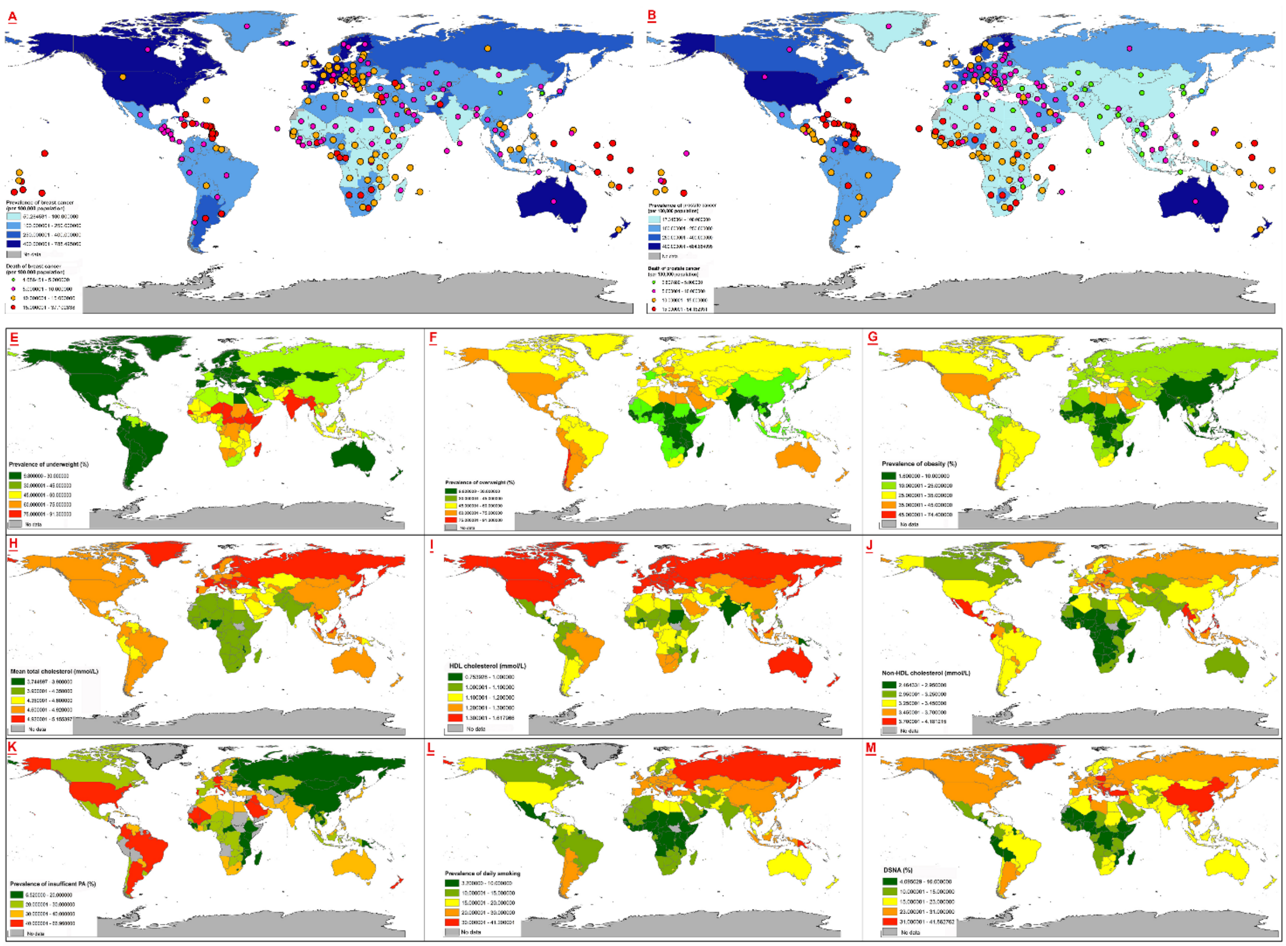

Fig. 1: National distribution of the ASPR and ASMR of four major cancers (A and B) and health-related risk factors (E-M)

Moreover, the ASPR of PC was 120.30 (113.11 – 125.65) in 2019. For more details, see Table S1-S3 in the supplementary file. The ASIR, ASPR, and ASMR of PC were greater among the population aged older than 75 yr than among the 15–49 and 50–74 age groups, and the lowest rates were observed among individuals aged 15 to 49 yr, with an increasing trend from 1990 to 2019 (Table S4-S6 in the supplementary file). Based on the age categories, the ASMRs for BC in the three age categories were 3.47 (95% CU: 3.79–3.17), 24.37 (95% CU: 26.26–22.69), and 66.02 (95% CU: 71.64–56.69) per 100,000, respectively. The scatter plots in Fig. S1 depicts also the mean values of cancer outcomes. Globally, the ASIR and ASPR of cancers gradually grew from 1990 to 2019, while the ASMR showed a downwards trend (Fig S2-4); However, the number of cancers increased between 1990 and 2019.

National and regional incidence, prevalence and mortality

In 2019, the highest ASIRs per 100,000 of BC (86.79, 65.37–115.55) and PC (84.68, 68.94–105.87) were reported in Monaco, whereas the lowest figures were indicated in Niger (6.76, 4.79–9.5) and Tajikistan (2.38, 1.52 – 3.61). In addition, Monaco (889.47, 708.99 – 1130.91) and Bermuda (669.92, 544.24 – 837.63) had the highest prevalence of BC and PC, respectively. Other figures are demonstrated in Table S1-3 the supplementary file. Approximately 67% and 65% of all countries and territories showed an upwards trend of ASMR for BC and PC, respectively, from 1990 to 2019 (Table S7-9 the supplementary file). Nationally, the highest EARC of ASIR (3.90, 2.51 – 5.73) and ASMR (1.30, 0.68 – 2.09) for BC was shown in Turkey. The highest EARC of the ASPR in PC was also seen in South Korea (5.14, 2.19 – 7.98).

By continent, America had the highest BC and PC incidence/prevalence in 1990, overtaken by Europe in 2019. Temporal EAPC trends (Fig. 2) showed the sharpest increases in BC ASIR in North Africa and the Middle East (1.90; 1.52–2.33), and in PC ASIR in Eastern Europe (1.88; 1.57–2.17). Additional data are in Table S10. The mean rate of change for independent variables for many regions was reported in Fig 3.

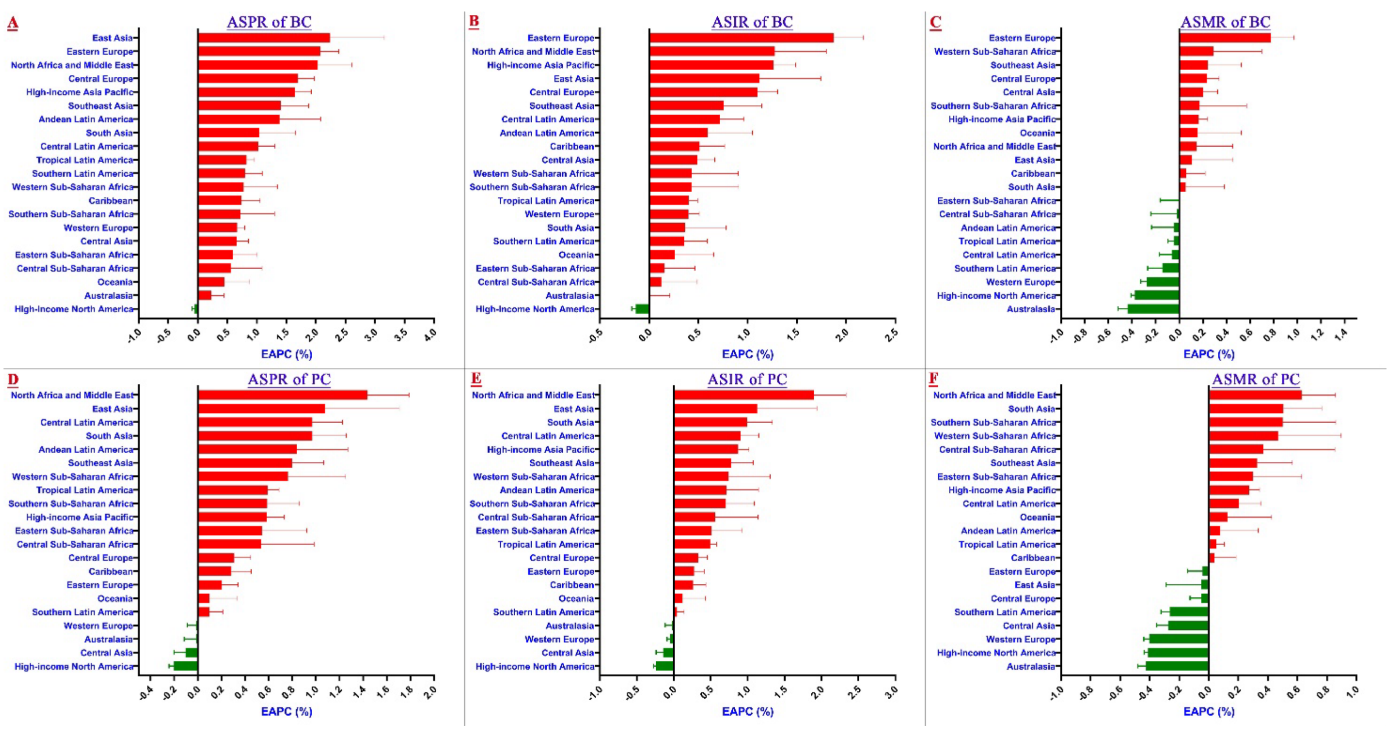

Fig. 2: Estimated annual percentage of change (EAPC) in prevalence, incidence, and mortality of breast and prostate cancers from 1990 to 2019

In 2019, Western Europe (16.64; 15.66–17.2) and the Caribbean (16.12; 14.83–18.08) had the highest ASMRs for BC and PC, respectively. High-income North America had the highest BC ASIR and ASPR in both 1990 and 2019, while Australia led in PC ASIR and ASPR in 2019 (Table S10, the supplementary file).

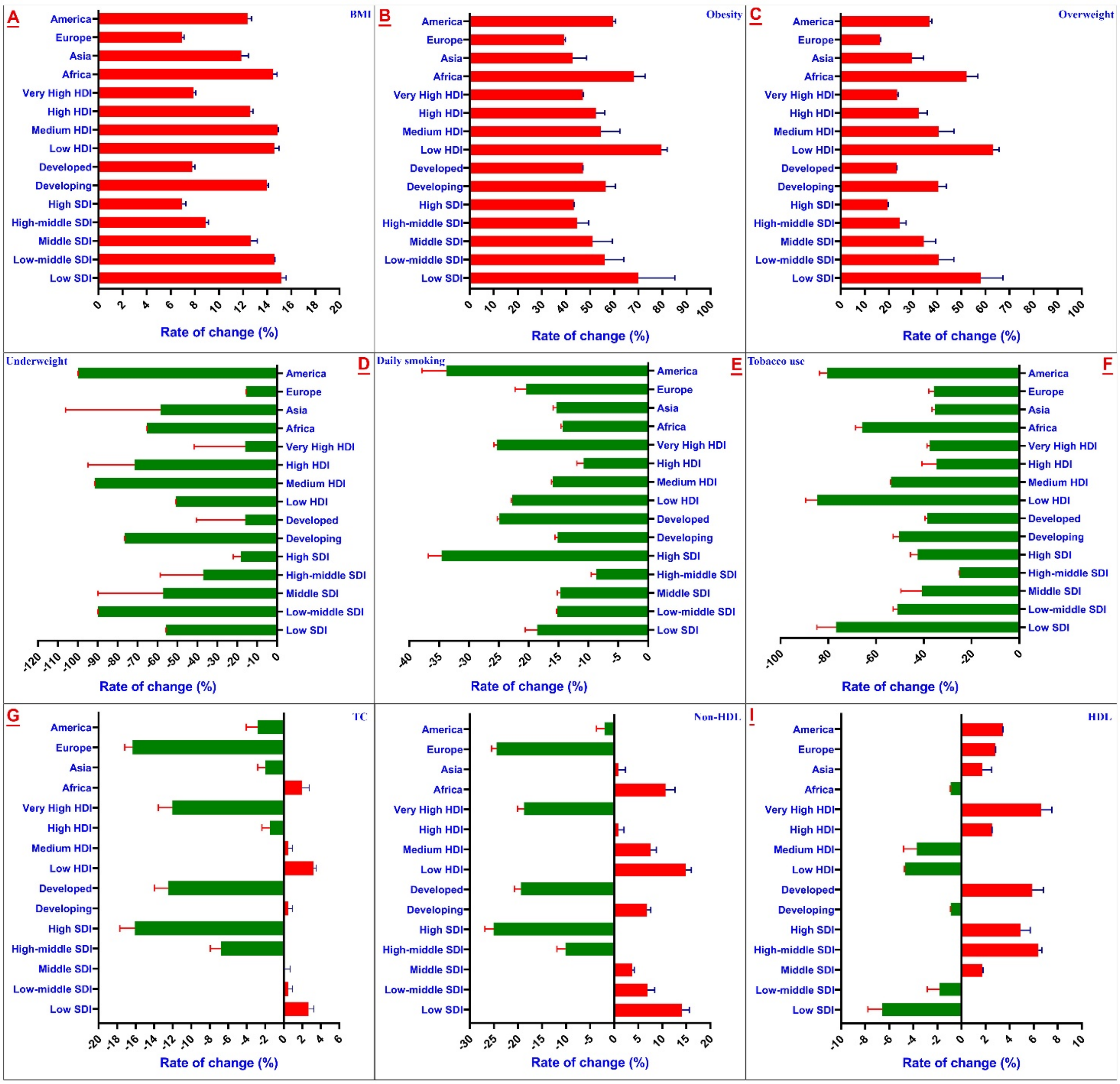

Fig. 3: Estimated annual rate of change (EARC) in health-related risk factor trends by SDI, HDI, Continent, and development level (A-I) for three decades

By SDI level, in 1990, High-SDI countries had the highest BC (13.44; 12.69–13.87) and PC (9.14; 8.61–9.43) ASMRs. In 2019, BC ASMR remained highest in High-SDI (8.69; 7.93–9.12), while PC ASMR peaked in Low-SDI countries (7.99; 5.23–9.89). High-SDI regions consistently showed the highest ASIR and ASPR for both cancers in 1990 and 2019. Commonwealth Income and World Bank classifications are detailed in Table S11, the supplementary file.

Correlation between modifiable HRRFs and cancers

The ASIR and ASPR of BC and PC were positively associated with HDI, BMI, obesity, overweight, underweight, IPA, and smoking-related factors (Fig. 4).

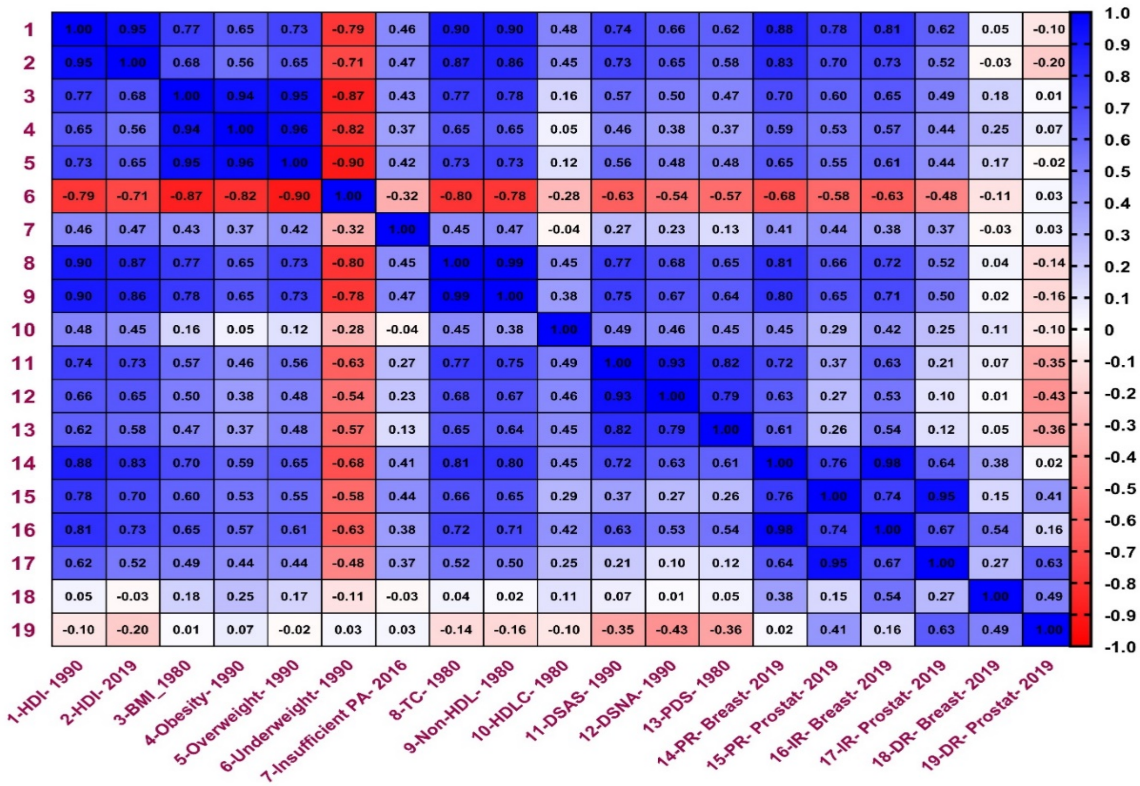

Fig. 4: Correlation between modifiable risk factors and different cancer outcomes

In 1990, BC and PC ASIR and ASPR increased with HDI (BC: r = +0.88, +0.81; PC: r = +0.78, +0.62; all *P*<0.001). ASIR and ASPR of BC also correlated with BMI (r = +0.70, +0.65; *P*<0.001), and negatively with underweight (r = –0.68, –0.63; *P* < 0.001). Correlations were generally stronger with older data (1980–1990). BC and PC ASPR showed strong positive correlations with non-HDL (r = +0.80, +0.65; *P*<0.001), but weaker with HDL (r=+0.45, +0.29; *P*<0.05). Notably, smoking-related factors negatively correlated with PC ASMR (r = –0.36; *P*<0.001). IPA was positively associated with PC (r=0.44, *P*<0.001) and BC (r=0.41, *P*<0.01) ASPR. Stronger associations were observed in high-middle and high-SDI countries. Regression results are shown in Fig. S5–S6, the supplementary file.

Linear regression displayed HDI, smoking, and HDL as predictors of ASIR and ASPR of BC (β > 0.50). Multivariable analysis in 2019 showed increased BC ASPR with HDI (β = 36.77, *P*<0.01), BMI (β = 0.71, *P*<0.05), and smoking (SADAS) (β =0.63, *P*<0.01). With all six key factors (Table 1), SADAS negatively predicted PC ASIR, ASPR, and ASMR (β =–0.71, –8.15, –1.35; *P*<0.001). Other analyses were shown in Table S12-14, the supplementary file.

Table 1: Multivariable adjusted analysis of the association between risk factors with the different outcomes of cancers using Backward Elimination regression

Variables	B (95% CI)	Beta	t	Sig.	VIF
ASPR of Breast Cancer					
HDI	440.08 (283.16–597.01)	0.46	5.54	<0.001	2.76
SADAS	6.43 (2.99–9.88)	0.24	3.69	<0.001	1.66
Mean HDL cholesterol	164.34 (40.18–288.49)	0.20	2.62	0.010	2.24
ASPR of Prostate Cancer					
HDI	684.19 (527.67–840.7)	0.73	8.64	<0.001	1.83
Mean BMI (kg/m²)	7.34 (-0.81–15.5)	0.12	1.78	0.077	1.24
SADAS	-8.15 (-12.38–-3.93)	-0.31	-3.81	<0.001	1.67
ASIR of Breast Cancer					
HDI	36.77 (23.17–50.36)	0.43	5.34	<0.001	1.83
Mean BMI (kg/m²)	0.71 (0–1.42)	0.13	1.98	0.05	1.24
SADAS	0.63 (0.24–0.97)	0.25	3.25	0.001	1.67
ASIR of Prostate Cancer					
HDI (2019)	70.73 (49.06–92.4)	0.59	6.45	<0.001	1.83
Mean BMI (kg/m²)	1.47 (0.35–2.6)	0.20	2.58	0.011	1.24
SADAS	-1.35 (-1.94–-0.77)	-0.40	-4.57	<0.001	1.67

ASPR: Age-standardized Prevalence rate, HDI: Human Development Index, BMI: body mass index, PA: physical activity, SADAS: share of all deaths attributable to smoking, HDL: high-density lipoprotein, RFM: remove from model using Backward Elimination regression

Discussion

This global, regional, and country-level time-trend analysis (GBD 2021) outlines 1990–2019 data and the ASPR, ASIR, and ASMR for breast (BC) and prostate cancer (PC) to national data on key modifiable HRRFs, offering actionable evidence for a major global health challenge. Between 1990 and 2019, ASMRs for BC and PC decreased worldwide despite a gradual rise in ASPR, especially for BC, with likely drivers including better health systems, new effective therapies, and wider preventive programs (12, 13); outcomes were highest in those aged ≥75 compared with ages 15–49 and 50–74, and while population ageing adds to the burden, HRRFs also make a substantial contribution.

Across the socioeconomic and demographic spectrum, higher-SDI/HDI regions had greater cancer burdens; for example, high-income North America shows substantial ASIRs and ASPRs for BC, and Australia displays similar patterns for PC in 2019, with regional variation partly associated to diet, metabolic factors, climate, air pollution, specific infections, and the uptake of advanced medical technologies (14, 15). However, disparities in cancer outcomes narrowed between low- and high-SDI regions by 2019, likely due to improvements in sociodemographic development, stronger health policies, and major cancer-control initiatives, such as National Cancer Control Plans, Universal Health Coverage, and the SDGs, that expanded early detection, treatment, and palliative care, bringing opportunities in many developing countries, including African nations, and possibly contributing to rising incidence and prevalence, which may help explain the upward changes in the EARC of prostate cancer (16-18).

Over the past three decades, BMI and obesity have risen significantly worldwide, especially in middle and high-middle SDI regions where higher ASIRs and ASPRs were observed, and the average rate of change shows sharp increases from 1980 to 2018, consistent with prior publications (10, 19, 20). These trends align with positive correlations between BMI/obesity and all cancer outcomes (Fig. 4); obesity and high BMI seem to be key modifiable risk factors for non-communicable diseases (20), and regions with higher BMI/obesity often show greater cancer prevalence, potentially influenced by co-exposures such as tobacco use (21, 22).

From 1990 to 2019, many impoverished countries experienced sharp declines in daily smoking and tobacco use, possible helping to reduce cancer ASIRs, although dropping mortality might also reflect poorer survival linked to smoking (23); moreover, during 1980–2019, low-SDI countries still had the highest smoking prevalence (approximately 80%), about twice that of high-SDI countries (Fig. 3). Consistent with reports showing an inverse link between physical activity and several cancers, outcomes (24, 25), our study found a positive univariate, but not multivariate, association between insufficient physical activity (IPA) and all cancer outcomes, while rising IPA and BMI remain serious issues and cholesterol levels seem to move from increasing (low-SDI) to stabilizing (middle-SDI) to decreasing (low-SDI).

Generally, total cholesterol showed an upward trend in low- and lower-middle-SDI/HDI countries but a downward trend in high-SDI settings, aligning with previous studies; meta-analyses report a negative association between TC and breast-cancer risk (26) yet a positive link between TC and dietary cholesterol intake among BC patients (27), and our sub analysis indicated divergent patterns for HDL and non-HDL, with mean ROC for non-HDL rising in low- to middle-SDI countries and falling in high-middle and high-SDI countries. These disparities may reflect higher overweight prevalence in lower-SDI groups, about three times that of high-SDI (Fig. 3), together with shifts toward high-fat, calorie-dense diets and expanding fast-food consumption (28, 29), where the highest prevalence is reported in Southeast Asia (17.7%) and the lowest in the Americas (8.3%) (30); notably, elevated non-HDL levels have been linked to breast cancer and prostate cancer.

Strengths and Limitations

Despite the valuable estimates of cancer outcomes provided by the GBD 2021 study, several main limitations should be mentioned. First, limited spatiotemporal data are available to estimate countries' ASRs for cancers, highlighting the importance of improving registration data related to cancers, especially in low- and middle-income countries. Second, national differences in cancer outcomes may be potentially biased due to variations in follow-up standards and data quality (2). Additionally, some limitations related to secondary data, including BMI, TC, and smoking-related data, were reported in previous studies (31, 32). It is essential for readers to understand the differences between correlation, association, and causation.

Conclusion

This country-level study shows clear disparities in ASIR, ASPR, and ASMR for BC and PC across men and women and across socioeconomic and demographic groups. From 1980 to 2019, obesity, insufficient physical activity, and mean BMI increased steadily, while tobacco use declined; non-HDL cholesterol also increased in low to middle SDI settings, underscoring lifestyle drivers such as diet and sedentary behaviour. Cancer control should reflect regional inequalities by developing preventive screening, strengthening health systems, improving access to new therapies, and managing modifiable high-risk related factors.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Availability of data and materials

All the data generated or analysed during this study are included in this published article except the supplematry material. Respected readers may contact the correspnding authors to apply for necessary data. The aggregated data analysed in this study are available from the WHO, United Nations Development Programme (UNDP), Global Burden of Disease (GBD), and Non-Communicable Diseases Risk Factor Collaboration databases. The data related to cancer variables are available on the https://vizhub.healthdata.org/gbd-results/ website.

Conflict of interests

The authors declare that they have no competing interests.

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