

Original Research



Sex difference of cancers over the years: age standardized incidence rates, trends, and exposure to risk factors in Sri Lanka

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Abstract

Introduction: Males have a higher chance of developing cancers compared to females. Aetiology of cancer is multifactorial. Lifestyle, constitutional characteristics of the individual and hereditary factors can contribute to development of cancer. One third of the cancers can be prevented through lifestyle change.

Objectives: To analyse male and female age-standardized rates (ASR) and average annual percentage change (AAPC) of cancer incidence during 2005-2019 and to describe exposure to lifestyle risk factors among males and females in Sri Lanka

Methods: Data from the National Cancer Registry, Sri Lanka (NCR-SL) from 2005 to 2019 were used to analyse male and female ASR. AAPC was analysed for males and females separately using Joinpoint regression program. National Survey data were used to describe the risk factor exposure among males and females and tobacco, alcohol, physical inactivity, obesity, and areca-nut use were considered in this paper.

Results: During 2005-2019, ASRs among males have increased from 68.1 to 132.6 per 100 000 population while ASRs for females have increased from 73.4 to 128.8. The AAPC of ASR among males 5.2% (95% CI: 0.7, 7.7; $p < 0.05$) was significantly higher than for females 3.8% (95% CI: 0.3, 7.5; $p < 0.05$). The considerable percentage of female only cancers are added to the total incidence and included cervical (ASR=8.3; 6%), uterine (ASR=7.4; 6%) and ovarian (ASR=7.3; 6%) cancers, which were placed 4th, 5th and 6th, respectively among the top ten cancers among females in year 2019. The ASRs for ovarian (ASR=5.9; 8%) and uterine (ASR=3.2; 2%) cancers in 2005 showed that the lower value of ASR in 2005 compared to 2019 and showed that gradual increase with time, except for a very slight reduction of cervical cancer with time (ASR=8.9; 12% in 2015). Out of the top ten cancers among males, prostate cancer adds a considerable amount to the total incidence from 2005-2019, while it remains in the fifth position out of all cancers among males from 3.5 in 2005 to 9.7 in 2019. Exposure to tobacco, alcohol and chewing betel quid which contains areca-nut & tobacco was higher among males, while obesity and chewing betel quid which contains only areca nut were higher among females in Sri Lanka. Physical inactivity was similar in both sexes.

Conclusions & Recommendations: The ASRs of all cancers and the AAPC showed an increase among both sexes, while the AAPC was higher among males than females. Regarding exposure to risk factors, use of tobacco, alcohol and betel quid which contains tobacco & areca-nut was higher among males, while obesity and use of betel quid which contains only areca-nut were higher among females. Separate interventions for both sexes need to be conducted, to prevent risk factors.

Key words: male and female cancers, age standardized incidence rate, annual percentage change, risk factors for cancers

Introduction

Globally and in Sri Lanka, the incidence and burden of cancers has gradually increased over the years to become a public health challenge. Both ageing and the growth of the population as well as the increasing prevalence of main risk factors for cancers contribute to this increase (1-2). Globally, according to GLOBOCAN, the estimated number of cases in 2020 among males was 10 065 305 (52%), and it was 9 227 484 (48%) among females. GLOBOCAN 2020 is an online database providing global cancer statistics and estimates of incidence and mortality for 185 countries for 36 types of cancer, and all cancer sites combined by the International Agency for Research on Cancer, World Health Organization. GLOBOCAN further estimated that ASR per 100 000 population for all cancers of all age groups were 222 for males and 186 for females worldwide and 185.2 for males and 156.7 for females in the Asian region in year 2020 (3). Southeast Asian (SEA) region showed an ASR of 110.3 for males and 110.8 for females, which was the lowest among males and females in all WHO regions in the global arena in 2020 (3).

According to the 2019 data of the NCR-SL, there were 14 845 (47%) males and 16 989 (53%) females diagnosed with cancer (4). Sri Lanka observed a female preponderance in the year 2019 (4). Global evidence showed that males are more prone to develop cancers than females (5). Worldwide, the incidence rate for all cancers was 19% higher in men (ASR of 222.0) than in women (ASR of 185.2) in 2020 (3). The contribution of multifactorial etiological causes leads to men being more prone to develop cancers than women (5-6). The aetiology of cancer is genetic damage, which is mainly acquired, but sometimes hereditary. With a few exceptions, cancers are derived from single somatic cells and their progeny. Genetic changes can be in tumour suppressor genes that regulate cell growth or alter the function of DNA repair genes, oncogenes and genes involved in the production of blood vessels (7). This multifactorial genetic damage can be classified as hereditary and constitutional characteristics of the individual and lifestyle factors including environmental exposures (8-10).

Hereditary factors account for about 5-10% of all cancers and contribution to the overall risk for total cancer incidence is extremely low. The sex-specificity of cancers is dependent on the type of cancer. For example, inherited mutations in the tumour suppressor genes lead to breast cancers. The presence of BRCA 1 and BRCA 2 lead to a more than 75% risk of breast cancer and ovarian cancer (11). However, females have more chances of developing breast cancer than males. Also, evidence shows that liver cancers, which have a higher incidence among males than among females occur due to hereditary factors. Lynch syndrome, often called hereditary nonpolyposis colorectal cancer is an inherited disorder that increases the risk of many other types of cancers, namely stomach, liver, small intestine, urinary tract, brain, ovary and endometrium (12). Because of its association with gynaecological malignancies, females with Lynch syndrome have a higher overall risk of developing cancer than men.

Lifestyle risk factors also increase a person's chance of developing cancers. It depends on the duration as well as the strength of exposure. Male and female exposure to lifestyle factors vary. Modifiable factors can lead to metabolic/physiological changes and alter the DNA of cells. Lifestyle habits such as the use of tobacco, alcohol and areca-nut, exposure to viruses & radiation and cancer-causing chemicals, obesity, hormones, and physical inactivity can cause genetic mutations (13). Preventing exposure lowers the risk of developing cancers. Individual constitutional factors that render an individual susceptible to genetic damage are non-modifiable, such as age, sex, ethnicity, early menarche, late menopause skin type, etc. (13).

The World Health Organization (WHO) reports that one-third of cancers are preventable by lifestyle modifications such as avoiding physical inactivity, weight reduction, stopping use of tobacco, areca nut and alcohol, healthy diet and protecting from certain infections (HPV infection and hepatitis B infection) (13). Easily preventable cancers are oral, lung, colorectal, prostate, cervical and breast cancers (14). The WHO has introduced “best buys” strategies to implement the prevention of non-communicable diseases including cancer (15). Lifestyle factors lead

to a higher risk of men than women due to socio-cultural facts which affect the exposure rates. Another factor that has contributed to this disparity is that Sri Lankan women typically have more frequent contact with health services than men, since maternal and child health services are provided at the field level with high coverage. It is evident that women have more health seeking behaviours than men (16). This makes it easier to miss preventive practices as well as detection of early signs of cancers among men than in women.

Sex differences in cancer epidemiology are a significant factor that helps to plan the risk reduction interventions as well as early detection programmes. Male and female annual trends are also important for measuring the successful efforts of these interventions. Data on ASR in cancer trends for all cancers among males and females are sparse in Sri Lanka. The aim of this study was to describe the ASR and AAPC of incidence during the year 2005 to 2019 of all cancers among males and females and to describe the risk factor exposure in Sri Lankans using national risk factor surveys.

Methods

The total number of male and female cancer incidence was obtained from NCR-SL for the years 2005-2019. All cancer cases were identified according to the International Classification of Diseases for Oncology (ICD-O) - 3rd edition, 1st revision which was introduced by the WHO (17). ASR was calculated for all cancers among all age groups using the data from the NCR-SL which uses Canreg 5 Software by standardization to 100 000 world population. The average annual percentage change of ASRs was analysed using Joinpoint Trend Analysis Software (version 4.9.0.0), introduced by National Cancer Institute, USA (18). The AAPC measured the trends in yearly cancer rates over time. Joinpoint regression analysis was used to identify the significant per cent change over time in both males and females. The significance of change was identified via p value with 95% confidence interval (CI) and $p < 0.05$ taken as significant.

The exposure to risk factors that are related to cancer among males and females were described using the results of the national risk factor surveys. This included the non-communicable disease risk factor survey also called STEPS Survey 2015 (19), Demographic & Health Survey (DHS) 2016 (20), DHS 2006 (21), National Alcohol Survey 2016 (22), Oral Health Survey 2015 (23) and Global Youth Tobacco Survey, 2015 (24). Risk factors accounted for in this study were tobacco (smoking & smokeless tobacco), alcohol, arecanut, obesity, and physical inactivity, which are risk factors that lead to common cancers in Sri Lanka.

Results

The NCR-SL during 2005-2019 included a total of 160 093 males (47%) and 177 321 (53%) females. The ASR for males for all cancers had increased almost two-fold from 68.1 per 100 000 population in 2005 to 132.6 in 2019. The all-cancer ASR for females has increased from 73.4 per 100,000 in 2005 to 128.8 in 2019, with a 1.7-fold rise. It is also noted that ASRs of all cancers in males and females increased with time, but during the 2011-2019 increase was higher among males compared to females. The picture was different in the previous years as ASRs for all cancers was higher for females from 2005 to 2010 (Figure 1).

The ASR of males showed one joinpoint model with two incidence trends. From 2005 to 2017, it showed an upward significant trend with an APC of 6.8% (95% CI: 5.7, 8.0; $p < 0.05$) and a non-significant decreasing trend of APC of -4.3% (95% CI: -20.0, 14.3; $p > 0.05$) from 2017-2019. However, AAPC showed an overall increasing significant trend of 5.2% (95% CI: 2.7, 7.7; $p < 0.05$). ASR of females observed two joinpoints model with three incidence trends. From 2005 to 2013, it showed an upward significant trend with an APC of 3.4% (95% CI: 1.5, 5.3; $p < 0.05$) and a non-significant decreasing trend of APC of 10.8% (95% CI: -6.2, 31.0; $p > 0.05$) from 2013-2016. From 2016 to 2019, it showed that non-significant trend with an APC of -1.6% (95% CI: -1.6, -9.5; $p > 0.05$). However, AAPC of females showed an overall increasing significant trend of 3.8% (95% CI: 0.3, 7.5; $p < 0.05$).

As shown in Figure 2, when different types of cancers are considered, NCR-SL showed that males have higher ASRs for oral, lung, oesophageal and colorectal cancers than for females during 2005-2019. In addition to that, a considerable percentage of female-only cancers are added to the total incidence every year. This included cervical (ASR=8.3; 6%), uterine (ASR=7.4; 6%) and ovarian (ASR=7.3; 6%) cancers, which were placed 4th, 5th and 6th respectively among the top ten cancers among females in the year 2019 (4). The ASRs for cervical (ASR=8.9; 12%), ovarian (ASR=5.9; 8%) and uterine (ASR=3.2; 2%) cancers in 2005 showed that the values have increased gradually with time from 2005 to 2019, except a slight reduction of cervical cancer. From 2005-2019, prostate cancer managed to remain in the 5th position out of all cancers among males. However, the ASR of prostate cancer has increased considerably from 3.5 in 2005 to 9.7 in 2019 (4) (Figure 3).

Risk factor exposure among males and females in Sri Lanka

The main risk factors relevant to cancer among Sri Lankan males and females as given in the STEPS survey (2015) are depicted in Table 1. Accordingly, females had lower exposure to tobacco in respect to current and daily tobacco use, the prevalence of current smoking and smokeless tobacco use, compared to males. However, exposure to second-hand smoking (SHS) at home during the last 30 days was almost similar in both sexes, while SHS at the workplace during the last 30 days indicated a 25% increase among males compared to females. Overall, it showed that males had more exposure to tobacco in all the indicators related to tobacco in the STEPS Survey (2015), compared to females. Oral Health Survey 2015 observed that smoking among males was higher than among females. It indicated that percentages of smoking among the 35-44-year male group and the 65-74-year male group as a habit were 30.9% and 34.6%, respectively, while in females, the same practice were 0.7% among the 35-44-year age group and 1.1% among the 65-74-year age group. Both surveys observed similar findings of higher smoking rates among males than among females. Global Youth Tobacco Survey (2015) recorded that

current smoking among the 13-15-year age group was 4% and 0.7% among males and females, respectively. Further, the Oral Health Survey (2015) recorded that chewing betel quid which contains tobacco & areca-nut among males was higher than among females. It further showed that chewing betel quid which contains tobacco & areca-nut among the 35-44-year male group and the 65-74-year male group were 49% and 60%, respectively, while females having the same practice was 14% among the 35-44-year age group and 37% among the 65-74-year age group. This survey further indicated that chewing betel quid which contains only areca-nut among the 35-44-year male group and the 65-74-year male group were 48% and 32%, respectively, while females having the same practice was 78% among the 35-44-year age group and 55% among the 65-74-year age group. This indicated that betel chewing which contain only areca-nut without tobacco was higher among females.

The Global Youth Tobacco Survey 2015 observed the current tobacco use among the 13-15-year age group to be 13% and 5% among males and females, respectively. In addition, this survey had reported that all indicators of usage and exposure to tobacco have decreased by more than double compared with the results of Global Youth Tobacco Survey from 1999 to 2015. The STEPS survey 2015, further revealed that current alcohol consumption during the last 30 days was 33 times higher among males (34%) compared to females (<1%). The National Survey on Alcohol Consumption conducted in 2016 showed that the prevalence of current drinkers was 39.6% among males and 2.4% among females. It was noted that alcohol consumption has increased since the last national survey on alcohol consumption conducted in 2008 (male: 26%; female: 1.2%). The National Survey on Alcohol Consumption in 2016 observed that alcohol consumption, among both male and female were slightly increased than in the STEPS Survey (2015). The female alcohol consumption showed a 2% increase compared to the results of the STEPS Survey (2015) and it accounted for <1%. The Oral Health Survey (2015) observed the consumption of alcohol to be higher among males than among females. It indicated that the alcohol consumption as a habit among the 35-44-year male

group and the 65-74-year male group were 51.7% and 43.4%, respectively, while females having the same practice were 1.5% among the 35-44-year age group and 1.8% among the 65-74-year age group. All these surveys revealed consumption of alcohol to be higher among males than among females.

The DHS Survey (2016) showed that 45% of ever-married women were overweight or obese (BMI>25 kgm⁻²). Thus, during a period of ten years, the

percentage of overweight women has increased from 24% in 2006-7 to 32% in 2016, while the percentage of obese ever-married women has increased from 7% to 13% during the same period. According to the WHO recommendations, STEPS Survey (2015) showed that a higher percentage of females (38.4%) were having inadequate physical activity compared to males (22.5%). The same survey showed that the mean waist circumference was almost similar in both males and females, and it was within normal limits.

Table 1: Behavioural risk factor exposure among males and females in STEPS Survey 2015

Risk factor	Male	Female
Tobacco use		
Current use of tobacco (both smoke & smokeless)	45.7%	5.3%
Daily tobacco users	35.3%	4.1%
Prevalence of current smoking	29.4%	0.1%
Smokeless tobacco	26.0%	5.0%
Second-hand smoking at home during the past 30 days	25.2%	21.6%
Second-hand smoking at their workplace in the past 30 days	36.1%	11.1%
Alcohol consumption		
Current alcohol users in the past 30 days	34.8%	<1.0 %
Lifetime abstainers of alcohol	40.2%	96.5%
Body mass index		
Overweight or obese	24.6%	34.3%
Obese	3.5%	8.4%
Overweight	21.0%	26.0%
Physical activity		
Did not meet the WHO recommendation of physical activity	22.5%	38.4%
Waist circumference		
Mean waist circumference (cm)	82.3	82.1

Figure 1: Male and female age standardized incidence rates (ASR) for all age and all cancers in Sri Lanka, 2005-2019

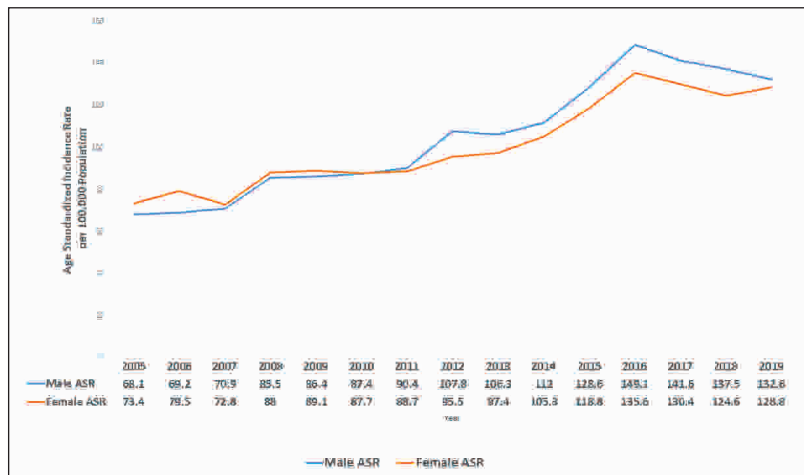


Figure 2: Joinpoint trend analysis for all age and all cancer age standardized rates (ASR) by sex in Sri Lanka, 2005-2019

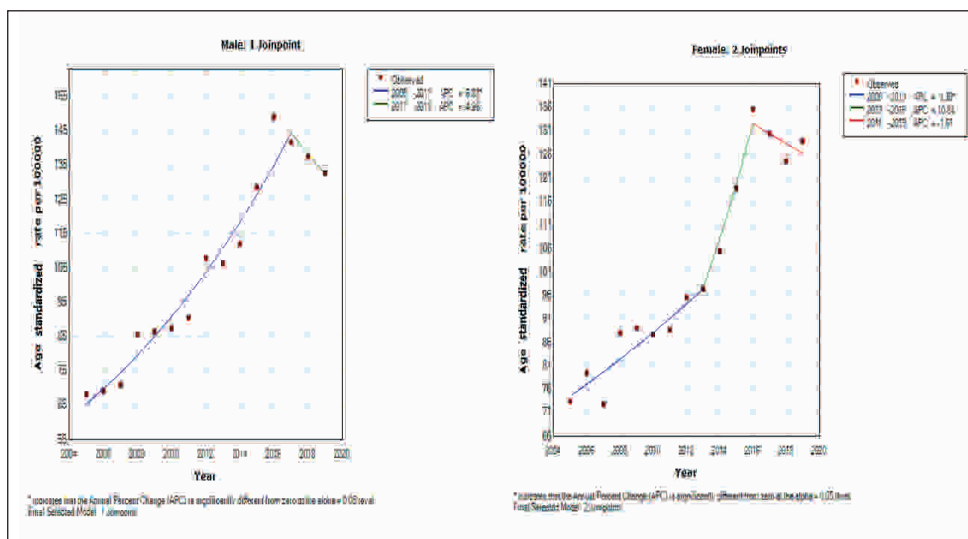
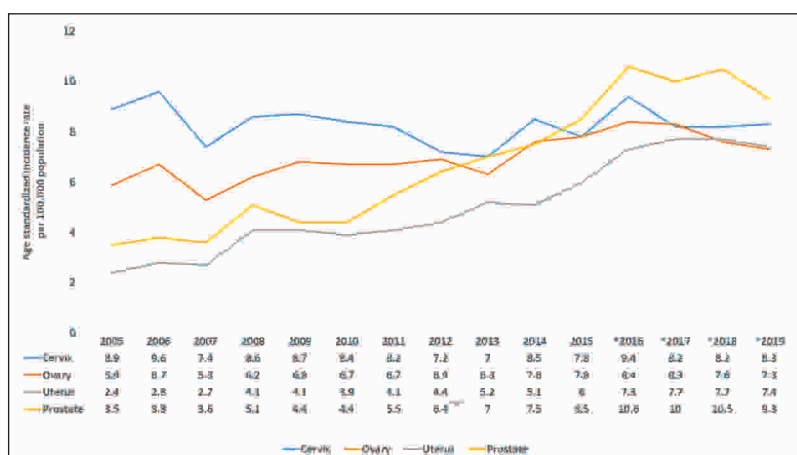


Figure 3: Age standardized rates (ASR) of common female only and male only cancers in Sri Lanka, 2005-2019



Discussion

Evidence showed that males have a higher cancer incidence than females (5). Global, regional and Sri Lankan incidence can be compared using ASR. The ASR is not influenced by the age structure of different countries, regions or worldwide. The ASR per 100 000 population ensures the differences in incidence between males and females in the same geographical area and that it is not due to differences in the age distribution of the populations being compared (25).

It is evident that the ASR among males (ASR=226) was higher than among females (ASR=186) worldwide, as well as in the Asian region in year 2020 (ASR in males=185.2 and ASR in females=156.7). The SEA Region showed a slightly lower value for all cancer ASR (ASR=110.3) among males than among females (ASR=110.8) in 2020. In Sri Lanka, the ASR was higher among males (ASR=132) than among females (ASR=128) in 2019, while it was similar to the global and Asian pattern of all cancer ASR in males. In addition to that, both male and female ASRs of Sri Lanka in 2019 were lower than the global and Asian region estimates in 2020. However, these figures were higher than the SEA figures. Higher ASR of Sri Lanka than in the SEA Region in 2020 could be due to an underestimated figure in the South Asian region in the GLOBOCAN because of the unavailability of incidence data in many SEA countries. Further, NCR-SL revealed that the ASR of males was higher than of females during the period from 2012 to 2019. In contrast, ASR of females was higher than of males in Sri Lanka during the period from 2005 to 2011. This observed difference could be due to the change in the denominator. From 2005-2010, due to the war situation in Sri Lanka, an estimated number for the total population in North & East Provinces was incorporated into the total Sri Lankan population instead of actual censuses data. From 2011 onwards, the actual population of the North and East Provinces were included instead of estimated population data.

Both global and Asian ASR, 2020 and Sri Lanka, 2019 showed that males have higher ASRs than females. The end results of multifactorial contributory factors may have been the reason to the

higher incidence in males. This difference of male and female ASRs could be due to the different levels of exposure to modifiable risk factors and non-modifiable factors like ethnicity. In addition to that, the ASRs of male and female cancers were contributed by male-only and female-only cancers both worldwide, and at the regional and Sri Lankan level.

The overall increase of ASR of each year was observed in both sexes in Sri Lanka from 2005 to 2019, and it could be due to the increasing life expectancy in Sri Lanka in both sexes, and the different exposure level for risk factors in both sexes. NCR-SL also recorded a higher ASR of oral, lung, colorectal and oesophageal cancers among males than females from 2005 to 2019 (4). It could be due to higher exposure to tobacco among males than females.

The AAPC of ASR in both sexes is useful for planning intervention. The AAPC of ASR was higher among males (5.2%) compared to females (3.8%) in Sri Lanka during the period of 2005 to 2019. This could be due to the different levels of exposure for risk factors, as well as a small percentage of other contributory factors including the male-only and female-only cancers.

Exposure to tobacco and alcohol could pose a significant risk for the development of cancers among males. Tobacco causes 15 types of cancers in the body and alcohol accounts for five types of cancers in the body (26). National surveys described above showed that exposure to risk factors were less among females than among males, except for obesity, use of betel quid which contain areca-nut and physical inactivity. Social gender norms can contribute to higher exposure to tobacco and alcohol in males, and it could be one reason for the higher ASR of males.

During 2006 to 2016, the obesity and overweight among females has increased from 33%. Obesity is one of the risk factors for breast cancer and thyroid cancer, and it could be one contributing reason for the increased ASR among female breast and thyroid cancers in Sri Lanka compared to males in 2019 (4). This is further enhanced by the second-hand smoking

at home among females, which accounts for the higher incidence of female breast cancer, despite the low incidence rate of current smoking among females.

During the recent years, Sri Lanka has accelerated actions to adopt evidence-based policies for risk factor reduction: strengthening tobacco control, promotion of physical activities & healthy diets, HPV vaccination, introduction of relevant legislation, improvements in living standards, education, and gender equity. They are implemented through the Ministry of Health in partnership with other ministries, NGOs, and community-based organizations. The expected outcome of these strategies is to achieve a significant reduction of cancer incidents among males and females in the future. One of the limitations of this study was not assessing the risk factors of cancer patients due to unavailability of data gathered in individual cancer patients in the NCR-SL.

Conclusions & Recommendations

In Sri Lanka, ASRs of all cancers among both sexes were increased from 2005 to 2019, and significant AAPC was observed for both sexes with a higher value among males than among females. Risk factor exposure of males was higher with regard to the use of tobacco, alcohol, and betel quid which contains areca-nut & tobacco, while obesity, physical inactivity, and betel quid which contains only areca-nut than females. Separate interventions for both sexes need to be conducted, to prevent risk factors. Secondary smoking at home was almost similar in both sexes, while males were exposed to secondary smoking more in working places.

Author Declarations

Competing interests: The authors declare that they have no competing interests.

Ethics approval and consent to participate: All the data in this paper were secondary data from National Cancer Registries from 2005- 2019, and data from National surveys on risk factors were used without any identification at individual level.

Public Health Implications

- Existing risk factor reduction strategies should be strengthened, and new strategies for use of tobacco and areca-nut, obesity and physical inactivity should be restructured, targeting males and females separately.
- Trend analysis should be conducted in identified intervals to plan the interventions for males and females.
- Research should be conducted to identify the association of risk factors by individual cancers.

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