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## POPULATION BASED LIFETIME RISK ESTIMATION OF MALIGNANT CANCERS IN BRUNEI DARUSSALAM.

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### ABSTRACT

**Introduction:** Since 2009, the leading cause of death in Brunei Darussalam has been cancer. This study aimed to estimate the lifetime risk of malignant cancers affecting men and women in Brunei Darussalam. **Methods:** De-identified data of malignant cancer cases were obtained from the population based cancer registry in Brunei Darussalam for the study period of 2011 to 2015. Adjusted multiple primaries method was applied to calculate a standardised estimate of lifetime risk of developing cancers. **Results:** The lifetime risk of being diagnosed with a type of malignant cancer is 28.0% or 1 in 4. The risk is 26.5% or 1 in 4 for men, and 29.2% or 1 in 3 for women. We found that at 5.0%, colorectal cancer poses the highest lifetime risk among men in Brunei Darussalam. This was followed by lung (4.5%) and prostate (3.7%) cancer. In women, the lifetime risk of developing breast cancer was 6.3%, colorectal cancer was 4.5% and cervical cancer was 1.8%. **Conclusion:** This study found significant population based lifetime risk of cancer in Brunei Darussalam; 1 in 4 Bruneians are at risk of being diagnosed with cancer at some point in his or her lifetime.

**Keywords:** Cancers, Lifetime risk, Malignant neoplasm, Population registers, Risk assessments.

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**Introduction:** Since 2009, the leading cause of death in Brunei Darussalam has been cancer. This study aimed to estimate the lifetime risk of malignant cancers affecting men and women in Brunei Darussalam. **Methods:** De-identified data of malignant cancer cases were obtained from the population based cancer registry in Brunei Darussalam for the study period of 2011 to 2015. Adjusted multiple primaries method was applied to calculate a standardised estimate of lifetime risk of developing cancers. **Results:** The lifetime risk of being diagnosed with a type of malignant cancer is 28.0% or 1 in 4. The risk is 26.5% or 1 in 4 for men, and 29.2% or 1 in 3 for women. We found that at 5.0%, colorectal cancer poses the highest lifetime risk among men in Brunei Darussalam. This was followed by lung (4.5%) and prostate (3.7%) cancer. In women, the lifetime risk of developing breast cancer was 6.3%, colorectal cancer was 4.5% and cervical cancer was 1.8%. **Conclusion:** This study found significant population based lifetime risk of cancer in Brunei Darussalam; 1 in 4 Bruneians are at risk of being diagnosed with cancer at some point in his or her lifetime.

**Keywords:** Cancers, Lifetime risk, Malignant neoplasm, Population registers, Risk assessments.

## INTRODUCTION

Brunei Darussalam has observed a shift in disease pattern from predominantly communicable diseases to non-communicable diseases over the past decades. Since 2009, the leading causes of death in Brunei have been cancer-related.<sup>1</sup> Economic burden of

cancer has been found to be substantial and is expected to increase significantly in the future due to population growth, increased life expectancy, ageing population, and rising costs of cancer treatment.<sup>2</sup> Healthcare services in Brunei Darussalam is currently provided free by the government, however, increasing economic burden of cancer and other non-communicable diseases has been a concern in term of the sustainability of the free healthcare services.

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This study is conducted to estimate

the lifetime risk of being diagnosed with malignant cancer in Brunei Darussalam. It aims to provide the overall lifetime risk of cancer in the population, by gender and for the most frequent cancers affecting men and women. The findings of the study will be relevant to the policy planners to evaluate cancer burden, to allocate resources for cancer preventive and control measures, to communicate cancer risk to the population to raise awareness on cancer risk, and encourage the population to exercise cancer preventive measures in the daily life.

## METHODS

### Data extraction

De-identified cancer data of Bruneians which included Brunei citizens and permanent residents were obtained from the Brunei Darussalam Cancer Registry (BDCR). BDCR is a population-based cancer registry in the Ministry of Health, Brunei Darussalam.<sup>3</sup> Data obtained for the study consisted of age, date of diagnosis, gender, disease codes using International Classification of Diseases 10<sup>th</sup> Revision (ICD-10), ICD-O topography and morphology codes, and the date of death. The data obtained were from malignant cancer cases registered in BDCR for the period 2011 to 2015. Sources of data for the BDCR included clinical reporting, histology and cytology reports and also the death registry. The specific cancer deaths were identified by the documented underlying cause of death based on ICD-10. Analyses of cancer site-specific incidence data were made using population census denominators obtained from the Department of Economic Planning and Development; population-based mortality data were obtained from the Death Registry of the Department of Immigration and National Registration.

### Lifetime risk Calculation

The calculation of lifetime risk of cancer is an estimation of the risk or probability that a

person may develop or being diagnosed with a type of cancer at some point during his or her life. Lifetime risk is calculated based on data of cancer incidence and deaths, deaths from all causes, and populations by gender and age groups. Lifetime risk is usually expressed as a percentage or the probability or odds of developing cancer during his or her lifetime, e.g. 20%, or 1 in 5.<sup>4,5</sup>

There are several methods of calculating lifetime risk namely cumulative risk, current probability, and the Adjusted Multiple Primaries methods.<sup>4</sup> For this study, the Adjusted Multiple Primaries (AMP) method is used. The method corrects for the inclusion of multiple primary cancers in the cancer incidence rates and provides a more accurate estimate of lifetime risk compared to more commonly used measures based on the average number of events. It requires the population numbers, all-cause mortality, site/group-specific cancer incidence and site/group-specific cancer mortality.<sup>6</sup> AMP method is applied for our study, it is a new method to estimate lifetime risk by adjusting for multiple primaries thus lowering the overestimation of risk based on other methods. There are assumptions made during the calculations such as assuming that the current rates, within each age group, will remain constant throughout the period of risk estimation.

This paper focused on estimating the lifetime risk for the three most frequent cancers affecting men and women from 2011 to 2015 in Brunei. For men, the most common malignant cancers were lung, colorectal and prostate. For women, these were breast, colorectal and cervical cancers.

The template for AMP calculation was downloaded from the Cancer Research UK site<sup>6</sup> and is calculated as follows using data in age bands:

For age group,  $i$ ,

$M_i$  denote the yearly number of deaths (all-

cause mortality);  
 $D_i$  denote the yearly number of cancer deaths (cancer mortality);  
 $R_i$  denote the yearly number of (registered) cancer cases;  
 $N_i$  denote the size of the mid-year population.

The estimated lifetime risk<sup>8</sup> is defined as:

$$\sum_{i=1}^f \frac{R_i}{R_i + M_i - D_i} \hat{S}_0^*(a_i) \times \left\{ 1 - \exp\left(-\frac{w_i}{N_i}(R_i + M_i - D_i)\right) \right\}$$

where at the  $i$ 'th interval is from  $a_i$  to  $a_{i+1}$ ,  $w_i=(a_{i+1}-a_i)$  and  $f$  is the final age group, and

$$\hat{S}_0^*(a_i) = \exp\left[-\sum_{j=1}^{i-1} \frac{R_j + M_j - D_j}{N_j}\right]$$

For this study, parameters  $M_i$ ,  $D_i$ ,  $R_i$  and  $N_i$  are based on their total values obtained from year 2011 to 2015.

## RESULTS

A total of 2,778 cases of malignant cancers among Bruneians were registered in BDCR during the study period from 2011 to 2015. Of these, 1,161 (42%) cases were men and 1,617 (58%) cases were women.

Table 1 shows a summary table of overall lifetime risk of any malignant cancers, and the 3 most common cancers by genders. The lifetime risk of being diagnosed with any cancer for both genders was 28.0% (1 in 4),

or 29.15% (1 in 3) among women and 26.49% (1 in 4) among men.

### Common cancers in men

Table 2 shows the lifetime risks of men diagnosed with the most frequent cancers (colorectal, lung and prostate) by age groups during the period 2011 to 2015.

### Colorectal cancer

Among men, 230 were diagnosed with colorectal cancer, with 109 deaths giving a lifetime risk of 1 in 20 men or 5.02%. The incidence peaks at the 55-59 age group with 42 malignant cases, the youngest case was in the age group of 10-14 years old.

### Lung cancer

There were 153 cases of lung cancer in men with 131 deaths recorded, and the lifetime risk was 4.54% or 1 in 22 men. The incidence peaks at the age group of 70-74 with 21 malignant cases with the youngest age being in the 25-29 years old age group.

### Prostate cancer

There were 101 cases with 60 deaths recorded for prostate cancers. The overall lifetime risk of being diagnosed with prostate cancer was 3.70% or 1 in 27. The youngest being diagnosed in the 40-44 age group, the numbers steadily increased with age, and highest number recorded in the 70-74 age group (27 cases).

**Table 1: Lifetime risk by gender and cancer types 2011-2015.**

Gender	Cancer	CR per 100,000 populations	ASR per 100,000 populations	Lifetime Risk (%)	Lifetime Risk (1 in x persons)
<b>Overall</b>	<b>All cancers</b>	172.90	240.95	28.00	4
<b>Male</b>	<b>Colorectal</b>	28.80	42.63	5.02	20
	<b>Lung</b>	19.16	32.22	4.54	22
	<b>Prostate</b>	12.65	24.18	3.70	27
	<b>All cancers</b>	144.11	222.64	26.49	4
<b>Female</b>	<b>Breast</b>	48.29	58.94	6.29	16
	<b>Colorectal</b>	24.14	32.85	4.47	22
	<b>Cervical</b>	18.51	20.33	1.78	56
	<b>All cancers</b>	201.66	258.54	29.15	3

CR=Crude Rate of cancer incidence; ASR= Age-Standardised Rate of cancer incidence

**Table 2: Lifetime risk of common cancers among men 2011-2015**

Age group	Ni	Mi	Type of cancer											
			Colorectal Cancer				Lung Cancer				Prostate cancer			
			Di	Ri	AMP method (%)	Current Probability (%)	Di	Ri	AMP method (%)	Current Probability (%)	Di	Ri	AMP method (%)	Current Probability (%)
0-4	73,174	193	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
5-9	81,749	19	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
10-14	88,137	21	0	1	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
15-19	86,945	34	1	2	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
20-24	80,250	72	0	1	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
25-29	68,971	87	0	2	0.0	0.0	0	1	0.0	0.0	0	0	0.0	0.0
30-34	59,908	100	1	5	0.0	0.0	3	3	0.0	0.0	0	0	0.0	0.0
35-39	50,479	121	1	8	0.1	0.1	2	1	0.0	0.0	0	0	0.0	0.0
40-44	45,353	173	8	15	0.2	0.2	6	6	0.1	0.1	0	2	0.0	0.0
45-49	42,031	229	11	17	0.2	0.2	4	10	0.1	0.1	1	1	0.0	0.0
50-54	38,444	269	11	29	0.3	0.3	17	17	0.2	0.2	1	1	0.0	0.0
55-59	30,610	281	16	42	0.6	0.6	10	15	0.2	0.2	4	4	0.1	0.1
60-64	19,214	288	13	31	0.6	0.7	10	17	0.4	0.4	1	6	0.1	0.1
65-69	12,681	308	10	23	0.7	0.7	13	16	0.5	0.5	6	12	0.3	0.3
70-74	9,103	348	13	23	0.8	0.8	18	21	0.7	0.7	19	27	0.9	0.9
75-79	6,084	391	6	10	0.4	0.4	20	16	0.6	0.6	14	21	0.8	0.8
80-84	3,590	329	10	13	0.6	0.6	13	16	0.7	0.7	10	21	0.9	1.0
85+	1,994	361	8	8	0.6	0.6	15	14	1.0	1.0	4	6	0.4	0.4
Total	798,716	3,624	109	230			131	153			60	101		
<b>Lifetime risk (%)</b>					5.02	5.11			4.54	4.56			3.70	3.76
<b>Lifetime risk (1 in X)</b>					19.92	19.55			22.04	21.94			27.07	26.60

Ni=total population; Mi=number of deaths (all causes); Di=number of cancer deaths; Ri=number of registered cancer cases. AMP= Adjusted Multiple Primaries

**Common cancers in women**

Table 3 shows the lifetime risks of women diagnosed with the most frequent cancers (breast, colorectal and cervical) by age groups during the period 2011 to 2015.

**Breast cancer**

6.29% or 1 in 16 women are at risk of being diagnosed with breast cancer during her lifetime. There were 386 cases of malignant breast cancer and 121 deaths recorded during the study period. The number increased with age from the youngest in 20-24 age group, and peaked at the 50-54 age group (70 cases).

**Colorectal cancer**

The lifetime risk was 1 in 22 Bruneian women

or 4.47%, there were 193 cases diagnosed with 89 deaths recorded during the study period. The youngest patient was diagnosed in the 20-24 age group, highest incidence (26 cases) was among the 55-59 age group.

**Cervical Cancer**

1 in 56 Bruneian women or 1.78% have the risk of developing malignant cervical during her lifetime. There were 148 cases with 46 deaths recorded. The highest number of cases was at the 35-39 age group (33 cases) and the youngest patient was in the 20-24 age group.

**DISCUSSION**

The study revealed that approximately 1 in 4



**Table 3: Lifetime risk of common cancers among women 2011-2015**

Age group	Ni	Mi	Type of cancer											
			Breast Cancer				Colorectal Cancer				Cervical cancer			
			Di	Ri	AMP method (%)	Current Probability (%)	Di	Ri	AMP method (%)	Current Probability (%)	Di	Ri	AMP method (%)	Current Probability (%)
0-4	68,100	135	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
5-9	76,679	22	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
10-14	81,043	15	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
15-19	82,464	24	0	0	0.0	0.0	0	0	0.0	0.0	0	0	0.0	0.0
20-24	76,593	28	0	1	0.0	0.0	0	2	0.0	0.0	0	2	0.0	0.0
25-29	69,046	44	3	5	0.0	0.0	1	5	0.0	0.0	1	13	0.1	0.1
30-34	61,216	68	1	16	0.1	0.1	3	12	0.1	0.1	4	15	0.1	0.1
35-39	54,084	57	7	21	0.2	0.2	2	10	0.1	0.1	4	33	0.3	0.3
40-44	51,703	127	10	43	0.4	0.4	5	9	0.1	0.1	6	24	0.2	0.2
45-49	46,429	139	18	56	0.6	0.6	8	18	0.2	0.2	4	21	0.2	0.2
50-54	41,634	185	28	70	0.8	0.8	9	22	0.2	0.2	7	12	0.1	0.1
55-59	32,786	216	19	64	0.9	0.9	10	26	0.4	0.4	6	9	0.1	0.1
60-64	21,487	225	8	43	0.8	0.9	11	24	0.5	0.5	6	9	0.2	0.2
65-69	12,509	247	8	32	1.0	1.0	9	19	0.6	0.6	1	3	0.1	0.1
70-74	10,434	285	8	18	0.6	0.6	6	14	0.5	0.5	6	5	0.2	0.2
75-79	7,172	392	5	9	0.4	0.4	7	13	0.5	0.5	0	1	0.0	0.0
80-84	3,550	342	2	4	0.2	0.2	10	9	0.5	0.5	0	0	0.0	0.0
85+	2,429	395	4	4	0.3	0.3	8	10	0.8	0.8	1	1	0.1	0.1
Total	799,361	2,946	121	386			89	193			46	148		
<b>Lifetime risk (%)</b>					6.29	6.45			4.47	4.54			1.78	1.79
<b>Lifetime risk (1 in X)</b>					15.90	15.50			22.38	22.04			56.15	55.78

Ni=total population; Mi=number of deaths (all causes); Di=number of cancer deaths; Ri=number of registered cancer cases. AMP= Adjusted Multiple Primaries

Bruneians (1 in 3 women and 1 in 4 men) is at risk of being diagnosed with a type of malignant cancer during his or her lifetime. The rates in other industrialised countries are: 1 in 10 men and 1 in 9 women in Malaysia<sup>7</sup>, 1 in 4 men and 1 in 5 women in Singapore,<sup>8</sup> 1 in 2 in the United Kingdom,<sup>9</sup> 1 in 3 in the United States<sup>10</sup>.

In Brunei, cancer cases started to increase from young age with significant proportion of cancer cases found among those aged 30-39, incidence peaked at 50 for female breast cancer and 55 for colorectal cancer for both genders (Table 1 and 2).

Worldwide, lung cancer is the most common diagnosed cancer with about 17 per-

cent of all cancers in men was lung cancer.<sup>11</sup> Several studies indicated that the incidence for lung cancer was higher in countries with very high Human Development Index (HDI) and economically developing countries.<sup>11,12</sup> In Table 4, the lifetime cancer risk in Brunei was lower (1 in 22) than the lifetime risks found in the United Kingdom (1 in 13), the United States (1 in 14), but higher than Malaysia (1 in 55) and Singapore (1 in 30). Smoking, passive smoking and air pollution have been found to increase the risk of lung cancer.<sup>13,14</sup> Tobacco control and early screening using low dose CT scan for those at higher risk have been found to reduce mortality due to lung cancer.<sup>15</sup>

Table 4 shows that Brunei recorded

**Table 4. Lifetime risks of common cancer in Brunei and in selected countries.**

Country	Men lifetime risk of developing cancer			Women lifetime risk of developing cancer		
	Colorectal	Lung	Prostate	Breast	Colorectal	Cervical
<b>Brunei</b>	5.0% (1 in 20)	4.5% (1 in 22)	3.7% (1 in 27)	6.3% (1 in 16)	4.5% (1 in 22)	1.8% (1 in 56)
<b>Malaysia<sup>7</sup></b>	1.8% (1 in 56)	1.8% (1 in 55)	0.9% (1 in 117)	3.4% (1 in 30)	1.3% (1 in 74)	0.9% (1 in 116)
<b>Singapore<sup>8</sup></b>	3.9% (1 in 26)	3.3% (1 in 30)	3.1% (1 in 32)	6.8% (1 in 15)	2.8% (1 in 36)	0.7% (1 in 137)
<b>UK<sup>9</sup></b>	7.3% (1 in 14)	7.7% (1 in 13)	13.7% (1 in 8)	13.0% (1 in 8)	5.5% (1 in 19)	0.8% (1 in 133)
<b>USA<sup>10</sup></b>	4.5% (1 in 22)	6.8% (1 in 15)	11.6% (1 in 9)	12.4% (1 in 8)	4.2% (1 in 24)	0.6% (1 in 161)

the highest lifetime risk for cervical cancer among the countries. The lifetime risk was lower in the other high income countries and likely due to several reasons including the availability of organised national screening program in 1988 in the United Kingdom and introduction of the Papanicolaou test in the United States in the mid-20th century.<sup>16,17</sup> Human Papilloma Virus (HPV) was reported as one of the most important risk factors in the development of cervical cancer.<sup>18</sup>

In Brunei, organised national cervical cancer screening programme was initiated in 2011 and HPV vaccination has been provided free of charge to female adolescents in year 7 of secondary school girls since 2012. Future studies will be useful to evaluate the impact of HPV vaccination on the trend of cervical cancer and to investigate possible risk factors which contributed to the higher lifetime risk of cervical cancer in Brunei, such as study on the impact of passive smoking<sup>19</sup> in view of the high adult smoking prevalence in Brunei (36% in men and 4% in women).<sup>20</sup>

The lifetime risk of breast cancer among Brunei women (Table 4) was lower than Singapore, the United Kingdom and the United States, but higher than Malaysia. Studies in the developed countries have found risk factors that contributed to the development of breast cancer, these include genes, obesity, childbearing, breastfeeding, physical inactivity, diet, alcohol, smoking, and

the use of hormonal replacement therapy.<sup>21,22,23</sup>

For colorectal cancer, the lifetime risks (Table 4) for both genders in Brunei were lower than Singapore and the United Kingdom. In Brunei, highest proportion of colorectal cancer cases were diagnosed among the age group 55-59 for both men and women. For prostate cancer, the lifetime risk of developing cancer in Brunei is lower than United States and United Kingdom but higher than Singapore (Table 4). The incidence of prostate cancer for men in Brunei was highest among age groups 70 years and above (Table 1).

Westernized or fast food diet (inadequate fruits and vegetables intake, and over consumption of meat and/or processed meats) and physical inactivity have been found to contribute to the development of many common cancers including colorectal and prostate cancers.<sup>24,25,26,27</sup> A recent national health survey found that a significant proportion of adult Bruneians have obesity (28.2%), inadequate consumption of fruits and vegetable (91.7%), physical inactivity (25.3%) and were smoking (19.9%).<sup>20</sup> If the risk factors (obesity, unhealthy diet and tobacco smoking) remain prevalent, cancer incidences in Brunei are likely to increase over the next few years with ageing population unless effective intervention is implemented to reduce the risk factors.

The availability of organized national health screening programme for targeted cancers has contributed to better pick up rates of cancer such as increase in the detection of ductal carcinoma in mammography<sup>28</sup> and early detection of colorectal cancer.<sup>29</sup> In Brunei Darussalam, several cancer prevention and control initiatives have been rolled out, such as the national screening programme for cervical cancer, national vaccination programme for HPV and Hepatitis B. Currently, colorectal and breast cancer screening are provided opportunistically in the healthcare institutions in Brunei, an organised national screening programme is recommended to enhance early detection and treatment of colorectal and breast cancer.

### **Strength of the study**

De-identified data on malignant cancer from the population-based cancer registry were captured from various sources including clinicians, laboratory and death registry. All deaths in Brunei Darussalam are reported, with the causes of deaths recorded. Under the Births and Deaths Registration Act, not reporting any death is an offence, enforcement is feasible due to the small geographical size and population of the country. The introduction of electronic medical record system in Brunei Darussalam, Brunei Darussalam Health Information Management System (BruHIMS), has allowed for electronic record of all registered patients encounters. In addition, the establishment of a national cancer centre, The Brunei Cancer Centre (TBCC), as the national referral centre for all malignant cancer cases have significantly improved cancer surveillance and comprehensive coverage of the national cancer registry.

Primary tumours diagnosed in each individual were captured and recorded by the national cancer registry and thus reducing the possibility of overestimation of lifetime risk. In addition, reliable population census data was used as denominators for this study. The

population-based cancer registry database has enabled analysis of cancer data by age groups and gender.

The strengths of the AMP method are that it takes the competing risk of death into account and corrects for all the primary tumours that arise in each individual. Therefore, unlike other methods, the AMP method tends to not overestimate lifetime risk for malignant cancers.

### **Limitations**

The lifetime risk calculation was based on cross-sectional age-specific cancer incidence, deaths and the all-cause mortality rates in the particular year cohort. This is assuming that age-specific cancer rates and all-cause mortality rates were stable over a long period of time. In addition, the time period and methods used in estimating lifetime risk from the other countries are not exactly the same as this study; hence direct comparison of figures should be interpreted with cautions.

The lifetime risk estimation method assumes that mortality rates due to conditions other than cancers are the same as those without cancer in the general population; and the risk of developing cancer is also the same in those who have never previously had cancer in the general population.<sup>4</sup> Other risk factors e.g. smoking and other lifestyle factors are likely to affect the incidence rates of some cancers and the death rates due to non-cancers such as cardiovascular diseases.

Lifetime cancer risk estimations in many developing countries are limited due to low screening rate, under diagnosis and reporting of cancers, which could contribute to underestimates of cancer incidence, particularly in the less developed countries.<sup>30</sup>

### **CONCLUSION**

The study revealed that the 1 in 4 Bruneians

(1 in 3 women or 1 in 4 men) was at risk of getting a type of malignant cancer during his or her lifetime. Estimates of lifetime risks of common cancers in Brunei Darussalam were relatively high and comparable with populations from industrialised countries. Cancer prevention and control initiatives should be strengthened in the areas of primary prevention and screening for early detection and management. The finding is relevant to policy planners and also healthcare professionals working in primary and secondary care, in planning for prevention measures, health messages, and capacity building; and in identifying target age groups for preventive measures and adopting healthy lifestyle. Communicating lifetime risks should be done in layman terms so that both healthcare providers and the public can step up preventive measures to reduce cancer risks.

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### DISCLOSURE

All authors have contributed to the manuscript equally. None of the authors have direct or financial conflicts of interest with this paper and material contained herein.

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