Cancers in Australia in 2010 attributable to tobacco smoke

Nirmala Pandeya,[1,2] Louise F. Wilson,[1] Christopher J. Bain,[1,3] Kara L. Martin,[4] Penelope M. Webb,[1,2] David C. Whiteman[1,2]

Abstract

Objectives: To estimate the population attributable fraction (PAF) and numbers of cancers occurring in Australia in 2010 attributable to tobacco smoking, both personal and by a partner.

Methods: We used a modified Peto-Lopez approach to calculate the difference between the number of lung cancer cases observed and the number expected assuming the entire population developed lung cancer at the same rate as never smokers. For cancers other than lung, we applied the standard PAF formula using relative risks from a large cohort and derived notional smoking prevalence. To estimate the PAF for partners' smoking, we used the standard formula incorporating the proportion of non-smoking Australians living with an ever-smoking partner and relative risks associated with partner smoking.

Results: An estimated 15,525 (13%) cancers in Australia in 2010 were attributable to tobacco smoke, including 8,324 (81%) lung, 1,973 (59%) oral cavity and pharynx, 855 (60%) oesophagus and 951 (6%) colorectal cancers. Of these, 136 lung cancers in non-smokers were attributable to partner tobacco smoke.

Conclusions: More than one in eight cancers in Australia is attributable to tobacco smoking and would be avoided if nobody smoked.

Implications: Strategies to reduce the prevalence of smoking remain a high priority for cancer control.

Key words: population attributable fraction, cancer, risk factor, tobacco use, second-hand smoke

The United States Surgeon General first concluded that tobacco smoke was the likely cause of lung cancer in 1957 and issued a definitive report in 1964 stating that cigarette smoking was causally related to lung cancer, noting that the magnitude of the effect of smoking far outweighed all other factors.[1] Other cancers have since been causally related to smoking. In their first monograph dedicated to tobacco smoking in 1986, the International Agency for Research on Cancer (IARC) declared that there was sufficient evidence that tobacco smoking causes cancers of the lung, bladder, renal pelvis, oral cavity, oropharynx, hypopharynx, oesophagus, larynx and pancreas.[2] Based on further evidence, subsequent monographs in 2004[3] and 2012[4] added nasopharynx, nasal cavity and sinuses, stomach, kidney (body), ureter, uterine cervix, myeloid leukaemia, colorectum, and ovary (mucinous) to this list. IARC also concluded that second-hand smoke causes lung cancer.[3,4] In addition, there is sufficient evidence to show that parental smoking (of mother and/or father during both the preconception period and pregnancy) causes hepatoblastoma, a rare embryonic cancer.[4]

The mechanisms through which smoking causes cancer are complex. Tobacco smoke releases more than 5,300 compounds, including neutral gases, carbon and nitrogen oxides, amides, aldehydes, phenols and nitrosamines.[4] More than 70 carcinogens have been identified in tobacco smoke, of which 16 have been formally evaluated as being carcinogenic to humans. Many of the carcinogens from tobacco smoke are absorbed into the blood stream and carried to distant organs; hence, the effects are not restricted to the airways. The carcinogens in tobacco smoke considered to make the greatest contribution to human disease are polycyclic aromatic hydrocarbons (PAHs), *N*-nitrosamines, aromatic amines, aldehydes and certain volatile organic compounds.[4] Cell culture and animal studies confirm that tobacco smoke is highly mutagenic, causing frameshift mutations, base-substitution mutations and sister chromatid exchanges. Emerging data from mutation databases demonstrate that lung tumours in smokers have significantly higher prevalence of mutations in *TP53, K-RAS* and loss of heterozygosity at *FHIT* than those in non-smokers. In addition to these specific genotoxic events, there is strong evidence that tobacco smoke has adverse effects on cell proliferation, differentiation, inflammation and apoptosis.

We calculated the proportion of cancers attributable to tobacco smoking for all of the cancers listed by IARC as causally related to smoking, except hepatoblastoma. The incidence of hepatoblastoma in Australia is very low; only eight cases were diagnosed

1. QIMR Berghofer Medical Research Institute, Queensland
2. School of Public Health, The University of Queensland
3. National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Australian Capital Territory
4. Cancer Epidemiology Centre, Cancer Council Victoria
Correspondence to: Professor David C. Whiteman, Cancer Control Group, QIMR Berghofer Medical Research Institute, Locked Bag 2000, Royal Brisbane and Women's Hospital, QLD 4029; e-mail: david.whiteman@qimrberghofer.edu.au
Submitted: March 2015; Revision requested: April 2015; Accepted: May 2015

The authors have stated they have no conflict of interest.

Aust NZ J Public Health. 2015; 39:464-70; doi: 10.1111/1753-6405.12446

each year on average between 1997 and 2006.[5] For second-hand smoking, we calculated the proportion of lung cancers in non-smokers attributable to exposure to cigarette smoke from a smoking partner living in the home.

Methods

Tobacco smoking

To calculate the population attributable fraction (PAF) and number of cancers attributable to tobacco smoking, we used the method developed by Peto and Lopez[6] and refined by Parkin in the United Kingdom burden of cancer project.[7] This approach was developed to overcome the complexities of estimating the proportions of former and current smokers when the strengths of the smoking-cancer associations differ depending on the duration and intensity of past smoking. It assumes that tobacco smoking is by far the most important cause of lung cancer, that the incidence of lung cancer among non-smokers is small (and similar across populations), and that the incidence of lung cancer is determined almost entirely by the cumulative exposure of any given population to tobacco smoke.[7] Thus, the number of cancer cases attributable to smoking is the difference between the number of cancer cases observed in the population and the number expected if the entire population developed cancer at the same incidence rate as 'never smokers'.

The calculations require, from the same population, incidence rates of lung cancer in never smokers and relative risks of specific cancers in smokers relative to never-smokers. As for both Parkin[7] and Peto and Lopez,[6] we used data from the American Cancer Society's second Cancer Prevention Study (CPS II) in our primary analyses. The CPS II is a prospective cohort study with approximately 1.2 million participants, aged 30 years and over at recruitment in 1982 (median age: 57yrs).[8,9] Incidence rates of lung cancer in never smokers were sourced from Parkin[7] who estimated these rates from death rates in the CPS II study for the follow-up period of 1982–2002.[8]

We conducted a sensitivity analysis using Australian data from the Melbourne Collaborative Cohort Study (MCCS) for incidence rates of lung cancer in never smokers. The MCCS is a prospective cohort study of approximately 40,000 participants aged between 40–69 years (median age: 56 yrs) at recruitment (1990–1994).[10,11] The follow-up for incident cancers in the MCCS analysis was the minimum of either diagnosis of cancer of interest, or the date of death, or the date of emigration from Australia, or 10 years post-baseline attendance. The average follow-up time for lung cancer, for example, was 9.23 years. We used MCCS data for sensitivity analyses rather than the primary analyses due to the small number of cancers diagnosed during the follow-up period and the restricted age group. The sample used to calculate incidence rates of lung cancer in never-smokers and the relative risks was 40,164 (41% men, 59% women); 25% of participants were of Southern European origin.[12] Where relative risks for site-specific cancers from the MCCS were less than 1.0 (stomach, ovary (mucinous) and myeloid leukaemia), we used the relative risks from CPS II.

Relative risk estimates

For comparability with the UK PAF project,[7] we used the relative risks of death from cancer for current smokers at baseline versus never smokers,[13-15] summarised in Table 1. While the relative risks for cancer mortality are likely conservative for cancer incidence, they have the advantage of being derived from a well-characterised cohort with a long duration of follow-up and a sample size sufficiently large to generate precise estimates of risk for less common cancers. For all these reasons, the mortality risk estimates of this cohort were considered the most desirable for our purposes. The only exception was for mucinous cancer of the ovary, a site for which no risk estimates have been published from the CPS II cohort. For that cancer site, we used the relative risk estimate for cancer incidence (not mortality) from a meta-analysis by Jordan and colleagues.[16] As above, we conducted sensitivity analyses using relative risks for incident (as opposed to fatal) cancers from the MCCS for each of the specified sites for current smokers versus never smokers (Table 1).

Statistical analysis

The number of lung cancer cases expected in Australian adults in the absence of smoking was calculated by applying the estimated incidence rates of lung cancer in never smokers in the CPS II study to

Table 1: Estimated relative risks (RR) for current smokers aged ≥35 years compared with never smokers.

Cancer (ICD-10 code)	Primary analysis				Sensivitiy analysis	
	Source	Study (follow-up period)	Relative Risks		Study (follow-up period)	Relative Risks[a]
			Males	Females		
oral cavity and pharynx (C00-C14)	US Department of Health and Human Services[15]	CPS II (1982-1988)	10.9	5.1	MCCS (average 10 yrs)[12]	2.84
oesophagus (C15)	US Department of Health and Human Services[15]	CPS II (1982-1988)	6.8	7.8	MCCS (average 10 yrs)[12]	3.96
stomach (C16)	Ezzati et al. (2005)[13]	CPS II (1982-1988)	2.2	1.5	CPS II (1982-1988)[13]	2.2 (M) 1.5 (F)
colorectum (C18-C20)	Hannan et al. (2009)[14]	CPS II Nutrition Cohort (1992-2005)	1.2	1.3	MCCS (average 10 yrs)[12]	1.09
liver (C22)	Ezzati et al (2005)[13]	CPS II (1982-1988)	2.3	1.5	MCCS (average 10 yrs)[12]	4.14
pancreas (C25)	Ezzati et al (2005)[13]	CPS II (1982-1988)	2.2	2.2	MCCS (average 10 yrs)[12]	1.15
larynx (C32)	US Department of Health and Human Services[15]	CPS II (1982-1988)	14.6	13.0	MCCS (average 10 yrs)[12]	4.69
lung (C34)	Ezzati et al (2005)[13]	CPS II (1982-1988)	21.3	12.5	MCCS (average 10 yrs)[12]	23.14
uterine cervix (C53)	Ezzati et al (2005)[13]	CPS II (1982-1988)		1.5	MCCS (average 10 yrs)[12]	1.12
ovary (mucinous) (C56)	Jordan et al (2006)[16]	Meta-analysis of 1 cohort, 6 case-control, and 1 pooled analysis of case-control studies		2.1	Meta-analysis of 1 cohort, 6 case-control, and 1 pooled analysis of case-control studies[16]	2.1
urinary bladder (C67)	Ezzati et al(2005)[13]	CPS II (1982-1988)	3.0	2.4	MCCS (average 10 yrs)	3.37
kidney and ureter (C64-C66)	Ezzati et al (2005)[13]	CPS II (1982-1988)	2.5	1.5	MCCS (average 10 yrs)[12]	1.17
myeloid leukaemia (C92)	Ezzati et al (2005)[13]	CPS II (1982-1988)	1.9	1.2	CPS II (1982-1988)[13]	1.9 (M) 1.2 (F)

Abbreviations: CPS II: American Cancer Society's Second Cancer Prevention Study, MCCS: Melbourne Collaborative Cohort Study, M: male, F: female.

a: Based on 677 cases in never smokers in the MCCS.

Table 2: Estimated notional prevalence (%) of smoking by age and sex: Australia 2010 and observed smoking prevalence, National Health Survey (NHS) 2007-08.

Age group (years)	Observed smoking prevalence (%) NHS 2007-08a				Estimated notional prevalence (%)	
	Current Smoker		Ex-Smoker			
	Males	Females	Males	Females	Males	Females
0-14	-	-	-	-	0	0
15-24	20	17	9	10	0	0
25-34	33	22	26	24	0	0
35-44	28	22	27	27	3	2
45-54	24	22	37	26	17	16
55-64	16	17	48	31	30	31
65-74	11	9	55	30	32	36
75+	5	5	61	28	23	21

a: Source: Australian Bureau of Statistics[29]

the population of Australia in 2010. The number and percentage of lung cancer cases attributable to smoking was then calculated by subtracting the expected number of cases from those actually observed in 2010.[17]

The Peto-Lopez method could not be used for other sites, as estimates of cancer incidence in never smokers for other sites were not available. So, to be able to apply the standard PAF formula for the remaining cancer sites, we estimated the 'notional prevalence' (P_e) of smoking for each age and sex category in the Australian population. The notional prevalence is an abstract construct that reflects the average past smoking experience of the population. Thus, P_e is the prevalence of smoking necessary to produce the incidence of cancer observed in the Australian population assuming the relative risks of the CPS II study had pertained. Essentially, it cumulates the person-time contributions of former smokers and current smokers into a single quantity. We calculated notional prevalence using the formula:[6,7]

$$P_e = \frac{I_o - I_e}{I_e\left(RR_{lung} - 1\right)}$$

Table 3: Population attributable fraction (PAF) and estimated number of lung cancers (C34) diagnosed in Australia in 2010 attributable to tobacco smoking.

Age group (years)	Population ('000s)	Observed Incidence (per 10^{-5}/yr)	Cases Observed	Expected Incidence[a] (per 10^{-5}/yr)	Cancers Expected[b]	Excess Cancers[c]	PAF[d]
Males							
0-14	2,171	0.1	1	0.0	0	1	0.0
15-24	1,620	0.1	2	0.0	0	2	0.0
25-34	1,613	0.7	11	0.7	11	0	0.0
35-44	1,575	4.7	74	2.9	46	28	38.1
45-54	1,508	26.5	399	6.0	91	308	77.2
55-64	1,260	100.4	1,265	14.1	178	1,087	85.9
65-74	794	250.6	1,990	33.0	262	1,728	86.8
75+	583	428.3	2,498	75.8	442	2,056	82.3
Total	11,124	56.1	6,240	-	1,030	5,210	83.5
Females							
0-14	2,060	0.1	2	0.0	0	2	0.0
15-24	1,530	0.2	3	0.0	0	3	0.0
25-34	1,586	0.5	9	0.5	9	0	0.0
35-44	1,594	4.6	74	3.8	60	14	18.8
45-54	1,537	20.9	321	7.4	114	207	64.5
55-64	1,278	67.8	866	14.7	188	678	78.3
65-74	826	150.3	1,241	28.9	239	1,002	80.7
75+	806	189.4	1,526	56.3	454	1,072	70.3
Total	11,218	36.0	4,042	-	1,064	2,978	73.7
Grand total			10,282		2,094	8,188	79.6

a: Incidence rates expected in a population that has never smoked, taken from US rates in CPS II
b: Lung cancers expected in 2010 a population that had never smoked
c: Excess lung cancers in 2010 attributable to tobacco smoking
d: PAF = Population attributable fraction (expressed as a percentage)

where I_o is the observed incidence of lung cancer, I_e is the incidence expected in the absence of smoking and RR_{lung} is the relative risk of lung cancer in current smokers versus never smokers from the CPS II study.

The notional prevalences of smoking in Australia are presented in Table 2. Using these notional prevalences and the relative risks for the additional cancers listed in Table 1, we used the standard formula to estimate the PAFs for each cancer site.[18]

$$\text{PAF} = \frac{\Sigma(p_e \text{ x ERR})}{1 + \Sigma(p_e \text{ x ERR})}$$

where p_e is the notional prevalence of smoking in the population and ERR the excess relative risk (RR–1) of cancer associated with current smoking.

To obtain the numbers of cancers attributable to smoking, the PAFs were multiplied by the total numbers of incident cancers at each site.

Exposure to partner smoking in the home

Estimating the fraction of cancer among never smokers attributable to smoking by others requires estimates of the relative risks of cancer from this pattern of tobacco smoke exposure, as well as the prevalence of exposure to other people's smoke. The most robust estimates of the effect of 'second-hand' smoke arise from studies reporting risks of lung cancer among never smokers who have lived with a smoking partner. We therefore restricted this analysis to estimate the number of cancers attributable to smoking among non-smokers currently living with a smoking partner, as described below.

Relative risks

Relative risks for lung cancer among never-smokers exposed to tobacco smoke from a smoking partner were obtained from pooled estimates published by the World Health Organization and IARC in 2004.[3] Based on the results of 11 studies (442 lung cancer cases), the pooled relative risk for males was 1.37 (95%CI 1.02-1.82, p=0.03). For females, the pooled relative risk was 1.24 (95%CI 1.14-1.34, p<0.001) based on the results of 46 studies (6,257 lung cancer cases).[3]

Prevalence estimates

We estimated the numbers of non-smoking Australians residing with a smoking partner using marital (and co-habiting) status data from the 2011 Population Census[19] and smoking status data from the 2011-12

Australian Health Survey,[20] following the approach of Parkin.[7]

Briefly, we assumed that smokers and non-smokers do not co-habit randomly, but rather that households tend to be concordant for smoking status. As proposed by Wald and colleagues[21] and used by Parkin,[7] we used an 'aggregation factor' of 3.0 to express the relative probability that couples have the same smoking status (In other words, ever smokers and never smokers are three times more likely to live with a partner of the same smoking status than with someone of the opposite smoking status). We further assumed that couples were of similar age. We thus estimated the proportions of never smokers in 2011 living with a partner who had ever smoked, by sex and age group.

From this, we calculated the fractions of lung cancers among never smokers attributable to living currently with an ever smoker.

Results

Tobacco smoking

An estimated 8,188 lung cancer cases (5,210 in men and 2,978 in women) from a total of 10,282 diagnosed in Australia in 2010 were attributable to tobacco smoking (Table 3). The corresponding PAFs were 84% in men and 74% in women. A further 7,201 cancers at 12 cancer sites other than lung (5,183 in men and 2,018 in women) from a total of 34,248 diagnosed were also attributable to smoking. Cancers other than lung with the highest PAFs were larynx (77%), followed by oesophagus (60%), oral cavity and pharynx (59%) and bladder (32%). Cancers other than lung with the greatest number of estimated cases attributable to smoking in 2010 were oral cavity and pharynx (1,973), colorectum (951) and oesophagus (855) (Table 4). Overall then, we estimated a total of 15,389 cases of cancer across thirteen sites in 2010 were attributable to tobacco smoking. This was 13% of all cancer cases (excluding basal cell and squamous cell carcinomas of the skin), 16% in males and 10% in females.

In sensitivity analyses using data from the MCCS and restricted to age groups 40–69 years, we estimated that the total number of cancers attributable to smoking was 6,284, or about 12% lower than the number estimated in the primary analyses for the same age groups (n=7,160) (Table 5). This was because several common cancers (oral cavity, pharynx, larynx, oesophagus, colorectum)

Table 4: Population attributable fraction (PAF) and estimated number of site-specific cancers (other than lung) diagnosed in Australia in 2010 attributable to tobacco smoking.

Age (yrs)	Oral Cavity & Pharynx (C00-C14)[a]			Oesophagus (C15)[a]			Stomach (C16)[a]			Colon-Rectum (C18-C20)[a]			Liver (C22)[a]			Pancreas (C25)[a]			Larynx (C32)[a]			Cervix (C53)[a]			Ovary – Mucinous (Est.) Only (C56)[a]			Bladder (C67)[a]			Kidney & Ureter (C64-C66)[a]			Myeloid Leukaemia (C92)[a]		
	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF	Obs.	Exp.	PAF
Males																																				
0-14	5	5	0.0	0	0	0.0	0	0	0.0	0	0	0.0	6	6	0.0	1	1	0.0	0	0	0.0							1	1	0.0	17	17	0.0	24	24	0.0
15-24	14	14	0.0	0	0	0.0	2	2	0.0	16	16	0.0	2	2	0.0	0	0	0.0	1	1	0.0							0	0	0.0	4	4	0.0	20	20	0.0
25-34	54	54	0.0	3	3	0.0	7	7	0.0	55	55	0.0	6	6	0.0	12	12	0.0	2	2	0.0							3	3	0.0	22	22	0.0	37	37	0.0
35-44	195	150	23.1	18	15	15.0	35	34	3.5	212	211	0.7	25	24	3.8	27	26	3.5	7	5	29.2							17	16	5.7	115	110	4.4	50	48	2.7
45-54	494	186	62.3	102	52	49.2	115	96	16.7	765	735	3.9	179	147	17.8	106	89	16.7	62	19	69.4							100	75	25.0	275	220	20.0	73	63	13.1
55-64	644	162	74.9	259	94	63.6	270	198	26.5	1,897	1,769	6.7	271	195	28.1	296	217	26.5	149	29	80.4							274	171	37.6	500	344	31.1	132	104	21.3
65-74	533	126	76.3	293	102	65.3	373	268	28.1	2,560	2,375	7.2	253	178	29.7	427	307	28.1	166	31	81.5							494	299	39.4	508	342	32.8	182	141	22.6
75+	419	128	69.4	332	143	57.1	512	401	21.6	2,752	2,608	5.2	282	217	22.9	539	423	21.6	155	38	75.7							946	649	31.4	484	360	25.6	275	228	17.1
Total	2,358	825	65.0	1,007	409	59.4	1,316	1,006	23.4	8,257	7,769	5.9	1,024	775	24.3	1,408	1,075	23.7	542	125	77.1							1,835	1,214	33.8	1,925	1,419	26.3	793	665	16.1
Females																																				
0-14	2	2	0.0	0	0	0.0	1	1	0.0	1	1	0.0	6	6	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	1	1	0.0	16	16	0.0	14	14	0.0
15-24	7	7	0.0	1	1	0.0	1	1	0.0	11	11	0.0	1	1	0.0	1	1	0.0	0	0	0.0	20	20	0.0	5	5	0.0	0	0	0.0	4	4	0.0	17	17	0.0
25-34	30	30	0.0	0	0	0.0	6	6	0.0	56	56	0.0	4	4	0.0	3	3	0.0	1	1	0.0	131	131	0.0	14	14	0.0	4	4	0.0	20	20	0.0	22	22	0.0
35-44	69	64	7.6	5	5	12.0	27	27	1.0	199	198	0.6	7	7	1.0	22	21	2.4	2	2	19.5	178	176	1.0	18	18	2.2	10	10	2.7	62	62	1.0	50	50	0.4
45-54	148	90	39.3	31	15	51.8	59	55	7.3	619	591	4.5	33	31	7.3	71	60	15.9	8	3	65.4	168	156	7.3	29	24	14.8	25	21	18.1	158	146	7.3	50	48	3.1
55-64	214	94	56.3	63	20	68.1	103	89	13.6	1,225	1,120	8.6	72	62	13.6	193	140	27.4	23	5	79.0	134	116	13.6	32	24	25.7	96	67	30.5	244	211	13.6	105	99	5.9
65-74	199	80	59.9	104	30	71.3	146	123	15.4	1,696	1,529	9.9	86	73	15.4	310	216	30.4	26	5	81.4	88	74	15.4	28	20	28.6	154	102	33.8	301	254	15.4	113	106	6.8
75+	302	164	45.7	213	89	58.3	342	310	9.3	2,794	2,632	5.8	171	155	9.3	654	524	19.8	24	7	71.1	100	90	9.3	30	25	18.4	334	259	22.3	378	343	9.3	238	228	3.9
Total	971	531	45.4	417	160	61.7	685	612	10.6	6,601	6,138	7.0	380	339	10.9	1,254	965	23.0	84	23	73.5	819	763	6.7	156	130	16.9	624	464	25.8	1,183	1,056	10.7	609	584	4.1
Total (Persons)	3,329	1,356	59.3	1,424	569	60.1	2,001	1,618	19.0	14,858	13,907	6.4	1,404	1,114	20.7	2,662	2,040	23.3	626	148	76.6	819	763	6.7	156	130	16.9	2,459	1,678	31.8	3,108	2,475	20.4	1402	1,249	10.9
Excess cases		1,973			855			383			951			290			622			478			56			26			781			633			153		

Total excess cases (12 cancers excl. lung)	**7,201**	**(5,183 males; 2,018 females)**
Total excess cases (lung cancer)	**8,188**	**(5,210 males; 2,978 females)**
Total excess cases (12 cancers + lung)	**15,389**	**(10,393 males; 4,996 females)**
PAF all cancers diagnosed in 2010[b]	**13.3%**	**(15.8% males; 10.0% females)**

Abbreviations: Obs. = observed cancers in 2010; Exp. = cancers expected in 2010 a population that had never smoked; PAF = population attributable fraction (expressed as a percentage)

a: International Classification of Diseases Code (ICD- 10)

b: excluding basal cell carcinoma and squamous cell carcinoma of the skin

Table 5: Sensitivity Analysis: comparison of results using data from the Melbourne Collaborative Cohort Study (MCCS) and the American Cancer Society's Second Cancer Prevention Study (CPSII) (restricted to age groups 40-69 yrs).

	Observed Cases (2010) 40-69 yrs	Sensitivity Analysis[a]		Primary Analysis[b]	
		Excess cases due to tobacco	% observed cases due to tobacco	Excess cases due to tobacco	% observed cases due to tobacco
Males (40-69 yrs)					
Oral cavity & pharynx (C00-C14)	1,559	458	29.4	902	57.9
Oesophagus (C15)	515	237	46.0	290	56.4
Stomach (C16)	600	86	14.4	138	23.1
Colorectum (C18-C20)	4,099	127	3.1	243	5.9
Liver (C22)	588	251	42.7	135	22.9
Pancreas (C25)	621	32	5.1	147	23.6
Larynx (C32)	305	157	51.5	222	72.9
Lung (C34)	2,636	2,354	89.3	2,219	84.2
Kidney and ureter (C64-C66)	1091	53	4.9	272	24.9
Bladder (C67)	597	262	43.9	206	34.6
Myeloid leukaemia (C92)	322	19	5.8	53	16.6
All cancers* in males 40-69 yrs	**34,378**	**4,036**	**11.7**	**4,827**	**14.0**
Females (40-69 yrs)					
Oral cavity & pharynx (C00-C14)	504	168	33.3	245	48.6
Oesophagus (C15)	147	75	51.3	96	65.1
Stomach (C16)	251	39	15.7	30	11.9
Colorectum (C18-C20)	2,790	99	3.6	218	7.8
Liver (C22)	148	73	49.4	18	12.4
Pancreas (C25)	420	26	6.2	108	25.8
Larynx (C32)	41	22	52.1	31	74.5
Lung (C34)	1,842	1,567	85.1	1,391	75.5
Uterine Cervix (C53)	429	12	2.7	38	8.9
Ovary (C56)	692	19	2.7	17	2.5
Kidney and ureter (C64-C66)	593	35	5.8	69	11.6
Bladder (C67)	205	99	48.4	61	29.6
Myeloid leukaemia (C92)	234	14	6.1	11	4.7
All cancers* in females 40-69 yrs	**26,856**	**2,248**	**8.4**	**2,333**	**8.7**
Persons (40-69 yrs)					
Oral cavity & pharynx (C00-C14)	2,063	626	30.3	1,147	55.6
Oesophagus (C15)	662	312	47.2	386	58.3
Stomach (C16)	851	125	14.8	168	19.8
Colorectum (C18-C20)	6,889	226	3.3	461	6.7
Liver (C22)	736	324	44.0	153	20.8
Pancreas (C25)	1,040	58	5.5	255	24.5
Larynx (C32)	346	179	51.6	253	73.1
Lung (C34)	4,478	3,921	87.6	3,610	80.6
Uterine Cervix (C53)	429	12	2.7	38	8.9
Ovary (C56)	692	19	2.7	17	2.5
Kidney and ureter (C64-C66)	1,685	88	5.2	341	20.2
Bladder (C67)	802	361	45.0	267	33.3
Myeloid leukaemia (C92)	556	33	5.9	64	11.6
All cancers* in persons 40-69 yrs	**61,234**	**6,284**	**10.3**	**7,160**	**11.7**

** excluding basal cell and squamous cell carcinomas of the skin*

a: Using incidence rates of lung cancer in never smokers and relative risks of specific cancers in smokers relative to smokers from the MCCS (except for stomach, ovary and myeloid leukaemia)

b: Using incidence rates of lung cancer in never smokers and relative risks of specific cancers in smokers relative to smokers from the CPS II Study

had considerably lower relative risks in MCCS than CPS II. The PAF from the sensitivity analysis was 10.3% compared with 11.7% in the primary analysis, an absolute difference of 1.4%.

Exposure to smoking by a partner

We estimated that about 17% of non-smoking men and 25% of non-smoking women in Australia resided with a partner who had ever smoked (Table 6). Using these estimates, 136 lung cancer cases diagnosed in never smokers in 2010 (63 in men and 73 in women) were attributable to smoking by a partner. This corresponds to 6.1% and 6.7% of lung cancers arising in never smoking men and women respectively.

Discussion

About 13% of all cancer cases occurring in Australia in 2010 (excluding basal cell and squamous cell carcinomas of the skin) were attributable to tobacco. Of the more than 15,500 cases of cancer attributable to tobacco, more than half (~8,300) were cancers of the lung, including about 130 due to smoking by a partner (about 6% of lung cancers occurring in never smokers). The PAFs appeared to differ slightly for men and women, accounting for 84% and 74% of lung cancer cases respectively. For cancers other than lung, PAFs were highest for larynx (77%), oesophagus (60%) and oral cavity and pharynx (59%), while in absolute terms the greatest number of cases attributable to smoking occurred in the oral cavity and pharynx (1,973).

Our findings can be compared with the UK PAF study, which used very similar methods and identical relative risk estimates. We found that overall, 16% of cancers in men and 10% of cancers in women were attributable to tobacco smoking, which is markedly lower than the UK PAF estimates of 23% of cancers in men and 15% of cancers in women.[7] It is important to note that the 'total smoking PAFs' for each population are calculated by summing the counts of attributable cancers at smoking-related sites, and dividing by the sum of the counts for all cancers. The denominator includes all cancers, not just those related to smoking, and there are differences in the relative frequencies of non-smoking-related cancers between Australia and the UK (notably prostate cancer and melanoma, for which Australia has the highest incidence in the world). Having these

cancers in the denominator serves to reduce the 'total smoking PAF' for Australia relative to the UK. Thus, while lower smoking prevalence in Australia explains the lower PAFs at all smoking-related cancer sites, it only partially explains the marked difference in total smoking PAFs between the two populations. Estimates of the fraction of cancers attributable to tobacco smoke in the French population in 2000 were 27% of cancers in men and 6% in women, albeit derived using very different methodology (including a 15-year latency; prevalence data 1985, estimated PAF for 2000).[22]

Using different approaches, others have estimated the burden of cancer in Australia due to smoking. Begg et al.[23] estimated that 20% of the disability-adjusted life years lost to cancers in 2003 were due to tobacco use, while Peto et al.[24] estimated that 23% of cancer deaths in 2000 were attributable to smoking. These figures are both higher than our overall estimate of 13% of incident cancers attributable to smoking, but again this is due to the fact that we were reporting on cancer diagnoses not cancer deaths.

Because smoking-related cancer sites have poorer survival than non-smoking related sites on average, the contribution of smoking to cancer mortality is higher than its contribution to cancer incidence.

The Peto-Lopez method[6] for estimating the fraction of cancer attributable to smoking assumes that the excess incidence of lung cancer, over and above the incidence among never smokers, is due solely to the cumulative effects of past and current tobacco smoking. The observed lung cancer incidence is then used to derive the 'notional prevalence of smoking', that is, the prevalence of smoking in the Australian population that would have been necessary to produce the observed incidence rates, assuming that the CPS II risk estimates for lung cancer had applied. To calculate the fraction of cancer attributable to smoking at each additional site, we applied the notional prevalence of smoking to the standard PAF formula,[18] along with the site-specific relative risks. This method is efficient and advantageous because it does not require detailed information about the proportions of current and former smokers in the population, nor separate relative risk estimates for the many categories of 'amount smoked' and 'time since quitting', each with attendant imprecision. The method is not without error however, since its application to populations with different smoking distributions may be imprecise, to an uncertain degree.

Another assumption is that the relative risks of cancer-specific mortality generated from CPS II (and used in previous studies) are appropriate for estimating PAFs for cancer incidence. Given the long duration of follow-up of the CPS II study (out to 20 years from baseline), and the generally high case-fatality rates for each of the smoking-related cancers considered, we contend that relative risks for mortality and incidence should be largely equivalent over the time. Nevertheless, we performed sensitivity analyses using relative risks for incident cancers derived from the MCCS. Being a smaller study than CPS II, and with a restricted age range, the MCCS risk estimates were less precise but, even so, the overall burden of cancer attributable to smoking estimated using those Australian data was of similar magnitude to those obtained using the US-based estimates. PAF estimates at specific cancer sites were not similar using the two approaches, reflecting differences in the relative risk estimates from the CPS-II and MCCS.

The PAF estimates for lung cancers attributable to exposure to smoking by a partner were based on data imputed from a number of secondary sources, and as such, may be subject to error. On the one hand, the PAFs calculated here may underestimate the true burden of lung cancer attributable to second-hand smoke because the relative risk estimates only accounted for current relationships and did not include possible hazards incurred from cohabiting with smokers in previous relationships. On the other hand, it is also possible that ever-smoking partners only smoked with former partners and not with their current partner as we have assumed. Finally, we estimated only the prevalence of cohabiting with a smoking partner and not the prevalence of cohabiting with other smokers since there are no prevalence data capturing such exposures in Australia. For these reasons, while the PAF estimates based on non-smokers with a current partner who had ever smoked are the best that can be derived with available data, it is likely that they underestimate the true impact of second-hand smoke on lung

Table 6: Prevalence estimates of cohabitation with smoking partner among never smokers in Australia and fraction of lung cancer cases among never smokers in Australia attributable to cohabitation with smoking partner.

Age Group (yrs)	% Population never smokers[a]	% Population living with partner[b]	Estimated prevalence Never-smokers living with ever smoking partner (%)[c]	PAF	Lung cancer cases expected in never smokers	Excess cases in never smokers due to exposure to partner smoking
Men						
15-24 yrs	71	8	1	0.6	0	0
25-34 yrs	48	57	16	5.6	15	1
35-44 yrs	47	76	25	8.4	46	4
45-54 yrs	40	75	27	9.2	91	8
55-64 yrs	36	77	21	7.3	178	13
65-74 yrs	36	78	19	6.7	262	17
75 + yrs	28	72	13	4.5	442	20
Total	46	61	17	6.1[d]	1,034	63
Women						
15-24 yrs	75	15	3	0.8	0	0
25-34 yrs	58	65	27	6.1	26	2
35-44 yrs	53	75	30	6.7	60	4
45-54 yrs	48	73	34	7.5	114	9
55-64 yrs	56	70	38	8.3	188	16
65-74 yrs	60	63	34	7.5	239	18
75 + yrs	67	36	24	5.4	454	24
Total	59	59	25	6.7[d]	1,081	73
Grand total				6.4[d]	2,115	136

Abbreviations: PAF = population attributable fraction amongst never smokers (expressed as a percentage).

a: 2011-12 National Health Survey[20]

b: generated from Australian Bureau of Statistics (2011)[19]

c: Estimates are based on cohabitation status and population smoking status, and assume couples are in the same broad age group as those in the table and the relative probability of couple being concordant for smoking status Is 3.021

d: Age-weighted population attributable fraction (expressed as a percentage)

cancer incidence in the Australian population. Importantly, our estimates of the burden of cancer attributable to environmental tobacco smoke do not account for smoking exposure in the workplace. This is because data on past occupational exposure to tobacco smoke were not available. It is worth noting that the prevalence of smoking has undergone profound changes over the past 80 years. Smoking increased rapidly in Australia after World War II, with smoking levels peaking in males in the 1950s (72%) and in females in the 1970s (31%).[25,26] Then followed steady declines in smoking prevalence so that by 2001, 24% of the Australian adult population were current smokers, 26% were ex-smokers and 49% were never smokers.[20] Rates have continued to decline, with 18% of the Australian adult population (18+ years) current smokers, 31% ex-smokers and 51% never smokers in 2011-12.[20] Recently, there have been declines in the incidence of smoking-related cancers[27] (except, notably, for lung cancer in women[28]), reflecting fewer people inhaling carcinogens from cigarettes and tobacco. Assuming these trends continue, then repeating these analyses in 10 years from now should be a rewarding experience.

Acknowledgements

This work was supported by a grant from Cancer Council Australia. NP, PMW and DCW were supported by Research Fellowships from the National Health and Medical Research Council of Australia (NHMRC). CJB was supported by a NHMRC Program Grant (552429). The funding bodies had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, or the preparation, review, or approval of the manuscript.

The Melbourne Collaborative Cohort Study was made possible by the contribution of many people, including the original investigators, the program manager, and the diligent team who recruited the participants and who continue working on follow-up. We would like to express our gratitude to the many thousands of Melbourne residents who continue to participate in the study. Cohort recruitment was funded by VicHealth and Cancer Council Victoria.

NP and LFW contributed equally to this manuscript and share first authorship.

PAF Project

Chief Investigators: David C. Whiteman, Penelope M. Webb, Adele C. Green, Rachel E. Neale, Lin Fritschi

Associate Investigators: Louise F. Wilson, Catherine M. Olsen, Christina M. Nagle , Nirmala Pandeya, Susan J. Jordan, Annika Antonsson, Bradley J. Kendall, Torukiri I. Ibiebele, Maria Celia B. Hughes, Kyoko Miura, Susan Peters, Renee N. Carey

Advisers: Christopher J. Bain, D. Max Parkin

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