Cancers in Australia in 2010 attributable to overweight and obesity

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Abstract

Objectives: To estimate the proportion and number of cancers occurring in Australia in 2010 attributable to overweight/obesity.

Methods: We estimated the population attributable fraction (PAF) and number of cancers causally associated with overweight/obesity. We used standard formulae incorporating Australian prevalence data for body mass index (BMI), relative risks associated with BMI and cancer. We also estimated the proportion change in cancer incidence (potential impact fraction [PIF]) that may have occurred assuming that the prevalence of overweight/obesity had remained at 1990 levels.

Results: An estimated 3,917 cancer cases (3.4% of all cancers) diagnosed in 2010 were attributable to overweight/obesity, including 1,101 colon cancers, 971 female post-menopausal breast cancers and 595 endometrial cancers (PAFs of 10%, 8% and 26%, respectively). Highest PAFs were observed for oesophageal adenocarcinoma (31%), endometrial cancer (26%) and kidney cancer (19%). If the prevalence of overweight/obesity in Australia had remained at levels prevailing in 1990, we estimate there would have been 820 fewer cancers diagnosed in 2010 (PIF 2%).

Conclusions: Overweight/obesity causes a substantial number of cancers in Australia.

Implications: Public health strategies to reduce the prevalence of overweight and obesity will reduce the incidence of cancer, particularly of the colon, breast and endometrium.

Key words: population attributable fraction, cancer, risk factor, obesity, potential impact fraction

Like many other industrialised countries, overweight and obesity is one of Australia's leading health issues,[1] with prevalence increasing steadily over the past 30 years.[2] Obesity is more prevalent among the most disadvantaged socioeconomic groups, such as people without post-school qualifications, Indigenous Australians and some migrant groups.[2]

In 2002, the International Agency for Research on Cancer (IARC) concluded that there was sufficient evidence that overweight and obesity cause cancers of the oesophagus (adenocarcinoma), endometrium, kidney (renal cell), colon and breast (post-menopausal).[3] The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) in 2007 supported these conclusions, finding the evidence for these cancers, as well as rectal and pancreatic cancer, convincing. They also found evidence for probable causality for cancer of the gall bladder.[4] The conclusions for breast, colon, rectal, pancreatic and endometrial cancer were maintained in subsequent WCRF Continuous Update Project Reports.[5-8] In March 2014, a WCRF Continuous Update for ovarian cancer published a new judgement that body fatness (marked by BMI) is probably a cause of ovarian cancer.[9] WCRF updates have not yet been completed for cancers of the oesophagus, kidney and gall bladder.

The association between obesity and pre-menopausal breast cancer is uncertain. The WCRF/AICR found that it is "probable" that body fatness decreases the risk of pre-menopausal breast cancer;[8] however, other studies have found a null or positive association with waist circumference and waist-hip ratio, both measures of central obesity.[10,11] In addition, this study aimed to analyse those cancers that are caused by obesity and therefore potentially preventable. For these reasons, we have not considered pre-menopausal breast cancer. Since the publication of the WCRF/AICR Second Expert Report, a number of meta-analyses have found a significant and consistent association between obesity and other cancers: thyroid cancer;[12,13] melanoma (men only);[12] non-Hodgkin's lymphoma (NHL);[12,14] multiple myeloma;[12,15] and leukaemia.[12,16]

Body mass index (BMI), is commonly used as a measure of body fatness.[4] BMI is calculated as weight in kilograms divided by the square of height in metres (kg/m^2). Overweight and obesity are defined as levels of abnormal or excessive fat accumulation that may impair health.[17] The WHO classifies adult overweight and obesity according to BMI: Normal weight 18.50–24.99 kg/m^2; Overweight 25.00–29.99 kg/m^2; and Obese ≥30 kg/m^2.[18]

In our primary analysis, we estimated the population attributable fractions (PAF) and numbers of cancers attributable to overweight and obesity for cancers designated by IARC or WCRF/AICR up until 30 June 2014 as being

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causally associated, namely cancers of the oesophagus (adenocarcinoma only), colon, rectum, gall bladder, pancreas, breast (post-menopausal only), endometrium, ovary and kidney. In our supplementary analysis, we included estimates for those cancers for which there is accumulating evidence of a causal effect, but for which no formal declaration has been made by IARC or WCRF. The cancers in the supplementary analysis were melanoma, non-Hodgkin lymphoma (NHL), multiple myeloma, leukaemia and thyroid cancer.

Methods

Relative risk estimates

The estimates of risk associated with overweight (BMI 25–29 kg/m^2) and obesity (BMI ≥30 kg/m^2), relative to normal weight (BMI <25 kg/m^2), for the nine cancers included in the primary analysis, are summarised in Table 1. The relative risk estimates for an increase of 5 kg/m^2 from the meta-analyses by WCRF in the global report[4] or more recent Continuous Updates[5-9] have been used for the 'overweight' category and the square of this value was taken for the 'obese' category (assuming a log-linear increase in risk with BMI). For a number of cancers (pancreatic, colon and rectal) there is a sex difference in relative risks; hence, sex-specific risks were used for these cancers.

Exposure prevalence estimates

The latent period between onset of overweight and obesity and cancer diagnosis is uncertain and may vary by cancer site. In a meta-analysis of BMI and cancer incidence,[12] the geometric mean follow-up per cancer site ranged from 8.4 years for post-menopausal breast cancer to 12.7 years for gall bladder, with typical follow-up exceeding 10 years. We used prevalence data from 2001 and cancer incidence data from 2010 for our analyses to give a nominal latent period of about 10 years. To account for population ageing with time since exposure and the latent period, we used prevalence data for the age category that was 10 years younger than the corresponding cancer incidence age category. (For example, cancer incidence in the 45–54 years age group in 2010 was attributed to overweight and obesity in the 35–44 years age group in 2001).

Data on the prevalence of overweight and obesity in the Australian population, by age and sex, were sourced from self-reported measures in the 2001 National Health Survey conducted by the Australian Bureau of Statistics from February to November 2001.[19] The most recent cancer incidence data (by age and sex) were sourced from the Australian Institute of Health and Welfare (2010).

Statistical analysis

The population attributable fraction (PAF) for each age-sex group was calculated for each cancer using the standard formula:[20]

$$\mathrm{PAF} = \frac{\Sigma(p_x \times \mathrm{ERR}_x)}{1 + \Sigma(p_x \times \mathrm{ERR}_x)}$$

where p_x is the proportion of the population in exposure level x (i.e. separate levels for overweight and obesity, respectively) and ERR_x the excess relative risk ($RR_x - 1$) associated with exposure level x.

To obtain the number of cancers attributable to overweight and obesity, the PAF was applied to the number of incident cancers (for each site) occurring in 2010[21] in each category of age (25–34 years, 35–44 years, 45–54 years … 85+ years) and sex. Because histology-specific incidence data for oesophageal cancers were not available for 2010, we applied the average age-specific incidence rates between 2006 and 2008 to the 2010 Australian estimated resident population (by age and sex) to estimate the number of incident oesophageal adenocarcinomas in 2010. The total number of cancers (all types combined) attributable to overweight and obesity was expressed as a percentage of the total number of all incident cancers among adults (excluding basal cell and squamous cell carcinoma of the skin) recorded in Australia in 2010.

Table 1: Relative risks for overweight and obesity.

Cancer Site (ICD-10 code)	Reference	Evidence Status	Relative Risks		
			Sub-group	Overweight	Obese
Oesophageal adenocarcinoma (C15[a])	WCRF (2007)[4]	Convincing	Persons	1.55	2.40
Colon (C18, C19)	WCRF CUP (2011)[5]	Convincing	Males	1.20	1.44
			Females	1.10	1.21
Rectum (C20)	WCRF CUP (2011)[5]	Convincing	Males	1.10	1.21
			Females	1.05	1.10
Gall bladder (C23)	WCRF (2007)[4]	Probable	Persons	1.23	1.51
Pancreatic Cancer (C25)	WCRF CUP (2012)[7]	Convincing	Males	1.13	1.28
			Females	1.10	1.21
Breast (post-menopausal) (C50)	WCRF CUP (2010)[8]	Convincing	Females	1.13	1.28
Endometrium (C54, C55)	WCRF (2013)[6]	Convincing	Females	1.50	2.25
Ovary (C56)	WCRF (2014)[9]	Probable	Females	1.06	1.12
Kidney (C64)	WCRF (2007)[4]	Convincing	Persons	1.31	1.72

a: Oesophageal cancer with histology codes 8140-8573

Supplementary analysis

Renehan and colleagues[12] conducted a comprehensive systematic review and meta-analysis of prospective observational studies to investigate the strength of associations between BMI and cancers at a greater number of sites than considered by IARC or WCRF/AICR. That study applied a uniform method and set of definitions across all cancer sites. In our supplementary analysis we estimated the PAFs and numbers of cancers attributable to overweight and obesity for cancers meeting both of the following conditions: (i) the p-values for the pooled effect estimates were significant and (ii) the IARC or WCRF/AICR had not classified the cancers as convincingly or probably caused by overweight or obesity. The cancers meeting these criteria were malignant melanoma (men only), thyroid cancer, non-Hodgkin's lymphoma, multiple myeloma and leukaemia (see supplementary file: Table S1, available with the online version of this article).

Potential impact of reducing overweight and obesity prevalence to 1990 levels

Reducing the BMI of all Australian adults to below 25 kg/m^2 is probably not possible. We therefore modelled the impact of a hypothetical scenario in which the prevalence of overweight and obesity had remained at the (self-reported) levels reported in the 1990 National Health Survey. Thus, we calculated the potential impact fraction (PIF) using the formula from Morgenstern and Bursic:[22]

$$PIF = \frac{\sum_{x=1}^{n} p_x RR_x - \sum_{x=1}^{n} p_x^* RR_x}{\sum_{x=1}^{n} p_x RR_x}$$

where p_x is the proportion of the population in age and sex category x, RR_x is the RR for that category and p^*_x is the population in age and sex category x at 1990 levels.

For each cancer site, we calculated the number of cancer cases that would have occurred in Australia in 2010, assuming that 1990 levels of overweight and obesity had prevailed in 2001. The PIF is then the

proportional difference between the observed number of cancers and the number expected under the alternative prevalence scenario.

Results

Prevalence of overweight and obesity

Estimates of the prevalence of overweight and obesity in the adult Australian population in 2001 are presented in Table 2. Overall, 52% of men and 37% of women were overweight or obese. A higher proportion of men than women were overweight (BMI 25–29 kg/m^2) in all age groups. In contrast, the overall prevalence of obesity (BMI ≥30 kg/m^2) was similar for men and women, although it was higher for women than men over the age of 55 years.

Proportion of cancers attributable to overweight and obesity

An estimated 3,917 cancer cases diagnosed in 2010 could be attributed to overweight and obesity in the Australian adult population. This was 3.4% of all cancer cases (excluding basal cell carcinoma and squamous cell carcinoma of the skin); 2.5% in men and 4.6% in women. The cancer sites contributing the greatest number of excess cancers were colon (1,101, PAF 10%), breast among postmenopausal women (971, PAF 8%) and endometrium (595, PAF 26%) (Table 3). The cancer sites with the highest fraction of cases attributable to overweight and obesity in the population were oesophageal adenocarcinoma (31%), endometrium (26%), kidney (19%) and gall bladder (14%).

Supplementary analysis

Assuming causal associations between overweight and obesity and the five additional cancers included in our supplementary analysis (thyroid cancer, leukaemia, multiple myeloma, non-Hodgkin's lymphoma and malignant melanoma in men), then the proportion of all cancers attributable to a high body mass index increases from 3.4% to 4.7% (4.2% in men and 5.3% in women); an increase in the number of excess cancer cases of 1,138 in men and 343 in women, bringing the total excess cases to 2,769 and 2,629, respectively (see supplementary file: Table S2, available online).

Potential impact if overweight and obesity prevalence had remained at 1990 levels

Altering the distribution of overweight and obesity in the Australian population had a moderate impact on estimated cancer incidence. In 2010, 38,878 adults over the age of 25 were diagnosed with cancers of the oesophagus (adenocarcinoma), colon, rectum, gall bladder, pancreas, breast, endometrium, ovary and kidney, of which we estimated 3,917 cases (10%) were directly attributable to levels of overweight and obesity prevailing in 2001. Assuming the prevalence of overweight and obesity had been at the levels prevailing in 1989–1990, we estimate 820 fewer cancers wold have been diagnosed (PIF 2.1%). This represents 21% of all cancers attributable to overweight and obesity. The proportion impacts were greatest for oesophageal adenocarcinoma and cancer of the endometrium (PIF of 7.4% and 6.1%, respectively), while the largest numbers of cases potentially prevented were for colon cancer (244). Further details of this analysis are included in the online supplementary file: Tables S3 and S4.

Discussion

We estimated that 3,917 cancer cases in Australian adults in 2010 could be attributed to overweight and obesity in the Australian population (3.4% of all cancers, excluding basal cell carcinoma and squamous cell carcinoma of the skin). This estimate could be as high as 5,398 cancers if overweight and obesity are confirmed to cause thyroid cancer, leukaemia, multiple myeloma, non-Hodgkin's lymphoma and malignant melanoma. The PAF was highest for oesophageal adenocarcinoma (31%) and endometrial cancer (26%). In absolute terms, the greatest numbers of cases attributable to overweight and obesity were for colon (1,101 cases) and post-menopausal breast cancer (971 cases). While it is implausible to have the entire population in the healthy weight range, we found that had the population remained at the levels pertaining in 1990, then the proportion of overweight and obesity-related cancers could have been reduced by around one-fifth (820 fewer cancers).

To avoid potentially subjective assessments of causality, we restricted our primary analyses to cancers causally associated with obesity as determined by independent agencies (IARC and WCRF; up until 30 June 2014) that have undertaken systematic and continual review of the evidence. We used summary risk estimates from those sources to calculate PAFs. In supplementary analyses, we calculated PAFs for cancers where there was a possible causal association with overweight/obesity, as identified by a comprehensive systematic review and meta-analysis of prospective observational studies.[12] We conducted supplementary analyses for five additional cancers for which suggestive evidence of causality was identified in a high quality meta-analysis.[12] Of note, while prostate cancer was considered in that meta-analysis, the effect size was small (1.03), not statistically significant (p=0.11) and there was marked heterogeneity across studies (73%). Hence, prostate cancer did not meet our *a priori* criteria for inclusion in these PAF analyses. However, a WCRF Continuous Update was published for prostate cancer in November 2014, after our analyses were completed. That report[23] found that body fatness (marked by BMI) is "probably" a cause of advanced prostate cancer, with an 8% increased risk per 5 kg/m^2 (RR 1.08; 95%CI 1.04-1.12). The ramifications of the WCRF declaration remain to be quantified, especially as national cancer incidence data for advanced prostate cancer do not exist. As an exercise to estimate the likely effect, we have undertaken a preliminary analysis using data published by the Melbourne Collaborative Cohort Study,[24] which reported that 29.6% of prostate cancers in their cohort were classified as 'aggressive' using a definition similar to WCRF. Assuming a causal association, then about 353 advanced prostate cancer cases (6% of all advanced prostate cancers; 1.8% of all prostate cancers) diagnosed in 2010 might be attributed to overweight and obesity in the Australian

Table 2: Prevalence (%) of overweight and obesity by age and sex, Australia 2001.

Age Group (years)	Males		Females	
	Overweight (BMI: 25<30 kg/m^2)	Obese (BMI: ≥30 kg/m^2)	Overweight (BMI: 25<30 kg/m^2)	Obese (BMI: ≥30 kg/m^2)
18-24	21.2	6.8	11.3	5.4
25-34	37.4	12.0	18.1	13.5
35-44	41.0	17.9	21.2	14.4
45-54	44.2	19.1	25.6	19.0
55-64	46.6	17.8	31.5	21.8
65-74	44.8	14.6	32.2	20.1
75+	35.3	8.9	23.9	10.5
18+	38.1	14.2	22.1	14.6

Source: Health Risk Factors Australia 2001 (Australian Bureau of Statistics)[19]

Table 3: Population attributable fraction (PAF) and estimated number of cancers diagnosed in Australia in 2010 attributable to overweight and obesity.

At outcome (years)[a]	Oesophagus (adenocarcinoma) (C15)[b,c]			Colon (C18, C19)[b]			Rectum (C20)[b]			Gall Bladder (C23)[b]			Pancreatic (C25)[b]			Breast (post-menopausal (C50)[b]			Endometrium (C54, C55)[b]			Ovary (C56)[b]			Kidney (C64)[b]			All Cancers[d]	
	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc.	PAF	Obs.	Exc	PAF	Obs.	Exc.	Obs.	Exc.
Males																													
25-34	17.5	2	0	6.7	37	2	3.4	18	1	7.7	0	0	4.4	12	1										10.3	22	2	1,042	6
35-44	27.2	17	5	11.3	134	15	5.9	79	5	12.9	0	0	7.6	27	2										16.8	111	19	2,214	46
45-54	32.3	62	20	13.8	469	65	7.3	296	22	15.7	5	1	9.3	106	10										20.3	263	53	6,632	171
55-64	33.8	140	47	14.7	1,187	175	7.8	709	55	16.6	18	3	9.9	296	29										21.5	469	101	16,279	410
65-74	33.6	158	53	14.6	1,817	266	7.7	744	58	16.6	30	5	9.9	427	42										21.4	433	92	19,513	516
75-84	31.1	149	46	13.3	1,557	208	7.0	538	38	15.1	37	6	9.0	383	34										19.6	307	60	14,520	392
85+	24.2	41	10	9.9	498	49	5.1	159	8	11.3	11	1	6.6	157	10										14.8	85	12	4,968	90
TOTAL		569	181		5,699	780		2,543	187		101	16		1,408	128											1,690	339	65,168	1,631
PAF_{aw}	31.9[e]																												
	18.1[f]			13.7			7.3			15.1			9.2												20.1			PAF_{aw}=	2.5
Females																													
25-34	12.1	1	0	2.2	40	1	1.1	16	0	5.1	1	0	2.2	3	0		258	0	11.0	19	2	1.3	39	1	6.9	20	1	1,401	5
35-44	22.4	2	0	4.4	134	6	2.2	65	1	10.0	2	0	4.4	22	1		1,420	0	20.6	103	21	2.7	77	2	13.3	62	8	3,637	39
45-54	24.2	8	2	4.9	422	21	2.5	198	5	10.9	12	1	4.9	71	3	6.3	3,385	214	22.2	362	80	3.0	196	6	14.4	150	22	7,812	354
55-64	28.9	14	4	6.1	908	56	3.1	317	10	13.5	34	5	6.1	193	12	7.9	3,893	308	26.8	721	193	3.7	284	11	17.7	226	40	11,042	639
65-74	32.4	28	9	7.2	1,346	97	3.7	350	13	15.6	67	10	7.2	310	22	9.2	2,845	262	30.1	556	167	4.4	285	12	20.2	249	50	11,073	642
75-84	31.5	39	12	6.9	1,522	105	3.5	319	11	15.0	61	9	6.9	415	29	8.9	1,617	144	29.2	355	104	4.2	275	12	19.6	198	39	9,819	465
85+	21.8	25	5	4.4	794	35	2.2	159	4	9.8	41	4	4.4	238	10	5.7	756	43	20.0	139	28	2.7	123	3	13.0	78	10	5,166	142
TOTAL		117	32		5,166	321		1,424	44		218	29		1,252	77		14,174	971		2,255	595		1,279	47		983	170	49,950	2,286
PAF_{aw}	28.6[e]															7.8[g]													
	8.0[f]			6.2			3.1			13.7			6.2			6.8[h]			26.4			3.6			17.4			PAF_{aw}=	4.6
Persons																													
25-34		3	0		77	3		34	1		1	0		15	1		258	0		19	2		39	1		42	3	2,443	11
35-44		19	5		268	21		144	6		2	0		49	3		1,420	0		103	21		77	2		173	27	5,850	85
45-54		70	22		891	86		494	27		17	2		177	13		3,385	214		362	80		196	6		413	75	14,444	525
55-64		154	51		2,095	232		1,026	65		52	8		489	41		3,893	308		721	193		284	11		695	141	27,321	1,049
65-74		186	62		3,163	363		1,094	71		97	15		737	65		2,845	262		556	167		285	12		682	142	30,586	1,158
75-84		188	58		3,079	313		857	49		98	15		798	63		1,617	144		355	104		275	12		505	99	24,340	857
85+		66	15		1,292	84		318	12		52	5		395	20		756	43		139	28		123	3		163	22	10,134	232
TOTAL		686	213		10,865	1,101		3,967	231		319	45		2,660	205		14,174	971		2,255	595		1,279	47		2,673	509	115,118	3,917
PAF_{aw}	31.4[e]															7.8[g]													
	15.1[f]			10.1			5.8			14.2			7.8			6.8[h]			26.4			3.6			19.1			PAF_{aw}=	3.4

Abbreviations: Obs. = observed cancers in 2010; exc. Excess cancers in 2010 attributable to overweight and obesity; PAF = population attributable fraction (expressed as a percentage); PAFaw = age-weighted population attributable fraction (expressed as a percentage).

a: Prevalence data age groups are 10 years younger than cancer incidence age groups, assuming a 10 year latent period; b: International Classification of Diseases code (ICD-10); c: Oesophageal cancer (adenocarcinoma) with histology codes 8140-8573; d: Excluding basal cell carcinoma and squamous cell carcinoma of the skin e: % of oesophageal adenocarcinomas (25+ years); f: % of all oesophageal carcinomas (25+ years); g: % of post-menopausal breast cancers (45+ years); h: % of all breast cancers (25+ years).

adult population. Clearly, this association will need deeper exploration in the future as more data come to hand.

The estimates of population attributable fractions for the Australian population can be compared with other published reports (Table 4).[25-28] There are some notable differences in PAF estimates across studies, reflecting population differences in the prevalence of overweight and obesity, and choices of relative risk estimates and exposure categories. For example, a higher proportion of the UK population than the Australian population was overweight or obese,[25] and proportions varied across age and sex categories. Hence, the PAF estimates for the UK differed from the Australian estimates, although the differences were not large. We used more recent estimates of relative risks than the previous studies, sourced from the WCRF Continuous Updates for breast, colon, rectum, pancreatic and endometrial cancer. Despite the differences in PAF estimates across populations, the overall rank orders of cancer sites were reasonably similar, with highest PAFs observed for oesophageal adenocarcinomas and cancers of the endometrium and kidney.

We used nationally representative data for BMI prevalence, although we note that we assumed a log-linear relationship between increasing BMI and cancer risk which may not be valid for all cancers.[6] Because the risks for endometrial cancer may be even greater with higher levels of obesity than predicted by a log-linear relation; we explored non-linear associations for endometrial cancer (not shown) and found only minor differences in the PAF.

A potential limitation of these data was that the prevalence of overweight and obesity was derived from self-reported measures of height and weight, which may result in under-estimates.[29] Countering this concern is the fact that the summary relative risks were derived mostly from studies using self-reported BMI measures, ensuring that any information biases are likely to be operating in the same direction.

BMI is the only measure of obesity for which national prevalence data are available. Fat distribution, particularly central or visceral obesity, appears to be important in the causation of some obesity-related cancers. Nationally representative data for central obesity (e.g. waist circumference and waist-to-hip ratio) are not available for the appropriate time periods, but would be useful measures to explore in future studies. In addition, there are insufficient numbers of studies reporting relative risks of cancer associated with such measures.

There are multiple likely mechanisms through which obesity may lead to cancer. Although previously regarded solely as a lipid storage organ, adipose tissue is now recognised as a highly active endocrine organ.[30] Adipose tissue contains adipocytes and stromal-vascular tissue containing pre-adipocytes, endothelial cells, and immune cells including macrophages.[31] It also secretes multiple products that can enter the circulation to have effects on distant tissue. These products include adipokines (leptin and adiponectin) and inflammatory cytokines (tumour necrosis factor-α, interlukin-6 and plasminogen activator inhibitor-1), all of which have been implicated in modulating cancer risk.[32-34] An additional consequence of obesity is insulin resistance with alteration in circulating levels of insulin, insulin-like growth factors and their binding proteins. These changes have effects on cellular proliferation and inhibit apoptosis, and have been associated with a number of cancers.[35] Secondary effects of obesity, including alterations in circulating levels and storage of lipids and activation of tissue macrophages, may also mediate obesity-related carcinogenesis.[36,37] Adipose tissue also secretes sex-steroid hormones, particularly oestrogen, which is likely to play an important role in breast and endometrial cancer.[38,39] Anovulation and changes in endogenous sex steroid hormone levels associated with obesity in pre-menopausal women may also play a role in the probable protective effect of obesity on pre-menopausal breast cancer.[4] Lastly, the changes in body habitus associated with obesity, particularly central obesity, may have a direct mechanical effect on increasing the risk of oesophageal adenocarcinoma via increased gastro-oesophageal reflux.[40] Thus there are multiple potential mechanisms through which obesity may increase cancer risk, and it is likely that these effects may vary according to cancer type and interaction with environmental factors.

The latent period between the onset of obesity and the onset of cancer is not known, and is likely to vary by cancer site and by mechanism.[41] We used obesity prevalence data that preceded cancer incidence by almost 10 years. While this interval was pragmatic and arbitrary, it was similar in magnitude to that used in other PAF studies[25] and was also similar to the follow-up periods for the cohort studies generating the risk estimates. Our estimates of the PAF assume that the effect of obesity is independent of other causal factors. We used relative risk estimates that were adjusted for the potentially confounding effects of other exposures, although it is possible that some residual confounding by factors such as smoking, poor diet and physical inactivity remains.[42] We could not model the effects of possible interactions and confounding given the available data. Finally, although the numbers of cancers attributable to overweight and obesity generated by these analyses appear precise, we remind readers that there is potential for error in these estimates due both to statistical uncertainty (precision) as well as variation in risk and prevalence estimates. We did not calculate confidence intervals for the PAF, as there is no universally agreed approach. Instead, we performed sensitivity analyses under various scenarios which convey a sense of the uncertainty of our estimates.

In summary, we estimate that overweight and obesity cause nearly 4,000 cancers annually in Australia. This, along with the other adverse health effects of obesity, results in substantial costs to the individual and the community. As Australia's population profile changes, with more people living to advanced age and greater proportions from non-European backgrounds, and with likely greater health inequalities between population groups,

Table 4: Comparison of PAF (%) reported for Australia, US, UK and France.

Cancer Site	Australia PAF Project		WCRF[27]				UK PAF Project[25]		IARC 2000 (France)[26]	
			US		UK					
	M	F	M	F	M	F	M	F	M	F
Oesophagus	32[a]	29[a]	32	38	29	33	27[a]	11[a]	28[a]	21[a]
Colon	14	6	17	15	15	13	14	12	7	5
Rectum	7	3								
Gallbladder	15	14	11	28	8	21	10	18		
Pancreas	9	6	17	20	14	16	13	12		
Breast		8[b]		17		16		9[b]		6[b]
Endometrium		26		50		38		34		18
Ovary		4		5		4				
Kidney	20	17	20	28	17	21	25	22	15	11

a: oesophagus adenocarcinoma only.

b: post-menopausal women (UK and Australian PAF projects – women over 45 yrs; IARC women – over 50 yrs).

it is likely that patterns of obesity will also change.[43] Strategies to reduce the prevalence of obesity are likely to generate substantial gains in health, but face formidable challenges in delivery.[44,45]

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PAF Project

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Supporting Information

Additional supporting information may be found in the online version of this article:

Supplementary Table 1: Summary of results from meta-analyses of the association between overweight and obesity and six cancers included in supplementary analysis.

Supplementary Table 2: Supplementary analysis of additional cancers: Summary of population attributable fraction (PAF) and estimated number of cancers in Australia in 2010 possibly attributable to overweight and obesity.

Supplementary Table 3: Prevalence (%) of overweight and obesity by age and sex, Australia 1990.