The Future Excess Fraction of Cancer Due to Lifestyle Factors in Australia

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Abstract

Background: Many cancers are caused by exposure to lifestyle, environmental, and occupational factors. Earlier studies have estimated the number of cancers occurring in a single year which are attributable to past exposures to these factors. However, there is now increasing appreciation that estimates of the future burden of cancer may be more useful for policy and prevention. We aimed to calculate the future number of cancers expected to arise as a result of exposure to 23 modifiable risk factors.

Methods: We used the future excess fraction (FEF) method to estimate the lifetime burden of cancer (2016-2098) among Australian adults who were exposed to modifiable lifestyle, environmental, and occupational risk factors in 2016. Calculations were conducted for 26 cancer sites and 78 cancer-risk factor pairings.

Results: The cohort of 18.8 million adult Australians in 2016 will develop an estimated 7.6 million cancers during their lifetime, of which 1.8 million (24%) will be attributable to exposure to modifiable risk factors. Cancer sites with the highest number of future attributable cancers were colon and rectum (n=717,700), lung (n=380,400), and liver (n=103,200). The highest number of future cancers will be attributable to exposure to tobacco smoke (n=583,500), followed by overweight/obesity (n=333,100) and alcohol consumption (n=249,700).

Conclusion: A significant proportion of future cancers will result from recent levels of exposure to modifiable risk factors. Our results provide direct, pertinent information to help determine where preventive measures could best be targeted.

Keywords: cancer, lifestyle factors, prevention, risk factors

1.1 Introduction

Cancer is a leading public health concern with a significant social and economic impact. It accounted for approximately 18% of the total disease burden in Australia in 2019 [1], with 145,000 cases estimated to have been diagnosed in 2020 [2]. A high proportion of these cancers are caused by exposure to lifestyle, and occupational factors [3]. Many of these factors are modifiable, meaning that the future number of cancers in our society could be reduced by minimising or, where possible, eliminating these exposures.

Historically, the most common approach to estimating the number of cancers caused by various risk factors has been the population attributable fraction (PAF) approach. This method is generally used to estimate the proportion of cancer cases occurring in a single year which is attributable to past exposures [4]. In Australia, previous studies have estimated that 32% - 44% of the cancer burden in a single year was attributable to lifestyle exposures [5-7]. This is comparable to estimates from other countries, including the United Kingdom (UK; 38% of cases in 2015) [8], United States (US; 42% of cases in 2014) [9] ,and Canada (41% of cases in 2012) [10].

There is now increasing appreciation that estimates of the future burden of cancer – that is, the number of cancer cases which might occur in the future as a result of current exposures – may be more useful for policy and prevention than estimates based on past cancer incidence and exposure [11]. A growing body of work has estimated the future burden of cancer using various methods, including work in Canada [12] and the UK [13]. In Australia, variations on the PAF method have been used to predict future cancers attributable to lifestyle exposures. For example, Laaksonen and colleagues used pooled cohort data to estimate the PAF of various cancers due to modifiable factors over 10 years (from 2017-2026) [14-16]. They found that smoking, overweight and obesity, and alcohol consumption contributed the highest number of cancers during that period [17]. In an alternative approach, Wilson and colleagues used a dynamic simulation model incorporating latency estimates to predict future cancers attributable to lifestyle factors over a 25 year period (2013-2037) [18, 19]. They estimated that 7-13% of weight-related cancers were attributable to overweight and obesity, 5-9% of activity-related cancers were attributable to physical inactivity, and 1-6% of alcohol-related cancers were attributable to alcohol consumption.

While these studies represent a valuable contribution to the literature, those previous estimates predicted the burden of cancer over finite periods of time extending into the future. An alternative approach, the future excess fraction (FEF) method, estimates the excess number of exposure-related cancers occurring over the lifetime of a population [20]. The FEF method is an extension of the lifetime risk approach [21, 22] and uses a life table to account for competing risks. This method provides an estimate of the proportion of future cancers in those members of a cohort who were exposed in a given year, and enables estimation of the future burden of cancer under current and hypothesised future scenarios [20].

The current study aims to estimate the future number of cancers resulting from recent levels of exposure to a comprehensive list of 23 modifiable lifestyle, environmental, and occupational risk factors.

1.2 Methods

We used the FEF method to estimate the lifetime burden of cancer resulting from recent levels of exposure to 23 modifiable factors among the 2016 Australian adult population. These risk factors were chosen based on evidence of a strong causal association with at least one cancer (according to the World Cancer Research Fund (WCRF; convincing or probable) or International Agency for Research on Cancer (IARC; Group 1 sufficient)) and availability of reliable Australian exposure prevalence data. The risk factors we examined are summarised in Table 1. In total, calculations were conducted for 26 different cancer sites and 78 cancer-risk factor combinations.

1.2.1 Data sources

The population of interest (or cohort) for this study was defined as the adult population (aged 18 and over) of Australia in 2016. The index year of 2016 was chosen as this was the most recent Census year [23]. The lifetime of the cohort was estimated to 2098, as this was the year in which the youngest in the cohort (those aged 18 in 2016) would turn 100.

We first constructed a series of life tables showing the probability that an individual of each age between 18 and 100 in 2016 would be alive at each future age over the lifetime of the cohort. We used double decrement life tables which adjusted for the competing probabilities of death from any cause (using life expectancy from Australian Bureau of Statistics (ABS) life tables) [24] as well as occurrence of the cancer of interest (using cancer incidence statistics from Australian Institute of Health and Welfare (AIHW)) [2]. Life tables were constructed separately by cancer site and sex, resulting in the creation of 47 such tables (21 cancer sites for both male and female plus five sex-specific cancer sites). The number of person-years at risk for the cohort (to 2098) were calculated by multiplying these life tables by the 2016 mid-year population statistics by sex and 5-year age group. Person-years at risk were calculated separately for each cancer site.

1.2.1.1 Exposure prevalence estimates

Information concerning the prevalence of exposure to each of the risk factors was collated from nationally representative data, including National Health Surveys (NHS) and surveillance reports. We used the most recent accurate data by sex and five-year age group available. Where sample weights were available (i.e. NHS [25], occupational exposures [26], breastfeeding [27] and menopausal hormone therapy (MHT) [28]), prevalence estimates were weighted to the 2016 adult population. For other data sources (e.g. infections), prevalence was extrapolated to the population by multiplying the proportion of the sample exposed by the number of adults in the 2016 Australian population.

Extrapolations were conducted separately by sex and age group. Sources of prevalence data are outlined in Table 1.

Exposures measured on a continuous scale (i.e. alcohol consumption, physical inactivity, fibre intake, red and processed meat consumption) were grouped into categories based on the range of values. We extracted the proportion of the population (by age group and sex) in each category of exposure, as well as the median value of each category. We used body mass index (BMI) to categorise the population into normal weight (BMI <25 kg/m^2), overweight (BMI 25<30 kg/m^2) and obese (BMI ≥30kg/m^2). Occupational exposures (including radiation) were divided into high and low exposure based on values provided in the prevalence data.

For insufficient breastfeeding, exposure was grouped by average number of months breastfeeding per child for parous women only (<1 through to 5 months; six groups total). Parous women with an average of six or more months breastfeeding per child were classified as unexposed, and the burden of breast cancer attributable to breastfeeding was calculated for parous women only (i.e. only parous women contributed person-years). For MHT, exposure (and therefore risk) is in postmenopausal women only; therefore the burden attributable to MHT use was calculated for postmenopausal women only (i.e. only postmenopausal women contributed person-years). A similar approach was taken for other combinations of cancer type and risk factor (e.g. overweight/obesity and breast cancer) where the association has been established for postmenopausal women only. The risk of breast cancer associated with combined oral contraceptive (OCP) use has been established for young women (aged under 35 years) only; therefore, only those women who were younger than 35 in the index year (2016) contributed person-years in this analysis.

1.2.1.2 Relative risk estimates

Risk estimates for each of the 78 combinations of cancer type and risk factor were sought from the literature (see Supplementary Table S1). Estimates derived from populations as similar as possible to Australia using definitions of exposure which accorded with those used in the prevalence data were obtained, with preference given to meta-analyses and estimates adjusting for the effects of known confounding factors. For estimates reported as dose-response (i.e. alcohol consumption, red and processed meat consumption) the risk estimates were converted to a common scale following the WCRF methods [29]. To do so, we assumed a log-linear relationship between exposure and risk, as follows:

$$Risk\ per\ unit\ increase = ln(RR_x)/x$$

where the original risk estimate (RR_x) was presented per x units.

Estimates presented as protective against cancer (i.e. breastfeeding, physical inactivity, dietary fibre intake) were converted to risk per unit deficit from target or optimal levels using the following formula:

$$Increase\ in\ risk\ per\ unit\ deficit = (ln(1/RR_x)/x$$

where the original risk estimate (RR_x) was presented per x units (Supplementary Table S1).

Risk estimates for each y exposure category (RR_y) were derived by taking the exponential of the product of the risk per unit (as calculated above) and the median value of each category (M_y), as follows:

$$RR_y = exp(risk\ per\ unit \times M_y)$$

For overweight/obesity, we used the risk estimates for an increase of 5kg/m^2 for the 'overweight' category (BMI 25<30kg/m^2) and the square of this value for the 'obese' category (BMI ≥30kg/m^2) (see also Supplementary Table S1). For occupational exposures, we assumed no excess risk (i.e. RR=1.0) where no risk estimate for low level exposure was available.

1.2.1.3 Cancer incidence

To estimate the future number of cancers in the cohort, we used cancer incidence projections available from AIHW [30]. These projections are available to the year 2020; for projections from 2021 to 2098, we used the 2020 incidence rate multiplied by the ABS population projections by age and sex [31] (i.e. assuming constant incidence rates). Where AIHW projections to 2020 were not available (e.g. for cancer sites including larynx and oral cavity), we multiplied the 2015 age- and sex-specific cancer incidence rates [2] by the ABS population projections [31]. Incidence was projected for each of the 26 cancer sites separately by sex.

In some cases, associations with risk factors are established for cancer subtypes rather than the cancer site as a whole (see Table 1). As incidence data were not available by cancer subtype, incidence counts were apportioned accordingly. For cervical cancer, the association with tobacco smoke has been established for squamous cell carcinoma (SCC) only; therefore, we divided the cervical cancer incidence according to the AIHW Cervical Screening Report 2014-15 [32]. For prostate cancer, the association with overweight/obesity is only established for advanced stage cancer (stages 3-4); data were apportioned according to Cancer Australia data on stage at diagnosis [33]. Incidence of oesophageal (adenocarcinoma versus SCC) and stomach cancer (cardia versus non-cardia) subtypes were divided according to analyses of the GLOBOCAN database [34, 35], while ovarian (mucinous versus nonmucinous) cancer incidence was divided according to a 2016 international review [36]. The association between *Helicobacter pylori* and non-Hodgkin lymphoma has been established for gastric mucosa-associated lymphoma tissues (MALT) only; incidence data were divided according to international data [37]. Finally, incidence data were only available for uterine cancer rather than endometrial cancer specifically; following the approach of previous studies [38], all uterine cancers were assumed to be endometrial.

For breast cancer, associations vary by menopausal status and parity. As menopausal status is not available in incidence data, we based age at menopause on the average age at menopause in Australia

(age 50) obtained from two cohorts, the Melbourne Collaborative Cohort Study [39] and the Australian Longitudinal Study on Women's Health [40]. Parity was based on the results of two large pooled studies which found that 16% of breast cancer cases occur in nulliparous women [41, 42]. The overall breast cancer incidence was then divided accordingly. Similarly, the link between OCP use and breast cancer is established for young women (aged under 35) only; we therefore divided the overall breast cancer incidence accordingly.

1.2.2 Statistical analyses

We used the FEF method to estimate the proportion of future cancers which will occur among the 2016 Australian adult population who were exposed to lifestyle, environmental, and occupational risk factors. This method has previously been described in detail [20, 43].

As a first step, the general lifetime risk (LR_P) of each cancer in the 2016 Australian adult population (the cohort), irrespective of exposure, was calculated by dividing the product of the estimated person-years at risk and age- and sex-specific cancer incidence rates by the number of people in the cohort (N_P). All calculations were conducted separately by sex and cancer site.

We then calculated the excess lifetime risk of each cancer due to exposure (LR_x) using the following formula:

$$LR_x = \frac{LR_P \times N_P \times (RR - 1)}{N_P + \left(N_e \times (RR - 1)\right)}$$

where $LR_P \times N_P$ is the number of expected cancers in the population; $RR - 1$ is the excess risk of cancer associated with exposure; and N_e is the number of people exposed to the risk factor. The future excess number of cases (FEN) was calculated by multiplying LR_x by N_e. Where multiple levels or categories of exposure were present, these calculations were conducted separately by exposure level and then summed to give an overall FEN for that cancer-risk factor combination. Future excess fractions (FEFs) were calculated by dividing the FEN by the total expected number of cases in the population regardless of exposure ($LR_P \times N_P$).

These calculations were conducted separately for each cancer-risk factor combination. To obtain a combined FEF for each cancer, adjusting for simultaneous exposure to more than one risk factor, the FEFs were combined across exposures by taking the complement of the product of complements [4]. In this method, for each risk factor k, the complement of the FEF was taken (i.e. 1-FEF$_k$). The resulting fractions were multiplied together, with the complement of these being the FEF$_{combined}$ (i.e. 1 - Π(1-FEF$_k$)$_k$). This method avoids double counting cancers that can be attributed to more than one exposure. The FEF$_{combined}$ was then multiplied by the number of expected cancers in the population ($LR_P \times N_P$) to obtain the combined FEN.

To determine the overall FEF of cancer attributable to lifestyle, environmental, and occupational risk factors, the combined FENs for each cancer site were summed to find the overall number of attributable cancers (over all cancer sites). This number was then divided by the sum of all expected cancers in the population (regardless of exposure) to obtain the overall FEF. We also followed this procedure to obtain an overall FEF separately by sex.

All analyses were undertaken using an R program we have written and which is available to other researchers on request.

Table 1. Modifiable risk factors considered in the current study, associated cancer sites, and sources of prevalence data

	Risk factor	Optimal exposure level	Source of exposure prevalence data	Associated cancer site(s)
	Alcohol consumption	Nil consumption	National Health Survey (NHS) 2014-15 [25]	Breast; colon and rectum; larynx; liver; oesophagus (SCC); oral cavity; pharynx; stomach
	Breastfeeding (insufficient)[a]	Average of 6+ months per child (parous women only)	Breast Cancer Employment and Environment Study (BCEES) 2009-11 [27]	Breast
	Overweight/obesity	Normal weight (BMI <25kg/m^2)	NHS 2014-15 [25]	Breast (postmenopausal); colon and rectum; endometrium; gallbladder; kidney; liver; oesophagus (AC); ovary; pancreas; prostate (stages 3-4); stomach (cardia)
	Physical inactivity[b]	≥30 MET-hours/week	NHS 2014-15 [25]	Breast (postmenopausal); colon; endometrium
	Tobacco smoke	Never smoker	NHS 2014-15 [25]	Bladder; cervix (SCC); colon and rectum; kidney; larynx; leukaemia; liver; lung; oesophagus; oral cavity; ovary (mucinous); pancreas; pharynx; stomach
Diet	Inadequate fibre[c]	≥30g/day for males; 25g/day females	NHS 2011-12 [44]	Colon and rectum
	Processed meat	Nil intake	NHS 2011-12 [44]	Colon; rectum
	Red meat[d]	≤65g/day	NHS 2011-12 [44]	Colon
Hormones	Combined oral contraceptives	Never use	NHS 2001 [45]	Breast; cervix; liver
	Menopausal hormone therapy	Never use	Velentzis et al, 2016 [28]	Breast; endometrium; ovary

Infection	*Helicobacter pylori*	No infection	Moujaber et al, 2008 [46]; Pandeya et al, 2011 [47]	non-Hodgkin lymphoma (gastric MALT); stomach (non-cardia)
	Hepatitis B virus	No infection	Kirby Institute Annual Surveillance Report 2017 [48]	Liver
	Hepatitis C virus	No infection	Kirby Institute Annual Surveillance Report 2017 [48]	Liver; non-Hodgkin lymphoma
	Human Immunodeficiency Virus (HIV)	No infection	Kirby Institute Annual Surveillance Report 2017 [48]	Anus; cervix; Hodgkin lymphoma; non-Hodgkin lymphoma
Occupation	Asbestos	No exposure	Australian Work Exposures Study (AWES) 2011-12 [26]	Larynx; lung; mesothelioma; ovary
	Benzene	No exposure	AWES 2011-12 [26]	Leukaemia (acute myeloid)
	Diesel engine exhaust	No exposure	AWES 2011-12 [26]	Lung
	Metals (arsenic, cadmium, chromium VI, nickel)	No exposure	AWES 2011-12 [26]	Lung; nasal
	Silica	No exposure	AWES 2011-12 [26]	Lung
	Trichloroethylene	No exposure	AWES 2011-12 [26]	Kidney
	Wood dust	No exposure	AWES 2011-12 [26]	Nasal; nasopharynx
Radiation (occupational)	Solar radiation	No exposure (or fully protected when exposed)	AWES 2011-12 [26]	Melanoma
	Ionising radiation	No exposure	AWES 2011-12[26]	Breast; leukaemia; lung; thyroid

AC: adenocarcinoma; MALT: mucosa-associated lymphoma tissue; SCC: squamous cell carcinoma

[a] Insufficient breastfeeding defined as breastfeeding for less than 6 months per child on average among parous women, in line with National Health and Medical Research Council (NHMRC) recommendations [49].

[b] Physical inactivity defined as less than 300 minutes of moderate intensity physical activity per week, based on Health Department recommendations [50]. This is equivalent to less than 30 MET-hours (metabolic equivalent of task-hours) per week.

[c] Inadequate fibre intake defined as less than 30g per day for males and less than 25g per day for females, in line with NHMRC recommendations [51].

[d] Risk associated with red meat consumption only modelled for consumption above Australian dietary guidelines (65g per day) [52].

1.3 Results

The cohort of Australian adults in 2016 comprised 9,219,712 males and 9,551,270 females (18,770,982 in total). An estimated 7,600,797 cancers were predicted to occur over their lifetime (4,233,308 cases in males and 3,367,489 in females).

Prevalence estimates weighted to the population are presented in Table 2. The prevalence of many modifiable risk factors approached or exceeded 50% of the Australian adult population, including alcohol consumption, physical inactivity, overweight and obesity, and inadequate fibre intake. Prevalence was generally higher in males than females.

The estimated numbers (FENs) and proportions (FEFs) for each cancer, adjusted for multiple exposures, are summarised in Table 3. Overall, for the cohort of Australian adults in 2016, we estimated that 24% (n=1,804,200) of all future cancers (registrations) will be caused by exposure to one or more of the modifiable risk factors listed in Table 1. A slightly higher proportion of future cancers was estimated to occur among males (25%) than females (22%; $p < .001$).

The cancer sites with the highest FEFs among males were colon and rectum (59%), liver (59%) and pharynx (54%) (Table 3). The highest FEFs among females were for cancers of the liver (58%), pharynx (45%) and endometrium (45%). Cancers with the highest FENs were colon and rectum (447,300), lung (226,500), and liver (64,500) for males, and colon and rectum (267,200), lung (153,600), and breast (83,200) for females. Across all cancer sites (with the exception of female sex-specific sites), the FEF was higher for males than females.

Table 4 presents the number of cases for each cancer site by risk factor. Overall, tobacco smoke will contribute the largest number of cancers (n=583,500), followed by overweight/obesity (n=333,100) and alcohol consumption (n=249,700). Results by sex show a similar pattern for the top three exposures (see Supplementary Tables S2 and S3), with a higher number of future attributable cancers in males than females. For overweight/obesity, however, the FEF is slightly higher among females (4.7%) than males (4.4%).

Physical inactivity also contributes more cancers for females (n=86,000; FEF=2.6%) than males (n=41,000; FEF=1.0%). Inadequate fibre intake contributes the fourth highest number of future cancer registrations in males (n=136,400; FEF=3.2%), while being ranked sixth overall for females (n=67,200; FEF=2.0%).

Table 2. Weighted prevalence (%) and 95% confidence intervals (CI) of modifiable risk factors by sex, adult population, Australia

Risk factor	Males (%, 95% CI)	Females (%, 95% CI)
Alcohol consumption [a]		
Non-drinker	36.7 (35.3-38.2)	52.2 (50.8-53.6)
>0 - 40 g/day	53.1 (51.5-54.6)	45.5 (44.1-46.9)
>40 g/day	10.2 (9.3-11.1)	2.2 (1.9-2.7)
Insufficient breastfeeding	-	60.3 (57.6-63.1) [b]
Parous women only	-	*48.0 (45.3-50.8)*
Overweight/obesity [c]		
Normal weight	42.4 (41.0-43.8)	53.2 (51.9-54.5)
Overweight	34.9 (33.6-36.2)	24.3 (23.2-25.4)
Obese	22.7 (21.6-23.9)	22.5 (21.4-23.6)
Physical activity [d]		
<300 minutes/week	64.5 (63.0-65.9)	72.2 (70.9-73.5)
≥300 minutes/week	35.5 (34.1-37.0)	27.8 (26.5-29.1)
Tobacco smoke		
Current smoker	18.2 (17.0-19.4)	12.8 (11.9-13.8)
Former/never smoker	81.8 (80.6-83.0)	87.2 (86.2-88.1)
Fibre intake [e]		
Inadequate	74.3 (72.7-75.7)	74.0 (72.6-75.4)
Adequate	25.7 (24.2-27.3)	26.0 (24.6-27.4)
Processed meat consumption [f]		
Any intake	42.9 (41.2-44.7)	35.4 (33.8-37.0)
No intake	57.1 (55.3-58.8)	64.6 (63.0-66.2)
Red meat consumption [g]		
≤65 g/day	63.4 (61.7-65.1)	72.7 (71.2-74.1)
>65 g/day	36.6 (34.9-38.3)	27.3 (25.9-28.8)
Combined oral contraceptive use		
Current use	-	12.5 (11.9-13.3)
Aged under 35 only	-	*18.9 (17.7-20.1)*
Menopausal hormone therapy (MHT) use [h]		
Current use of combined MHT	-	0.9 (0.8-1.1)
Postmenopausal women only	-	*2.2 (1.8-2.6)*

Current use of oestrogen-only MHT	-	1.6 (1.4-1.8)
Postmenopausal women only	-	*3.6 (3.1-4.1)*
Helicobacter pylori infection [i]	25.3 (19.4-28.1)	17.4 (13.0-19.2)
Hepatitis B infection [j]	1.4	1.1
Hepatitis C infection [j]	1.4	0.7
Human Immunodeficiency Virus (HIV) [j]	0.3	0.02
Occupational exposure [26]		
Arsenic (metal)	1.1 (0.8-1.5)	-
Asbestos	5.4 (4.6-6.3)	0.1 (0.0-0.3)
Benzene	13.5 (12.3-14.8)	5.1 (4.3-6.1)
Cadmium (metal)	0.4 (0.2-0.7)	0.04 (0.0-0.2)
Chromium VI (metal)	6.2 (5.3-7.1)	0.2 (0.1-0.4)
Diesel engine exhaust	28.6 (27.9-30.3)	6.0 (5.1-7.1)
Nickel	3.6 (3.0-4.4)	0.1 (0.0-0.4)
Silica	11.6 (10.5-12.9)	1.0 (0.7-1.5)
Trichloroethylene	1.6 (1.2-2.1)	0.2 (0.1-0.4)
Wood dust	9.6 (8.6-10.8)	0.7 (0.4-1.2)
Radiation exposure (occupational) [26]		
Ionising radiation	2.7 (2.2-3.4)	2.3 (1.8-3.0)
Solar radiation	37.0 (35.2-38.8)	7.9 (6.9-9.1)

[a] Note that 10 categories of alcohol consumption used in analysis; these are summary data. 40 g per day is equivalent to 4 standard drinks, the recommended maximum daily intake of alcohol according to NHMRC [53].

[b] Proportion of all adult females, includes non-parous adult females as having insufficient breastfeeding. Prevalence in parous women only was used in analysis; that is, burden was only calculated for parous women.

[c] Weight categories defined by body mass index (BMI), whereby normal weight BMI < 25 kg/m^2; overweight BMI $25 < 30$ kg/m^2; obese BMI ≥ 30 kg/m^2

[d] 5 categories of physical activity used in analysis. 300 minutes per week is the minimum recommended amount of moderate intensity physical activity per week for adults according to Health Department guidelines [50].

[e] 11 categories of fibre intake used in analysis. Inadequate fibre intake defined as less than 30 g per day for males and less than 25 g per day for females, in line with NHMRC recommendations [51].

[f] 4 categories of processed meat intake used in analysis.

[g] 5 categories of red meat intake used in analysis. 65 g is recommended maximum daily intake according to Australian dietary guidelines [52].

[h] Proportion of women aged 50-69 from Velentzis et al [28] applied to 2016 Australian adult female population (aged 18-100+).

[i] Prevalence estimated from rates presented in Moujaber et al [46] and Pandeya et al [47] applied to 2016 Australian adult population.

[j] Prevalence of hepatitis and HIV infection by sex estimated from rates presented in The Kirby Institute report [48]; no confidence intervals available.

Table 3. Estimated future excess fractions (FEF) and future excess numbers (FEN) arising from modifiable factors among the cohort of Australian adults in 2016, adjusting for multiple exposures, by sex and cancer site

Cancer site	Males		Females		Overall	
	FEF (%)	FEN[a]	FEF (%)	FEN[a]	FEF (%)	FEN[a]
Anus	6.3	800	0.7	100	3.2	900
Bladder	22.8	41,700	18.5	13,000	21.6	54,700
Breast	0.0	0	9.3	83,200	9.3	83,200
Cervix	0.0	0	10.6	4,200	10.6	4,200
Colon and rectum	58.8	447,300	39.0	267,200	49.7	717,700
Endometrium	0.0	0	44.6	78,800	44.6	78,800
Gallbladder	20.0	1,900	17.2	3,800	18.1	5,700
Hodgkin lymphoma	2.5	300	0.2	<100	1.5	300
Kidney	29.3	54,300	24.8	19,500	28.0	74,000
Larynx	47.7	20,800	39.4	2,400	46.7	23,200
Leukaemia	4.6	8,600	2.6	3,000	3.8	11,600
Liver	58.5	64,500	58.2	39,200	58.1	103,200
Lung	38.8	226,500	33.3	153,600	36.4	380,400
Melanoma of the skin [b]	1.0	7,000	0.1	500	0.7	7,500
Mesothelioma	26.0	21,100	0.1	<100	21.4	21,100
Nasal	11.0	600	0.2	<100	7.1	600
Nasopharynx	2.1	100	0.0	0	1.6	100
non-Hodgkin lymphoma	3.9	8,800	2.1	3,600	3.1	12,400
Oesophagus	52.5	48,400	37.7	18,000	47.5	66,400
Oral cavity	43.3	10,700	33.4	7,200	38.8	18,000
Ovary	0.0	0	5.9	6,500	5.9	6,500
Pancreas	18.3	23,600	14.7	22,400	16.4	46,000
Pharynx	54.0	8,500	45.1	2,300	52.3	10,900
Prostate	7.1	19,600	0.0	0	7.1	19,600
Stomach	38.1	38,800	32.2	17,900	36.0	56,800
Thyroid	0.0	0	0.0	<100	0.0	<100
Overall	24.9	1,054,100	22.2	746,500	23.8	1,804,200

[a] All numbers rounded to the nearest 100 to avoid a false sense of precision. Totals may not add up due to rounding and methods of adjusting for multiple exposures.

[b] This represents the future number and fraction of melanoma cases attributable to <u>occupational</u> solar radiation exposure only; the true fraction of avoidable melanoma cases is likely to be much higher.

Table 4. Estimated future excess numbers (FEN) arising from modifiable factors among the cohort of Australian adults in 2016, by risk factor and cancer site (including only those cancer sites with at least 500 attributable cases), shown in thousands

Risk factor	Colon and rectum (C18-C20)	Lung (C33-C34)	Breast (C50)	Liver (C22)	Endometrium (C54-C55)[a]	Kidney (C64)	Oesophagus (C15)	Stomach (C16)	Bladder (C67)	Pancreas (C25)	Larynx (C32)	Mesothelioma (C45)	Prostate (C61)	Oral cavity (C03-C06)	non-Hodgkin lymphoma (C82-C86)	Leukaemia (C92-C94)[b]	Pharynx (C10, C11, C13)	Melanoma of the skin (C43)	Ovary (C56)	Gallbladder (C23)	Cervix (C53)	Anus (C21)	Nasal (C30)	Total attributable registrations
Tobacco smoke	26.3	369.3	-	12.3	-	19.1	22.6	13.5	54.7	25.4	16.7	-	-	9.8	-	4.9	6.8	-	0.5	-	1.7	-	-	**583.5**
Overweight/obesity	60.8	-	28.0	39.2	53.5	59.2	26.7	12.6	-	22.7	-	-	19.6	-	-	-	-	-	5.1	5.7	-	-	-	**333.1**
Alcohol consumption	144.7	-	30.5	18.6	-	-	17.1	12.7	-	-	9.7	-	-	10.3	-	-	6.1	-	-	-	-	-	-	**249.7**
Insufficient fibre	203.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**203.5**
Processed meat	187.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**187.6**
Physical inactivity	85.8[c]	-	15.1	-	26.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**127.0**
Red meat	89.6[c]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**89.6**
Hepatitis C	-	-	-	29.4	-	-	-	-	-	-	-	-	-	-	3.3	-	-	-	-	-	-	-	-	**32.7**
Hepatitis B	-	-	-	28.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**28.9**
Asbestos	-	4.0	-	-	-	-	-	-	-	-	0.1	21.1	-	-	-	-	-	-	-	-	-	-	-	**25.2**
Helicobacter pylori	-	-	-	-	-	-	-	19.1	-	-	-	-	-	-	5.7	-	-	-	-	-	-	-	-	**24.8**
OCP	-	-	0.2	13.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.5	-	-	**16.2**
MHT	-	-	6.4	-	7.1	-	-	-	-	-	-	-	-	-	-	-	-	-	0.9	-	-	-	-	**14.4**

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(continued)	Colon and rectum (C18-C20)	Lung (C33-C34)	Breast (C50)	Liver (C22)	Endometrium (C54-C55)[a]	Kidney (C64)	Oesophagus (C15)	Stomach (C16)	Bladder (C67)	Pancreas (C25)	Larynx (C32)	Mesothelioma (C45)	Prostate (C61)	Oral cavity (C03-C06)	non-Hodgkin lymphoma (C82-C86)	Leukaemia (C92-C94)[b]	Pharynx (C10, C11, C13)	Melanoma of the skin (C43)	Ovary (C56)	Gallbladder (C23)	Cervix (C53)	Anus (C21)	Nasal (C30)	**Total attributable registrations**
Insufficient breastfeeding	-	-	9.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**9.6**
Solar radiation[d]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7.5	-	-	-	-	-	**7.5**
Benzene	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7.2	-	-	-	-	-	-	-	**7.2**
Silica	-	5.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**5.4**
Diesel engine exhaust	-	5.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**5.1**
HIV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.4	-	-	-	-	-	<0.1	0.9	-	**4.7[e]**
Metals[f]	-	2.8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	**3.4**
Ionising radiation[d,g]	-	-	0.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**0.4**
Wood dust	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.1	**0.2[h]**
Trichloroethylene	-	-	-	-	-	0.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**0.1**

HIV: Human Immunodeficiency Virus; MHT: Menopausal hormone therapy; OCP: combined Oral Contraceptive Pill. Totals may not always add up due to rounding. These numbers are not adjusted for multiple exposures and so totals may not always add up to those presented in Table 3.
[a] All cases of uterine cancer (ICD-10 codes C54-C55) assumed to be endometrial.
[b] Definition of leukaemia restricted to acute myeloid leukaemia (ICD-10 codes C92,0, C92.3-C92.6, C92.8, C93.0, C94.0, C94.2, C94.4-C94.5).
[c] All cases of colorectal cancer attributable to physical inactivity and red meat consumption are cancers of the colon (C18).
[d] Limited to occupational exposure.
[e] Total cases attributable to HIV includes cases of Hodgkin lymphoma (n=300; not presented in Table).
[f] Comprising arsenic, cadmium, chromium VI, and nickel.
[g] Ionising radiation exposure also linked to leukaemia, lung cancer, and thyroid cancer, but negligible numbers of attributable cases found (n≤10) and so not included in total estimate.
[h] Total cases attributable to wood dust exposure includes cases of nasopharyngeal cancer (n≈100; not presented in Table).

1.4 Discussion

Of the 7.6 million cancers predicted to occur over the lifetime of the population of adult Australians in 2016, we estimated that around one-quarter will result from exposure to modifiable factors. This amounts to around 1.8 million future cancers. The sites contributing the greatest number of cases to the overall excess burden were cancers of the colon and rectum, lung, and liver. The leading preventable risk factor was tobacco smoke, which will contribute more than 580,000 future cancers. Other important contributors include overweight and obesity, alcohol consumption, and inadequate fibre intake, each of which will contribute more than 200,000 future cases.

We found a higher proportion of future cancers in males (25%) than females (22%) to be attributable to modifiable factors. Across all cancer sites, the FEF was higher for males than females, with the exception of female sex-specific cancers. For individual risk factors, we found a higher proportion of cancers attributable to physical inactivity among females than males. While the prevalence of physical inactivity was slightly higher among females, this is likely due to the strong association between physical inactivity and cancers of the breast and endometrium.

To our knowledge, no previous Australian studies have presented an overall estimate of the future burden of cancer attributable to modifiable exposures. Baade and colleagues estimated the future number of cancers in Australia in one year (2025) that were attributable to diet, physical activity, and obesity by applying PAF estimates published for the US and UK to Australian cancer incidence data [54]. They found that 25% of future cancers were preventable by changes in diet and physical activity. However, this method does not take into account prevalence of exposure to risk factors, or potential differences in exposure prevalence between different countries.

Other studies in Australia have investigated the future burden due to specific exposures, rather than providing an overall estimate. Wilson and colleagues estimated the future burden of cancer attributable to overweight/obesity, physical inactivity, and alcohol consumption in Australia over 25 years (2013-2037) [18, 19]. While their numbers are not directly comparable to ours as they used a different denominator (proportion of risk factor-related cancers versus all cancers), their results are similar to ours in terms of the relative ranking of cancer sites. For example, Wilson and colleagues found that the cancer sites with the highest fraction of cases attributable to overweight and obesity were oesophageal, liver, kidney, and endometrial [18]; these were also the top four cancer sites attributable to overweight/obesity in our results. Similarly, the cancer sites with the highest fraction of cases attributable to alcohol consumption (oesophagus, oral cavity, and pharynx) [19] were similar in both studies.

Recent studies in Australia have also estimated the future burden at a number of specific cancer sites over 10 years (2017-2026). Using a modified PAF method, Laaksonen and colleagues estimated that 19% of colorectal cancers [55], 31-63% of lung cancers [15], 19% of premenopausal breast cancers,

24% of postmenopausal breast cancers [56], 33% of kidney cancers, and 24% of bladder cancers were attributable to modifiable factors [16]. Our estimates accord closely to many of these findings (36% lung, 25% postmenopausal breast, 28% kidney, 22% bladder); however, we estimated a much higher attributable burden for colorectal cancer (50%). This is likely due to the risk factors considered: while we included smoking, physical activity, overweight/obesity, red and processed meat consumption, alcohol consumption, and inadequate fibre intake, Vajdic and colleagues estimated the burden due only to smoking, body mass index, and alcohol [55]. Many of the additional risk factors we included accounted for a sizeable proportion of the burden (e.g. processed meat and inadequate fibre intake each accounted for 14% of colorectal cancers).

Internationally, studies in Canada and the Nordic countries have used various methods to calculate the future attributable burden of cancer [57-59]. For example, Soerjomataram and colleagues estimated the future burden of lung and breast cancer due to smoking and alcohol in Denmark in 2050 and found that 44% of lung cancers and 7.3% of breast cancers could be prevented by avoiding smoking and excessive alcohol consumption, respectively [58]. These estimates are broadly similar to our estimates (35% of lung cancers and 8% of breast cancers). Another study in the Nordic countries estimated the cancers due to overweight and obesity over 30 years (2016-2045) and found that oesophageal adenocarcinoma had the highest proportion of avoidable cancers [59], similar to our results. In Canada, Poirier and colleagues used the population attributable risk method to calculate the future burden of cancer in 2042 [57]. They found that 31% of future cancer cases among the 2015 adult population (aged 30+) were attributable to modifiable factors, higher than our estimate of 24%. Disparities between these estimates may stem from a variety of factors, including the risk factors considered (for example, we did not include residential radon due to negligible exposure in Australia) and differing cancer incidence rates between countries. Regardless, the top risk factors in Poirier's study [57] were tobacco smoking, physical inactivity, and overweight/obesity, while cancers of the lung and colon and rectum were the top sites, similar to our results.

While we have attempted to compare our findings with those of past studies, it is clear that our estimates are not directly comparable with other studies of burden of disease due to the differing methods and assumptions. These include differences in the denominators used (proportion of all cancers versus risk factor-related cancers) and/or minimum risk threshold. For example, we used 1800 MET-minutes/week as the threshold for physical inactivity, while Wilson and colleagues used 1000 MET-minutes/week [18]. In addition, there may be differences in cancer incidence rates, levels of exposure, and risk factors examined. For example, while Laaksonen and colleagues estimated the future burden of lung cancer due to fruit consumption and physical inactivity [15], we excluded these risk factors as the updated WCRF evidence shows only a suggestive relationship [60]. We also excluded risk factor/cancer combinations where a protective effect has been found and the risk factor

could not be conceptualised in terms of insufficient exposure (for example, oestrogen-only MHT and cancer of the colon and rectum [29]; OCP use and ovarian and endometrial cancers) [61].

The FEF method used here has a number of strengths and advantages. We focused on those risk factor/cancer combinations with sufficient or convincing evidence, based on the most recent determinations from IARC and WCRF. These determinations are based on systematic reviews of all available evidence and are updated regularly. Our minimum risk level was based on the relevant Australian recommendations and guidelines, which allows us to more accurately communicate health promotion information. Further, our method does not require any assumptions regarding latency or lag, and accounts for competing risk of death through the use of double decrement life tables.

As with all burden of cancer studies, the FEF approach used here relies on a number of assumptions. While we have used the best-available exposure prevalence estimates, we have necessarily excluded cancer registrations from those in the cohort who were unexposed in the index year but had been exposed in the past or would be exposed in the future. That is, this approach provides an estimate of the proportion of future cancers only in those members of the cohort who were exposed in the index year. In doing so, we assume a normal distribution around this prevalence with regards to length of exposure, such that many but not all of those exposed in the index year are assumed to have been exposed in the past and to continue to be exposed in the future. It is possible, however, that this has led to an underestimate of exposure prevalence and hence the future burden of cancer in this cohort. In addition, we did not explicitly include a latency period in our estimates, as we assumed that some of those exposed in the index year had been exposed for some time in the past and therefore may have developed cancer soon after the index year. Further, in order to provide an overall FEF for each cancer, we combined exposures using the complement of the product of complements method [4]. While this method avoids double counting cancers that can be attributed to more than one exposure, it also assumes independence of exposures and does not allow for effect modification between exposures.

Like other future burden methods, the FEF method also required us to project cancer incidence rates and numbers forward to 2098 (the year in which the youngest members of our cohort would turn 100) in order to represent risk over the lifetime of the cohort. We chose to project forward on the basis of demographic change only, an approach adopted in previous Australian and international work [19, 54, 62]. Although this may result in a slight misestimation of future cancers, this approach does not require assumptions to be made about continuing trends and patterns in cancer incidence. However, the accuracy of these projections is unknown. It is possible that contributing factors, including the prevalence of risk factors, population demographics, and competing causes of death, may undergo substantial changes over this extended period of time. Our previous work compared projections made on the basis of demographic change only with those using 'Canproj', a program which takes into account observed trends in cancer registrations, and found the former to result in a slightly higher FEF

and FEN [43]. Further, Cameron and Baade projected the future incidence of seven cancer types (breast, colorectal, liver, lung, non-Hodgkin lymphoma, melanoma, and stomach) in Australia to 2031 using Bayesian age-period cohort models [63]. They found decreases in the age-standardised rate for colorectal and male lung cancer, and substantial increases for liver and female lung cancer. Thus, the impact of the projection method used will differ by cancer type.

The results presented here depend on the validity of other key inputs, including the exposure prevalence data and relative risks used. Whilst we have used relative risks derived from large international meta-analyses wherever possible, the relevance of these to Australian exposure circumstances may vary. Further, for some risk factors, including OCP use and breastfeeding, estimates of the prevalence of exposure were not recent, although all attempts were made to source the best available data. While rates of breastfeeding are not likely to have changed significantly over time [64], OCP use has decreased [65], and so the results presented here may overestimate the future burden due to OCP use. In addition, we were unable to measure some potentially important risk factors, including recreational solar radiation exposure and exposure to ionising radiation from medical sources, due to a lack of suitable exposure prevalence data. This means that the future burden due to these exposures is underestimated, most notably the FEF of melanoma. We also aggregated exposure prevalence data over all age groups, which may have led to a slight misestimation of the future burden due to differences in exposure prevalence by age.

Our results show that a significant proportion of future cancers will be attributable to exposure to lifestyle, environmental, and occupational risk factors. These cancers are considered preventable, and there are clear opportunities for policy action to reduce the number of cancers occurring in the community. Our results have shown which cancers will contribute most to the overall future burden of disease, as well as which risk factors are the most important contributors. This provides direct, pertinent information to help determine where preventive measures could best be targeted. For example, our results suggest that a continued focus on smoking cessation is likely to be beneficial in preventing future cancers, and that future interventions should also focus on the ongoing obesity epidemic.

The approach used here has provided an estimate of the future number of cancer cases arising from contemporary exposures, rather than current cases based on past exposures as in many previous estimates of the burden of cancer. Such an estimate is likely to be more useful to policymakers and other health decision makers, as changes in contemporary rather than historical exposures are easier to conceptualise when deciding on priorities for future research and funding. The results of this study can be used as a baseline to model the impact of potential behavioural and policy interventions to reduce exposure to modifiable risk factors, as well as to inform future economic analyses including exploring the cost-effectiveness of different interventions for reducing future cancers.

References

[1]   Institute for Health Metrics and Evaluation (IHME), GBD Compare Data Visualization. http://vizhub.healthdata.org/gbd-compare, 2020 (accessed 5 March 2021).

[2]   Australian Institute of Health and Welfare (AIHW), Cancer data in Australia, AIHW, Canberra, 2020.

[3]   V.J. Cogliano, R. Baan, K. Straif, Y. Grosse, B. Lauby-Secretan, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, N. Guha, et al., Preventable exposures associated with human cancers, J Natl Cancer Inst. 103 (2011) 1827-39. https://doi.org/10.1093/jnci/djr483.

[4]   K. Steenland, B. Armstrong, An overview of methods for calculating the burden of disease due to specific risk factors, Epidemiol. 17 (2006) 512-9. https://doi.org/10.1097/01.ede.0000229155.05644.43.

[5]   D.C. Whiteman, P.M. Webb, A.C. Green, R.E. Neale, L. Fritschi, C.J. Bain, D.M. Parkin, L.F. Wilson, C.M. Olsen, et al., Cancers in Australia in 2010 attributable to modifiable factors: Summary and conclusions, Aust N Z J Public Health. 39 (2015) 477-84. https://doi.org/10.1111/1753-6405.12471.

[6]   L.F. Wilson, A. Antonsson, A.C. Green, S.J. Jordan, B.J. Kendall, C.M. Nagle, R.E. Neale, C.M. Olsen, P.M. Webb, et al., How many cancer cases and deaths are potentially preventable? Estimates for Australia in 2013, Int J Cancer. 142 (2018) 691-701. https://doi.org/10.1002/ijc.31088.

[7]   Australian Institute of Health and Welfare (AIHW), Australian Burden of Disease Study: Impact and causes of illness and death in Australia 2015, AIHW, Canberra, 2019.

[8]   K.F. Brown, H. Rumgay, C. Dunlop, M. Ryan, F. Quartly, A. Cox, A. Deas, L. Elliss-Brookes, A. Gavin, et al., The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015, Br J Cancer. 118 (2018) 1130-1141. https://doi.org/10.1038/s41416-018-0029-6.

[9]   F. Islami, A. Goding Sauer, K.D. Miller, R.L. Siegel, S.A. Fedewa, E.J. Jacobs, M.L. McCullough, A.V. Patel, J. Ma, et al., Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, CA: Cancer J Clin. 68 (2018) 31-54. https://doi.org/10.3322/caac.21440.

[10]   A. Grundy, A.E. Poirier, F. Khandwala, X. Grevers, C.M. Friedenreich, D.R. Brenner, Cancer incidence attributable to lifestyle and environmental factors in Alberta in 2012: Summary of results, CMAJ Open. 5 (2017) E540-E545. https://doi.org/10.9778/cmajo.20160045.

[11]   C.D. Mathers, D. Loncar, Projections of global mortality and burden of disease from 2002 to 2030, PLoS Med. 3 (2006) e442. https://doi.org/10.1371/journal.pmed.0030442.

[12]   D.R. Brenner, C.M. Friedenreich, Y. Ruan, A.E. Poirier, S.D. Walter, W.D. King, E.L. Franco, P.A. Demers, P.J. Villeneuve, et al., The burden of cancer attributable to modifiable

risk factors in Canada: Methods overview, Prev Med. 122 (2019) 3-8.
https://doi.org/10.1016/j.ypmed.2019.03.007.

[13] S. Hutchings, L. Rushton, Toward risk reduction: Predicting the future burden of occupational cancer, Am J Epidemiol. 173 (2011) 1069-1077. https://doi.org/10.1093/aje/kwq434.

[14] M.A. Laaksonen, M.E. Arriaga, K. Canfell, R.J. Maclnnis, J.E. Byles, E. Banks, J.E. Shaw, P. Mitchell, G.G. Giles, et al., The preventable burden of endometrial and ovarian cancers in Australia: A pooled cohort study, Gynecol Oncol. 153 (2019) 580-588. https://doi.org/10.1016/j.ygyno.2019.03.102.

[15] M.A. Laaksonen, K. Canfell, R. MacInnis, M.E. Arriaga, E. Banks, D.J. Magliano, G.G. Giles, R.G. Cumming, J.E. Byles, et al., The future burden of lung cancer attributable to current modifiable behaviours: A pooled study of seven Australian cohorts, Int J Epidemiol. 47 (2018) 1772-1783. https://doi.org/10.1093/ije/dyy136.

[16] M.A. Laaksonen, R.J. MacInnis, K. Canfell, G.G. Giles, P. Hull, J.E. Shaw, R.G. Cumming, T.K. Gill, E. Banks, et al., The future burden of kidney and bladder cancers preventable by behavior modification in Australia: A pooled cohort study, Int J Cancer. 146 (2020) 874-883. https://doi.org/10.1002/ijc.32420.

[17] M.A. Laaksonen, M.E. Arriaga, K. Canfell, R. MacInnis, P. Hull, E. Banks, G.G. Giles, P. Mitchell, R.G. Cumming, et al., A large linked study to evaluate the future burden of cancer in Australia attributable to current modifiable behaviours, Int J Popul Data Sci. 3 (2018). https://doi.org/10.23889/ijpds.v3i4.729.

[18] L.F. Wilson, P.D. Baade, A.C. Green, S.J. Jordan, B.J. Kendall, R.E. Neale, C.M. Olsen, D.R. Youlden, P.M. Webb, et al., The impact of changing the prevalence of overweight/obesity and physical inactivity in Australia: An estimate of the proportion of potentially avoidable cancers 2013-2037, Int J Cancer. 144 (2019) 2088-2098. https://doi.org/10.1002/ijc.31943.

[19] L.F. Wilson, P.D. Baade, A.C. Green, S.J. Jordan, B.J. Kendall, R.E. Neale, C.M. Olsen, D.R. Youlden, P.M. Webb, et al., The impact of reducing alcohol consumption in Australia: An estimate of the proportion of potentially avoidable cancers 2013-2037, Int J Cancer. 145 (2019) 2944-2953. https://doi.org/10.1002/ijc.32204.

[20] L. Fritschi, J. Chan, S.J. Hutchings, T.R. Driscoll, A.Y. Wong, R.N. Carey, The future excess fraction model for calculating burden of disease, BMC Public Health. 16 (2016) 386. https://doi.org/10.1186/s12889-016-3066-1.

[21] J. Esteve, E. Benhamou, L. Raymond, Statistical methods in cancer research. Volume IV. Descriptive epidemiology, IARC Sci Publ. (1994) 1-302.

[22] I.D. Goldberg, M.L. Levin, P.R. Gerhardt, V.H. Handy, R.E. Cashman, The probability of developing cancer, J Natl Cancer Inst. 17 (1956) 155-73. https://doi.org/10.1093/jnci.17.2.155.

[23] Australian Bureau of Statistics, Census 2016, ABS, Canberra, 2016.

[24]   Australian Bureau of Statistics, 3302.0.55.001 - Life tables, States, Territories and Australia, 2014-2016, ABS, Canberra, 2017.

[25]   Australian Bureau of Statistics, National Health Survey 2014-15, ABS, Canberra, 2015.

[26]   R.N. Carey, T.R. Driscoll, S. Peters, D.C. Glass, A. Reid, G. Benke, L. Fritschi, Estimated prevalence of exposure to occupational carcinogens in Australia (2011-2012), Occup Environ Med. 71 (2014) 55-62. https://doi.org/10.1136/oemed-2013-101651.

[27]   L. Fritschi, T.C. Erren, D.C. Glass, J. Girschik, A.K. Thomson, C. Saunders, T. Boyle, S. El-Zaemey, P. Rogers, et al., The association between different night shiftwork factors and breast cancer: A case-control study, Brit J Cancer. 109 (2013) 2472-2480. https://doi.org/10.1038/bjc.2013.544.

[28]   L.S. Velentzis, E. Banks, F. Sitas, U. Salagame, E.H. Tan, K. Canfell, Use of menopausal hormone therapy and bioidentical hormone therapy in Australian women 50 to 69 years of age: Results from a national, cross-sectional study, PLoS ONE. 11 (2016). https://doi.org/10.1371/journal.pone.0146494.

[29]   World Cancer Research Fund International/American Institute for Cancer Research, Continuous Update Project report: Diet, nutrition, physical activity and colorectal cancer, WCRF, London, 2017.

[30]   Australian Institute of Health and Welfare (AIHW), Cancer incidence projections: Australia, 2011 to 2020. Cancer Series no. 66. Cat. No. CAN 62, AIHW, Canberra, 2012.

[31]   Australian Bureau of Statistics, 3222.0 Population Projections, Australia, 2012 (base) to 2101, ABS, Canberra, 2013.

[32]   Australian Institute of Health and Welfare, Cervical screening in Australia 2014-2015. Cancer series no. 105. Cat. no. CAN 104, AIHW, Canberra, 2017.

[33]   Cancer Australia, Distribution of cancer stage. https://ncci.canceraustralia.gov.au/diagnosis/distribution-cancer-stage/distribution-cancer-stage, 2018 (accessed 11 June 2020).

[34]   A. Colquhoun, M. Arnold, J. Ferlay, K.J. Goodman, D. Forman, I. Soerjomataram, Global patterns of cardia and non-cardia gastric cancer incidence in 2012, Gut. 64 (2015) 1881-8. https://doi.org/10.1136/gutjnl-2014-308915.

[35]   M.C.S. Wong, W. Hamilton, D.C. Whiteman, J.Y. Jiang, Y. Qiao, F.D.H. Fung, H.H.X. Wang, P.W.Y. Chiu, E.K.W. Ng, et al., Global incidence and mortality of oesophageal cancer and their correlation with socioeconomic indicators temporal patterns and trends in 41 countries, Sci Rep. 8 (2018) 4522. https://doi.org/10.1038/s41598-018-19819-8.

[36]   W. Xu, J. Rush, K. Rickett, J.I. Coward, Mucinous ovarian cancer: A therapeutic review, Crit Rev Oncol Hematol. 102 (2016) 26-36. https://doi.org/10.1016/j.critrevonc.2016.03.015.

[37]   R. Newton, J. Ferlay, V. Beral, S.S. Devesa, The epidemiology of non-Hodgkin's lymphoma: Comparison of nodal and extra-nodal sites, Int J Cancer. 72 (1997) 923-30. https://doi.org/10.1002/(SIC)1097-0215(19970917)72:6<923::AID*IJC1>3.0.CO;2-R.

[38]   N. Allen, R. Peto, V. Beral, S.W. Kan, G. Reeves, S. Sweetland, R. Stevens, T.O. Yang, R. Stevens, et al., Endometrial cancer and oral contraceptives: An individual participant meta-analysis of 27 276 women with endometrial cancer from 36 epidemiological studies, Lancet Oncol. 16 (2015) 1061-1070. https://doi.org/10.1016/S1470-2045(15)00212-0.

[39]   J.A. Simpson, D.R. English, R.J. MacInnis, D.M. Gertig, J.L. Hopper, G.G. Giles, A comparison of different methods for including 'age at menopause' in analyses of the association between hormone replacement therapy use and breast cancer, J Fam Plan Reprod Health Care. 33 (2007) 11-6. https://doi.org/10.1783/147118907779399828.

[40]   G.D. Mishra, H.F. Chung, Y.A. Gelaw, D. Loxton, The role of smoking in the relationship between intimate partner violence and age at natural menopause: A mediation analysis, Womens Midlife Health. 4 (2018) 1. https://doi.org/10.1186/s40695-017-0031-9.

[41]   O. Brouckaert, A. Rudolph, A. Laenen, R. Keeman, M.K. Bolla, Q. Wang, A. Soubry, H. Wildiers, I.L. Andrulis, et al., Reproductive profiles and risk of breast cancer subtypes: A multi-center case-only study, Breast Cancer Res. 19 (2017) 119. https://doi.org/10.1186/s13058-017-0909-3.

[42]   Collaborative Group on Hormonal Factors in Breast Cancer, Breast cancer and breastfeeding: Collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease, Lancet. 360 (2002) 187-95. https://doi.org/10.1016/S0140-6736(02)09454-0.

[43]   R.N. Carey, S.J. Hutchings, L. Rushton, T.R. Driscoll, A. Reid, D.C. Glass, E. Darcey, S. Si, S. Peters, et al., The future excess fraction of occupational cancer among those exposed to carcinogens at work in Australia in 2012, Cancer Epidemiol. 47 (2017) 1-6. https://doi.org/10.1016/j.canep.2016.12.009.

[44]   Australian Bureau of Statistics, National Health Survey 2011-12, ABS, Canberra, 2012.

[45]   Australian Bureau of Statistics, National Health Survey 2001, ABS, Canberra, 2001.

[46]   T. Moujaber, C.R. MacIntyre, J. Backhouse, H. Gidding, H. Quinn, G.L. Gilbert, The seroepidemiology of Helicobacter pylori infection in Australia, Int J Infect Dis. 12 (2008) 500-4. https://doi.org/10.1016/j.ijid.2008.01.011.

[47]   N. Pandeya, D.C. Whiteman, Australian Cancer Study, Prevalence and determinants of Helicobacter pylori sero-positivity in the Australian adult community, J Gastroenterol Hepatol. 26 (2011) 1283-9. https://doi.org/10.1111/j.1440-1746.2011.06726.x.

[48]   The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2017, The Kirby Institute, Sydney, 2017.

[49] National Health and Medical Research Council, Infant feeding guidelines, NHMRC, Canberra, 2012.

[50] Department of Health, Australia's physical activity and sedentary behaviour guidelines for adults (18-64 years), Department of Health, Canberra, 2019.

[51] National Health and Medical Research Council, Nutrient reference values for Australia and New Zealand, NHMRC, Canberra, 2017.

[52] National Health and Medical Research Council, Australian dietary guidelines, NHMRC, Canberra, 2013.

[53] National Health and Medical Research Council, Australian guidelines to reduce health risks from drinking alcohol, NHMRC, Canberra, 2019.

[54] P.D. Baade, X.Q. Meng, C. Sinclair, P. Youl, Estimating the future burden of cancers preventable by better diet and physical activity in Australia, Med J Aust. 196 (2012) 337-340. https://doi.org/10.5694/mja11.11082.

[55] C.M. Vajdic, R.J. MacInnis, K. Canfell, P. Hull, M.E. Arriaga, V. Hirani, R.G. Cumming, P. Mitchell, J.E. Byles, et al., The future colorectal cancer burden attributable to modifiable behaviors: A pooled cohort study, JNCI Cancer Spectr. 2 (2018). https://doi.org/10.1093/jncics/pky033.

[56] M.E. Arriaga, C.M. Vajdic, K. Canfell, R.J. MacInnis, E. Banks, J.E. Byles, D.J. Magliano, A.W. Taylor, P. Mitchell, et al., The preventable burden of breast cancers for premenopausal and postmenopausal women in Australia: A pooled cohort study, Int J Cancer. 145 (2019) 2383-2394. https://doi.org/10.1002/ijc.32231.

[57] A.E. Poirier, Y. Ruan, K.D. Volesky, W.D. King, D.E. O'Sullivan, P. Gogna, S.D. Walter, P.J. Villeneuve, C.M. Friedenreich, et al., The current and future burden of cancer attributable to modifiable risk factors in Canada: Summary of results, Prev Med. 122 (2019) 140-147. https://doi.org/10.1016/j.ypmed.2019.04.007.

[58] I. Soerjomataram, E. de Vries, G. Engholm, G. Paludan-Muller, H. Bronnum-Hansen, H.H. Storm, J.J. Barendregt, Impact of a smoking and alcohol intervention program on lung and breast cancer incidence in Denmark: An example of dynamic modeling with Prevent, Eur J Cancer. 46 (2010) 2617-2624. https://doi.org/10.1016/j.ejca.2010.07.051.

[59] T.M. Andersson, E. Weiderpass, G. Engholm, A.Q. Lund, E. Olafsdottir, E. Pukkala, M. Stenbeck, H. Storm, Avoidable cancer cases in the Nordic countries - The impact of overweight and obesity, Eur J Cancer. 79 (2017) 106-118. https://doi.org/10.1016/j.ejca.2017.03.028.

[60] World Cancer Research Fund International/American Institute for Cancer Research, The associations between food, nutrition and physical activity and the risk of lung cancer, WCRF, London, 2016.

[61]   Y. Grosse, R. Baan, K. Straif, B. Secretan, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, N. Guha, L. Galichet, et al., A review of human carcinogens-Part A: pharmaceuticals, Lancet Oncol. 10 (2009) 13-14. https://doi.org/10.1016/S1470-2045(08)70286-9.

[62]   B.D. Smith, G.L. Smith, A. Hurria, G.N. Hortobagyi, T.A. Buchholz, Future of cancer incidence in the United States: Burdens upon an aging, changing nation, J Clin Oncol. 27 (2009) 2758-65. https://doi.org/10.1200/JCO.2008.20.8983.

[63]   J.K. Cameron, P. Baade, Projections of the future burden of cancer in Australia using Bayesian age-period-cohort models, Cancer Epidemiol. 72 (2021) 101935. https://doi.org/10.1016/j.canep.2021.101935.

[64]   Public Health Association of Australia, Breastfeeding: Background paper, PHAA, Deakin ACT.

[65]   Family Planning NSW, Contraception in Australia 2005-2018, FPNSW, Sydney, 2020.