Breast Cancer: Targets and Therapy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Ranking of Modifiable Lifestyle Risk Factors for Breast Cancer in Saudi Women: Population Attributable Risk and Nomogram

Rawabi M Alsayer[1], Edward B De Vol[2], Amani Almeharish[2], Areej Alfattani[2], Alaa J Alghamdi[1], Luluh Behlal AlBehlal[3], Shatha Alhaddab[4], Yasmin Altwaijri[2]

[1]Population, Public and Environmental Health, Ministry of Defense Health Services (MODHS), Riyadh, Saudi Arabia; [2]Department of Biostatistics, Epidemiology and Scientific Computing, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; [3]Scientific Research Center, Prince Sultan Military Medical City, Riyadh, Saudi Arabia; [4]Saudi Bio-Bank, King Abdullah International Medical Research Center, Riyadh, Saudi Arabia

Correspondence: Yasmin Altwaijri, Biostatistics, Epidemiology and Scientific Computing Department, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, MBC 03, Riyadh, 11211, Saudi Arabia, Email YasminT@Kfshrc.edu.sa

Purpose: Breast cancer is the most common cancer among women in the Saudi Arabia, and over 50% of the cases are detected at a late stage. This study aimed to estimate population attributable risk percentage (PAR%) of modifiable lifestyle risk factors for breast cancer in Saudi Arabia.

Patients and Methods: A secondary analysis of previously published papers was performed . Relative risks (RR) and odds ratios (OR) were obtained from published international epidemiological studies, and the prevalence of each risk factor in Saudi Arabia was obtained from various sources (eg, national surveys and published literature) to calculate PAR%. A nomogram was used to visually translate the RRs/ORs and their prevalence into PAR% using a practical tool.

Results: Seven modifiable lifestyle risk factors for breast cancer were identified in Saudi Arabia. The identified risk factors included lack of physical activity (sedentary lifestyle), oral contraception (current use), obesity (postmenopausal), hormone replacement therapy (current use), passive smoking, age at first birth (≥ 35 years), and tobacco smoking (current or daily smoking). The PAR% for these risk factors ranged from 0.5% for tobacco smoking to 23.1% for a lack of physical activity. Few modifiable lifestyle risk factors were excluded from this study, due to limited nor unavailable data in Saudi Arabia (eg, alcohol consumption, breastfeeding patterns and childbearing patterns, obesity according to menopausal status, and night-shift work).

Conclusion: Physical inactivity has the most significant modifiable health impact and is a major risk factor for breast cancer. Removing this risk factor would reduce the prevalence of breast cancer in the Saudi population by 23%. There is an immense need to prioritize cancer control strategies based on local needs, current data on cancer risk factors, and the disease burden.

Keywords: breast cancer, population attributable risk, lifestyle risk factors, nomogram, Saudi Arabia

Introduction

Breast cancer is the most common type of cancer among women worldwide,[1] constituting approximately one-quarter of all cancers. Every year, approximately 43 cases are diagnosed per 100,000 people worldwide. With a mortality rate of 12.9 per 100,000 individuals, Breast cancer is one of the leading causes of death in females globally.[2] The implications of breast cancer affect both individuals and societies in various ways, physically, psychologically, and economically. It is estimated that almost one-third (30.7%) of females with breast cancer experience depression in their lifetime.[3] In 2009, the global economic burden of breast cancer was 15 billion Euros, accounting for 12% of the total global burden of all types of cancer.[4]

In Saudi Arabia, breast cancer ranks first among all types of cancers in women, regardless of age. Breast cancer accounts for 30.1% of all cancers[5] and is responsible for 2.92% of all mortalities.[6]

Previous studies have investigated risk factors for breast cancer. Some of these risk factors are modifiable, while others are not. Non-modifiable risk factors included age, sex, age at menarche < 11 years, age at menopause > 54 years,

Received: 6 February 2024
Accepted: 13 August 2024
Published: 2 September 2024

environmental factors, family history, and race. Modifiable risk factors include obesity, smoking, oral contraceptive use, maternal age at first birth > 35 years, lack of physical activity, and little or no breastfeeding.[7] These lifestyle risk factors can be modified to alleviate the burden of breast cancer in Saudi women and society.

PAR% is an epidemiological measure widely used to assess the public health impact of exposure in populations. It is defined as the number of cases in a population that are attributable to a specific exposure and would therefore not have occurred in the population if the exposure (risk factor) was eliminated. Consequently, this result is known as the preventable fraction.[8,9] A similar approach has been used in other countries like New Zealand,[10] United States,[11] and Europe.[12]

The primary aim of this study was to determine the impact of modifiable lifestyle risk factors on breast cancer in Saudi Arabia by calculating the PAR% of every well-established risk factor (exposure). Additionally, a nomogram was developed to predict modifiable breast cancer risk factors that were ranked based on their impact on breast cancer among Saudi women. A nomogram is a graphical statistical instrument that measures variables to calculate the precise risk probability for a specific outcome. This instrument is vital for decision making in modern medicine.[13]

This study will assist in identifying modifiable lifestyle risk factors with the highest effect on breast cancer among Saudi women, which can be factored into the design of public health measures to combat these factors and minimize the burden of breast cancer.

Material and Methods

Modifiable Lifestyle Risk Factors (Sources of Data)

The electronic databases (MEDLINE and EMBASE) were searched using keywords related to modifiable lifestyle risk factors of breast cancer (eg "lack of physical activity", "oral contraception", "obesity", "hormone replacement therapy", "tobacco", "age at first birth ≥ 35", etc). The main search strategy include the following Keyword ("Lack of physical activity" OR "sedentary" AND "Breast cancer"), ("Obesity" AND "postmenopausal" AND "Breast cancer"), ("Oral contracept*" AND "current use" AND "Breast cancer"), ("Hormone replacement therapy" AND "current use" AND "Breast cancer"), ("Passive Smok*" AND "Breast cancer"), ("Tobacco Smoke*" AND "Breast cancer"), ("Age at first birth ≥35" AND "Breast cancer"). A few modifiable lifestyle risk factors were excluded from this study, due to limited nor unavailable data in Saudi Arabia (eg, alcohol consumption, breastfeeding patterns and childbearing patterns, obesity according to menopausal status, and night-shift work)

Prevalence in Saudi Arabia

The most recent information on the prevalence of each risk factor in Saudi women was obtained from numerous sources (conducted between 2013 and 2019), such as population-based surveys: the Ministry of Health (MOH) Saudi Health Interview Survey (SHIS)[14] the General Authority for Statistics (GaStat) Household Sport Practice Survey,[15] and specific studies undertaken in Saudi Arabia investigating the prevalence of breast cancer risk factors (reproductive risk factors in particular).[16]

Risk Parameter

This project was not intended to provide a comprehensive literature review. While it was a secondary data analysis to identify robust estimates of RRs/ORs with 95% CI, thus calculating the PAR%. Relative risks (RR) and odds ratios (OR) were obtained from a total of seven international epidemiological studies conducted between 2003 and 2015. RRs and ORs that had been adjusted for confounding factors were assigned a priority. RRs were reported in well-designed cohort studies and meta-analyses of observational studies, and ORs were reported in case-control studies. The Newcastle-Ottawa Scale (NOS) for cohort and case-control studies assessment tool were used to validated the included studies quality.[17]

PAR% Calculation

The prevalence of risk factors in Saudi Arabia and estimates of relative risks from the literature were used to calculate PAR%[18,19]

$$\mathbf{PAR}\% = \frac{\mathrm{Pe}(\mathrm{RR}-1)}{\mathrm{Pe}(\mathrm{RR}-1)+1} \times 100$$

Where

Pe = the prevalence of exposure to the risk factor among women in Saudi Arabia

RR = the relative risk for exposed, compared with the risk for unexposed

When the relative risk was unavailable, the odds ratio replaced the relative risk in the PAR% equation. The PAR% equation is a point estimate. The confidence interval for PAR% was estimated using a simulation method (based on bootstrapping). Specifically, the reported 95% confidence interval for the risk parameters (relative risk or odds ratio) was used to calculate the standard deviation of each risk parameter. The population of the RRs (or ORs) was assumed to have a normal distribution with an expectation equaling the point estimate and a standard deviation determined from the 95% confidence interval. PAR% values were then simulated 1000 times, and the 2.5th and 97.5th percentiles of the resulting distribution were taken as the 95% confidence intervals for PAR%.

Sensitivity Analyses

The parameter values and assumptions of any model are subject to change and error. Sensitivity analyses were conducted to provide bounds on the possible ranges of PAR%, and these were based on minima and maxima for the constituent parameters (ie, Pe, RR, OR, etc) that were included in the formula for PAR%.

Attributable Fraction Nomograms

The nomogram model is used to graphically illustrate PAR%, facilitate visual assessment of relative risk factor burden according to prevalence, and present odds ratio estimates. The estimate of the log odds ratio/relative risk is applied to the rule of Bayes (that is, prior odds x Likelihood = posterior odds), a dependence that has been exploited in the nomograms suggested by Fagan [R].[13] This analogy was used to display the relationships between approximate PAF, prevalence, and the estimated log-OR. Upon taking logs of both sides of the equation, it was determined that log-OR is proportional to the average of the log prevalence and the log approximate PAF. This observation facilitated the creation of a log-scale plot where prevalence, odds ratios, and approximate PAFs for each risk factor are connected with lines.

All analyses were conducted using the R Studio software (version 1.4; R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel (2016).

Modifiable Lifestyle Risk Factors

Lack of Physical Activity (Sedentary Lifestyle)

Insufficient physical activity is one of the ten leading risk factors for mortality worldwide. Lack of physical activity was associated with an increased risk of breast cancer (RR: 1.34; 95% CI 1.25–1.43). The risk of developing breast cancer is increased by 30% in sedentary women compared to that in active women.[20] In 2019, GaStat reported that only 11.62% of Saudi females (aged 15 years or above) practiced sports for 150 minutes or more per week, revealing that 88.38% of Saudi females do not engage in sufficient levels of physical activity.[15]

Oral Contraception (Current Use)

The risk of breast cancer is higher among current users of oral contraceptive pills (OCP). According to a large prospective cohort study of 116,608 premenopausal women conducted by nurses, current use of any OCP is associated with an increased breast cancer risk. This association is most evident among current users, with an RR of 1.33 (1.03–1.73).[21] The risk of developing breast cancer is 30% higher among women who have used OCP than women who have never used OCP.[22] In Saudi Arabia, it has been reported that the use of OCP is the most common risk factor for breast cancer among primary health care (PHC) attendees, with a prevalence of 51.2%.[16]

Obesity (Postmenopausal)

Obesity is a global public health problem that plays a significant role in the development of various health disorders including breast cancer. The association between the body mass index (BMI), which reflects general obesity, and the risk of developing breast cancer varies between premenopausal and postmenopausal women. Most studies have found either no relationship or a weak inverse relationship between BMI and breast cancer risk in premenopausal women. In postmenopausal women, the risk of developing breast cancer is almost 30% higher for women with a BMI over 30 kg/m2 (RR: 1.29; 95% CI 1.22–1.36) than for women with a BMI of 22.5–24.9 kg/m2.[10,23] In contrast to BMI, waist-hip ratio (WHR) as a central obesity indicator is associated with an increased risk of breast cancer in both pre- and postmenopausal women.[24] The prevalence of obesity (BMI ≥ 30 kg/m2) in Saudi Arabia ranges from 13.6% in young adults to 48.0% in adults, with 33.5% of Saudi women having a BMI above 30 kg/m2.[14]

Hormone Replacement Therapy (Current Use)

The current use of hormone replacement therapy (HRT) is also associated with an increased risk of breast cancer. Compared with non-users of HRT, current users of HRT have a 66% increased risk of developing breast cancer with an adjusted of RR 1.66 (1.58–1.75).[25] In Saudi Arabia, reports of HRT use vary. In 2004, 42% of women underwent HRT at some point after menopause.[26] In contrast, the use of HRT was reported to be only 8% among PHC attendees in the Eastern province of Saudi Arabia in 2015.[16]

Age at First Birth (≥ 35 years)

In women aged ≥ 40 years, the risk of breast cancer was higher for those who had their first birth at age ≥ 30 with an adjusted RR of 1.15 (1.02–1.29).[27] It increased the chance of developing breast cancer by 40% compared to those who had their first birth before the age of 20 years, with an RR 1.4 (1.2–1.7).[28] Globally, it has been reported that the prevalence of women aged > 35 years at first birth was 13.5%, although it was only 9.3% among Saudi women in 2006.[29] This statistic appears to be declining, with a 2015 study finding a prevalence of 4.8% among Saudi women.[16]

Tobacco Smoking (current or daily smoking)

Active smoking for at least 20 years and smoking ten or more cigarettes per day increases the risk of developing breast cancer, with an RR of 1.34 (1.06–1.70) compared with never smokers.[30] The Saudi national survey reported that the prevalence of smoking among women was lower (1.5%) than that among men (22.7%).[14] In Saudi society (as in several other societies), gender plays an essential role in the low smoking rate among females. Tobacco smoking is considered to be a social stigma among Saudi females. Therefore, the reported figures from the KSA are very low. Due to this low prevalence, it is difficult to assess the true burden of smoking among Saudi females.

Passive Smoking

Passive smoking was also associated with a heightened risk of breast cancer, with an adjusted OR of 1.35 (1.11–1.65). A strong association with breast cancer risk was primarily observed in postmenopausal women.[31] The Saudi national survey reported that 13.5% (95% CI:12.1–15.0) of women were exposed to passive smoking for at least one day during the past seven days at home, work, or school.[14]

Breastfeeding

Extended breastfeeding has been associated with a reduced risk of breast cancer. Evidence shows that breastfeeding is protective regardless of age at diagnosis.[27] The longer the duration of breastfeeding, the higher the protection against breast cancer; the relative risk of breast cancer is reduced by an estimated 4.3% for each year that a woman breastfeeds.[32] Breastfeeding is influenced by various components (eg, patterns of childbearing and breastfeeding duration) and is limited in being realistically modifiable. In addition, the data were either limited or inconsistent; this risk was not considered in this study.

Parity

A woman's parity is defined as the total number of children she has birthed, including live births and stillbirths. Increased parity is a protective factor against breast cancer; nulliparous women have a higher risk of breast cancer than parous women do.[33] The relative risk of breast cancer was reduced by 7.0% (95% CI 5.0–9.0; p<0.0001) for each birth.[32] Several circumstances determine the decision to have children (eg, socio-economic factors) and are unlikely to include the desire to reduce the risk of breast cancer. Therefore, parity risk was excluded as a modifiable risk factor in this study.

Diet

Based on previous research findings, the association between diet and breast cancer has been inconsistent. It evinced possible dietary determinants of risk, such as the consumption of meat, fiber, fruit and vegetables, phytoestrogens, and dairy products. However, studies on the role of specific dietary factors in breast cancer causality are limited.[34–37] Hence, diet was not considered a risk factor in this study.

Alcohol

The International Agency for Research on Cancer (IARC) classifies alcoholic beverages as carcinogenic to humans.[38] Alcohol intake is associated with an increased risk of breast cancer. With an intake of 35–44 g (3–5 drinks) per day, the risk increased by 1.3% (1.2–1.5). There was a 7.1% increase in the risk of breast cancer for each additional 10 g intake per day.[39] The World Health Organization (WHO) reported that Saudi Arabia is one of the nine countries where alcohol consumption is completely prohibited by law.[40] Therefore, alcohol consumption was not considered a risk factor in this study.

Occupation (Night-Shift Work)

Long-term night-shift work in diverse occupations is associated with an increased risk of breast cancer.[41] There is evidence about the characteristics of night-shift work that are associated with the occurrence of breast cancer in France between 2005 and 2008, showing that women who worked the night-shift for 4.5 or more years (and fewer than three nights per week on average) were at increased odds (OR 1.40 [1.01–1.92]).[42] Currently, studies investigating this risk factor in Saudi Arabia are not available; thus, this risk was not considered further in this study.

Results

Lack of Physical Activity (Sedentary Lifestyle)

The results of this study indicate that among the studied modifiable risk factors, lack of physical activity is the highest risk factor for developing breast cancer in Saudi Arabia. According to PAR%, 23.1% (95% CI 18.0–27.0) of breast cancer cases could have been prevented if Saudi women were physically active (Table 1).

Oral Contraception (Current Use)

OCP was ranked as the second-highest risk factor for developing breast cancer among all measured risks. In Saudi Arabia, 14.5% (95% CI 0.0–27.0) of breast cancer cases may be attributed to the current use of OCP (Table 1).

Obesity (Postmenopausal)

The PAR% calculation found obesity to be the third highest risk factor for developing breast cancer among postmenopausal women. This suggests that in Saudi Arabia, 8.9% (95% CI 7.0–11.0) of breast cancer cases could be prevented if women had a BMI of less than 30 (Table 1).

Hormone Replacement Therapy (Current Use)

HRT was the fourth-highest risk factor for developing breast cancer, as calculated by PAR%. Therefore, in Saudi Arabia, 5.2% (95% CI 4.0–6.0) of breast cancer cases could be prevented if women were not using HRT (Table 1).

Table 1 Breast Cancer Risk Factors, Prevalence, and PAR% for Saudi Women

Risk Factor	Relative Risk (RR) (95% CI)	Odd Ratio (OR) (95% CI)	Prevalence of Risk Factor in Saudi Arabia (95% CI)	PAR% (95% CI)	Comments
Lack of physical activity (sedentary)	1.34 (1.25–1.43)[20]		88.3% (88.3–88.3)a	23.1% (18.0–27.0)	Sedentary/low physical activity is <150 minutes of physical activity in the last 7 days
Oral contraception (current use)	1.33 (1.03–1.73)[21]		51.2% (47.2–55.1)b	14.5% (0.0–27.0)	Current use of any oral contraception
Obesity (postmenopausal)	1.29 (1.22–1.36)[10,23]		33.5% (32.6–34.3)c	8.9% (7.0–11.0)	BMI ≥30 kg/m2
Hormone replacement therapy (current use)	1.66 (1.58–1.75)[25]		8.0% (5.0–10.0)b	5.2% (4.0–6.0)	Adjusted RR
Passive smoking		1.35 (1.11–1.65)[31]	13.5% (12.8–14.1)c	4.5% (1.0–8.0)	Women who were exposed to passive smoke for at least one day during the past 7 days at home, work, or school
Age at first birth ≥ 35	1.15 (1.02–1.29)[27]		4.8% (3.0–6.5)b	0.7% (0.0–1.0)	Age adjusted RR
Tobacco smoking (current, daily smoking)	1.34 (1.06–1.70)[30]		1.5% (1.2–1.7)c	0.5% (0.0–1.0)	RR for women who smoked for at least 20 years and who smoked 10 cigarettes or more daily

Notes: a 95% CI, estimate based on a sample of over 26,000 individuals. b 95% CI: estimated based on a sample of 600 individuals. c 95% CI: estimate based on a sample of over 10,000 individuals.
Abbreviations: CI, confidence interval; PAR%, population attributable risk fraction; BMI, Body mass index; RR, Relative risks; OR, odds ratios; kg/m2, kilogram per square meter.

Passive Smoking

Passive smoking was ranked as the fifth highest risk factor for developing breast cancer in Saudi Arabia, with a PAR of 4.5%. This suggests that, in Saudi Arabia, 4.5% (95% CI 1.0–8.0) of breast cancer cases could be prevented if women avoid exposure to passive smoking (Table 1).

Age at First Birth (≥ 35 years)

Being an age equal to or more than 35 years at the first birth was calculated to be the sixth-highest risk factor (among all calculated risk factors) for developing breast cancer in Saudi Arabia, with a PAR% of 0.7% (95% CI 0.0–1.0). This suggests that in Saudi Arabia, 0.7% of breast cancer cases could be prevented if women have their first birth before the age of 35 years (Table 1).

Tobacco Smoking (current or daily smoking)

Tobacco smoking ranked seventh and last of all the studied risk factors for developing breast cancer in Saudi Arabia, with a PAR of 0.5%. This suggests that, in Saudi Arabia, 0.5% (95% CI 0.0–1.0) of breast cancer cases could be prevented if women avoid smoking. The results of this study showed that passive smoking has more detrimental effects on Saudi women than active smoking (Table 1).

Discussion

In this study, seven modifiable lifestyle risk factors for breast cancer were identified: lack of physical activity (sedentary lifestyle), OCP (current use), obesity (post-menopausal), HRT (current use), passive smoking, age at first birth ≥ 35, and tobacco smoking. (Figure 1).

The PAR% for these risk factors ranged ascendingly from 0.5% for tobacco, 0.7% for age at first birth ≥35 years, 4.5% for passive smoking, 5.2% for current use of HRT, 8.9% for postmenopausal obesity, 14.5% for current use of OCP, and 23.1% for lack of physical activity (Table 1).

The clustering of risk factors (factors with similar prevalence, OR/RR, and esti-mated PAR%) is represented by the effective equality of the corresponding lines. When the two risk factors had similar PAR% but differed in prevalence and relative risks, the corresponding lines had distinctly different slopes. However, they nearly intersect at the same approximate PAR% vertical HRT and passive smoking (Figure 2).

These results corroborate that lack of physical activity (sedentary lifestyle) and current use of OCP are modifiable lifestyle risk factors among Saudi women, leading to a higher incidence of breast cancer. Moreover, the PAR% of obesity among postmenopausal women is alarmingly high. Similar PAR% values for breast cancer have been reported in New Zealand,[10] the United States[11] and Italy.[43] Lifestyle changes, such as a reduction in the prevalence of physical inactivity, obesity, and use of OCP, have the potential to reduce the incidence of breast cancer among the respective populations.

The Continuous Update Project (CUP), the world's largest ongoing source of scientific research, provides insights into cancer prevention and survivorship by investigating certain lifestyle factors (eg, diet, weight, and level of physical activity) that can affect the risk of developing breast cancer.[34] The Evidence reveals that a total vigorous physical activity is likely protective against postmenopausal breast cancer. However, the type and amount of exercise required to provide this protective factor is poorly defined.[20,34]

The GaStat, Bulletin of Household Sport Practice Survey (2019) reports that in Saudi Arabia,[15] 20.2% of Saudis aged 15 years and above exercise for a minimum of 150 minutes per week. Only (11.6%) of Saudi females who exercised. Saudi women aged 25–29 years reported the highest engagement in exercise (14.1%), followed by women aged 20–24 years (13.8%). However, Saudi women aged ≥ 65 years had the lowest percentage (2.9%).

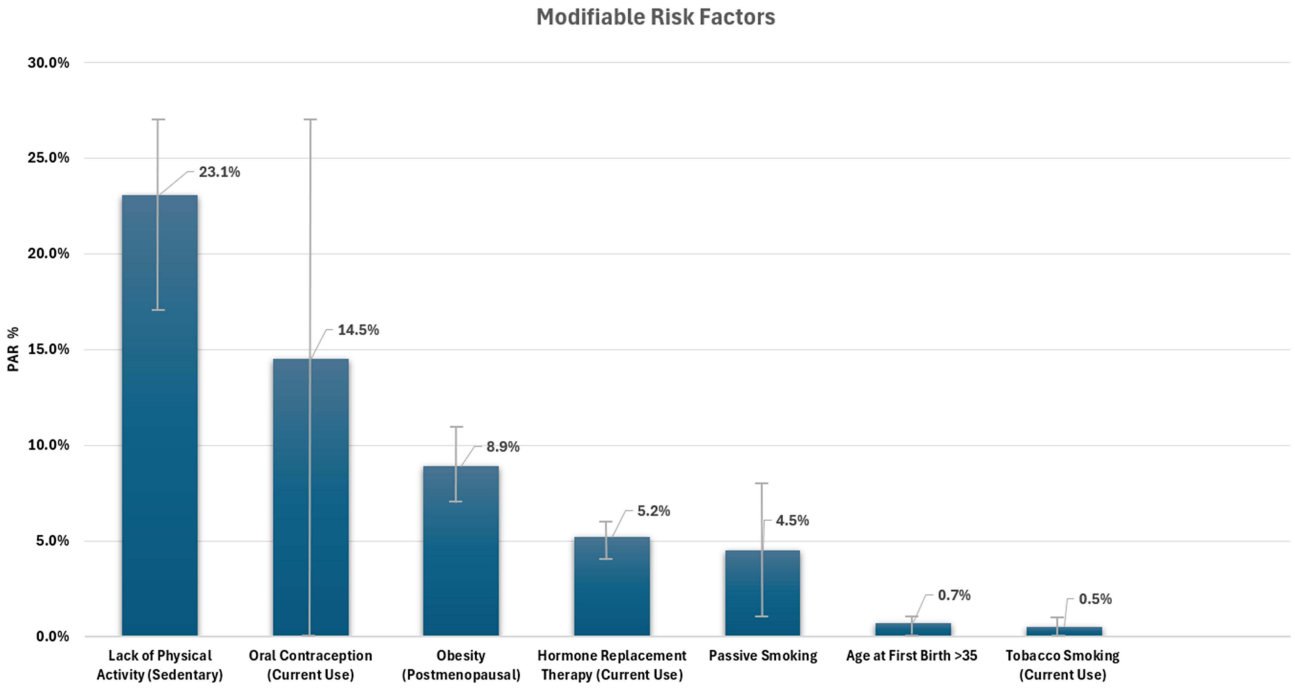

Figure 1 Ranking of modifiable lifestyle risk factors for breast cancer in Saudi Women, PAR%.

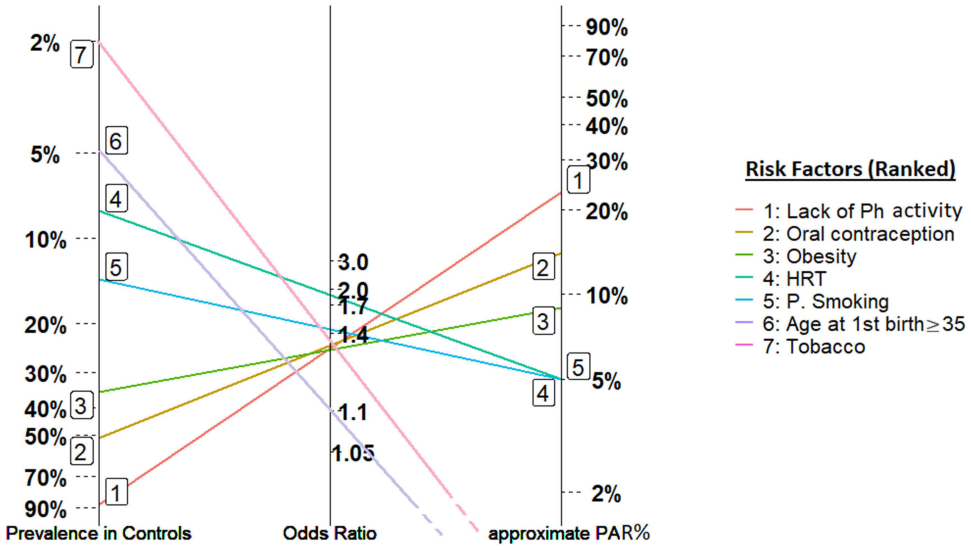

Figure 2 Attributable fraction nomogram displaying estimates of risk factor prevalence, average Odds Ratio, and approximate PAR% for the 7 of modifiable lifestyle risk factors for breast cancer in Saudi Arabia.

Accordingly, the GaStat report states that the most common reason for Saudis' lack of physical activity is the absence of the desire to do so, which accounted for (44.0%) of all Saudis. With insufficient time to exercise (24.62%), health reasons (15.20%) and lack of accessible exercise facilities accounted for (14.80%) of Saudis.[15]

These percentages reflect the social, cultural, and environmental restrictions of women practicing physical activity in Saudi Arabia. This is partly due to sociocultural factors that restrict Saudi women's opportunities to exercise and encourage participation in professional sports clubs.[44,45] Additionally, physical education for Saudi females was only included as part of the curriculum in schools in 2019.[45] This study emphasizes the importance of the social determinants of health, cultural, and environmental changes that would promote healthier lifestyles.[46,47] Creating safe neighborhood play spaces for adults and children where they can be physically active and affordable health clubs for both women and men can help promote healthy lifestyles.[48,49] Additionally, regulation of healthy food prices may promote the choice of healthy options over unhealthy ones.[50]

Reports from the CUP state that the use of OCP could lead to a slight increase in breast cancer risk among young women (current and recent users only).[34] The relationship between OCP levels and the risk of breast cancer remains controversial. Some evidence has suggested that the use of OCP increases the risk of breast cancer between 24–30% compared to never used.[7,22] The differences between analyses could be associated with changes in the formulations of OCP during the past decades and the duration of OCP use.

PAR% calculations require good evidence of causal associations and prevalence of risk factors. The strength of this study includes the use of nationally representative data on exposure prevalence, which will aid policymakers in endorsing health policies to address common ailments and thereby prevent them. However, this study has several limitations, including the data source. The selected prevalence source was based on self-reports, which tend to underestimate the prevalence of behavioral risk factors, and thus risk underestimation of the calculated PAR%. The availability of adjusted prevalence data that exactly reflects the risk factor measurements used in epidemiological studies (eg, breastfeeding patterns and childbearing patterns, obesity according to menopausal status, and night-shift work) was limited or unavailable. Therefore, some risk factors were excluded from this study. Furthermore, an accurate estimation of the recent prevalence of OCP use and HRT in Saudi Arabia is unavailable. Therefore, the estimates provided in this manuscript may not reflect the full scope of current use.

The Nomogram model serves as an efficient method for calculating PAR% and impact fractions, while also demonstrating that risk factor prevalence and risk factor/disease log-odds ratio equally contribute to PAR%. (Figure 2)[13] However, this presentation has its limitations. First, the estimations derived were only valid for logistic disease models, with no effect modification between the risk factors and confounders. Second, the approximations used may be inaccurate for larger odds ratios. These limitations indicate that the optimal used for these plots is as a visual accompaniment to, and not a replacement for, the exact calculations of attributable fractions.

Conclusion

Physical inactivity significantly affects health negatively on national and global levels. Elimination of this risk factor could reduce the incidence of breast cancer by 23% in the Saudi population. Disease burden can be significantly reduced by effectively modifying exposure to risk factors through the promotion of healthy lifestyles. Therefore, modifying these lifestyle factors must be prioritized as a major strategy for reducing the incidence of breast cancer in the Saudi population. There is an immense need for public health interventions towards achieving such changes considering, local needs, current data on cancer risk factors, and the disease burden.

Acknowledgments

The authors would like to thank Dr. Alanoud Khuthaila for her contribution and support in the initial phase of the project.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Fitzmaurice C, Allen C, Barber RM. Collaboration GBoDC. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study global burden of cancer 2015 global burden of cancer 2015. *JAMA Oncol*. 2017;3(4):524–548. doi:10.1001/jamaoncol.2016.5688
2. Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. *Asian Pac J Cancer Prev*. 2016;17(S3):43–46. doi:10.7314/APJCP.2016.17.S3.43
3. Nikbakhsh N, Moudi S, Abbasian S, Khafri S. Prevalence of depression and anxiety among cancer patients. *Caspian j intern med*. 2014;5(3):167.
4. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol*. 2013;14(12):1165–1174. doi:10.1016/S1470-2045(13)70442-X
5. Registry SC. Cancer incidence report Saudi Arabia 2015. *Saudi Health Council*. Available from: https://nhic.gov.sa/eServices/Documents/E%20SCR%20final%206%20NOV.pdf. Accessed, 2024.
6. (IHME) IfHMaE. GBD Compare. 2015; Available from: https://vizhub.healthdata.org/gbd-compare/. Accessed August 24, 2024.
7. Kaminska M, Ciszewski T, Lopacka-Szatan K, Miotla P, Staroslawska E. Breast cancer risk factors. *Przeglad menopauzalny*. 2015;14(3):196–202. doi:10.5114/pm.2015.54346
8. Friis RH, Sellers TA. *Epidemiology for Public Health Practice*. Jones & Bartlett Publishers; 2014.
9. Mansournia MA, Altman DG. Population attributable fraction. *BMJ*. 2018;360:757. doi:10.1136/bmj.k757
10. Hayes J, Richardson A, Frampton C. Population attributable risks for modifiable lifestyle factors and breast cancer in N ew Z ealand women. *Internal Med J*. 2013;43(11):1198–1204. doi:10.1111/imj.12256
11. Clarke CA, Purdie DM, Glaser SL. Population attributable risk of breast cancer in white women associated with immediately modifiable risk factors. *BMC Cancer*. 2006;6(1):170. doi:10.1186/1471-2407-6-170
12. Barnes BB, Steindorf K, Hein R, Flesch-Janys D, Chang-Claude J. Population attributable risk of invasive postmenopausal breast cancer and breast cancer subtypes for modifiable and non-modifiable risk factors. *Cancer Epidemiol*. 2011;35(4):345–352. doi:10.1016/j.canep.2010.11.003
13. Ferguson J, O'Leary N, Maturo F, Yusuf S, O'Donnell M. Graphical comparisons of relative disease burden across multiple risk factors. *BMC Med Res Methodol*. 2019;19(1):186. doi:10.1186/s12874-019-0827-4
14. Health Mo. Saudi health interview survey results *Kingdom of Saudi Arabia: Ministry of Health* 2013Available from: http://www.healthdata.org/sites/default/files/files/Projects/KSA/Saudi-Health-Interview-Survey-Results.pdf.. Accessed August 24, 2024.
15. statistics GAf. Bulletin of household sport practice survey. 2019.
16. Aldabal BK, Koura MR. Risk factors of breast cancer among the primary health-care attendees in Eastern Saudi Arabia. *Int J Med Sci Public Health*. 2016;5(2):276–281. doi:10.5455/ijmsph.2016.16092015102
17. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. *World J Meta-Analysis*. 2017;5(4):80–84. doi:10.13105/wjma.v5.i4.80
18. Lilienfeld DE, Lilienfeld DE, Stolley PD, Lilienfeld AM. *Foundations of Epidemiology*. USA: Oxford University Press; 1994.
19. Kelsey WE, Kelsey JL, Whittemore AS, Evans AS, Thompson WD. *Methods in Observational Epidemiology*. Monographs in Epidemiology and; 1996.
20. Lee I-M, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet (London, England)*. 2012;380(9838):219–229. doi:10.1016/S0140-6736(12)61031-9
21. Hunter DJ, Colditz GA, Hankinson SE, et al. Oral contraceptive use and breast cancer: a prospective study of young women. *Cancer Epidemiol Prev Biomarkers*. 2010;19(10):2496–2502. doi:10.1158/1055-9965.EPI-10-0747

22. Kumle M, Weiderpass E, Braaten T, Persson I, Adami H-O, Lund E. Use of oral contraceptives and breast cancer risk: the Norwegian-Swedish Women's Lifestyle and Health Cohort Study. *Cancer Epidemiol Prev Biomarkers*. 2002;11(11):1375–1381.
23. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D. Cancer incidence and mortality in relation to body mass index in the million women study: cohort study. *BMJ*. 2007;335(7630):1134. doi:10.1136/bmj.39367.495995.AE
24. Amadou A, Hainaut P, Romieu I. Role of obesity in the risk of breast cancer: lessons from anthropometry. *J Oncol*. 2013;2013:1–19. doi:10.1155/2013/906495
25. Collaborators MWS. Breast cancer and hormone-replacement therapy in the million women study. *Lancet*. 2003;362(9382):419–427.
26. Alkhenizan A. Evidence-based medicine and hormone replacement therapy. *Ann Saudi Med*. 2004;24(3):164. doi:10.5144/0256-4947.2004.164
27. Warner ET, Colditz GA, Palmer JR, Partridge AH, Rosner BA, Tamimi RM. Reproductive factors and risk of premenopausal breast cancer by age at diagnosis: are there differences before and after age 40? *Breast Cancer Res Treat*. 2013;142(1):165–175. doi:10.1007/s10549-013-2721-9
28. Ewertz M, Duffy SW, Adami HO, et al. Age at first birth, parity and risk of breast cancer: a meta-analysis of 8 studies from the Nordic countries. *Int J Cancer*. 1990;46(4):597–603. doi:10.1002/ijc.2910460408
29. Andrieu N, Goldgar DE, Easton DF, et al. Pregnancies, breast-feeding, and breast cancer risk in the International BRCA1/2 carrier cohort study (IBCCS). *J National Cancer Inst*. 2006;98(8):535–544. doi:10.1093/jnci/djj132
30. Gram IT, Braaten T, Terry PD, et al. Breast cancer risk among women who start smoking as teenagers. *Cancer Epidemiol Prev Biomarkers*. 2005;14(1):61–66. doi:10.1158/1055-9965.61.14.1
31. Li B, Wang L, M-s L, et al. Passive smoking and breast cancer risk among non-smoking women: a case-control study in China. *PLoS One*. 2015;10(4):e0125894. doi:10.1371/journal.pone.0125894
32. HFiB CC. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50 302 women with breast cancer and 96 973 women without the disease. *The Lancet*. 2002;360(9328):187–195.
33. Shen S, Zhong S, Xiao G, Zhou H, Huang W. Parity association with clinicopathological factors in invasive breast cancer: a retrospective analysis. *Onco Targets Ther*. 2017;10:477. doi:10.2147/OTT.S123888
34. Research WCRFAIf C. *Continuous update project expert report 2018. diet, nutrition, physical activity and breast cancer*.
35. Key TJ, Allen NE, Spencer EA, Travis RC. Nutrition and breast cancer. *Breast*. 2003;12(6):412–416. doi:10.1016/S0960-9776(03)00145-0
36. Gandini S, Merzenich H, Robertson C, Boyle P. Meta-analysis of studies on breast cancer risk and diet: the role of fruit and vegetable consumption and the intake of associated micronutrients. *Eur. J. Cancer*. 2000;36(5):636–646. doi:10.1016/S0959-8049(00)00022-8
37. Almutlaq BA, Almuazzi RF, Almuhayfir AA, et al. Breast cancer in Saudi Arabia and its possible risk factors. *J Cancer Policy*. 2017;12:83–89. doi:10.1016/j.jcpo.2017.03.004
38. Scoccianti C, Straif K, Romieu I. Recent evidence on alcohol and cancer epidemiology. *Future Oncol*. 2013;9(9):1315–1322. doi:10.2217/fon.13.94
39. HFiB CC. Alcohol, tobacco and breast cancer–collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. *Br. J. Cancer*. 2002;87(11):1234.
40. Unit WHOMoSA. *Global Status Report on Alcohol and Health, 2014*. World Health Organization; 2014.
41. Grundy A, Richardson H, Burstyn I, et al. Increased risk of breast cancer associated with long-term shift work in Canada. *Occup Environ Med*. 2013;70(12):831–838. doi:10.1136/oemed-2013-101482
42. Menegaux F, Truong T, Anger A, et al. Night work and breast cancer: a population-based case–control study in France (the CECILE study). *Int J Cancer*. 2013;132(4):924–931. doi:10.1002/ijc.27669
43. Maura M, Boyle P, La Vecchia C, Decarli A, Talamini R, Franceschi S. Population attributable risk for breast cancer: diet, nutrition, and physical exercise. *JNCI J National Cancer Inst*. 1998;90(5):389–394. doi:10.1093/jnci/90.5.389
44. Al-Eisa ES, Al-Sobayel HI. Physical activity and health beliefs among Saudi women. *J Nutr Metab*. 2012;2012:642187. doi:10.1155/2012/642187
45. Al-Hazzaa HM. Physical inactivity in Saudi Arabia revisited: a systematic review of inactivity prevalence and perceived barriers to active living. *Int J Health Sci*. 2018;12(6):50–64.
46. Organization WH. *Social Determinants of Health: The Solid Facts*. World Health Organization. Regional Office for Europe; 2003.
47. Davis SL, Chapa DW. Social determinants of health: knowledge to effective action for change. *J Nurse Practit*. 2015;11(4):424–429. doi:10.1016/j.nurpra.2015.01.029
48. Alahmed Z, Lobelo F. Physical activity promotion in Saudi Arabia: a critical role for clinicians and the health care system. *J Epidemiol Glob Health*. 2018;7(Suppl 1):S7–S15. doi:10.1016/j.jegh.2017.10.005
49. Alqahtani BA, Alenazi AM, Alhowimel AS, Elnaggar RK. The descriptive pattern of physical activity in Saudi Arabia: analysis of national survey data. *Int Health*. 13 2020.
50. Kern DM, Auchincloss AH, Stehr MF, et al. Neighborhood prices of healthier and unhealthier foods and associations with diet quality: evidence from the multi-ethnic study of atherosclerosis. *Int J Environ Res Public Health*. 2017;14(11):1394. doi:10.3390/ijerph14111394