The future burden of lung cancer attributable to current modifiable behaviours: a pooled study of seven Australian cohorts

Running title: Preventable lung cancer burden in Australia

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KEY MESSAGES

- We ascertained the future Australian lung cancer burden attributable to current, modifiable behaviours using a novel population attributable fraction method that accounts for competing risk of death and allows burdens for population subgroups to be compared statistically.
- We show that despite the declining smoking prevalence in Australia, smoking continues to cause the majority of the lung cancer burden.
- Several large population subgroups have a higher smoking-attributable burden and are likely to benefit the most from measures that prevent smoking uptake and facilitate quitting.
- Inadequate fruit intake and physical inactivity, two highly prevalent behaviours, appear to explain a substantial proportion of the lung cancer burden.
- Unhealthy behaviours can cluster and people with such risk factor clustering have a higher lung cancer burden and thus the most to gain from health promotion activities.

ABSTRACT

Background: Knowledge of preventable disease and differences in disease burden can inform public health action to improve health and health equity. We quantified the future lung cancer burden preventable by behavioural modifications across Australia.

Methods: We pooled seven Australian cohort studies (n=367 058) and linked them to national registries to identify lung cancers and deaths. We estimated Population Attributable Fractions and their 95% confidence intervals (CIs) for modifiable risk factors using risk estimates from the cohort data and risk factor exposure distribution from contemporary national health surveys.

Results: During the first 10-years follow-up, there were 2025 incident lung cancers and 20 349 deaths. Stopping current smoking could prevent 53.7% (95% CI 50.0-57.2%) of lung cancers over 40 years and 18.3% (11.0-25.1%) in 10 years. The smoking-attributable burden is highest in males, those who smoke < 20 cigarettes per day, are < 75 years of age, unmarried, of lower educational attainment, live in remote areas, or are healthy weight. Increasing physical activity and fruit consumption, if causal, could prevent 15.6% (6.9-23.4%) and 7.5% (1.3-13.3%) of the lung cancer burden, respectively. Jointly, the three behaviour modifications could prevent up to 63.0% (58.0-67.5%) of lung cancers in 40 years, and 31.2% (20.9-40.1%) or 43 300 cancers in 10 years. The preventable burden is highest among those with multiple risk factors.

Conclusions: Smoking remains responsible for the highest burden of lung cancer in Australia. The uneven burden distribution distinguishes subgroups that could benefit the most from activities to control the world's deadliest cancer.

Key words: Cancer burden, lung cancer, risk factors, risk groups, cohort studies, population attributable fraction

INTRODUCTION

Lung cancer is the fifth most frequent cancer in Australia and the leading cause of cancer death in Australia and worldwide.[1,2] Prevention and early detection are key strategies for reducing the burden. Smoking is an established cause of lung cancer[3] and Australian tobacco control activities have played an important role in reducing smoking prevalence from 28% to 16% between 1990 and 2015,[4,5] similar to trends in other industrialised countries.[6] Other behaviours, such as inadequate fruit consumption and physical inactivity have probable or suggestive evidence of increasing lung cancer risk.[7] These health-risk behaviours often coexist in individuals, so it is possible that the lung cancer burden may be greatest in those with multiple exposures.[8–10]

Several studies have assessed the individual effects of behaviours on the lung cancer burden by estimating population attributable fractions (PAFs)[11–21] but have not accounted for the competing risk of death, which may bias PAF estimates.[22] Most studies have used non-representative, non-contemporary prevalence data, thereby hindering generalisation and relevance of the findings. Only two studies have assessed the joint effects of behaviours on the lung cancer burden,[19,23] showing their effects are not independent,[19] as usually assumed in PAF estimations.[11,13,24] No study has assessed the difference in lung cancer burden between population subgroups.

To identify those who could benefit most from cancer control activities, we quantified and compared across sample subgroups the future burden of lung cancer avoidable by individual and joint modifications to behaviours. Using Australian cohorts and the most recent representative exposure prevalence data,[25–27] we applied a PAF method that accounts for competing risk of death and risk factor interdependence and allows for the evaluation of PAF effect modification.[22,28,29]

METHODS

Data sources

We used data from the Australian cancer-PAF cohort consortium,[25] which comprises of seven well-established Australian prospective cohort studies with comprehensive information on behaviours or lifestyle risk factors: Melbourne Collaborative Cohort Study (MCCS),[30] Blue Mountains Eye Study (BMES),[31] Australian Longitudinal Study on Women's Health (ALSWH),[32] Australian Diabetes, Obesity and Lifestyle Study (AusDiab),[33] North West Adelaide Health Study (NWAHS),[34] Concord Health and Ageing in Men Project (CHAMP),[35] and the 45 and Up Study (45&Up)[36]. Together they formed a study sample of 369 515 adult Australians. The final sample was 364 411 individuals after exclusion of 2457 people enrolled in more than one cohort, 1885 people who did not consent to record linkage, and 762 individuals with prevalent lung cancer (Table 1).

We obtained the most recent available risk factor prevalence estimates from the representative National Health Survey (NHS; 2014-2015)[26] and National Drug Strategy Household Survey (NDSHS; 2013)[27] (Table 1, Supplementary Table 1).

We obtained ethical approval for the study (Australian Institute of Health and Welfare EC2013/4/62).

Data harmonisation

We examined modifiable behaviours with convincing, probable or suggestive evidence of a causal association with lung cancer, as judged by expert review panels[3, 7, 37] if they were measured both in our cohort and the health surveys. These behaviours were smoking,[3] inadequate fruit consumption,[7] and physical inactivity.[7] We harmonised these exposures, measured at baseline, across the cohorts and external data sources (Supplementary Table 1), classifying them according to the current Australian recommendations for healthy living, i.e. not smoking, eating at least two serves (i.e. 300 g) of fruits per day, and doing at least 150 minutes of moderate or 75 minutes of vigorous physical activity per week.[25]

We also harmonised non-modifiable exposures such as country of birth, marital status, educational attainment, socio-economic status[38] and residential location (rurality)[39] to allow subgroup analyses (Supplementary Table 1).

Data linkage

We linked the cohort to the Australian Cancer Database and National Death Index to identify cancers and deaths using an established probabilistic linkage algorithm.[40] These records were available until the end of 2012, providing 8-22 years follow-up (Table 1).

Statistical methods

We classified lung cancers on the basis of International Classification of Diseases for Oncology codes (ICD-O; C33-34).

We defined follow-up as the time from baseline to the date of lung cancer diagnosis, death or end of follow-up, whichever occurred first. We estimated the strength of association between the behaviours and lung cancer using a piecewise constant hazards model,[41] and expressed them as hazard ratios (HR) and their 95% confidence intervals (CI). We restricted the analyses to the first 10-years follow-up to generate comparable estimates across the cohorts, and tested heterogeneity among the cohort-specific HRs using the asymptotic DerSimonian and Laird Q statistic.[42] In a sensitivity analysis we excluded the first 12 months follow-up to evaluate the potential for reverse causality.

We defined two main effects models. The first model included age, sex, study and separately each of the behaviours. We then modelled age, sex, study and all behaviours, with behaviours associated with lung cancer retained in the final model. We computed the corresponding exposure prevalence (PR) estimates from the NHS or NDSHS. We then combined the strength of association and exposure prevalence estimates to estimate the future burden of lung cancer that could be avoided if the current exposure distribution could be changed using our recently developed method[22] and program[43] for calculation of PAFs and their 95% CIs, accounting for competing risk of death and risk factor interdependence (see Appendix A).

We evaluated both the burden attributable to all exposure (attributable burden) and the burden attributable to modifiable exposure (preventable burden). We calculated PAFs both for the individual and joint contribution of behaviours to these burdens. For smoking, we evaluated attributable burden scenarios in which ever (i.e. former and current) smokers or former smokers (eventually) had the same lung cancer risk as never smokers. In preventable burden scenarios, current smokers had the same lung cancer risk as never smokers (long-term scenario) or recent former smokers (short-term scenario), or current smokers of 20 cigarettes or more a day had the same risk as those who smoked fewer than 20 cigarettes a day. For other behaviours, we evaluated scenarios in which those currently not adhering to the Australian recommendations adhered to them. As all exposure to these behaviours was modifiable, the attributable and preventable burden scenarios were the same. We estimated the number of lung cancers that could be prevented in Australia by multiplying the preventable burden estimates by the projected numbers of lung cancers over the next 10 years (2017-2026) using a published method and data.[44]

We tested for potential effect modification of PAFs by other behaviours, sex, age, country of birth, marital status, educational attainment, socio-economic status and residential location. This was done by including an interaction term between the risk factor and the potential effect modifying factor in the model and calculating the 95% confidence interval of the difference of the PAF estimates between the categories of the effect modifying factor.[28,29]

We carried out all statistical analyses using SAS 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

During the first 10-years follow-up of the pooled cohort we observed 2025 incident lung cancers and 20 349 deaths (Table 1). There was no heterogeneity between the cohort-specific HRs of lung cancer in relation to behaviours (Supplementary Table 2).

Strength and prevalence of exposures

Non-adherence to Australian healthy living recommendations on smoking, fruit consumption and physical activity increased the risk of lung cancer (Table 2). Compared with never-smokers, current smokers had 24-fold increased risk of developing lung cancer if they smoked 20 cigarettes or more per day and 13-fold increased risk if they smoked less than 20 cigarettes per day. Former smokers remained at increased risk of lung cancer for up to 40 years compared with never-smokers, with risk approximately halving every 10 years after quitting smoking. People who ate two or more serves of fruits per day had on average a 13% lower risk of lung cancer compared with those who ate less than two serves of fruits per day. People whose physical activity complied with the recommendations had, on average, an 18% lower risk of lung cancer. The strength of these associations did not change materially after excluding the first 12 months follow-up (data not shown).

Ever-smoking and physical inactivity were moderately associated, and inadequate fruit consumption was weakly associated, with risk of death (Supplementary Table 3). These three risk factors were highly prevalent (47%, 50% and 74%, respectively) (Table 2) and 59% of Australians (63% men, 56% women) had at least two of them.

Avoidable lung cancers

Individual contribution of risk factors

Most of the future lung cancer burden (PAF, 78.0%; 95% CI, 74.8-80.8%) is attributable to former (PR, 31%; PAF, 24.3%) or current (PR, 16%; PAF, 53.7%) smoking (Tables 2 and 3). The majority of current smokers (78%) reported smoking fewer than 20 cigarettes a day, therefore contributing most (PAF, 32.1%) of the lung cancer burden. Given the extended period of excess risk for former smokers, these figures correspond to the burden avoidable in 50 years' time. In the next 10 years, 18.3% (95% CI, 11.0-25.1%) or 25 400 lung cancers in Australia could be avoided if all current smokers were to quit. The burden would reduce by 8.2% (95% CI, 4.7-11.6%) or 11 400 lung cancers if those who currently smoked 20 or more cigarettes per day smoked fewer than 20 cigarettes per day.

Fruit intake below Australian recommendations, if causal, explains 7.5% (95% CI, 1.3-13.3%) of the lung cancer burden, or up to10 400 preventable lung cancers over the next 10 years (Table 3). Similarly, physical activity below Australian recommendations, if causal, contributes 15.6% (95% CI, 6.9-23.4%) of the lung cancer burden, or up to 21 700 cancers (Table 3).

Combined contributions of risk factors

Jointly, ever-smoking, inadequate fruit consumption and physical inactivity appear to explain 82.5% (95% CI, 79.2-85.2%) of the future lung cancer burden (Table 3). Quitting smoking and increasing fruit consumption and physical activity combined could potentially eliminate up to 63.0% (95% CI, 58.0-67.5%) of lung cancers over 50 years and 31.2% (95% CI, 20.9-40.1%) or 43 300 cases in Australia over the next 10 years.

Contributions of risk factors across population subgroups

The burden attributable to ever-smoking and current smoking is higher for men than for women (83.9% versus 71.1%, and 59.8% versus 46.2%, *P*-difference <0.001, respectively) (Table 3). For both men and women, the burden attributable to ever-smoking and current smoking appear to accumulate with the presence of other risk factors, being higher for those not adhering to Australian fruit intake recommendations compared with those adhering to them (83.7% versus 72.5%, *P*-difference <0.001, and 58.5% versus 48.5%, *P*-difference = 0.01, respectively) and those not adhering to Australian exercise recommendations compared with those adhering to them (82.9% versus 64.3%, and 57.5% versus 30.5%, *P*-difference <0.001, respectively) (Tables 4a and 4b). The burden attributable to current smoking is also higher for those with healthy weight compared with those overweight (58.2% versus 48.9%, *P*-difference = 0.01). These subgroup differences are due to both a higher smoking prevalence and a higher lung cancer risk related to smoking in the high-burden subgroups (Supplementary Table 4).

The burden of lung cancer attributable to ever-smoking and current smoking is also higher among those <75 years of age, unmarried, of low educational attainment, and living in inner regional areas compared with other cohort members (Tables 4a and 4b). Additionally, Australian-born persons have a higher burden attributable to ever-smoking.

In the next 10 years, quitting smoking would result in a higher reduction of the lung cancer burden for those aged <65 years compared to those ≥65 years of age, due to differences in both smoking prevalence and risk (Supplementary Tables 5a and 5b).

The lung cancer burden attributable to inadequate fruit consumption is higher for those who do not adhere to exercise recommendations compared with those who do (13.4% versus 1.8%, *P* for difference = 0.03). No notable disparities in the burden of lung cancer attributable to inadequate fruit consumption or physical inactivity were observed for other subgroups (data not shown).

DISCUSSION

Smoking is the single greatest attributable risk factor to the burden of lung cancer in Australia, supporting tobacco control as the primary means of prevention. We discovered high burden subgroups that have the most to gain from not taking up smoking or from stopping smoking. We also revealed that inadequate fruit consumption and physical inactivity, if causal, contribute to the burden of lung cancer in Australia, and also modify the burden attributable to smoking.

We estimate 78% of the future lung cancer burden for Australian men and women is attributable to current and former smoking. Three recent studies reported PAF estimates of 87%, 82% and 82% in the UK[11], Europe,[12] and Australia[13] respectively. These estimates were based on higher prevalence estimates for current smokers (around the year 2000), and a PAF method that did not account for competing risk of death.

Only current smoking is modifiable, and there is a lag in the risk reduction after quitting smoking. We showed that the risk halves with every 10 years since quitting, in line with prior studies,[45] taking 40 years to reach the level of never smokers. This strongly supports the dual importance of preventing smoking uptake and encouraging quitting. We quantified the Australian lung cancer burden under several scenarios, demonstrating the benefits of smoking cessation relative to reductions in smoking intensity. We found 54% of lung cancers could be avoided in the long-term and 18% in the short-term, if all current smokers were to quit. An 18% reduction in the long-term burden could also be achieved if current smokers who smoke 20 cigarettes or more a day were to quit, shrinking to an 8% reduction if they cut their smoking to less than 20 a day. The largest reduction in lung cancer burden could be achieved if all people who currently smoked fewer than 20 cigarettes a day were to quit. Together, such estimates inform the likely short- and long-term impact of smoking control activities as well as the future health service requirements.

We demonstrated for the first time that the burden of lung cancer attributable to both ever-smoking and current smoking is higher for men than women. Prior studies have assessed the smoking-attributable burden for men only,[15–18] for women only,[14,19] for men and women together,[12] or for men and women separately but without assessing their difference or providing confidence intervals for the PAFs[11,13,20,21]. We also showed that the burden of lung cancer attributable to ever-smoking is highest for people who are <75 years of age, especially those aged 65-74 years, in line with previously published point estimates.[46] We further showed that the largest reduction in lung cancer burden in the short-term and long-term could be achieved by targeting smoking cessation activities at current smokers aged <65 years. There are no previous PAF estimates for other population subgroups. We identified multiple subgroups defined by sociodemographic characteristics contributed most to the smoking-attributable lung cancer burden. These subgroups, if confirmed in other studies, are likely to benefit most from tobacco control and early detection activities.

Whereas smoking has decreased continuously over the last 15 years, inadequate fruit intake and physical activity are both common and increasing in prevalence in Australia and globally.[4,5,6,24] If causally related, we estimate these behaviours contribute 8% and 16% of the future Australian lung cancer burden, respectively. A recent Australian study with the same fruit intake categories produced a similar estimate (10%),[13] and a French study with a physical activity cut-off twice as high as ours a higher estimate (23%).[19]

Notably, both current and former smokers with either inadequate fruit intake or physical activity, and those with inadequate fruit intake and physical activity, had a higher burden of lung cancer, and these unhealthy behaviours appeared to cluster at the level of the individual. People with such risk factor clustering have thus the most to gain from health promotion activities and potentially also lung cancer screening.[47,48]

The harmonised individual-level data from a large, prospective cohort consortium,[25] enabling risk factor interaction and subgroup analyses, is a key strength of our study. Additionally, matching the strength of association estimates from cohort data with corresponding contemporary, representative exposure prevalence estimates enhanced the generalisability of our PAF estimates to the present-day Australian population. The use of an advanced PAF method that accounted for the simultaneous effects of risk factors and their modification both on lung cancer incidence and death also increased the accuracy of the PAF estimates.[22,25] Also, assessment of the statistical uncertainty of these estimates allowed us to identify differences in the distribution of the lung cancer burden.

Despite the large data sample, we did not have information or only had information from individual cohorts on some convincing, probable or suggestive lung cancer risk factors, such as occupational or environmental exposures, passive smoking[3], and intake of beta-carotene supplements or cruciferous vegetables[7]. The possibility of residual confounding due to these or other factors, including imprecise smoking history, cannot be excluded. Exposures measured at baseline may also have changed during follow-up, but such changes are likely to have been small over 10-years. Some suggestive risk factors, for example red and processed meat consumption, were available from some cohorts but not from representative Australian health surveys.[25] The most recent IARC report concluded insufficient evidence for an association between body fatness, approximated by BMI, and lung cancer,[37] and hence we did not evaluate BMI as a potential causal factor. We did evaluate BMI as an effect modifier and found healthy weight current smokers to have a higher lung cancer burden than overweight current smokers, in line with prior evidence.[49]

PAF estimation traditionally assumes an immediate risk reduction to the level of those unexposed following the hypothetical exposure modification. However, as shown for smoking cessation, in reality there is a lag in risk reduction, and we took that into account in our PAF estimation and interpretation for this behaviour. Reliable evidence on the lag in risk reduction following other behaviour modifications is needed to better evaluate their short- and long-term impacts.

In conclusion, although the prevalence of smoking is declining, health promotion and cancer prevention policies and efforts to discourage smoking, and possibly also increase fruit intake and physical activity, could be strengthened and targeted at high-burden subgroups to further and more rapidly reduce the burden of this poor prognosis malignancy.

AUTHOR CONTRIBUTIONS

MAL, CMV, KC, and RM designed the study. GGG, RM, EB, PM, RGC, VH, JEB, DJM, JES, AWT, TKG, MAL, CMV, KC, MEA, SM, and BA contributed to the acquisition, analysis, or interpretation of data. MAL analysed the data. MAL and CMV drafted the report. KC, RM, EB, GGG, PM, RGC, VH, JEB, DJM, JES AWT, TKG, MEA, SM, and BA critically revised the report for important intellectual content. All authors approved the final submitted version.

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CONFLICT OF INTEREST

None declared

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Table 1. Characteristics of the individual and pooled cohort and representative external data sources

	COHORT DATA								EXTERNAL DATA	
CHARACTERISTIC	**MCCS**	**BMES**	**ALSWH**	**AusDiab**	**NWAHS**	**CHAMP**	**45&Up**	**Pooled**	**NHS**	**NDSHS**
Baseline year(s)	1990-1994	1992-1993	1996	1999-2000	1999-2003	2005-2007	2006-2009	1990-2009	2014-2015	2013
Population (n)	41 481	3652	38 336	11 189	4030	1613	264 110	364 411	14 560	22 696
Incident lung cancers (n)[a]	256	51	180	78	35	34	1391	2025		
Deaths (n)[a]	2119	689	2618	785	277	419	13 442	20 349		
State/Territory	VIC	NSW	All	All	SA	NSW	NSW	All	All	All
Age at baseline, mean (range)	55 (27-76)	66 (45-97)	45[b] (18-75)	51 (25-95)	50 (18-90)	77 (70-97)	62 (45->100)	59 (18->100)	46 (18-85)	46 (18-84)
Women (%)	59	57	100	55	52	0	53	59	51	51

45&Up, 45 and Up Study; ALSWH, Australian Longitudinal Study on Women's Health; AusDiab, Australian Diabetes, Obesity and Lifestyle Study; BMES, Blue Mountains Eye Study; CHAMP, Concord Health and Ageing in Men Project; MCCS, Melbourne Collaborative Cohort Study; NDSHS, National Drug Strategy Household Survey; NHS, National Health Survey; NSW, New South Wales; NWAHS, North West Adelaide Health Study; SA, South Australia; VIC, Victoria

[a] During the first 10-years follow-up

[b] The ALSWH recruited three cohorts aged 18-23, 45-50 and 70-75 so the age distribution is not continuous

Table 2. Risk factor exposure prevalence and hazard ratios for lung cancer incidence by exposure level over 10-years follow-up

	MEN AND WOMEN			MEN			WOMEN		
	PR	HR (95% CI)		PR	HR (95% CI)		PR	HR (95% CI)	
RISK FACTORS		**MODEL 1[a]**	**MODEL 2[b]**		**MODEL 1[a]**	**MODEL 2[b]**		**MODEL 1[a]**	**MODEL 2 [b]**
Smoking status									
Never smoker	53%	1	1	45%	1	1	60%	1	1
Former smoker	31%	4.78 (4.23, 5.41)	4.52 (3.89, 5.25)	36%	5.12 (4.21, 6.22)	5.19 (4.11, 6.56)	27%	4.66 (3.96, 5.49)	4.19 (3.42, 5.13)
Current smoker	16%	17.3 (15.0, 19.8)	15.6 (13.1, 18.6)	19%	19.8 (16.0, 24.5)	19.7 (15.2, 25.6)	13%	15.6 (13.0, 18.6)	12.8 (10.1, 16.3)
Time since quitting smoking[c]									
Never smoker	53%	1	1	45%	1	1	60%	1	1
Former smoker, who quit									
≥ 40 years ago	5%	1.21 (0.90, 1.63)	1.15 (0.80, 1.63)	6%	1.21 (0.83, 1.77)	1.32 (0.85, 2.04)	3%	1.58 (0.97, 2.60)	1.18 (0.60, 2.31)
30-39 years ago	5%	2.16 (1.72, 2.71)	2.24 (1.72, 2.92)	6%	2.30 (1.70, 3.12)	2.53 (1.77, 3.60)	4%	2.28 (1.58, 3.29)	2.28 (1.49, 3.48)
20-29 years ago	6%	4.00 (3.37, 4.76)	4.20 (3.43, 5.15)	6%	4.60 (3.61, 5.88)	4.91 (3.67, 6.55)	5%	3.61 (2.77, 4.71)	3.90 (2.87, 5.31)
10-19 years ago	6%	6.74 (5.75, 7.90)	6.68 (5.49, 8.12)	7%	7.96 (6.32, 10.0)	8.26 (6.24, 10.9)	6%	5.85 (4.63, 7.38)	5.57 (4.14, 7.49)
0-9 years ago	10%	11.8 (10.1, 13.7)	11.4 (9.43, 13.8)	11%	14.2 (11.3, 17.7)	14.5 (11.0, 19.1)	9%	10.1 (8.20, 12.5)	9.21 (6.96, 12.2)
Current smoker	16%	19.0 (16.6, 21.9)	17.5 (14.7, 20.9)	19%	21.8 (17.6, 27.0)	22.1 (17.0, 28.7)	13%	17.4 (14.6, 20.9)	14.5 (11.4, 18.5)
Current smoking frequency[d]									
Never	56%	1	1	52%	1	1	61%	1	1
Former smoker, who quit									
≥ 40 years ago	2%	1.21 (0.90, 1.63)	1.14 (0.80, 1.63)	3%	1.19 (0.82, 1.74)	1.30 (0.84, 2.01)	1%	1.57 (0.96, 2.57)	1.17 (0.60, 2.29)
30-39 years ago	3%	2.17 (1.73, 2.73)	2.25 (1.73, 2.93)	4%	2.29 (1.69, 3.11)	2.52 (1.77, 3.59)	3%	2.28 (1.58, 3.29)	2.28 (1.49, 3.48)
20-29 years ago	5%	4.04 (3.40, 4.81)	4.23 (3.45, 5.18)	5%	4.61 (3.61, 5.89)	4.91 (3.67, 6.56)	5%	3.63 (2.79, 4.74)	3.93 (2.89, 5.34)
10-19 years ago	6%	6.83 (5.82, 8.00)	6.74 (5.54, 8.20)	6%	8.01 (6.35, 10.1)	8.29 (6.26, 11.0)	6%	5.90 (4.67, 7.44)	5.62 (4.17, 7.56)
0-9 years ago	10%	12.0 (10.3, 14.0)	11.6 (9.56, 14.0)	10%	14.3 (11.4, 18.0)	14.6 (11.1, 19.2)	10%	10.3 (8.31, 12.7)	9.34 (7.06, 12.4)
Current smoker									
0-19 cigarettes/day	14%	12.8 (10.8, 15.3)	13.2 (10.6, 16.6)	16%	15.1 (11.5, 19.8)	17.4 (12.5, 24.2)	11%	11.5 (9.14, 14.6)	10.7 (7.81, 14.6)
≥ 20 cigarettes/day	4%	27.4 (23.5, 31.9)	23.6 (19.3, 28.9)	5%	29.1 (23.1, 36.6)	28.0 (20.9, 37.4)	4%	27.2 (22.2, 33.2)	21.1 (15.9, 28.1)
Fruit consumption									
< 2 serves/day	50%	1	1	56%	1	1	45%	1	1
≥ 2 serves/day	50%	0.67 (0.61, 0.74)	0.87 (0.78, 0.97)	44%	0.68 (0.60, 0.77)	0.82 (0.71, 0.95)	55%	0.66 (0.56, 0.77)	0.93 (0.78, 1.12)
Physical activity[e]									
< 150 min/week	74%	1	1	69%	1	1	79%	1	1
≥ 150 min/week	26%	0.79 (0.71, 0.88)	0.82 (0.73, 0.92)	31%	0.72 (0.62, 0.82)	0.76 (0.66, 0.88)	21%	0.92 (0.77, 1.08)	0.91 (0.77, 1.09)

CI, Confidence interval; HR, Hazard ratio; PR, Prevalence

[a] Age, sex, study and the risk factor of interest

[b] Age, sex, study, smoking, fruit consumption and physical activity

[c] Evaluated in the subset of former smokers (95%) who provided information on time since quitting.

[d] Evaluated in the subset of current smokers (93%) who provided information on smoking frequency. Prevalence of smoking frequency was estimated from the National Drug Strategy Household Survey and therefore differs from prevalence for smoking status and time since quitting smoking estimated from the National Health Survey

[e] Australian recommendation: ≥ 150 min/week of moderate physical activity or ≥ 75 min/week of vigorous physical activity or combination of the two

Note: Some percentages do not add up to 100 because of rounding

Table 3. Fractions of lung cancers attributable to all exposure (attributable burden) and current exposure (modifiable burden)

	MEN AND WOMEN		MEN		WOMEN	
	PAF (95% CI)		PAF (95% CI)		PAF (95% CI)	
RISK MODIFICATION	**MODEL 1[a]**	**MODEL 2[b]**	**MODEL 1[a]**	**MODEL 2[b]**	**MODEL 1[a]**	**MODEL 2[b]**
Attributable burden						
Smoking						
Former and current smokers to never smokers[c]	79.3 (76.9, 81.4)	78.0 (74.8, 80.8)	83.3 (80.1, 86.1)*	83.9 (79.9, 87.1)*	74.5 (71.0, 77.7)	71.1 (65.9, 75.5)
Former smokers to never smokers[c]	24.8 (22.6, 26.9)	24.3 (21.5, 26.9)	24.6 (21.7, 27.4)	24.1 (20.6, 27.5)	25.2 (22.0, 28.3)	24.9 (20.5, 29.0)
Fruit consumption						
< 2 fruits/day to ≥ 2 fruits/day	20.2 (15.2, 25.0)	7.5 (1.3, 13.3)	21.1 (14.3, 27.4)	11.0 (2.4, 18.9)	18.8 (11.5, 25.4)	3.3 (-5.8, 11.6)
Physical activity[d]						
< 150 min/week to ≥ 150 min/week	16.3 (8.9, 23.1)	15.6 (6.9, 23.4)	21.7 (11.9, 29.6)	20.7 (10.1, 30.1)	6.8 (-6.8, 18.7)	7.3 (-7.8, 20.3)
Ever-smoking, fruit consumption and physical activity		82.5 (79.2, 85.2)		88.3 (84.8, 90.9)*		73.9 (67.2, 79.2)
Preventable burden						
Smoking						
Current smokers to never smokers[c]	54.5 (51.7, 57.1)	53.7 (50.0, 57.2)	58.8 (55.1, 62.2)*	59.8 (55.1, 64.0)*	49.3 (45.4, 53.0)	46.2 (40.5, 51.4)
Current smokers < 20 cigarettes per day to never smokers[c,e]	30.3 (26.8, 33.6)	32.1 (27.4, 36.5)	33.9 (28.5, 38.9)*	37.4 (30.5, 43.5)*	26.7 (22.2, 31.0)	27.0 (20.6, 32.9)
Current smokers ≥ 20 cigarettes per day to never smokers[c,e]	20.4 (18.3, 22.5)	17.9 (15.3, 20.5)	20.1 (17.2, 23.0)	18.3 (14.7, 21.7)	20.6 (17.6, 23.4)	17.4 (13.5, 21.2)
Current smokers to recent former smokers[f]	23.6 (17.6, 29.1)	18.3 (11.0, 25.1)	22.4 (13.9, 30.1)	19.3 (9.3, 28.3)	24.7 (16.4, 32.1)	17.7 (6.7, 27.4)
Current smokers ≥ 20 to <20 cigarettes per day	11.3 (8.5, 13.9)	8.2 (4.7, 11.6)	10.0 (6.0, 13.9)	7.1 (2.2, 11.9)	12.3 (8.5, 15.9)	9.1 (4.0, 13.8)
Fruit consumption						
< 2 fruits/day to ≥ 2 fruits/day	20.2 (15.2, 25.0)	7.5 (1.3, 13.3)	21.1 (14.3, 27.4)	11.0 (2.4, 18.9)	18.8 (11.5, 25.4)	3.3 (-5.8, 11.6)
Physical activity[d]						
< 150 min/week to ≥ 150 min/week	16.3 (8.9, 23.1)	15.6 (6.9, 23.4)	21.7 (11.9, 29.6)	20.7 (10.1, 30.1)	6.8 (-6.8, 18.7)	7.3 (-7.8, 20.3)
Current smoking, fruit consumption and physical activity						
Current smokers to never smokers[c]		63.0 (58.0, 67.5)		70.6 (65.0, 75.3)*		51.4 (41.4, 59.7)
Current smokers to recent former smokers[f]		31.2 (20.9, 40.1)		37.7 (24.7, 48.5)		22.0 (4.6, 36.2)

* Burden in men differs from burden in women, i.e. the 95% confidence interval of the difference of the PAF estimates for men and women does not include zero

CI, Confidence interval; PAF, Population Attributable Fraction

[a] Age, sex, study and the risk factor of interest

[b] Age, sex, study, smoking, fruit consumption and physical activity

[c] Smokers were no longer at excess risk of lung cancer 40 years after quitting smoking (see Table 2), i.e. their risk equaled the risk of never smokers

[d] Australian recommendation: ≥ 150 min/week of moderate physical activity or ≥ 75 min/week of vigorous physical activity or combination of the two

[e] Evaluated in the subset of current smokers (93%) who provided information on smoking frequency. Prevalence of smoking frequency was estimated from the National Drug Strategy Household Survey and therefore differs from prevalence for smoking status and time since quitting smoking estimated from the National Health Survey

[f] Smokers who quit < 10 years ago. Evaluated in the subset of former smokers (95%) who provided information on time since quitting.

Table 4a. Fractions of lung cancers attributable to ever-smoking by potential effect modifying factors

EFFECT MODIFIER	PAF (95% CI)[a]				
	SUBGROUP 1	SUBGROUP 2	SUBGROUP 3	SUBGROUP 4	SUBGROUP 5
Fruit consumption	< 2 serves/day	≥ 2 serves/day			
	83.7* (79.5, 87.0)	72.5 (67.4, 76.8)			
Physical activity[b]	< 150 min/week	≥ 150 min/week			
	82.9* (78.7, 86.3)	64.3 (58.5, 69.2)			
Alcohol consumption	≤ 2 drinks/day	> 2 drinks/day			
	75.7 (72.0, 78.9)	80.4 (69.3, 87.5)			
Body fatness (BMI)	< 25 kg/m^2	≥ 25 kg/m^2			
	78.2 (73.4, 82.2)	77.6 (72.9, 80.8)			
Age	< 65 years	65-74 years	≥ 75 years		
	75.4 (69.3, 80.3)	78.0# (72.1, 82.6)	68.6# (61.8, 74.2)		
Country of birth	Australia	Other			
	80.8* (77.3, 83.8)	68.8 (60.9, 75.2)			
Marital status	Not married	Married/de facto			
	81.1* (76.0, 85.1)	75.0 (70.6, 78.7)			
Educational attainment	Low	Intermediate	High		
	82.2 (78.4, 85.4)	77.5 (70.9, 82.5)	66.2* (55.2, 74.6)		
Socio-economic status	Quintile 1 (low)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (high)
	81.0 (74.8, 85.6)	85.1 (78.7, 89.5)	70.6*[c] (61.8, 77.4)	80.7 (73.2, 86.1)	68.7*[c] (58.8, 76.2)
Residential location	Major city	Inner regional	Outer regional		
	73.3# (68.0, 77.6)	85.4# (80.8, 88.8)	79.9 (72.8, 85.2)		

* Burden in this subgroup differs from all other subgroups; # Burden between these two subgroups differs, i.e. the 95% confidence interval of the difference of the PAF estimates for the subgroups does not include zero

BMI, Body mass index; CI, Confidence interval; PAF, Population Attributable Fraction

[a] Age, sex, study, smoking, fruit consumption and physical activity

[b] Australian recommendation: ≥ 150 min/week of moderate physical activity or ≥ 75 min/week of vigorous physical activity or combination of the two

[c] Burden in quintiles 3 and 5 does not differ from one another, i.e. the 95% confidence interval of the difference of these PAF estimates includes zero,

Table 4b. Fractions of lung cancers avoidable by modification of current smoking by potential effect modifying factors

EFFECT MODIFIER	PAF (95% CI)[a]				
	SUBGROUP 1	SUBGROUP 2	SUBGROUP 3	SUBGROUP 4	SUBGROUP 5
Fruit consumption	< 2 serves/day	≥ 2 serves/day			
	58.5* (53.8, 62.2)	48.5 (42.3, 54.0)			
Physical activity[b]	< 150 min/week	≥ 150 min/week			
	57.5* (52.2, 62.2)	30.5 (25.6, 34.9)			
Alcohol consumption	≤ 2 drinks/day	> 2 drinks/day			
	50.3 (46.1, 54.2)	56.7 (47.9, 64.0)			
Body fatness (BMI)	< 25 kg/m^2	≥ 25 kg/m^2			
	58.2* (52.7, 63.1)	48.9 (43.5, 53.8)			
Age	< 65 years	65-74 years	≥ 75 years		
	57.8* (52.0, 62.8)	35.2* (29.6, 40.4)	18.9 (14.0, 23.5)		
Country of birth	Australia	Other			
	53.6 (49.0, 57.8)	51.0 (43.7, 57.4)			
Marital status	Not married	Married/de facto			
	63.0* (57.3, 67.9)	44.6 (39.7, 49.1)			
Educational attainment	Low	Intermediate	High		
	60.5* (55.6, 64.8)	46.9 (40.2, 52.8)	46.3 (35.5, 55.4)		
Socio-economic status	Quintile 1 (low)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (high)
	62.8 (56.1, 68.5)	58.5 (50.6, 65.2)	35.6*[c] (27.7, 42.6)	56.7 (47.6, 64.2)	47.4*[c] (37.4, 55.7)
Residential location	Major city	Inner regional	Outer regional		
	49.9[#] (44.3, 55.0)	62.1[#] (56.0, 67.3)	54.0 (45.8, 60.9)		

* Burden in this subgroup differs from all other subgroups; [#] Burden between these two subgroups differs, i.e. the 95% confidence interval of the difference of the PAF estimates for the subgroups does not include zero

BMI, Body mass index; CI, Confidence interval; PAF, Population Attributable Fraction

[a] Age, sex, study, smoking, fruit consumption and physical activity

[b] Australian recommendation: ≥ 150 min/week of moderate physical activity or ≥ 75 min/week of vigorous physical activity or combination of the two

[c] Burden in quintiles 3 and 5 does not differ from one another, i.e. the 95% confidence interval of the difference of these PAF estimates includes zero,