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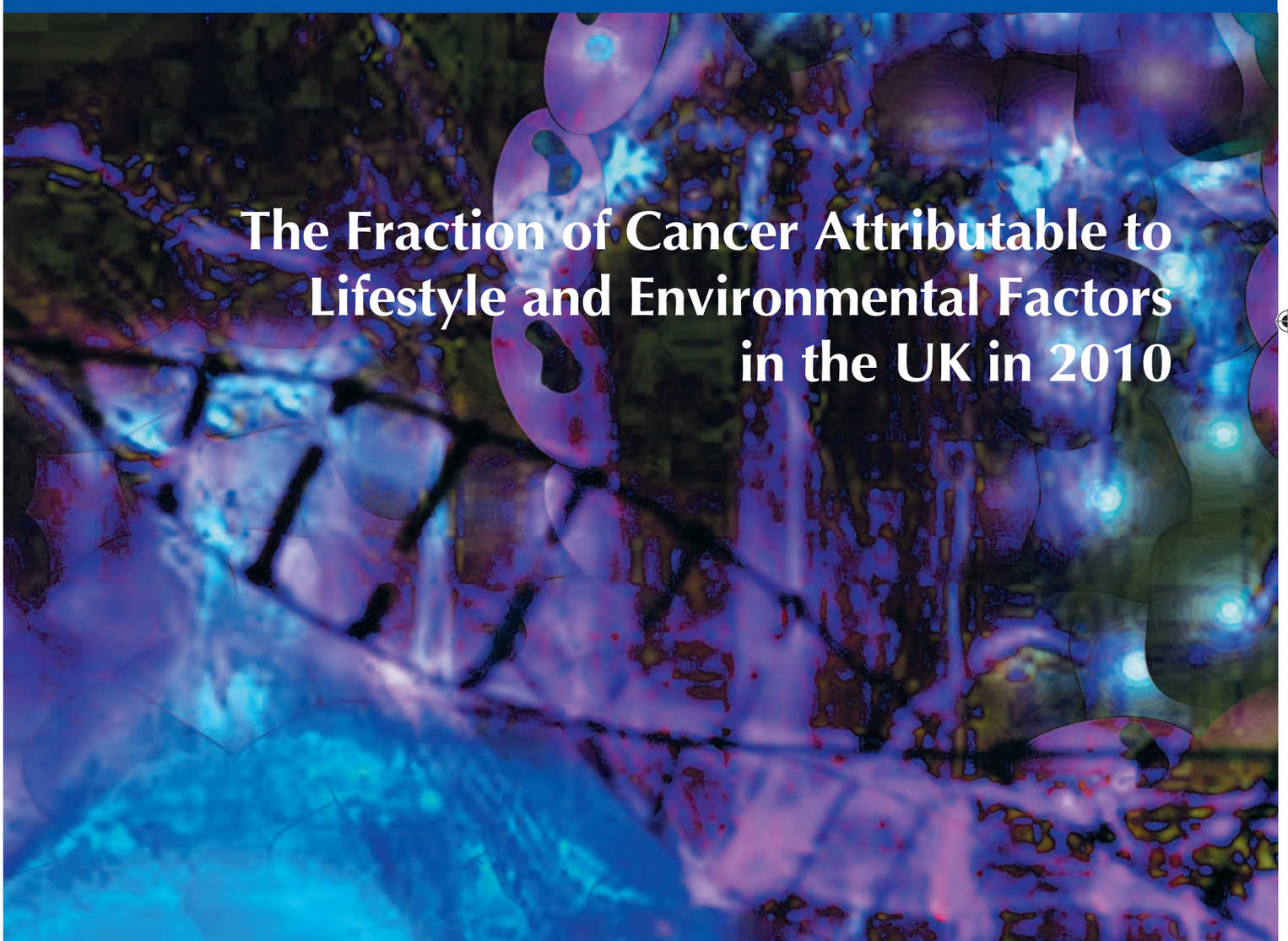

The Fraction of Cancer Attributable to Lifestyle and Environmental Factors in the UK in 2010

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The Fraction of Cancer Attributable to Lifestyle and Environmental Factors in the UK in 2010

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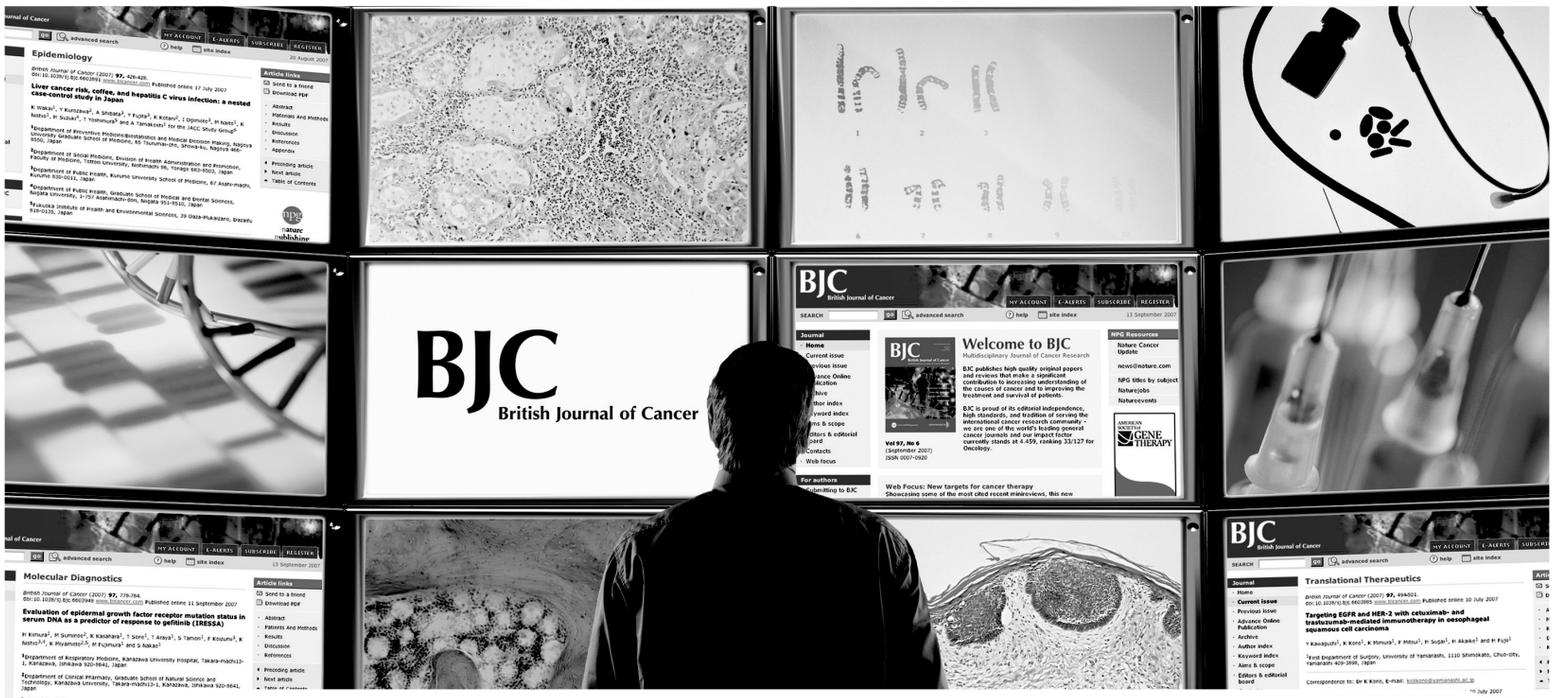

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Foreword

The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010

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This supplement provides up-to-date estimates of the numbers (and percentages) of new cancer cases in the UK that are attributable to factors that have been established by international consensus as potentially avoidable causes of the disease. It therefore offers a useful guide to the relative imporance of different preventive interventions.

Excluded from consideration are factors that, although known to be effective in reducing the risk of numerically important cancers, do not offer acceptable or practical preventive strategies at present. Early and multiple childbearing (to prevent breast cancer) and the widespread use of anti-androgen drugs (to prevent prostate cancer) come under this category. What remains is a limited number of important factors that can, at least to some extent, be affected by personal or political choices. The most important among these is continuation of the significant reduction in tobacco exposure. Next in importance are reductions in obesity and in heavy alcohol consumption, and certain other dietary changes. Each of these four main strategies for cancer control would also substantially reduce the burden of other non-communicable diseases, particularly cardiovascular, diabetic, renal and hepatic disease.

Whether, and to what extent, changes in these major causes of cancer can be achieved is another consideration. Thus, for example, although substantial progress has been made in reducing the number of young people who start smoking, and in helping those who smoke to escape their addiction in time to avoid most of the risk of premature death, tobacco still remains the most important avoidable cause of cancer, responsible for almost 20% of all cases of cancer (and, although this supplement does not quantify cancer mortality, for about 25% of all deaths from cancer, plus similar numbers of deaths from other diseases).

Taken together, the causative factors reviewed in this supplement account for an estimated 43% of all new cases of cancer in the UK (approximately 134 000 new cases in 2010), and about 50% of all cancer deaths. Most of these cases of cancer (excluding a few thousand due to the natural background of ionising radiation, or due to certain infections that are currently neither preventable nor treatable) could have been prevented by methods that would also prevent many premature deaths from other non-communicable disease. Over the past 40 years in the UK, the probability of death before the age of 70 years has been halved, and over the next few decades it could be halved again by continued improvements in the treatment of disease and by paying appropriate attention to the few major avoidable causes of disease. This supplement will help focus the attention of researchers, individuals and policy makers on the relative importance of the currently known causes of cancer.

Conflict of interest

The author declares no conflict of interest.

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1.

The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010

Introduction

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The overall objective of the study is to estimate the percentage of cancers (excluding non-melanoma skin cancer) in the UK in 2010 that were the result of exposure to 14 major lifestyle, dietary and environmental risk factors: tobacco, alcohol, four elements of diet (consumption of meat, fruit and vegetables, fibre and salt), overweight, lack of physical exercise, occupation, infections, radiation (ionising and solar), use of hormones and reproductive history (breast feeding). The number of new cases attributable to suboptimal exposure levels in the past, relative to a theoretical optimum exposure distribution, is evaluated. For most of the exposures, the attributable fraction was calculated based on the distribution of exposure prevalence (around 2000), the difference from the theoretical optimum (by age group and sex) and the relative risk per unit difference. For tobacco smoking, the method developed by Peto *et al* (1992) was used, which relies on the ratio between observed incidence of lung cancer in smokers and that in non-smokers, to calibrate the risk. This article outlines the structure of the supplement – a section for each of the 14 exposures, followed by a Summary chapter, which considers the relative contributions of each factor to the total number of cancers diagnosed in the UK in 2010 that were, in theory, avoidable.
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Keywords: cancer; environment; lifestyle; risk factors; UK

The purpose of this study is to estimate the fraction (or percentage) of cancers occurring in the UK in 2010 that were the result of exposure to common and, for the most part, modifiable lifestyle and environmental exposures. A total of 14 major modifiable lifestyle, dietary and environmental metabolic risks are considered (Table 1).

The analyses in the chapters that follow estimate the number of cancer cases diagnosed in the UK in 2010 that were due to such exposures in the past (or that would have been prevented if risk factor exposures had been at some hypothetical alternative optimal distribution from those actually present). The proportion (or percentage) of such avoidable cancers is known as the population-attributable fraction (PAF), which provides a quantification of the total effects of a risk factor (direct, as well as mediated through other factors).

The inputs to each analysis are as follows:

(1) The aetiological effect of risk factor exposures on cancer-specific risk.
(2) The population distribution of risk factor exposure in the past
(3) An alternative exposure distribution.
(4) The projected total number of cancer cases (by type) in the UK population in 2010.

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SELECTION OF RISK FACTORS

Among dietary, lifestyle and environmental factors, those that fulfilled the following criteria were selected:

(i) There was sufficient evidence on the presence and magnitude of likely causal associations with cancer risk from high-quality epidemiological studies.
(ii) Data on risk factor exposure were available from nationally representative surveys.
(iii) There were achievable alternative exposure levels that would modify the risk.

Several other risk factors were considered but were not included because the evidence on causal effects was less convincing, or because their effects on national cancer incidence were likely to have been small and estimates of relevant past exposures difficult to obtain. This is discussed further below.

SOURCES OF DATA

(1) The risks of exposure (aetiological effect sizes) were taken from published systematic reviews and meta-analyses of epidemiological studies.
(2) Risk factor exposure distributions were obtained from nationally representative health examination and interview surveys. Data on prevalence of risk factors from epidemiological studies (cohort or case – control) were not used, as such

studies will almost never provide information relevant to the general population of the UK.

(3) The number of cancer cases in 2010 (by cancer type, sex and 5-year age group) was projected using UK incidence rates for the 15-year period from 1993 to 2007. For such a short-term projection (3 years), most established methods will provide very similar results. For all but two cancers (breast and prostate) the R-based software, 'Nordpred' (Møller *et al*, 2002), was used to project incidence rates from 2008 to 2012, on the basis of the incidence rates from 1993 to 2007, aggregated into three 5-year time periods. National population projections (2008 based) for the UK by sex, 5-year age group and year, from 2008 to 2012, were obtained from the population projections of the Office for National Statistics (Office of National Statistics (ONS), 2009). The estimate for 2010 was taken as the average annual number of cases projected for the period 2008–2012. For cancers of the prostate and female breast, a different approach was used, because recent rates have been modified to a great extent by the increased use of PSA testing and extensions to the breast cancer screening programme. An age–period cohort model based on observations for single years was fitted, but incidence rates from age groups and time periods that were assumed to have been affected by the introduction of screening were not used in the model building (Mistry *et al*, 2011).

Table 2 compares the numbers of cases diagnosed in 2007 with the projected numbers for 2010.

Table 1 Exposures considered, and theoretical optimum exposure level

Exposure	Optimum exposure level
Tobacco smoke	Nil
Alcohol consumption	Nil
Diet	
1 Deficit in intake of fruit and vegetables	$\geqslant$5 servings (400 g) per day
2 Red and preserved meat	Nil
3 Deficit in intake of dietary fibre	$\geqslant$23 g per day
4 Excess intake of salt	$\leqslant$6 g per day
Overweight and obesity	BMI $\leqslant$25 kg m^{-2}
Physical exercise	$\geqslant$30 min 5 times per week
Exogenous hormones	Nil
Infections	Nil
Radiation – ionising	Nil
Radiation – solar (UV)	As in 1903 birth cohort
Occupational exposures	Nil
Reproduction: breast feeding	Minimum of 6 months

AETIOLOGICAL EFFECTS OF RISK FACTORS ON DISEASE-SPECIFIC INCIDENCE

The relative risk (RR) per unit of exposure or for each exposure category (for risks measured in categories) was obtained for cancers with probable or convincing causal associations with each risk factor. The studies used for aetiological effect sizes were observational studies (prospective cohort studies whenever possible) that estimated the effects relative to baseline exposure. The RRs used in the analyses represent the best evidence for the impact of risk factor exposure on cancer risk in the UK population, based on the current causes and determinants of the population distribution of exposure. Relative risks adjusted for major potential confounders were used to estimate the causal components of risk factor–disease associations. With respect to diet, for example, the relative risks for specific components – for example, meat – have generally been adjusted for intake of other components with which they may be confounded, as well as for total energy intake. However, if there is also a correlation between exposure and risk of a specific cancer, due to correlations of exposure with other risks or other unobserved factors, the above equations may result in under- (when there is positive correlation) or over-estimation (negative correlation) of the true PAF when used with adjusted RRs (Bruzzi *et al*, 1985).

The cancers that occur in a particular year, related to specific risk factors, are presumably related to cumulative exposures to the factor concerned over a period of many years. For tobacco smoking, for example, the risk of lung cancer relates to the

Table 2 Numbers of cancers diagnosed in the UK in 2007 (20 most common sites) and estimates for 2010

	Males			Females		
Cancer site	**2007**	**2010 (estimate)**	**Change (%)**	**2007**	**2010 (estimate)**	**Change (%)**
Breast (female)	—	—	—	45 695	48 385	6
Lung	22 355	22 273	0	17 118	18 132	6
Colorectal cancer	21 014	22 127	5	17 594	17 787	1
Prostate	36 101	40 750	13	—	—	—
Non-Hodgkin lymphoma	5881	6297	7	5036	5305	5
Malignant melanoma	4975	6095	23	5697	6822	20
Bladder	7284	6713	−8	2807	2572	−8
Kidney	5165	5697	10	3063	3365	10
Oesophagus	5226	5713	9	2740	2819	3
Stomach	4988	4467	−10	2796	2577	−8
Pancreas	3748	4084	9	3936	4280	9
Uterus (corpus and unspecified)	—	—	—	7536	8195	9
Leukaemias	4069	4639	14	2932	3201	9
Ovary	—	—	—	6719	6820	2
Oral cavity and pharynx	4083	4571	12	2136	2359	10
Brain and CNS	2663	2799	5	2013	1902	−6
Multiple myeloma	2223	2506	13	1817	1994	10
Liver	2152	2270	5	1255	1298	3
Cervix uteri	—	—	—	2828	2691	−5
Mesothelioma[a]	1977	2077	5	424	462	9
All[b]	149 356	158 667	6	148 635	155 584	5

[a]Number of cases estimated from the UK population (2010) and rates in England in 2008. [b]Excluding non-melanoma skin cancer.

cumulative exposure to tobacco smoke (duration and dose), including the time since quitting in ex-smokers. Similarly, the total lifetime exposure to ionising radiation for individuals in each age group in 2010 was estimated on the basis of known or estimated levels of exposure in the past. Such detailed quantification of risk is not available for most exposures, and, even if it was, it would be impossible to partition the 2010 UK population according to the appropriate categories of past exposure. Therefore, for several exposures, an arbitrary latent period was included, which is the average interval between 'exposure' and the appropriate increase in risk of the cancers concerned. The most appropriate period was deemed to be the mean interval between measurement of exposure and cancer outcome in the prospective studies that were used as the source of data on relative risks. For most exposures, this was around 10 years, and thus the effects on cancers occurring in 2010 of suboptimal levels of exposure in 2000 were examined. When there was evidence about the duration between exposure and change in risk (for example, for exposure to radiation, or exogenous and endogenous sex hormones), the appropriate interval was used to select the year for which exposure data were obtained. The method used for estimating the attributable fraction of the most important exposure – tobacco smoking – does not require estimation on the basis of past exposure, and so no such assumptions are needed (although, in fact, the latency between exposure to cigarette smoking and lung cancer risk (at least) is well documented).

Many calculations of PAFs are based on *current* levels of exposure to risk factors; for example, the work of the Global Burden of Disease/Comparative Risk Assessment Group (Ezzati *et al*, 2002; Danaei *et al*, 2005) or the World Cancer Research Fund (WCRF/AICR, 2009). Although this simplifies the business of obtaining data on prevalence of the different exposures, the effect being imputed must relate to cancers that will be caused by these exposures at some variable, and undefined, period in the future.

To measure the effects of non-optimal levels of exposure, one must define, for each exposure, an optimal exposure distribution, sometimes referred to as the theoretical-minimum-risk exposure distribution (TMRED), against which the excess risk due to actual exposure is evaluated. The optimal exposure may be zero for risk factors for which zero exposure is imaginable, and results in minimum risk (e.g., no tobacco smoking, alcohol drinking or consumption of red meat). For some exposures (e.g., BMI, solar radiation, salt consumption), zero exposure is physiologically impossible. For these risks, we used optimal exposure levels corresponding to accepted recommendations for the UK population, or, for UV radiation, corresponding to those observed in a population with an attainable low level of exposure (Table 1). The 'optimum' exposure levels for factors with protective effects (physical activity, and dietary fruit and vegetable and fibre intake) were selected as the intake and activity levels recommended for the UK population (Table 1). Strictly speaking, these baselines should be called 'recommended levels', as benefits may continue to accrue at higher (for preventive exposures) or lower (for carcinogenic exposures) levels, but the terminology of 'optimum' is retained for consistency. The optimum exposure levels (TMREDs) should obviously be identical in calculations for the effect of the same exposure on different cancers.

The fraction of cancer cases considered to be attributable to a given exposure is based on estimating the effect of bringing all those individuals at suboptimal levels to the exact level of the optimum baseline, without changing (improving) the exposure (and risk) of those individuals who already exceed it. This approach is a conservative one. In other studies, for example, that of the WCRF (2009), attributable fractions are based on the estimated effect of moving all those in suboptimal exposure categories to the most favourable one (in which the *mean* exposure is considerably higher than the optimum baseline).

The analyses use data on the fraction of the UK population at different levels of exposure, and estimates of the risk associated with each, relative to the optimum exposure. The PAF is given by the following equation:

$$\frac{(p_1\times \mathrm{ERR}_1)+(p_2\times \mathrm{ERR}_2)+(p_3\times \mathrm{ERR}_3)\ \ldots\ +(p_n\times \mathrm{ERR}_n)}{1+[(p_1\times \mathrm{ERR}_1)+(p_2\times \mathrm{ERR}_2)+(p_3\times \mathrm{ERR}_3)\ \ldots\ +(p_n\times \mathrm{ERR}_n)]}$$

where p_x is the proportion of the population in exposure level x and ERR_x the excess relative risk (relative risk−1) at exposure level x.

The calculation is carried out separately by sex and age group (the choice of which depended on availability of exposure data).

The method of estimation of PAF follows the same principle for the different exposures, although some variations to the formula above are necessary depending on the type of exposure and the availability of pertinent data; they are presented in detail in each chapter. For tobacco smoking, the method developed by Peto *et al* (1992) was used, which relies on the ratio between observed incidence of lung cancer in smokers and that in non-smokers, to calibrate the risk.

Because the current (2010) cancer risk is, for most of the factors considered, related to past exposures that occur only in adulthood (age 15+), or for which data are available only for adults, PAFs can be calculated only for ages $\geqslant$25, when the latency between exposure and outcome is 10 years. Even where a fraction of cases occurring at ages $<$25 are related to childhood exposure, the effect of ignoring these on the estimate of the total PAF (at all ages) will be very small, owing to the rarity of cancer in the age group of 15–24 years.

A separate section is devoted to each lifestyle/environmental factor, for which the number of cases of different cancers attributable to suboptimal levels exposure is estimated. This is expressed also as a percentage of the observed number of cases in 2010. The total number of cancer cases (all sites) attributable to each risk factor was obtained by summing the numbers at the individual sites. Cases of different cancers attributable to a single risk factor are additive because each cancer case is assigned to a single ICD category.

In a summary chapter, the estimates for the 14 different exposures are listed together, and the numbers of cancer cases caused by all of them functioning individually, or in combination, are estimated.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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2.
Tobacco-attributable cancer burden in the UK in 2010

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In 2004, the International Agency for Research on Cancer (IARC) judged that there was sufficient evidence in humans that tobacco smoking causes cancers of the lung, larynx, oral cavity and pharynx, paranasal sinuses, oesophagus, stomach, pancreas, liver, kidney, ureter, bladder, uterine cervix and bone marrow (myeloid leukaemia; IARC, 2004). At a recent expert review (to be published as IARC Monograph 100E), the list of cancers for which the evidence for tobacco smoking being causative was considered to be 'sufficient' was updated to include cancers of the colon and rectum, and mucinous tumours of the ovary (Secretan *et al*, 2009).

In the 2004 evaluation, the IARC judged that there was sufficient evidence that involuntary smoking – that is, exposure to second-hand or 'environmental' tobacco smoke (ETS) – causes lung cancer in humans (IARC, 2004). In this monograph, the results of meta-analyses were reported, showing a statistically significant and consistent association between lung cancer risk in spouses of smokers and exposure to second-hand tobacco smoke from the spouse who smokes. The relative risk was 1.24 in women and 1.37 in men after controlling for some potential sources of bias and confounding. The excess risk increases with increasing exposure. For lung cancer in never smokers exposed to ETS at the workplace, the relative risks were 1.19 in women and 1.12 in men. For children exposed to smoke from their parents smoking, the evidence for an increased risk of lung cancer was less consistent.

The reported increases in risk of lung cancer from ETS exposure pertain to non-smokers (indeed, usually to persons who have never smoked). It would be impossible to directly quantify the tiny increment in risk that a smoker might suffer from exposure to another person's smoke (as well as his own). Thus, calculation of attributable fractions will be undertaken only for lung cancer cases in never smokers. This makes sense in that the ultimate aim is to estimate how much cancer is caused by smoking, and this comprises the cases caused by direct smoking and those caused by involuntary smoking in never smokers. Even if a theoretical estimate of the total effect of other persons' smoking was made (including the incremental risk to current and past smokers), this latter component would have to be deducted from the total tobacco-attributable fraction, as involuntary smoking cannot occur without active smoking by others.

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TOBACCO SMOKING

Methods

The numbers and percentage of cancers caused by tobacco smoking are estimated using the method developed by Peto *et al* (1992). This is based on the assumption that tobacco smoking is overwhelmingly the most important cause of lung cancer, and that the incidence of this disease in the absence of smoking would be more or less the same in all populations, so that contemporary incidence (or mortality) rates from lung cancer simply reflect the cumulative exposure of a particular population to tobacco smoking. A set of data is required for the calculation, comprising, from the same population, incidence rates of lung cancer in persons who have never smoked and relative risks of different cancers in smokers relative to never smokers. Similar to Peto *et al* (1992), we use the data from the follow-up during 1982–1988 of the American Cancer Society's second 'Cancer Prevention Study' (CPS II; Thun *et al*, 1997), the largest cohort study carried out until now, involving more than a million volunteers aged $\geqslant$30 years at the time of enrolment in 1982 (Garfinkel, 1980; Burns *et al*, 1997). Lung cancer incidence in never smokers has been estimated from the death rates in the CPS II study, for a slightly longer period of follow-up (1982–2002; Thun *et al*, 2006; Figure 1).

The relative risks of death from different cancers during the follow-up period (1984–1988); and the sources are shown in Table 1. Most values listed here were those published in Ezzati *et al* (2005). For cancers of the colon and rectum, the values were those from the follow-up of the CPS II Nutrition Cohort to June 2005 (Hannan *et al*, 2009), in which the multivariate hazard ratios in current smokers were 1.24 in men and 1.30 in women. No data for the risk of mucinous carcinomas of the ovary in smokers have been published based on the CPS II cohort; the value used (2.1) was that from a meta-analysis published by Jordan *et al* (2006).

The first step is to calculate the number of lung cancer cases expected in the UK in the absence of smoking, by applying the age- and sex-specific never-smoker rates (in Figure 1) to the population of the UK in 2010. The number of cases attributable to smoking (and the attributable fraction) is then derived by subtracting the expected cases from the number actually observed in 2010. The results are shown in Table 2.

For the other cancers, the rates in non-smokers are not known, and thus the usual formula for calculating the population

attributable fraction (PAF) is used:

$$\mathrm{PAF} = \frac{P_e(r-1)}{1+P_e(r-1)}$$

where P_e is the prevalence of exposure and r is the relative risk in smokers.

Using the attributable fractions of lung cancer, already estimated (Table 2) by age group and sex, and the relative risks for lung cancer in smokers from the American cohort (Table 1), the above formula enables calculation of P_e for each age/sex group. This may be thought of as the 'notional' prevalence of smoking (ever *vs* never) in the UK population – more specifically, the prevalence that would have been necessary in the UK population to produce the observed incidence rates if the relative risks of the CPS II study had pertained.

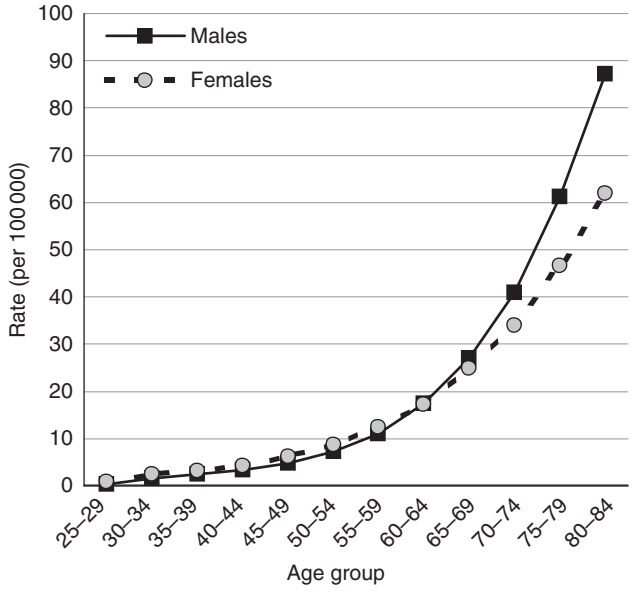

Figure 1 Age-specific incidence rates of lung cancer in the lifelong never smokers (CPS-II) in the US.

Finally, we use the same formula, the values of prevalence (P_e) and the relative risks for the other cancers (Table 1) to estimate their PAF and, consequently, the numbers of cases attributable to smoking.

'Notional prevalence' (P_e) is an artificial concept that may be quite different from the true prevalence, depending on how different the past experience of tobacco smoking in the population under study was from that in the volunteers of the CPS II study. It can, in fact, even be >1 if a particular age/sex/population cohort has a higher prevalence of smoking and/or a higher relative risk of lung cancer than the CPS II subjects.

Results

For lung cancer (Table 2), the results suggest that about 85% of the lung cancer cases in men are attributable to smoking, and in women the percentage is 80%.

Table 3 shows the estimated numbers of cancer cases at sites other than the lung, and the fractions due to tobacco smoking. (No estimate is made for cancers of the paranasal sinuses, owing to the lack of relevant data on the risk of tobacco smoking; the number of cases concerned would be very few: the total number of cases registered in England in 2008 was 125.)

Table 1 Estimated relative risks (RR) for current smokers aged ⩾35 compared with never-smokers

Cancer	Male	Female
Lung[a]	21.3	12.5
Oral cavity and pharynx[b]	10.9	5.1
Oesophagus[b]	6.8	7.8
Stomach[a]	2.2	1.5
Liver[a]	2.3	1.5
Pancreas[a]	2.2	2.2
Colon–rectum[c]	1.24	1.30
Larynx[b]	14.6	13.0
Cervix[a]	—	1.5
Ovary (mucinous)[d]	—	2.1
Urinary bladder[a]	3.0	2.4
Kidney and renal pelvis[a]	2.5	1.5
Acute myeloid leukaemia[a]	1.9	1.2

[a]From Ezzati *et al* (2005). [b]From US Department of Health and Human Services (2004). [c]From Hannan *et al* (2009). [d]From Jordan *et al* (2006).

Table 2 Cases of lung cancer attributable to smoking, by sex and age group (UK, 2010)

Age group (years)	Population (thousands)	Rates observed	Cases observed	Rates expected[a]	Cases expected[a]	Excess attributable cases	PAF (%)
Males							
0–14	5548	0.0	1	0.0	0	1	0
15–34	8365	0.5	38	0.5	38	0	0
35–44	4387	4.9	215	2.9	128	87	40
45–54	4202	27.1	1138	6.0	252	886	78
55–64	3580	116.9	4184	14.3	513	3705	89
⩾65	4526	368.9	16 697	51.5	2331	14 366	86
Total	30 609	72.8	22 273	—	3262	19 011	85
Females							
0–14	5292	0.0	2	0.0	0	2	0
15–34	8048	0.4	42	0.5	42	0	0
35–44	4452	4.5	224	3.8	168	56	25
45–54	4331	26.7	1088	7.4	320	768	71
55–64	3731	85.3	3441	14.9	556	2885	84
⩾65	5759	218.0	13 335	42.9	2471	10 864	81
Total	31 614	53.1	18 132	—	3557	14 575	80

Abbreviations: PAF = population-attributable fraction. [a]Expected in a population that had never smoked.

Table 3 Other cancers: cases attributable to smoking in 2010

Age (years)	Cases attributable to smoking for specific cancers: Oral cavity and pharynx Obs.	Exp.	PAF (%)	Oesophagus Obs.	Exp.	PAF (%)	Stomach Obs.	Exp.	PAF (%)	Liver Obs.	Exp.	PAF (%)	Pancreas Obs.	Exp.	PAF (%)	Colon–rectum Obs.	Exp.	PAF (%)	Larynx Obs.	Exp.	PAF (%)	Cervix Obs.	Exp.	PAF (%)	Ovary Obs.	Exp.	PAF (%)	Bladder Obs.	Exp.	PAF (%)	Kidney and ureter Obs.	Exp.	PAF (%)	Myeloid leukaemia Obs.	Exp.	PAF (%)
Males																																			
0–14	5	5	0	0	0	0	0	0	0	15	15	0	0	0	0	1	1	0	0	0	0	—	—	—	—	—	1	1	0	54	54	0	41	41	0
15–34	77	77	0	12	12	0	14	14	0	23	23	0	9	9	0	163	163	0	2	2	0	—	—	—	—	—	8	8	0	37	37	0	97	97	0
35–44	244	183	25	86	72	16	82	79	4	43	41	4	67	64	4	397	394	1	35	24	31	—	—	—	—	—	58	54	6	206	196	5	89	86	3
45–54	902	332	63	469	234	50	251	208	17	166	136	18	278	230	17	1436	1379	4	195	58	70	—	—	—	—	—	235	175	26	612	486	21	150	130	13
55–64	1458	325	78	1308	430	67	677	476	30	493	338	31	818	575	30	4129	3807	8	535	92	83	—	—	—	—	—	961	564	41	1295	847	35	348	264	24
⩾65	1887	471	75	3836	1389	64	3443	2524	27	1530	1097	28	2910	2133	27	15999	14912	7	1035	202	81	—	—	—	—	—	5448	3390	38	3493	2400	31	1321	1038	21
Total	4573	1393	70	5711	2137	63	4467	3300	26	2270	1650	27	4082	3011	26	22125	20656	7	1802	378	79	—	—	—	—	—	6711	4191	38	5697	4020	29	2046	1656	19
Females																																			
0–14	6	6	0	0	0	0	0	0	0	18	18	0	0	0	0	2	2	0	0	0	0	0	0	0	12	12	0	1	1	0	57	57	0	43	43	0
15–34	75	75	0	5	5	0	29	29	0	12	12	0	12	12	0	164	164	0	2	2	0	739	739	0	273	273	0	6	6	0	37	37	0	86	86	0
35–44	131	117	11	27	23	16	64	63	1	29	29	1	53	51	3	402	399	1	12	9	26	679	669	1	438	435	1	31	30	4	110	108	1	90	89	1
45–54	354	191	46	147	61	59	129	117	9	70	64	9	221	177	20	1230	1158	6	53	15	71	411	372	9	926	901	3	104	80	23	298	270	9	142	136	4
55–64	593	208	65	398	98	75	287	234	18	199	163	18	633	411	35	2755	2427	12	105	16	84	317	259	18	1506	1451	4	303	186	39	639	521	18	210	193	8
⩾65	1196	466	61	2240	622	72	2067	1735	16	969	813	16	3361	2304	31	13233	11871	10	210	38	82	547	459	16	3665	3571	3	2126	1385	35	2223	1866	16	1025	952	7
Total	2355	1063	55	2817	808	71	2576	2178	15	1298	1099	15	4280	2955	31	17786	16020	10	382	80	79	2693	2498	7	6820	6643	3	2571	1688	34	3364	2860	15	1596	1500	6

Abbreviations: Exp. = cases expected; Obs. = cases observed; PAF (%) = population-attributable fraction.

Table 4 Relative risks of lung cancer from exposure to ETS (IARC, 2004)

Source of exposure to ETS	RR by sex: Males	Females
At home (spouse)	1.37	1.24
At work (occupational)	1.12	1.19

Abbreviations: ETS = environmental tobacco smoke; RR = relative risk.

Taking these figures together, we can estimate that, in total, 36 102 (22.8% of the total) cancers in men and 23 722 (15.2% of the total) in women are attributable to smoking tobacco (currently, or in the past).

Discussion

The method of estimation developed by Peto *et al* (1992, 2000) is based on the assumption that the excess mortality (or incidence) from lung cancer, above that which would have been observed in persons who have never smoked, is the result of smoking (past and current). Thus, the attributable fraction of lung cancer can be estimated as

$$(\text{cases observed} - \text{cases expected})/\text{cases observed}$$

and used to estimate the attributable fractions of other cancers. It should be noted that it is of no consequence that the data set used for estimates of PAF in 2010 is derived from study results pertaining to the period 1984–1988, so long as the two components (mortality/incidence of lung cancer in non-smokers, and relative risks of different cancers in smokers *vs* never-smokers) derive from the same population. On the other hand, it is important that the non-smoker rates observed in the US volunteers in 1984–1988 are appropriate to the UK population in 2010. The only large cohort study in the UK was for British Doctors – almost all of them being men. The US CPS II non-smoker rates predicted 19.03 lung cancer deaths in 40 years of follow-up, *vs* 19 actually observed (Peto *et al*, 2000), confirming that non-smoker rates in the UK are likely to be very similar to those in the US CPS II cohort.

The main advantage of the Peto method is that it does not require detailed information of the current relative risks of different cancers in relation to smoking history in the UK population. The risk of tobacco smoking depends on cumulative exposure to carcinogens in tobacco smoke, and therefore varies with the amount smoked, duration of smoking and time since cessation (in ex-smokers), as well as with the type of cigarette smoked. Factors such as these differ between countries, and over time, and thus one cannot be sure that relative risks taken from studies in different populations (geographic or temporal) would be appropriate for the UK in 2010. In the USA, the relative risk of lung cancer in current smokers (relative to never smokers) was 11.5 in men and 2.7 in women in the Cancer Prevention Study I (CPS I) conducted by the American Cancer Society during 1959–1965, whereas it was 23.3 in men and 12.7 in women in CPS II (US Department of Health and Human Services, 2004). In the British Doctors study, the relative risk in current smokers rose from 15.5 during 1951–1971 to 18.5 during 1971–1991 (Doll *et al*, 1994). In fact, one might have expected the switch to cigarettes delivering low tar to have reduced the hazard of lung cancer, but this effect is being offset by the 'maturing' of the smoking epidemic, and thus smokers still alive in more recent years have had a longer history of regular consumption of cigarettes than men of the same ages would have had during the 1950s and 1960s. Another factor that may be important in the maturing of the epidemic (but which is impossible to quantify) is a change in the way cigarettes have been smoked in recent decades. The minority of doctors who continued

to smoke cigarettes in the latter half of the study may have tended to be those who smoked them in a way different from that of the greater number who had stopped smoking them earlier.

Using the ratio of mortality rates from lung cancer in never, former and current smokers after the 50-year follow-up of British doctors (Doll *et al*, 2005), and the prevalence of smoking among British men in 2008 (22% current smokers, 30% ex-smokers; General Lifestyle Survey 2008/ONS 2010, 2010), the estimate of the PAF of lung cancer is 80%. This is somewhat lower than the 85% estimate of the current analysis, and that of Peto *et al* (2006), who, using essentially the same methodology, estimated that 88% of lung cancer deaths in men in the UK in the year 2007 were due to smoking, and 84% of deaths in women. The reason, as noted above, is that the relative risks observed in British doctors are unlikely to be the same as the averages for the UK population in 2010.

ENVIRONMENTAL TOBACCO SMOKE (ETS)

Methods

Estimation of the fraction of cancer caused by exposure to ETS in lifelong non-smokers uses the traditional method for attributable fractions, incorporating estimates of relative risk (of exposure to tobacco smoke) and the prevalence of such exposure among never smokers. The formula for calculating PAF is as follows:

$$\mathrm{PAF} = \frac{P_e(r-1)}{1+P_e(r-1)}$$

where P_e is the prevalence of exposure and r is the relative risk of lung cancer in those exposed to ETS. The attributable fraction is applied to the number of lung cancer cases estimated to occur among never smokers. From the section on tobacco smoking, this was estimated to be 6819 (3262 in men and 3557 in women) in the UK in 2010 (Table 2).

We may estimate two components:

(1) Cases of lung cancer (in never smokers) caused by domestic exposure to ETS.
(2) Cases of lung cancer (in never smokers) caused by exposure to ETS in the workplace.

The relative risks from the IARC (2004) meta-analyses, described in the Introduction, are used (Table 4).

Exposure to ETS at home Most studies investigate the risk of lung cancer in lifelong non-smokers (never-smokers) living with a smoking spouse, and it was on a meta-analysis of such studies that the estimated relative risks in the IARC monograph were based. There appear to be no survey data upon which one can estimate the prevalence of such exposures in the UK. A range of approaches have been used by others, from using the exposure prevalence of control subjects in case–control studies (IARC, 2007) to extrapolation from exposure of children to ETS at home (Jamrozik, 2005). Trédaniel *et al* (1997) estimate the exposure from spouse smoking based on the prevalence of smoking in men and women, and the probability that couples would be discordant for their smoking status. This seems to be the method most likely to yield exposures equivalent to those for which relative risks have been estimated, as well as allowing estimates specific to the UK (which controls from case–control studies cannot). Using data from the General Household Survey for 2008, we may obtain the prevalence of current, ever or never smokers by age group, as well as the probability of being married or cohabiting currently or ever in the past. We use the 'aggregation factor' of 3.0 proposed by Wald *et al* (1986) to express the relative probability of couples being concordant for smoking status.

Table 5 shows the percentage of the UK population who are currently married or cohabiting (column 1), and the percentage

Table 5 Prevalence estimates of cohabitation with smoking partner among non-smokers in UK, and fraction of lung cancer cases attributable to cohabitation with a smoking partner

	Cohabitation status of never-smokers (%)[a]		Population smoking status (%)[a]		Estimated prevalence of never-smokers cohabiting with smoking partner and lung cancer cases attributable to cohabitation with smoking partner (%)[b]					
	1	2	3	4	5	6	7	8	9	10
Age group (years)	Living with a partner	Ever had a partner	Current smokers	Never smokers	Never-smokers living with current smoking partner	PAF	Never-smokers living with ever smoking partner	PAF	Never-smokers ever living with smoking partner	PAF
Men										
16–24	8	8	24	69	1	0.5	2	0.6	2	0.6
25–34	61	63	30	53	10	3.5	19	6.4	19	6.6
35–44	77	82	24	51	11	3.8	25	8.3	26	8.8
45–54	77	88	24	48	11	3.8	24	8.1	27	9.1
55–64	79	93	18	41	7	2.5	16	5.6	19	6.5
65–74	77	94	13	37	4	1.3	20	6.9	25	8.3
⩾75	60	93	13	37	8	2.8	14	5.0	22	7.5
Total	63	72	22	49	6	2.0	17	6.0	20	6.8
Women										
16–24	18	19	26	71	3	1.0	4	1.5	4	1.5
25–34	68	72	29	57	12	4.1	24	8.1	25	8.6
35–44	75	87	25	56	8	3.0	29	9.8	34	11.2
45–54	75	93	24	57	10	3.4	31	10.3	38	12.4
55–64	72	96	22	55	4	1.6	29	9.7	39	12.5
65–74	63	96	13	56	7	2.5	32	10.7	50	15.5
⩾75	29	94	13	56	4	1.6	14	5.1	47	14.8
Total	59	79	21	57	7	2.5	23	7.8	31	10.1

Abbreviations: PAF = population-attributable fraction. [a]Cohabitation status and population smoking status from General Lifestyle Survey 2008/ONS 2010 (2010). [b]Estimates are based on cohabitation status and population smoking status, and assume couples are in the same broad age groups as those in the table and the relative probability of couples being concordant for smoking status is 3.0 (Wald *et al*, 1986).

who have ever been married (or cohabiting; column 2), by age group. Column 3 shows the prevalence of current smokers, and column 4 the percentage of persons who have never smoked.

Under the assumption that couples are in the same broad age groups as those in the table, and that the 'aggregation factor' described above is 3.0, we can estimate the percentage of never smokers who belong to the following categories:

- Currently living with a smoking partner (column 5)
- Currently living with a partner who has ever smoked (column 7)
- Has ever lived with a partner who was a smoker at some point of time (column 9).

The corresponding attributable fractions of lung cancers among never smokers are shown in columns 6, 8 and 10. They range from 2% of lung cancer cases in non-smoking men (due to their current partner's smoke) to 10.1% of lung cancers in non-smoking women, as a consequence of ever having had a partner who was a smoker at some point of time.

Although the relative risks derive from studies of non-smokers with current partners who smoked, the corresponding estimates of PAF in Table 5 (column 6) are probably an underestimate, because of the following factors:

- They take account only of current partnerships, and it is likely that past partnerships with a smoker would have had some adverse effects, particularly when separation had occurred only recently
- Some non-smoking partners may have quit relatively recently, and their past smoking would have had an adverse effect
- There may be other members of the household smoking, even though the partner does not.

For these reasons, the attributable fractions in column 8 (based on non-smokers with a current partner who was ever a smoker) are taken as the relevant estimate for the UK population.

Exposure to ETS at work Jamrozik (2005) gives the prevalence of passive smoking at work as 11%, an estimate that probably derives from the survey commissioned by ASH in April 1999, which revealed that approximately 3 million people in the UK are regularly exposed to ETS at work (ASH, 2004). There are otherwise very few data on workplace exposure to ETS in the UK. Chen *et al* (2001), in a small sample derived from participants in the fourth Scottish MONICA survey of 1995, found that any (regular) exposure of adults aged 25–64 years to environmental tobacco smoke at work was 68.1% for men and 57.5% for women (of which 21.5% of men and 17.4% of women classified such exposure as 'some' or 'a lot'). The EPIC study collected data on exposure to ETS at the time of recruitment among 123 000 non-smokers from 11 centres (none of them in UK) during 1993–1998, 78% of whom were women; 67% reported exposure at work (Vineis *et al*, 2005). The proportion of non-smoker controls in the multi-centre

Table 6 Lung cancer cases attributable to exposure of non-smokers to ETS in UK in 2010

	Source of exposure										
							Both				
	Spouse			Workplace			Independent ETS exposure			Correlated ETS exposure	
Age group (years)	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	Obs.	Excess attributable cases	PAF (%)	Excess attributable cases	PAF (%)
Men											
16–24	0.01	0	0	0.08	0	0	0	0	—	0	—
25–34	0.06	38	2	0.08	38	3	38	5	13.7	5	12.9
35–44	0.08	128	11	0.08	128	10	128	20	15.5	19	14.6
45–54	0.08	252	20	0.08	252	20	252	38	15.3	36	14.4
55–64	0.06	513	28	0.08	513	40	513	66	12.9	62	12.0
65–74	0.07	854	59	0.08	854	67	854	121	14.2	114	13.3
⩾75	0.05	1478	74	0.08	1478	115	1478	183	12.4	170	11.5
All ages		3262	195		3262	255	3262	434	—	406	—
% of total (all ages)			6.0			7.8		13.3		12.4	
Women											
16–24	0.01	0	0	0.09	0	0	0	0		0	
25–34	0.08	42	3	0.09	42	4	42	7	16.5	7	15.6
35–44	0.10	168	16	0.09	168	15	168	30	18.0	29	17.1
45–54	0.10	320	33	0.09	320	29	320	59	18.5	56	17.6
55–64	0.10	556	54	0.09	556	51	556	100	18.0	95	17.1
65–74	0.11	822	88	0.09	822	75	822	155	18.9	148	18.0
⩾75	0.05	1649	84	0.09	1649	151	1649	227	13.8	212	12.8
All ages		3557	279		3557	325	3557	578	—	547	—
% of total (all ages)			7.8			9.1		16.3		15.4	
Persons											
16–24		0	0		0	0	0	0		0	
25–34		80	6		80	7	80	12	15.2	6	7.3
35–44		296	27		296	25	296	50	16.9	27	9.1
45–54		572	53		572	49	572	98	17.1	53	9.3
55–64		1069	82		1069	91	1069	166	15.5	82	7.7
65–74		1676	147		1676	142	1676	276	16.5	147	8.8
⩾75		3127	158		3127	266	3127	410	13.1	158	5.0
All ages		6820	474		6820	580	6820	1013	—	952	—
% of total (all ages)			6.9			8.5		14.8		14.0	

Abbreviations: ETS = environmental tobacco smoke; Obs. = observed cases; PAF = population-attributable fraction.

European case–control study of Boffetta *et al* (1998) who reported ever being exposed to ETS at work was 71% in men and 47% in women.

It is difficult, based on such incomplete data, and the varying definition of 'exposure', to decide an appropriate prevalence for the UK. On the basis of the average of the results from Boffetta *et al* (1998), Chen *et al* (2001) and Vineis *et al* (2005), 71% for men and 53% for women, 8% of lung cancers in never-smoking men and 9% in women would be due to workplace exposure to ETS. With the much lower exposure estimate of Jamrozik (11%), the attributable fractions would be 1.3% and 2.0% in men and women, respectively.

RESULTS

Estimate of attributable fraction in lifelong non-smokers

Table 6 shows the final estimates of lung cancer attributable to ETS from the spouse, and at work, with the assumptions described above. With respect to combined exposure, it is assumed that the relative risks are simply multiplicative (no interaction). The exposures are assumed to be either

- independent of each other or
- correlated, in that individuals exposed at home are more likely to be exposed at work. In fact, the concordance between exposures at the two sites is rather weak: on the basis of the results among the control subjects in the study by Boffetta *et al* (1998), the κ value is -0.005 for women and $+0.05$ for men.

In total, 14–15% of lung cancer cases among individuals who have never smoked are estimated to be due to exposure to ETS.

DISCUSSION

The estimate of the effect of exposure to spousal smoking is based on current (2008) data on the proportion of persons married or cohabiting, and an estimate of the likelihood that their current partner has ever smoked. The percentages are 17% for men (aged over 16) and 23% for women. Self-reported exposure to spousal smoke among controls in the multi-centre European case–control study of Boffetta *et al* (1998) was reported as 12.8% for men and 62.7% for women – but these are values for those ever exposed, which were used in estimating the PAF in France (IARC, 2007). In the EPIC study, 28.5% of non-smokers (78% women) from 11 centres in Europe (not UK) reported ETS exposure (probably at the time of recruitment) at home (Vineis *et al*, 2005). The estimates of Jamrozik (2005) – 37% of adults under 65 exposed at home – are clearly inappropriate, as they relate to exposure of children to smoke at home from either parent. In the UK, Jarvis *et al* (2003), in a sample of adults from the general population of England in 1994 and 1996, found that among 9556 married or cohabiting non-smokers 14.5% had a partner who was a current cigarette smoker. This is similar to the indirect estimate of 17% (men) and 23% (women) who would be expected to have a smoking partner, based on the current prevalence in 2008, and an aggregation factor of 3, on which the result in Table 5 is based. Smoking prevalence has declined over time, and exposure to smoke from a smoking spouse would have been greater in the past (among individuals developing lung cancer in 2010), especially for women, as smoking has declined among men much more than among women. However, as the estimate is based on the probability of the current partner ever having been a smoker, any bias will be small.

The estimate of the role of exposure to ETS in the workplace uses the relative risks from the meta-analysis of case–control studies conducted by IARC (2004). A somewhat more recent meta-analysis of 22 studies (Stayner *et al*, 2007) suggested a similar magnitude of relative risk (1.24). The definition of 'exposure' in the studies included in these analyses varies, and, in any case, estimates of the PAF depend on the prevalence of workplace exposure to ETS in the UK population, for which there are no representative data.

A previous estimate for deaths attributable to passive smoking in the UK was made by Jamrozik (2005). The results are rather different from those obtained here – 1372 deaths from lung cancer due to exposure at home and 160 due to exposure at work. The

Table 7 Cases of lung cancer attributable to tobacco, by sex and age group (UK 2010)

				Total attributable cases	
Age group (years)	**Observed cases**	**Smoking attributable cases**	**ETS attributable cases**	**Excess attributable cases**	**PAF (%)**
Males					
0–34	38	0	5	5	14
35–44	215	87	20	107	50
45–54	1138	886	38	924	81
55–64	4184	3671	66	3737	89
⩾65	16 697	14 366	305	14 671	88
Total	22 273	19 011	434	19 445	87
Females					
0–34	42	0	7	7	17
35–44	224	56	30	86	39
45–54	1088	768	59	827	76
55–64	3441	2885	100	2985	87
⩾65	13 335	10 864	382	11 246	84
Total	18 132	14 575	578	15 153	84
Persons					
0–34	80	0	12	12	15
35–44	439	143	50	193	44
45–54	2226	1654	98	1752	79
55–64	7625	6556	166	6722	88
⩾65	30 032	25 230	687	25 917	86
Total	40 405	33 586	1013	34 599	86

Abbreviations: ETS = environmental tobacco smoke; PAF = population-attributable fraction.

Table 8 Cancer cases caused by exposure to tobacco smoke (by smoking, or environmental), UK 2010

Cancer	Cases in UK, 2010		
	Observed cases	Excess attributable cases Number (% at this site)	Population-attributable fraction (% of all cancers)
Males			
Lung	22 273	19 445 (87)	12.3
Oral cavity and pharynx	4573	3180 (70)	2.0
Oesophagus	5711	3574 (63)	2.3
Stomach	4467	1167 (26)	0.7
Liver	2270	620 (27)	0.4
Pancreas	4082	1071 (26)	0.7
Colon–rectum	22 125	1469 (7)	0.9
Larynx	1802	1424 (79)	0.9
Cervix uteri	—	—	—
Ovary	—	—	—
Bladder	6711	2520 (38)	1.6
Kidney	5697	1677 (29)	1.1
Leukaemia	4639	390 (8)	0.2
All cancers	158 667	36 537 (23.0)	23.0
Females			
Lung	18 132	15 153 (84)	9.7
Oral cavity and pharynx	2355	1292 (55)	0.8
Oesophagus	2817	2009 (71)	1.3
Stomach	2576	398 (15)	0.3
Liver	1298	199 (15)	0.1
Pancreas	4280	1325 (31)	0.9
Colon–rectum	17 786	1766 (10)	1.1
Larynx	382	302 (79)	0.2
Cervix uteri	2693	195 (7)	0.1
Ovary	6820	177 (3)	0.1
Bladder	2571	883 (34)	0.6
Kidney	3364	504 (15)	0.3
Leukaemia	3201	96 (3)	0.1
All cancers	155 584	24 300 (15.6)	15.6
Persons			
Lung	40 405	34 599 (86)	11.0
Oral cavity and pharynx	6928	4472 (65)	1.4
Oesophagus	8528	5583 (65)	1.8
Stomach	7043	1565 (22)	0.5
Liver	3568	819 (23)	0.3
Pancreas	8362	2396 (29)	0.8
Colon–rectum	39 911	3235 (8)	1.0
Larynx	2184	1726 (79)	0.5
Cervix uteri	2693	195 (7)	0.1
Ovary	6820	177 (3)	0.1
Bladder	9282	3403 (37)	1.1
Kidney	9061	2181 (24)	0.7
Leukaemia	7840	487 (6)	0.2
All cancers	314 251	60 837 (19.4)	19.4

reasons for this are different assumptions concerning prevalence of exposure (as mentioned above) and relative risk, and the attribution of no lung cancer deaths after the age of 64 years to workplace exposures. What is more, Jamrozik estimates lung cancer deaths attributable to passive smoking in the whole population – including among current and past smokers; as noted in the introduction, this is illogical, as such deaths would not occur among non-smokers if no one smoked.

SUMMARY

Table 7 summarizes the findings with respect to lung cancer and exposure to tobacco smoke. In total, 34 599 cases of lung cancer in the UK (86% of the total) were due to exposure to tobacco smoke in 2010, the great majority of which (97.4%) are due to active smoking (current or in the past). The figures for men are 87% cases due to exposure to tobacco (of which 97.7% were due to smoking), and for women 84% cases due to exposure to tobacco (of which 96.2% were due to smoking).

Table 8 shows the final summary of the estimate of tobacco-attributable cancer in the UK. In total, the estimate is of 60 837 cancer cases (19.4% of all new cancer cases) attributable to tobacco: 36 537 (23.0%) of cancers in men and 24 300 (15.6%) of cancers in women.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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3.
Cancers attributable to consumption of alcohol in the UK in 2010

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In 1988, the International Agency for Research on Cancer (IARC) Monograph on the carcinogenic risk to humans of alcohol drinking concluded that the occurrence of malignant tumours of the oral cavity, pharynx, larynx, oesophagus and liver was causally related to the consumption of alcoholic beverages. In an updated review (Baan *et al*, 2007; Secretan *et al*, 2009), they noted the consistent finding of an increased risk of breast cancer with increasing alcohol intake, and that an association between alcohol consumption and colorectal cancer had been reported by more than 50 prospective and case–control studies, with no difference in the risk for colon and rectal cancers (Baan *et al*, 2007). The World Cancer Research Fund report (WCRF, 2007) considered that the evidence for an association of alcohol intake with these sites was convincing and, for liver cancer, probable.

METHODS

Quantitative risk of alcohol

Table 1 shows the increase in risk associated with consumption of 1 g per day of alcohol. The estimates in these studies had been adjusted for major confounders, notably smoking.

With respect to breast cancer, the estimate was derived from a meta-analysis of 53 studies, conducted by the Collaborative Group on Hormonal Factors in Breast Cancer (Hamajima *et al*, 2002), which found that the risk was increased by 7.1% for every 10 g of daily alcoholintake. The values observed in subsequent studies are not substantially different. A pooled analysis of six cohort studies with data on alcohol and dietary factors found that the risk of breast cancer increased monotonically with increasing intake of alcohol; the multivariate relative risk (RR) for a 10-g per day increase in alcohol was 1.09 (95% CI = 1.04–1.13; Smith-Warner *et al*, 1998). The EPIC study (Tjønneland *et al*, 2007) found that the risk was 1.03 (95% CI = 1.01–1.05) per 10-g per day recent alcohol intake, whereas in the Million Women Study the increase in risk associated with 10 g per day intake was 12% (Allen *et al*, 2009).

With respect to cancers of the colorectum, a pooled analysis of eight cohort studies reported a borderline statistically significant 16% risk increase for people drinking 30–45 g per day of alcohol and a significant 41% risk increase for people drinking $\geqslant$45 g per day (Cho *et al*, 2004). A more recent meta-analysis of cohort studies found a 15% increase in the risk of colon or rectal cancer for an increase of 100 g alcohol intake per week (Moskal *et al*, 2007), with no difference between men and women. In the EPIC study (Ferrari *et al*, 2007), the effect was a bit weaker, with alcohol intake at study baseline increasing colorectal cancer risk by 9% per 15 g per day, a risk greater for rectal cancer than for cancer of the distal colon, which in turn was greater than the risk for cancer of the proximal colon. In the WCRF (2007) report, a meta-analysis of eight studies of colon cancer yielded a combined RR of 1.09 (1.03–1.14) per 10 g intake per day, and a meta-analysis of nine studies of rectal cancer yielded an RR of 1.06 (1.01–1.12) per 10 g intake per day.

The means in the meta-analyses of Cho *et al* (2004), Moskal *et al* (2007), the EPIC study (Ferrari *et al*, 2007) and WCRF (2007) are 0.75% per gram alcohol per day for colon cancer and 0.85% per gram per day for rectal cancer. As these estimates are similar, the global figure of 0.8% per gram (increase of 0.008 per gram per day) was used for colorectal cancer as a whole (Table 1).

For the remaining cancers, the meta-analysis of Corrao *et al* (2004) was used to estimate the RRs. They present RRs associated with a mean intake of 0, 25, 50 and 100 g of alcohol per day. The RR per gram of alcohol intake was estimated by assuming a log–linear relationship between exposure and risk, so that:

$$\text{Relative risk}\,(x) = \exp(\ln(\text{risk per unit}) \times \text{exposure level}\,(x))$$

where x is the exposure level (in grams per day).

Prevalence of exposure to alcohol

The latent period or interval between 'exposure' to alcohol and the appropriate increase in risk of these cancers is not known. We chose to assume that this would be, on average, 10 years, and thus examine the effects on cancers occurring in 2010 from non-optimal levels of alcohol consumption in the year 2000.

There are two main ways of measuring the amount of alcohol consumed: asking people how much alcohol they drink or counting how much alcohol is sold. As the estimates of the effect of past alcohol drinking on cancer risk are based on epidemiological studies in which alcohol intake is estimated from questionnaire data, it is most appropriate to base the exposure prevalence on data from a similar source.

We have used data from the National Diet and Nutrition Survey, a survey of the diet and nutrition of a representative sample of adults in the age group of 19–64 years living in private households in Great Britain, carried out between July 2000 and June 2001

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(Henderson *et al*, 2003). For the age group >65 years, we used data on the proportion of non-drinkers, and average alcohol consumption from the General Household Survey (for England) (Goddard, 2006). From these tables, an estimate was prepared of the proportions of individuals (by age group and sex) consuming different quantities of alcohol in terms of grams per day, assuming that 1 unit of alcoholic beverages contains 8 g of pure alcohol (Table 2).

The same data are shown in Figure 1, as the cumulative percentages of men and women of different ages with different levels of alcohol intake in 2000, as grams per day of alcohol.

Estimation of population attributable fractions (PAFs)

For the six cancer types, PAFs were calculated for each sex–age group according to the usual formula:

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

where p_x is the proportion of the population in consumption level x ($x = 1-12$) and ERR_x the excess relative risk ($\mathrm{RR}_x - 1$) in consumption level x ($x = 1-12$).

The ERR of alcohol consumption for each level x of alcohol consumption given in Table 2 was calculated as follows:

$$\mathrm{ERR}_x = \exp(R_g \times G_x) - 1$$

where R_g is the increase in risk per gram of alcohol intake (Table 1) and G_x the intake of alcohol (grams per day) in consumption category x (Table 2).

Table 1 Increase in risk of cancer associated with 1 gram of alcohol per day

Cancer type	Studies	Increase in risk per gram alcohol per day
Oral cavity and pharynx	Corrao *et al* (2004)	0.0185
Larynx	Corrao *et al* (2004)	0.0136
Oesophagus	Corrao *et al* (2004)	0.0129
Colorectal cancer	Cho *et al* (2004) Moskal *et al* (2007) Ferrari *et al* (2007) WCRF (2007)	0.0080
Breast	Collaborative Group (Hamajima *et al*, 2002)	0.0071
Liver	Corrao *et al* (2004)	0.0059

RESULTS

Table 3 shows for each sex and age group the numbers of cases of the six alcohol-related cancers in the UK in 2010, the PAFs due to alcohol consumption 10 years earlier (2000–2001) and the corresponding number of excess cases (calculated as (observed × PAF)).

Because of the high risk of upper aero-digestive tract cancer associated with alcohol drinking, cancers of the mouth and pharynx, as well as larynx, had the highest percentages of alcohol-attributable cases (30.4% of cancers of the oral cavity and pharynx, 24.6% of laryngeal cancers). Although the fractions of colorectal (11.6%) and breast (6.4%) cancers were much lower, the actual numbers of alcohol-attributable cases were much greater – together, they account for about 7700 alcohol-attributable cases in 2010 (or 62% of all alcohol-related cancers).

Table 4 sums the excess numbers of cases at the six sites, caused by alcohol consumption, and expresses these numbers as a fraction of the total burden of (incident) cancer. The estimates are 4.6%

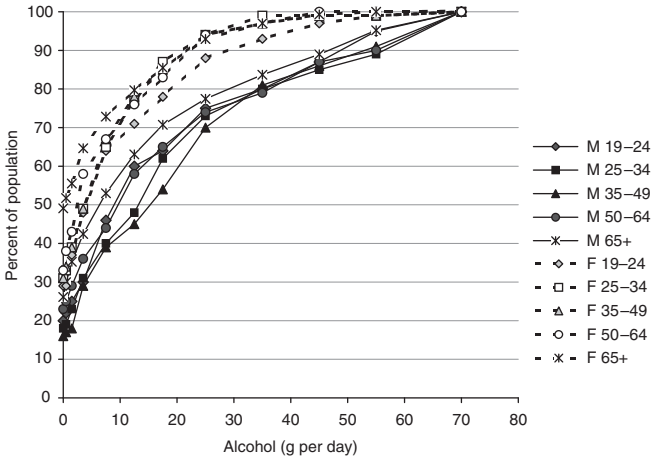

Figure 1 Cumulative percentage of population with different alcohol intakes.

Table 2 Estimated percentage of the population at 12 levels of alcohol consumption

		% of population consuming the specified grams per day alcohol in Great Britain during 2000–2001											
Alcohol consumption		Men by age (years)						Women by age (years)					
Level	Grams per day	19–24	25–34	35–49	50–64	65+	All 19+	19–24	25–34	35–49	50–64	65+	All 19+
1	0	20	18	16	23	26	20	29	31	31	33	49	35
2	0.5	2	1	1	2	4	2	0	2	3	5	3	3
3	1.5	3	4	1	4	5	3	8	6	5	5	4	5
4	3.5	5	8	11	7	7	8	11	10	10	15	9	11
5	7.5	16	9	10	8	11	10	16	16	18	9	8	13
6	12.5	14	8	6	14	10	10	7	12	11	9	7	9
7	17.5	4	14	9	7	8	9	7	10	7	7	6	7
8	25	11	11	16	9	7	11	10	7	9	11	7	9
9	35	5	7	11	5	6	7	5	5	3	3	4	4
10	45	7	5	5	8	5	6	4	0	2	3	2	2
11	55	8	4	5	3	6	5	2	0	0	0	1	0
12	70	5	11	9	10	5	8	1	1	1	0	0	0
Mean grams per day		20.4	22.2	23.1	21.1	12.6	23.6	11.4	9.1	9.2	8.6	7.7	11.6

Data for 19–64-year-olds from Henderson (2003); data for >65-year-olds from Goddard (2006).

Table 3 Cancer cases diagnosed in 2010 attributable to alcohol consumption in 2000–2001

Age (years)		Cases attributable to alcohol consumption for each cancer																	
		Oral cavity and pharynx			Oesophagus			Colon–rectum			Liver			Larynx			Breast		
At exposure	At outcome (+10 years)	PAF	Obs.	Excess attrib. cases	PAF	Obs.	Excess attrib. cases	PAF	Obs.	Excess attrib. cases	PAF	Obs.	Excess attrib. cases	PAF	Obs.	Excess attrib. cases	PAF	Obs.	Excess attrib. cases
Men																			
15–24	25–34	0.36	55	19.6	0.25	11	2.8	0.16	133	20.8	0.12	19	2.1	0.26	2	0.5			
25–34	35–44	0.39	244	96.1	0.28	86	24.0	0.17	397	69.2	0.13	43	5.5	0.29	35	10.3			
35–49	45–59	0.40	1591	631.8	0.28	970	274.9	0.18	2921	521.1	0.13	351	46.4	0.30	407	121.3			
50–64	60–74	0.38	1888	709.1	0.26	2535	668.2	0.16	9481	1548.0	0.12	1011	121.4	0.28	914	253.9			
⩾65	⩾75	0.32	768	249.1	0.22	2108	473.7	0.14	9162	1262.7	0.10	828	83.7	0.24	444	105.3			
Total			4571	1705.9		5713	1443.5		22 127	3421.8		2270	259.1		1803	491.3			
%				37.3			25.3			15.5			11.4			27.3			
Women																			
15–24	25–34	0.23	50	11.4	0.16	4	0.6	0.10	136	13.0	0.07	12.11	0.9	0.17	2	0.3	0.08	715.1	60.7
25–34	35–44	0.18	131	23.2	0.12	27	3.3	0.07	402	29.9	0.05	29.48	1.6	0.13	12	1.5	0.07	3857	254.0
35–49	45–59	0.18	622	113.5	0.12	303	37.9	0.08	2292	174.8	0.06	142.8	8.0	0.13	99	13.1	0.07	14 628	987.4
50–64	60–74	0.17	855	146.3	0.12	922	108.5	0.07	6116	440.7	0.05	453	23.9	0.12	168	20.9	0.06	17 194	1096.9
⩾65	⩾75	0.16	666	105.2	0.11	1560	166.8	0.06	8810	568.8	0.05	642.4	30.2	0.11	101	11.4	0.06	11 952	681.3
Total			2359	399.7		2819	317.2		17 787	1227.3		1298	64.6		386	47.3		48 385	3080.3
%				16.9			11.3			6.9			5.0			12.2			6.4
Persons																			
15–24	25–34		105	31.1		15	3.4		269	33.8		31	3.0		4	0.9		715	60.7
25–34	35–44		375	119.3		113	27.3		799	99.1		72	7.1		47	11.8		3857	254.0
35–49	45–59		2213	745.4		1273	312.8		5213	695.9		494	54.3		506	134.4		14 628	987.4
50–64	60–74		2743	855.5		3457	776.7		15 597	1988.8		1464	145.4		1082	274.8		17 194	1096.9
⩾65	⩾75		1434	354.3		3668	640.5		17 972	1831.5		1470	113.9		545	116.7		11 952	681.3
Total			6930	2105.6		8532	1761		39 914	4649		3568	324		2189	539		48 385	3080
%				30.4			20.6			11.6			9.1			24.6			6.4

Abbreviations: attrib. = attributable; Obs. = observed cases; PAF = population-attributable fraction.

Table 4 Estimated total numbers of cancers in the UK in 2010, PAFs due to alcohol consumption 10 years earlier (2000–2001), and the corresponding number and percentage of excess cases, by age group and sex

Age (years)		All cancers[a]		
Exposure	Outcome (+10 years)	Observed cases	Excess attributable cases	PAF (%)
Men				
15–24	25–34	2109	46	2.2
25–34	35–44	4124	205	5.0
35–49	45–59	22 388	1596	7.1
50–64	60–74	68 043	3301	4.9
⩾65	75+	60 149	2175	3.6
Total		158 667	7322	4.6
Women				
15–24	25–34	3284.1	87	2.6
25–34	35–44	8619.2	313	3.6
35–49	45–59	31 631	1335	4.2
50–64	60–74	54 966	1837	3.3
⩾65	75+	55 437	1564	2.8
Total		155 584	5136	3.3
Persons				
15–24	25–34	5393	133	2.5
25–34	35–44	12 743	519	4.1
35–49	45–59	54 019	2930	5.4
50–64	60–74	123 009	5138	4.2
⩾65	75+	115 586	3738	3.2
Total		314 251	12 458	4.0

Abbreviations: PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

cancers in men and 3.3% in women due to alcohol consumption, or 4.0% cancers overall.

DISCUSSION

The estimates of the RR of alcohol consumption for various cancers are an 'average' taken from widely cited meta-analyses; more extreme values can be found in specific studies.

Table 5 compares the excess RRs of 1 g of alcohol consumption per day as used in this study with those from the Million Women Study (Allen *et al*, 2009) and the EPIC study (Ferrari *et al*, 2007; Tjonneland *et al*, 2007), as well as with those derived from various meta-analyses by WCRF (2007). The values for cohort studies are shown for cancers of the breast, colon, rectum and liver. For upper aero-digestive and oesophageal cancers, meta-analyses were based on case–control studies only.

For the most part, the risks associated with consumption of alcohol used in the present study are similar to those in the three comparative studies listed in Table 5. The ERRs reported in the Million Women Study (Allen *et al*, 2009) are rather higher than those in Table 1 for cancers of the oesophagus, liver and larynx, although the values used in the current analysis (Table 1) lie within the relevant 95% confidence intervals; for colon cancer, however, the value is considerably lower.

With respect to cancer of the oesophagus, some of the differences may relate to the differing proportions of squamous cell and adenocarcinomas in the series of cancers in various studies. Although squamous cell carcinomas are clearly related to alcohol exposure, the risk of adenocarcinoma is much lower, or nil (Lagergren *et al*, 2000; Wu *et al*, 2001; Lindblad *et al*, 2005; Pandeya *et al*, 2009). Currently, adenocarcinomas comprise

Table 5 Estimates of excess relative risk associated with 1 gram alcohol intake per day

Cancer	Excess relative risk (ERR)			
	This study	MWS 2009[a]	WCRF/AICR 2007[b]	EPIC[c]
Breast	0.0071	0.0114	0.0095	0.0030[d]
Colon	0.0081	0.0010	0.0086	0.0045
Rectum	0.0081	0.0096	0.0058	0.0070
Liver	0.0059	0.0217	0.0095	
Oesophagus	0.0129	0.0201	0.0183[e]	
Oral cavity and pharynx	0.0185	0.0258		
Larynx	0.0136	0.0371	0.0138[e]	

[a]Million Women Study, Allen *et al* (2009). [b]WCRF (2007). [c]European Prospective Investigation into Cancer and Nutrition, Ferrari *et al* (2007). [d]Tjonneland *et al* (2007). [e]Based on meta-analysis of case–control studies only.

Table 6 UK alcohol consumption per adult

Year	General Household Survey[a]		HM Revenue and Customs[b]	
	Units per week	Litres of pure alcohol per year	Units per week	Litres of pure alcohol per year
1990	10.8	5.3	19.2	10
2000	12.0	6.2	20.2	10.5
2005	10.8	5.6	21.9	11.4

[a]General Household Survey (Goddard, 2006). [b]HM Revenue and Customs (HMRC, 2008).

approximately 70% of oesophageal cancers in men in the UK, and 40% in women (see section 8, in Cancers attributable to overweight and obesity). However, the studies currently used to estimate the RR of oesophageal cancer in relation to alcohol do not distinguish between the histological subtypes, and no correction to the estimate for the UK has been made on this basis.

We chose to use the estimates of alcohol consumption in the UK based on population survey data (the National Diet and Nutrition Survey). However, it is well known that surveys produce figures far lower than would be expected from alcohol sales. Alcohol sales are estimated based on clearance data produced by HM Revenue and Customs (HMRC). Not all alcohol that is cleared is actually consumed; for example, it is conceivable that some of it may be thrown away when it passes its best-before date. Conversely, not all alcohol that is consumed in the UK is cleared by HMRC; for example, home brew and illegally imported alcohol.

Table 6 compares consumption as estimated by the General Household Survey (Goddard, 2006) and from clearance data produced by HM Revenue and Customs (HMRC, 2008). The large difference between the two sets of data is unlikely to be due to large amounts of purchased alcohol not being consumed. Both the General Household Survey and the Government's alcohol strategy (HMG, 2007) believe that many people underestimate the amount of alcohol they drink. However, as estimates of risk are generally based on responses to questionnaires, they are likely to overestimate the risk in relation to actual alcohol consumption. It is more appropriate, therefore, to use estimates of alcohol intake from (self-reported) survey data than the more accurate clearance data.

The current estimate (3.6% of new cancers in 2010 related to alcohol) is similar to the figure published by Doll and Peto (2003) – that around 6% of UK cancer deaths could be avoided if people did not drink. The estimation is based on the attribution to alcohol of 2/3 deaths from alcohol-related cancers (mouth, pharynx, larynx, oesophagus) in men and 1/3 in women, plus 'a small proportion' of liver cancer deaths. A recent publication, based on the risks of alcohol consumption observed in the EPIC study, estimates a rather higher fraction of cancers attributable to alcohol in the UK – especially in men: 8% of cancer in men and 3% in women (Schütze *et al*, 2011). The difference appears to be mainly because of the rather higher level and prevalence of alcohol consumption that were used to estimate attributable fractions (an average intake of 35.2 g per day in men and 17.6 g per day in women, cf. Table 2). These were calculated from data available on the World Health Organisation website, which appear to be derived from clearance data, with levels of consumption equivalent to those in Table 6 (on average, annually 13.4 l of alcohol per capita in 2003–5). As noted above, it would seem more appropriate to use self-reported consumption, even though this is an underestimate of the true situation, as the RR estimates in EPIC (as in other cohort studies) are also based on questionnaire data.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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4.
Cancers attributable to dietary factors in the UK in 2010

I. Low consumption of fruit and vegetables

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There is considerable controversy over the protective effect of diets rich in fruit, vegetables and fibre, and the respective roles of the different components (including micronutrients such as folate). The report of the Committee on Medical Aspects of Food Nutrition Policy (COMA) (Department of Health, 1998) recommended increasing consumption of all of them, an advice that seems to have motivated the Department of Health in promoting its '5-a-day' programme (Department of Health, 2005). The original consensus of the probable decrease in risk of several cancers of the gastrointestinal tract (oral cavity and pharynx, oesophagus, stomach and colorectum) associated with increased consumption of fruit and vegetables (WHO/FAO, 2003) was based on the results of multiple case–control studies and a few prospective studies. The IARC Handbook of Cancer Prevention (IARC, 2003) concludes its review of the evidence as follows:

> There is *limited evidence* for cancer-preventive effect of consumption of fruit and vegetables for cancers of the mouth and pharynx, oesophagus, stomach, colorectum, larynx, lung, ovary (vegetables only), bladder (fruit only) and kidney.
> There is *inadequate evidence* for a cancer-preventive effect of consumption of fruit and vegetables for all other sites.
> More specifically, this evidence indicates that higher intake of fruit *probably* lowers the risk of cancers of the oesophagus, stomach and lung, while higher intake of vegetables *probably* lowers the risk of cancers of the oesophagus and colorectum.
> Likewise a higher intake of fruit *possibly* lowers the risk of cancers of the mouth, pharynx, colorectum, larynx, kidney and urinary bladder. An increase in consumption of vegetables *possibly* reduces the risk of cancers of the mouth, pharynx, stomach, larynx, lung, ovary and kidney.

The conclusions of the WCRF report (2007) are more or less in line with these, except with respect to large-bowel cancer, for which the evidence for protective effects of both vegetables and fruit was considered 'limited' (in contrast to 'conclusive' or 'probable' – implying that a causative relationship is uncertain). More emphasis was placed on the importance of the protective effects of consumption of foods containing dietary fibre than on vegetables *per se*. The summary conclusions were as follows:

> Non-starchy vegetables probably protect against cancers of the mouth, pharynx, and larynx, and those of the oesophagus and stomach. There is limited evidence suggesting that they also protect against cancers of the nasopharynx, lung, colorectum, ovary, and endometrium.
> Fruit in general probably protects against cancers of the mouth, pharynx, and larynx, and those of the oesophagus, lung, and stomach. There is limited evidence suggesting that fruit also protects against cancers of the nasopharynx, pancreas, liver, and colorectum.

In this analysis, we follow the WCRF in considering ONLY the effect of a deficit of fruit and vegetables on cancers of the mouth and pharynx, oesophagus, stomach and larynx, and of a deficit of fruit on cancers of the lung.

The advice from the Department of Health (2005) is to increase the average consumption of a variety of fruit and vegetables to at least five portions per day, corresponding to 5×80 or 400 g per day. In this section, we estimate the population-attributable fraction (PAF) of these five cancers (and of all cancer) that results from consumption of fruit and vegetables lower than this target.

METHODS

The risks associated with consumption of 1 g per day of fruit or of vegetables are shown in Table 1. As we are concerned with quantifying the effect of a deficit in consumption, they are presented as the risk associated with a decreased intake of 1 g per day.

These risks derive from the simple means of the values from three meta-analyses: those of Riboli and Norat (2003), WCRF (2007) and, except for laryngeal cancer, Soerjomataram *et al* (2010). (The value for the protective effect of vegetables on cancers of the oral cavity and pharynx in the meta-analysis of Soerjomataram *et al* (2010) was quite implausible, implying a reduction in risk of 1.4% per gram per day. We substituted the value for upper aero-digestive tract cancers from the multi-centre

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European prospective study (EPIC) of 0.29% per gram per day (Boeing *et al*, 2006)). The values from the latter were reported as relative risk per gram increase in daily consumption of fruit and vegetables. For the others, the excess relative risk for a decrease of 1 g of vegetables or fruit consumed was estimated by assuming a log-linear relationship between exposure and risk, so that:

$$\text{Risk per gram per day} = (\ln(1/\text{RR}_x))/x$$

where x is the exposure level (in grams per day) and RR_x the relative risk for x grams per day.

The latent period (or interval between 'exposure' to fruit and vegetables and the appropriate decrease in risk of these cancers) is not known. Prospective studies of diet and cancer (from which the estimates of relative risk are mostly drawn) involve follow-up periods (between estimated dietary intake and cancer onset) of several years. For the cohort studies contributing to the meta-analyses of WCRF, 10 studies of lung cancer and 6 of stomach cancer reported the mean duration of follow-up; the simple means were 15.2 and 10.3 years, respectively. There are a few cohort studies on upper GI cancers: the follow-up periods in the EPIC study (González *et al*, 2006) and Japanese JPHC studies (Yamaji *et al*, 2008) were 6.5 and 7.7 years, respectively. For the purposes of estimating attributable fraction, we assume a mean latency of 10 years, and thus examine the effects on cancers occurring in 2010 of sub-optimal levels of fruit and vegetable consumption in 2000. Consumption of fruit and vegetables, in grams per week, by age group and sex, is available for 2000–2001 from the National Diet & Nutrition Survey (FSA, 2004; Table 2.1). The mean consumption, by age group, is shown in Table 2. The target consumption of 400 g per day was not achieved at any age, and the young, in particular, had a low consumption of such items.

Table 1 Estimated risks associated with a decreased consumption of 1 g per day of fruits and non-starchy vegetables

	Risks associated with 1 g per day decrease in consumption	
Cancer type	**Fruit**	**Vegetables[a]**
Oral cavity and pharynx	0.00488	0.00416
Oesophagus	0.00504	0.00266
Stomach	0.00234	0.00320
Colon–rectum	0	0
Larynx	0.00322	0.00370
Lung	0.00146	0

[a]Non-starchy vegetables.

Table 2 Mean consumption of fruit and non-starchy vegetables by sex and age group, Great Britain 2000–2001

	Mean consumption (grams per day) by age group (years)				
Vegetables or fruit	**19–24**	**25–34**	**35–49**	**50–64**	**19–64**
Men					
Vegetables	95	122	144	162	137
Fruit	27	61	99	122	87
Women					
Vegetables	89	130	139	143	132
Fruit	54	74	98	151	103
Persons					
Vegetables	92	126	141	153	135
Fruit	40	68	99	137	95

Table 3 Proportions of the Great Britain population in seven categories of fruit and vegetable consumption in 2000–2001, and estimated deficit in consumption in each category from the recommended 400 g per day

	Consumption categories in 2000–2001						
Sex and age (years)	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Men 19–49							
Proportion of the population	0.01	0.22	0.29	0.20	0.11	0.08	0.09
Vegetables (g per day)	0	27.8	83.3	138.8	194.3	249.8	305.3
Deficit from 256 g per day	256	228	172	117	61	6	0
Fruit (g per day)	0	15.8	47.3	78.8	110.3	141.8	173.3
Deficit from 144 g per day	144	129	97	66	34	3	0
Men 50–64							
Proportion of the population	0.01	0.06	0.22	0.16	0.15	0.16	0.24
Vegetables (g per day)	0	24.5	73.5	122.5	171.5	220.5	269.5
Deficit from 228 g per day	228	204	155	106	57	8	0
Fruit (g per day)	0	18.5	55.5	92.5	129.5	166.5	203.5
Deficit from 172 g per day	172	153	116	79	42	5	0
Women 19–49							
Proportion of the population	0.01	0.06	0.22	0.16	0.15	0.16	0.24
Vegetables (g per day)	0	25.8	77.3	128.8	180.3	231.8	283.3
Deficit from 242 g per day	242	217	165	114	62	11	0
Fruit (g per day)	0	16.8	50.3	83.8	117.3	150.8	184.3
Deficit from 158 g per day	158	141	107	74	40	7	0
Women 50–64							
Proportion of the population	0.01	0.19	0.26	0.21	0.12	0.08	0.12
Vegetables (g per day)	0	21	63	105	147	189	231
Deficit from 195 g per day	195	174	132	90	48	6	0
Fruit (g per day)	0	22.3	66.8	111.3	155.8	200.3	244.8
Deficit from 205 g per day	205	183	139	94	50	5	0

The National Diet & Nutrition Survey also provides the distribution of intake of fruit and vegetables in the British population, in terms of the cumulative percentage of individuals (by sex and age group) consuming 0, <1, <2, …, >5 portions of fruit and vegetables daily (FSA, 2004; Table 2.3). The populations of each sex were dichotomised into two age groups (<50 and 50–64), and 'portions' were converted into grams (of fruit and vegetables), such that the mean daily intake corresponded to the values in Table 2. Table 3 shows the results in terms of the proportions of the population at seven different levels of consumption of fruit and vegetables.

To calculate the deficit in consumption of fruit and vegetables relative to a target of 400 g per day for both, the deficit in each sex and age group (19–49, 50–64) was calculated from Table 2. For example, the deficit in older men (50–64) was, on average, 216 g per day (400−(162+122)). The total deficit is partitioned into deficits of fruit and vegetables, so that the same ratio of vegetables to fruit that was being eaten in 2000–1 is maintained. Thus, the 400 g per day target for consumption in men in the age group of 50–64 years is partitioned in the ratio of 162:122 (Table 2); i.e., 228 g per day vegetables and 172 g per day fruit (Table 3). The deficit of each in the different consumption categories in men and women aged <50 years and in the age group of 50–64 is shown in Table 3.

For each cancer, the relative risk in 2010 in the four age–sex strata is calculated from the deficit in consumption 10 years earlier (2000–2001), with the risk for fruit and vegetables calculated separately according to the following formula:

$$\mathrm{RR} = (\exp(R_g \times G_x))$$

where R_g is the relative risk for a deficit of 1 g per day of fruit or vegetables (Table 1) and G_x is the deficit in consumption (as shown in Table 3) in consumption category x.

The benefits of fruit and vegetables are considered to be multiplicative in their effect, so that

$$\mathrm{RR}(f \text{ and } v) = \mathrm{RR}(f) \times \mathrm{RR}(v)$$

Population-attributable fractions were calculated for each of the four sex–age groups in Table 3 according to the following formula:

$$\mathrm{PAF} = \frac{\begin{array}{c}(p_1 \times \mathrm{ERR}_1)+(p_2 \times \mathrm{ERR}_2)+(p_3 \times \mathrm{ERR}_3)+(p_4 \times \mathrm{ERR}_4)\\ +(p_5 \times \mathrm{ERR}_5)+(p_6 \times \mathrm{ERR}_6)+(p_7 \times \mathrm{ERR}_7)\end{array}}{\begin{array}{c}1+[(p_1 \times \mathrm{ERR}_1)+(p_2 \times \mathrm{ERR}_2)+(p_3 \times \mathrm{ERR}_3)+(p_4 \times \mathrm{ERR}_4)\\ +(p_5 \times \mathrm{ERR}_5)+(p_6 \times \mathrm{ERR}_6)+(p_7 \times \mathrm{ERR}_7)]\end{array}}$$

where p_x is the proportion of population in consumption category x and ERR_x the excess relative risk (RR(f and v)−1) in consumption category x.

RESULTS

Table 4 shows the PAFs and the estimated number of cases 'caused' in 2010 by these deficits in consumption of fruit and vegetables 10 years earlier. The cancers for which the greatest proportion of cases may be related to low intake of fruit and vegetables are the oral cavity and pharynx (56%), oesophagus (46%) and larynx (45%). Although only 9% of lung cancer cases may be related to low intake of fruit (there is no excess risk of lung cancer from low intake of vegetables), the actual number of cases (3567) represents almost one-quarter of the total number of cancers attributable to low intake of fruit and vegetables (14 902: Table 5).

Table 5 sums the excess numbers of cases at the five sites, caused by low consumption of fruit and vegetables, and expresses these numbers as a fraction of the total burden of (incident) cancer. The estimate is 6.1% cancers in men and 3.4% in women, or 4.7% of cancers overall.

Table 4 Cancer cases in 2010 at six sites caused by deficient intake of fruit and vegetables in 2000–2001

Age (years)		Oral cavity and pharynx			Oesophagus			Stomach			Colon–rectum			Larynx			Lung		
At exposure	At outcome (+10 years)	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases
Men																			
19–49	29–59	0.65	1874	1223	0.56	1064	596	0.49	587	285	0	3410	0	0.56	443	249	0.11	2839	300
50–64	⩾60	0.52	2656	1393	0.45	4643	2067	0.35	3875	1367	0	18 643	0	0.43	1358	578	0.08	19 417	1584
Total (%)			4571	2616 (57.2%)		5713	2663 (46.6%)		4467	1651 (37.0%)		22 127	0 (0.0%)		1803	827 (45.9%)		22 273	1884 (8.5%)
Women																			
19–49	29–59	0.64	786	503	0.55	332	184	0.47	325	151	0	2791	0	0.54	113	61	0.11	2550	280
50–64	⩾60	0.50	1521	762	0.44	2482	1088	0.32	2243	722	0	14 926	0	0.40	269	106	0.09	15 562	1403
Total (%)			2359	1265 (53.6%)		2819	1272 (45.1%)		2577	874 (33.9%)		17 787	0 (0.0%)		386	168 (43.5%)		18 132	1683 (9.3%)
Persons																			
19–49	29–59		2660	1725		1396	779		912	436		6201	0		556	310		5389	579
50–64	⩾60		4177	2155		7125	3155		6118	2089		33 569	0		1627	684		34 979	2987
Total (%)			6930	3881 (56.0%)		8532	3935 (46.1%)		7044	2525 (35.8%)		39 914	0 (0.0%)		2189	995 (45.4%)		40 405	3567 (8.8%)

Abbreviations: Obs = observed cases; PAF = population-attributable fraction.

Table 5 Number of all cancer cases in 2010 caused by deficient intake of fruit and vegetables in 2000–2001

Age group (years)		All cancers[a]		
At exposure	At outcome (+10 years)	Observed cases	Excess attributable cases	PAF (%)
Men				
19–49	29–59	27 845	2651	9.5
50–64	60+	128 192	6990	5.5
Total		158 667	9641	6.1
Women				
19–49	29–59	42 499	1179	2.8
50–64	60+	110 403	4082	3.7
Total		155 584	5261	3.4
Persons				
19–49	29–59	70 344	3830	5.4
50–64	60+	238 595	11 071	4.6
Total		314 251	14 902	4.7

Abbreviations: PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

Table 6 Percentage of cancers in UK in 2002 attributable to low consumption of fruits and vegetables

	Oesophagus	Mouth, pharynx, larynx	Lung	Stomach
Non-starchy vegetables	21 (4–40)	34 (2–57)		21 (0–41)
Fruits	5 (2–9)	17 (0–43)	33 (17–51)	18 (3–33)

From WCRF/AICR (2009).

DISCUSSION

As we note in the Introduction, the protective role of the consumption of fruit and vegetables against cancer is controversial. The first report of the World Cancer Research Fund (WCRF)/AICR Panel (1997) considered that the evidence for a protective effect of fruit and/or vegetables against cancers of the upper aero-digestive tract, stomach and lung was 'convincing'. As we describe, although the preventive recommendation remains to 'eat at least five portions/servings (at least 400 g) of a variety of non-starchy vegetables and of fruits every day', this evaluation had been downgraded to 'probable' in the latest report (WCRF, 2007). This is because of the subsequent publication of some cohort studies that failed to find statistically significant associations. Key (2011) suggests that, as all of the relevant cancers are also caused by smoking, and that smokers have a lower intake of fruit and vegetables than non-smokers, the observed associations could be due to residual confounding (failure to control adequately for this risk factor in the analysis, generally due to the use of rather broad groups for categorising smoking status). With respect to lung cancer (the malignancy with the strongest smoking-associated risk), for example, recent cohort studies show conflicting results: no association (Wright *et al*, 2008) or protective effects of fruit (and vegetables) in all subjects or in smokers only (Büchner *et al*, 2010). Miller *et al* (2004) have even suggested that the strength of the association between smoking and lung cancer can overwhelm a real, but much smaller, association with diet. Fruit and vegetables are the main dietary source of many micronutrients and other metabolically active chemicals. The types and quantities of these compounds vary between items, which may explain why most studies measuring cancer risk in relation to overall intake tend to show only a weak association (McCullough and Giovannucci, 2004).

In any case, in this section, we have followed the results of the current consensus reviews by WHO/FAO (2003), IARC (2003) and WRCF (2007) with respect to those cancers that might reasonably be caused, in part, by a deficient intake of these dietary elements. The latter report considered that the evidence for a protective effect of vegetables (and, even more so, fruit) on the risk of colon cancer was 'limited', and placed more emphasis on the importance of the protective effects of consumption of foods containing dietary fibre than on vegetables *per se*. This concurs with more recent reviews of the evidence from epidemiological studies (Koushik *et al*, 2007; Huxley *et al*, 2009), and in this section, therefore, we consider that no cases of colorectal cancer are attributable to sub-optimal consumption of vegetables or fruit.

An estimate of the fraction of cancer in UK attributable to low intake of fruit and vegetables was recently published by the WCRF (2009) (Table 6). There are several reasons for the differences in results from the current estimates. WCRF selected 'representative' studies from which to take the relative risks, rather than those from their own meta-analyses. Exposure prevalence was taken from data for the same year as outcome (2002). Finally, the baseline category (optimum consumption) varied by site – $\geqslant$160 g vegetables per day for oesophagus and stomach cancer; $\geqslant$120 g per day for upper aero-digestive cancers; $\geqslant$57.1 g fruit per day for stomach cancer; and $\geqslant$160 g fruit per day for lung cancer. Given the estimates by site in Table 6, the overall AF (for all cancers) due to low consumption of vegetables and fruits would be 7.1% – of which almost 60% are lung cancers, because of the large attributable fraction (33%) and high incidence of this cancer.

See acknowledgements on page Si.

Conflict of interest

The authors declare no conflict of interest.

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5.
Cancers attributable to dietary factors in the UK in 2010

II. Meat consumption

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The current consensus based on several published meta-analyses is that consumption of red meat (all fresh, minced, and frozen beef, veal, pork and lamb), especially processed meat (any meat preserved by methods other than freezing, including marinating, smoking, salting, air-drying or heating (includes ham, bacon, sausages, pate and tinned meat)), is associated with an increased risk of bowel cancer (Department of Health, 1998; WHO/FAO, 2003; WCRF, 2007). Sandhu *et al* (2001) observed significant positive associations with all meat and red meat (an increased risk of around 15% per 100 g per day intake of red meat), and a stronger increase for processed meat (49% risk increase for a 25-g per day serving). Norat *et al* (2002) found a significant increase in risk for colorectal cancer with higher consumption of red meat (1.24 per 120 g per day) and processed meat (1.36 per 30 g per day). Larsson and Wolk (2006) considered 15 prospective studies, and found a relative risk of 1.28 for an increase of 120 g per day intake of red meat and 1.09 for an increase of 30 g per day intake of processed meat. Consumption of red meat and processed meat was positively associated with the risk of both colon and rectal cancer, although the association with red meat appeared to be stronger for rectal cancer.

There are no dietary guidelines concerning recommended levels of consumption of red and processed meat; as for alcohol, it is assumed that 'less is better' and that there is no threshold below which consumption presents no risk. In this section, we assume that the optimum (or target) is zero consumption. Currently, about 10% of the adult population are vegetarian, or consume only fish and poultry products (DEFRA, 2007).

METHODS

The relative risk of meat consumption for colorectal cancer is taken from the WCRF report (2007), and is based on the effect of red meat in a meta-analysis of three prospective studies (1.29 per 100 g red meat per day). Under the assumption that the increase in risk is a logarithmic function of intake of meat, the risk is increased by 0.0025 for each gram of meat consumed. The effect of processed meat, based on five studies, was 1.21 per 50 g per day (the excess risk corresponds to 0.0038 per gram).

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The latent period, or interval between 'exposure' to meat and the increased risk of colorectal cancer, is not known. In the cohort studies included in the meta-analyses by WCRF (2007), the mean duration of follow-up was 8.9 years. In studies contributing to the meta-analysis by Larsson and Wolk (2006), the mean duration of follow-up (when this was given) was 8.7 years. We chose to assume a mean latency of 10 years, and estimate the effects on cancers occurring in 2010 from meat consumption in 2000.

Information on consumption of meat in the UK is available for 2000–2001 from the National Diet and Nutrition Survey (Food Standards Agency, 2002) as mean consumption, in grams of different types of meat per week, by age group and sex. The relevant data are shown in Table 1.

The population distribution of protein consumption, in grams per day, by age group and sex, is available from the National Diet and Nutrition Survey (Volume 2, Table 3.1; Food Standards Agency, 2003). This was converted to grams of meat per day, based on the average intake of meat (Table 1) and protein (NDNS Volume 2, Table 3.4) in each age–sex group.

The estimate for 2000 is shown in Table 2 (as the percentage of the population in different age–sex groups consuming specified amounts of red and processed meat), and in Figure 1 as the cumulative frequency (percentage) of the population in each age–sex group at different consumption levels.

The relative risk of meat consumption for each of the x consumption categories shown in Table 2 was calculated according to the following formula:

$$\mathrm{RR}_x = \exp(R_g \times G_x)$$

where R_g is the increase in risk of colon cancer per gram of meat (0.0025) and G_x is the consumption of meat in gram per day in category x.

Population-attributable fractions (PAFs) were calculated for each sex–age group according to the following formula:

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

where p_x is the proportion of population in consumption category x and ERR_x the excess relative risk ($\mathrm{RR}_x - 1$) in consumption category x.

Table 1 Total quantities of meat consumed by age of respondent, including non-consumers (Great Britain, 2000–2001)

	Grams per day consumed, by age (years)									
	Men					Women				
Meat	**19–24**	**25–34**	**35–49**	**50–64**	**All men**	**19–24**	**25–34**	**35–49**	**50–64**	**All women**
Red meat[a] (including liver)	63	72	74	77	73	45	37	50	52	47
Processed meat[b]	63	50	43	35	45	32	24	21	19	23
Red (including processed)	125	122	118	111	118	77	62	71	71	69
All meat products[a]	144	142	137	133	138	86	70	81	80	78

[a]Excludes poultry. [b]Bacon, ham, sausages, burgers, kebabs.

Table 2 Distribution of meat (red and processed) consumption by age group and sex, grams

	Consumption of red and processed meat by age group (years)									
	19–24		**25–34**		**35–49**		**50–64**		**All ages**	
Consumption category	**grams per day**	**%**	**grams per day**	**%**	**grams per day**	**%**	**grams per day**	**%**	**grams per day**	**%**
Men										
1	0	6	0	0	0	2	0	3	0	2
2	79	6	66	2	64	4	62	3	66	4
3	88	0	74	3	71	1	68	1	73	1
4	97	11	81	14	79	6	76	7	81	9
5	113	22	95	14	91	9	88	14	94	14
6	129	19	108	16	105	19	100	19	107	18
7	145	19	122	21	118	23	113	13	120	19
8	161	9	135	13	131	14	125	16	134	13
9	177	7	149	8	144	8	138	8	147	9
10	193	1	162	3	157	6	151	10	161	5
11	217	0	182	6	176	8	169	6	181	6
Mean gram per day	125		122		118		111		118	
Women										
1	0	7	0	7	0	4	0	2	0	4
2	52	9	42	13	44	6	42	6	44	9
3	59	4	48	1	50	2	49	1	50	1
4	66	17	54	22	56	15	54	11	55	16
5	77	28	63	26	65	21	63	25	65	24
6	90	19	74	17	76	26	74	25	76	23
7	103	9	84	9	87	16	84	16	87	13
8	116	6	95	3	98	6	95	10	98	7
9	129	1	105	1	109	3	106	4	109	2
10	148	0	121	1	125	1	121	0	125	1
Mean gram per day	77		62		71		71		69	

RESULTS

Table 3 shows PAFs of colorectal cancer resulting from meat consumption in 2000–2001, and the estimated number of cases 'caused' in 2010. The final three columns show the excess numbers of cases of colorectal cancer caused by meat consumption expressed as a fraction of the total burden of (incident) cancer. The estimate is 3.5% cancers in men and 1.9% in women, or 2.7% of cancers overall.

DISCUSSION

The association between consumption of red and processed meat and the risk of cancer of the colon and rectum is now well established. Although the risk for processed meat products (such as ham, bacon, sausages, pate and tinned meat) is greater than that for fresh meat, in this analysis we have considered both together,

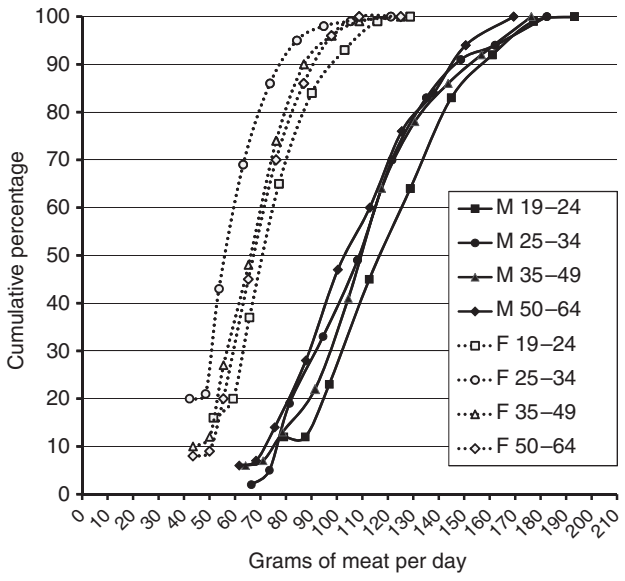

Figure 1 Estimated consumption of red and processed meat, by age group and sex, expressed as grams per day.

partly because separate estimates of intake (by age group and sex) would be difficult, and partly because it would not affect the overall estimate, which is concerned with the proportion of colorectal cancer related to any meat consumption (i.e., over and above a diet including poultry and fish, as sources of animal protein).

The estimation of attributable fraction is against a baseline of a diet that would contain no red meat, and is based on the relative risks of consumption of red meat, according to the review by WCRF (2007). The values for red meat consumption (1.29 per 100 g per day) are rather higher than those in the more recent meta-analysis of Larsson and Wolk (1.29 per 120 g per day, when adjusted for BMI, physical activity, smoking, energy intake and so on). These values would have given a total of 18% of colon cancers due to consumption of red meat (rather than 21.1%, as in Table 3).

Norat *et al* (2002) estimated the proportion of colorectal cancer risk attributable to current (1995) red meat consumption in North and Central Europe as 7.8% in men and 5.8% in women, much lower than the estimated percentages in the UK, but estimated per caput red meat consumption of this population (47.3 g per day in men and 35 g per day in women) was around one-half of that in the UK in 2000 (Table 1). WCRF (2009), based on the relative risks from the EPIC study (Norat *et al*, 2005; 1.49 per 100 g red meat, 1.70 per 100 g processed meat), estimated that 15% of colorectal cancer in the UK in 2002 was due to consumption in excess of 10 g per day of red meat and 10 g per day of processed meat.

Several other cancers have been linked to consumption of red or processed meat. However, at the time of the review by WCRF

Table 3 Colorectal cancer diagnosed in 2010, attributable to meat consumption in 2000–2001

Age (years)		Colon–rectum				All cancers[a]		
At exposure	At outcome	PAF	Observed cases	Excess attributable cases	PAF (%)	Observed cases	Excess attributable cases	PAF (%)
Men								
19–24	29–34	0.27	92	24.8	26.9	1333	24.8	1.9
25–34	35–44	0.26	397	102.5	25.8	4124	102.5	2.5
35–49	45–59	0.26	2921	756.7	25.9	22 388	756.7	3.4
50–64	⩾60	0.25	18 643	4611.3	24.7	128 192	4611.3	3.6
All ages			22 127	5495.3	24.8	158 667	5495.3	3.5
Women								
19–24	29–34	0.17	97	16.9	17.5	2248	16.9	0.8
25–34	35–44	0.14	402	57.0	14.2	8619	57.0	0.7
35–49	45–59	0.16	2292	376.0	16.4	31 631	376.0	1.2
50–64	⩾60	0.17	14 926	2465.6	16.5	110 403	2465.6	2.2
All ages			17 787	2915.5	16.4	155 584	2915.5	1.9
Persons								
19–24	29–34		189	42	22.1	3582	42	1.2
25–34	35–44		799	160	20.0	12 743	160	1.3
35–49	45–59		5213	1133	21.7	54 019	1133	2.1
50–64	⩾60		33 569	7077	21.1	238 595	7077	3.0
All ages			39 914	8411	21.1	314 251	8411	2.7

Abbreviations: PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

(2007), the evidence with respect to cancers of the oesophagus, lung, pancreas, endometrium, stomach and prostate was considered to be 'limited'. Only the associations between consumption of red and processed meat with an increased risk of colorectal cancer were considered to be 'convincing'.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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6.
Cancers attributable to dietary factors in the UK in 2010

III. Low consumption of fibre

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Dietary fibre has long been thought to be associated with a reduced risk of colorectal cancer (Burkitt, 1971). However, analytic epidemiological studies of dietary fibre and the risk of colorectal cancer have not yielded consistent associations. The first comprehensive meta-analysis of prospective studies showed no significant reduction in the risk of colorectal cancer with high consumption of fibre, but very low fibre intake (less than 10 g per day) did significantly increase bowel cancer risk (Park *et al*, 2005). The results of subsequent cohort studies seem to be split between those suggesting a protective effect of fibre (Bingham *et al*, 2003, 2005; Nomura *et al*, 2007; Wakai *et al*, 2007) and those showing no benefit (Otani *et al*, 2006; Shin *et al*, 2006). In some studies, null findings may be due to an insufficient range of fibre intake or other methodological problems; alternatively, other features of a high-fibre diet (a plant-based diet rich in fruits, vegetables and whole grains) could be responsible for the protective effect. The World Cancer Research Fund (WCRF) review (2007) concluded that, although there was a clear association, residual confounding could not be excluded as an explanation for the dose – response relationship between risk and fibre intake. In a subsequent study combining data from seven UK cohort studies (Dahm *et al*, 2010), fibre intake was ascertained by food diaries (rather than the less reliable food frequency questionnaires used in most studies), and issues of confounding (by anthropometric and socioeconomic factors, and dietary intake of folate, alcohol and energy) were addressed. A clear protective effect of fibre intake was observed, with a risk of colorectal cancer of 0.66 in the highest relative to the lowest quintile of intake.

Almost 20 years ago, the Committee on Medical Aspects of Food Nutrition Policy (COMA) Panel on Dietary Reference Values proposed that the diet of the UK adult population should contain on average 18 g per day non-starch polysaccharides, with an individual range of 12 – 24 g per day, from a variety of foods (Department of Health, 1991). This recommendation was repeated in the report of the COMA Working Group on Diet and Cancer (Department of Health, 1998), which had recommended 'an increase in average intake of non-starch polysaccharide in the adult population from 12 grams per day to 18 grams per day'. A measure of 18 g per day of NSP is equivalent to 23 g of fibre per day. The recommendation published by the Department of Health in 'Choosing a better diet: a food and action plan' (Department of Health, 2005) is to 'increase the average intake of dietary fibre to 18 grams per day (currently 13.8 grams per day)'. Presumably, this actually refers to dietary NSP, for which the average intake in 2000 – 2001 was 13.8 g (FSA, 2003).

In this section, we examine the potential effects of a deficit in consumption of fibre (below the recommended 23 g per day) on the incidence of colorectal cancer in the UK in 2005.

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METHODS

The relative risk of fibre intake, calculated by WCRF, was 0.9 per 10 g per day increment of dietary fibre (95% confidence interval 0.84 – 0.97). In the study of Dahm *et al* (2010), the value from the fully adjusted model was 0.84 (95% confidence interval 0.70 – 1.0). This is equivalent to a decline in risk of 2.9% per gram of fibre, and this value has been chosen for the estimation.

The latent period, or interval between 'exposure' to fibre and development of cancer, and the appropriate decrease in risk of cancers of the colon and rectum are not known. In the eight cohort studies contributing to the WCRF (2007) meta-analysis, the mean duration of follow-up was about 11 years. Therefore, an interval of 10 years is assumed, and the 2010 fraction of avoidable cancers is based on an estimate of the fibre intake in 2000.

Consumption of NSP, as grams per day, by age group and sex, is available for 2000 – 2001 from the National Diet and Nutrition Surveys (FSA, 2004; Tables 3.14 and 3.15). The relevant data are shown in Table 1.

The mean daily intake of NSP was significantly lower for women ($P < 0.01$) than for men. The youngest group had significantly lower mean intakes of NSP than those in any other age group. Median values were generally close to the mean within sex and age groups.

The three main sources of NSP, accounting for about three-quarters of the dietary intake, were cereals and cereal products (43%), vegetables excluding potatoes (20%), and potatoes and savoury snacks (16%). Within the cereals and cereal products group, whole-grain and high-fibre breakfast cereals provided 11% of the intake and white bread provided a further 9%. There were

Table 1 Average daily NSP intake (g) by sex and age of respondent, Great Britain 2000–2001

	Percentage of the population by age group				
NSP intake	**19–24**	**25–34**	**35–49**	**50–64**	**All**
Men (g per day)					
<6	6	0	2	1	2
6<8	10	8	6	5	6
8<10	17	15	11	8	12
10<12	9	15	11	11	12
12<14	26	12	14	13	15
14<16	21	16	16	11	15
16<18	5	11	10	12	10
18<20	2	10	9	11	9
20<22	1	3	5	12	6
22<24	3	4	5	5	5
⩾24	0	6	11	11	8
Mean					
NSP	12.3	14.6	15.7	16.4	15.2
Fibre	15.7	18.7	20.1	21.0	19.5
Women (g per day)					
<6	9	6	7	5	5
6<8	16	17	9	5	12
8<10	27	16	13	12	15
10<12	15	18	18	19	18
12<14	12	19	18	16	17
14<16	13	10	12	13	12
16<18	4	6	8	10	8
18<20	3	4	7	8	5
20<22	1	1	3	4	3
⩾22	0	3	5	8	5
Mean					
NSP	10.6	11.6	12.8	14	12.6
Fibre	13.6	14.8	16.4	17.9	16.1

Abbreviation: NSP = non-starch polysaccharide. Data from National Diet and Nutrition Survey, FSA (2004).

Table 2 NSP content of diet, Great Britain 2000–2001

Food items	**Grams NSP per gram food item**	**Grams NSP per day**	**% NSP intake**
Cereals and cereal products	0.023	5.91	43
Pasta, rice, miscellaneous cereals	0.006	0.42	3
Pasta	0.010	0.28	2
Other pasta, rice	0.003	0.14	1
Bread	0.028	2.82	20
White bread	0.019	1.27	9
Wholemeal bread	0.054	0.84	6
Other bread	0.037	0.70	5
Breakfast cereals	0.058	1.69	12
Other cereal products	0.018	0.99	7
Meat and meat products	0.005	0.84	6
Fish and fish products	0.005	0.14	1
Vegetables and vegetable dishes (excluding potatoes)	0.021	2.82	20
Baked beans	0.035	0.56	4
Other vegetables (not baked beans)	0.019	2.25	16
Potatoes and savoury snacks	0.020	2.25	16
Potato chips	0.020	0.70	5
Fried/roast potatoes and fried potato products	0.012	0.14	1
Other potatoes	0.017	0.99	7
Savoury snacks	0.038	0.28	2
Fruit and nuts	0.014	1.41	10
Sugar, preserves, confectionery	0.009	0.14	1
Miscellaneous[a]	—	0.28	2
Total	—	13.80	100

Abbreviation: NSP = non-starch polysaccharide. Data are from National Diet and Nutrition Survey, Vol. 2, FSA (2004). [a]Miscellaneous food items include powdered beverages (except tea and coffee), soups, sauces, condiments and artificial sweeteners.

no significant sex or age differences in the proportion of NSP provided by different food types (Table 2).

Assuming that 1 g of NSP corresponds to 1.28 g of fibre, the deficit (in grams) from the recommended 23 g per day can be estimated for each row of Table 1. Population-attributable fractions (PAFs) were calculated for each sex–age group in Table 2 according to the usual formula:

$$\mathrm{PAF} = \frac{(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) \ldots + (p_n \times \mathrm{ERR}_n)}{1 + [(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) \ldots + (p_n \times \mathrm{ERR}_n)]}$$

where p_x is the proportion of population in consumption category x and ERR_x is the excess relative risk in consumption category x.

ERR_x is calculated as follows:

$$\{\exp(R_g \times G_x) - 1\}$$

where R_g is the increase in risk for a deficit of 1 g per day of fibre (0.029) and G_x is the deficit in consumption (<23 g per day) in consumption category x.

RESULTS

Table 3 shows the estimated PAF and the number of cases of colorectal cancer 'caused' in 2010 by the deficit in consumption of fibre in 2000, by age group and sex. The excess number of cases is also expressed in terms of cancer as a whole. About 12.2% of colorectal cancer, or 1.5% of all cancers in 2010, is due to fibre consumption falling below the recommended daily intake of an average of 23 g (or 18 g NSP).

As discussed in Section 4 of this supplement (Parkin and Boyd, 2011), the benefit of consumption of fruits and vegetables on the risk of colorectal cancer may be, in part, due to their content of fibre. In calculating the cancer cases attributable to a deficient intake of dietary fruit and vegetables, the increased consumption that would have been necessary to achieve the '5-a-day' target (equivalent to 400 g of fruit and vegetable intake daily) was estimated. On the basis of the content of NSP in fruits and vegetables (in 2000–2001), we may estimate the additional consumption of fibre that is implied (Table 4). The increase is considerable – on average 4.1 g per day of fibre for men and 3.8 for women. With this addition to the distribution of fibre intake shown in Table 1, the mean intake (for all age groups 19–64) would be 23.6 g per day fibre for men, with only 30% consuming less than 23 g per day, and 16.4 g per day for women, with 58% consuming less than 23 g per day.

In Table 5, the numbers of cancer cases that would have been avoided by a diet containing 400 g per day of fruit and vegetable intake is presented, assuming that the benefit is due to the reduction in risk from the fibre content. Overall, the increase in dietary fibre intake from increasing the intake of fruits and vegetables to 400 g per day is estimated to reduce colorectal cancer by ~4.9% (4.4% in men and 5.5% in women). This is about two-fifths of the total benefit achievable from increasing the intake of fibre to 23 g per day, for those consuming less than this.

Table 3 Projected number of colorectal and all cancer cases in UK in 2010 and proportion due to deficient intake of NSP

Age (years)		Colorectal cancer			All cancer[a]		
At exposure	At outcome	Observed cases	Excess attributable cases	PAF (%)	Observed cases	Excess attributable cases	PAF (%)
Men							
19–24	29–34	92	14	15.1	1333	14	1.0
25–34	35–44	397	42	10.6	4124	42	1.0
35–49	45–59	2921	276	9.5	22 388	276	1.2
50–64	⩾60	18 643	1932	10.4	128 192	1932	1.5
	All ages	22 127	2264	10.2	158 667	2264	1.4
Women							
19–24	29–34	97	19	19.5	2248	19	0.8
25–34	35–44	402	82	20.5	8619	82	1.0
35–49	45–59	2292	364	15.9	31 631	364	1.1
50–64	⩾60	14 926	2127	14.2	110 403	2127	1.9
	All ages	17 787	2592	14.6	155 584	2592	1.7
Persons							
19–24	29–34	189	33	17.3	5096	33	0.6
25–34	35–44	799	124	15.6	18 704	124	0.7
35–49	45–59	5213	640	12.3	73 321	640	0.9
50–64	⩾60	33 569	4059	12.1	183 745	4059	2.2
	All ages	39 914	4856	12.2	314 251	4856	1.5

Abbreviations: NSP = non-starch polysaccharide; PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

Table 4 Estimated additional consumption of fibre from increasing fruit and vegetable intake to 400 g per day from the levels observed in 2000–2001

	Increase in fibre consumption (g per day) by age group				
	19–24	25–34	35–49	50–64	All ages
Males	7.9	5.5	3.9	2.7	4.1
Females	6.8	3.8	3.9	2.4	3.8

Table 5 Projected number and proportion of colorectal cancer cases avoidable in 2010 from the fibre intake associated with five servings (400 g) of fruit and vegetables daily

Age (years)		Colorectal cancer		
			Reduction in cases	
At exposure	At outcome	Observed cases	Number	%
Men				
19–24	29–34	92	11	11.7
25–34	35–44	397	31	7.7
35–49	45–59	2921	163	5.6
50–64	⩾60	18 643	771	4.1
	All ages	22 127	975	4.4
Women				
19–24	29–34	97	13	13.4
25–34	35–44	402	34	8.4
35–49	45–59	2292	184	8.0
50–64	⩾60	14 926	748	5.0
	All ages	17 787	978	5.5
Persons				
19–24	29–34	189	24	12.6
25–34	35–44	799	64	8.1
35–49	45–59	5213	346	6.6
50–64	⩾60	33 569	1519	4.5
	All ages	39 914	1954	4.9

DISCUSSION

In the analysis presented here, we examine both the possible number of colorectal cancers due to a deficit in consumption of fibre less than the recommended 23 g per day and the effect of a deficit in consumption of fruit and vegetables (below the recommended '5 a day'), assuming that the benefit of fruit and vegetables is solely the result of their fibre content. The latter depends not only on the supposition that fibre is indeed protective against colorectal cancer, but also on the assumption that all forms of fibre are equally protective. This is not universally accepted; in the study by Schatzkin *et al* (2007), for example, only fibre from grains was associated with a lower risk of colorectal cancer.

The UK-recommended average intake of NSP in the adult population is 18 g per day (equivalent to 23 g per day of fibre). The WCRF (2007) set a much more ambitious public health goal, as 'a population average of at least 25 grams non-starch polysaccharide daily' (equivalent to 32 g of dietary fibre). In their estimates of 'preventability' of colorectal cancer in the UK in 2002 (WCRF, 2009), an estimated 12% of colorectal cancer was stated as preventable by increasing fibre intake to 30 g per day, based on the effects estimated by Park *et al* (2005): a relative risk of 1.14 for an intake of ⩽10 g per day relative to ⩾30 g per day.

Although there is no direct evidence from intervention studies of the effect of dietary and supplemental fibre on colorectal cancer, several trials have been carried out on the effects of fibre supplements on recurrence of colonic adenomas. The results as reported were negative (Maclennan *et al*, 1995; Alberts *et al*, 2000; Schatzkin *et al*, 2000), although the period of supplementation and follow-up was very short (2–4 years). A pooled reanalysis of the two US trials showed a statistically significant interaction by sex, and a beneficial effect of the intervention in men (odds ratio = 0.81, 95% CI = 0.67–0.98; Jacobs *et al*, 2006).

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Conflict of interest

The authors declare no conflict of interest.

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7.
Cancers attributable to dietary factors in the UK in 2010

IV. Salt

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In a large international ecological study, comparing urinary sodium excretion and stomach cancer mortality in 39 countries, Joossens *et al* (1996) concluded that 'Salt intake, measured as 24-hour urine sodium excretion, is likely the rate-limiting factor of stomach cancer mortality at the population level'. On the basis of human observational and animal experimental data, as well as mechanistic plausibility, the 2003 report from the joint World Health Organization/Food and Agriculture Organization Expert Consultation (WHO/FAO) concluded that salt-preserved food and salt 'probably' increase the risk of gastric cancer (WHO/FAO, 2003). In fact, there is substantial evidence that the risk of gastric cancer is increased by high intakes of some traditionally preserved salted foods, especially meats and pickles, and with salt *per se* (Palli, 2000; Tsugane, 2005). The World Cancer Research Fund (WCRF) report (2007) concluded that 'salt is a probable cause of stomach cancer', and that there is robust evidence for the mechanisms operating in humans.

In the UK, the Committee on Medical Aspects of Food Policy (COMA) panel on Dietary Reference Values (Department of Health, 1991) advised that sodium (Na) intakes should be maintained below 3.2 g (or 8.0 g of salt) per day and set the reference nutrient intake (RNI) for men and women at 1.6 g of sodium (or 4.0 g of salt) per day. Following this, COMA's Cardiovascular Review Group recommended that salt intake should be gradually reduced further to a daily average of 6 g (Department of Health, 1994). This recommendation was also accepted in the food and health action plan 'Choosing a better diet' (Department of Health, 2005).

In this section, we consider the population-attributable fraction of stomach cancer associated with an intake of salt >6 g per day.

METHODS

The relative risk (RR) of stomach cancer in relation to salt intake has been taken from the meta-analysis of cohort studies (WCRF, 2007), suggesting a RR of 1.08 per g per day, an excess RR of 0.08 per g. The durations of follow-up in the two studies contributing to this pooled value (van den Brandt *et al*, 2003; Tsugane *et al*, 2004) were 6.3 and 11 years, respectively. The latent period, or interval between 'exposure' to salt and the appropriate increase in risk of cancers of the stomach, is therefore taken to be 10 years, and the 2010 fraction of avoidable cancers is based on an estimate of salt intake in 2000 – 2001. Table 1 shows the results from the 2000 – 2001 National Diet and Nutrition Survey in which average daily urinary excretion of salt was 11 g per day in men and 8.1 g per day in women (Food Standards Agency, 2003).

On the basis of an excess risk of 0.08 per gram of salt per day, the risk of stomach cancer associated with an intake of x g salt per day in excess of the recommended 6 g per day is as follows:

$$\exp(0.08x)/\exp(0.08\times 6)$$

so that, in the lowest consumption category (women in the age group of 50 – 64 years), where average salt intake (x) is 7.5 g per day, the RR is as follows:

$$\exp(0.08\times 7.5)/\exp(0.08\times 6)$$
$$1.84/1.62 = 1.13$$

Table 2 shows the estimated intake of salt in 2000 – 2001 (Food Standards Agency, 2003), and the RRs of stomach cancer (by sex and age group) associated with the excess intake, compared with the recommended level of 6 g per day.

RESULTS

Table 3 shows the estimated number of cases of stomach cancer 'caused' in 2010 by the excessive consumption of salt in 2000 – 2001. These excess cases are calculated as (observed – expected), where the number expected = (observed/RR). Approximately 24% of stomach cancer cases can be attributed to this cause.

The excess number of cases is also expressed in terms of cancer as a whole. About 0.5% of cancers in 2010 are due to salt consumption in excess of the recommended daily maximum of an average of 6 g.

DISCUSSION

The difficulties in estimating salt consumption in epidemiological studies probably contribute to the very heterogeneous findings;

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nevertheless, the consensus view, most recently expressed in the WCRF report (2007), is that salt intake (as well as sodium intake and salty and salted foods) is a probable cause of gastric cancer. The 'optimum exposure level', against which the risk of actual exposure was evaluated, was chosen as that recommended in the report of the Committee on Medical Aspects of Food Policy (Department of Health, 1994) and the UK government's food and health action plan 'Choosing a better diet' (Department of Health, 2005). This recommendation (less than 6 g of salt per day) was based on general health considerations, and mostly guided by the well-established link between salt and blood pressure. High salt intake is a major contributor to high blood pressure, which increases the risk of heart disease and stroke (MacGregor, 1999), and there is evidence that reductions in dietary salt can reduce blood pressure and the long-term risk of cardiovascular events (Cook *et al*, 2007). Nevertheless, it seems to be a reasonable (and attainable) target with respect to reduction in the risk of gastric cancer. The calculation of excess risk assumes a simple log-linear increase in the risk of gastric cancer with increasing salt intake. The evidence for this is somewhat equivocal: it is apparent for total salt use in cohort but not case–control studies, whereas for sodium intake it was also apparent in case–control studies; for salted and salty foods, the reverse was observed (dose–response relationship in case–control but not cohort studies; WCRF, 2007).

In general, diets of Western communities contain amounts of sodium that are far in excess of any physiological need and many times the recommended daily sodium requirement. The likely adverse effect on cancer risk in the UK is small, as the incidence of gastric cancer is low (gastric cancer ranks only 13th in terms of incidence in the UK, with incidence rates well below the European average (CRUK, 2011)). Average consumption in the UK is around 10 g per day, and had shown little change between 1986–7 and 2001 (Food Standards Agency, 2004). Although individuals can limit their personal consumption by avoiding salt in cooking, or adding salt at the table, around 75% of salt in the diet is from processed foods. In 2005, the Food Standards Agency developed proposals for voluntary targets for salt levels in a wide range of food categories (85 categories in total) as a guide for the food industry. There has subsequently been some progress on voluntary salt reductions by the industry (Department of Health, 2009). There is no direct evidence from intervention studies of the benefit of reduced salt intake with respect to gastric cancer. In Japan, the national dietary policy has resulted in declines in dietary salt intake, and there has been an equivalent reduction in the incidence of gastric cancer (Tominaga and Kuroishi, 1997); however, there have been other changes in prevalence of gastric cancer risk factors – notably in prevalence of infection with *Helicobacter pylori* (Kobayashi *et al*, 2004) – and thus the part played by salt reduction is far from clear.

See acknowledgements on page Si.

Table 1 Urinary salt excretion in grams per day in Great Britain, 2000–2001

	Urinary salt excretion (grams per day) by age group (years)				
Sex	**19–24**	**25–34**	**35–49**	**50–64**	**19–64**
Men	11.0	11.4	11.1	10.5	11.0
Women	9.1	8.7	8.0	7.5	8.1

From National Diet and Nutrition Survey, Food Standards Agency (2003).

Table 2 Salt intake (grams per day, 2000–2001) and associated relative risk of stomach cancer

	Age group (years)				
Salt intake 2000–2001	**19–24**	**25–34**	**35–49**	**50–64**	**19–64**
Men					
Mean grams per day	11.0	11.4	11.1	10.5	11.0
Excess grams per day	5.0	5.4	5.1	4.5	5.0
RR for this excess	1.49	1.54	1.50	1.43	1.49
Women					
Mean grams per day	9.1	8.7	8.0	7.5	8.1
Excess grams per day	3.1	2.7	2.0	1.5	2.1
RR for this excess	1.28	1.24	1.17	1.13	1.18

Abbreviations: RR = relative risk (of stomach cancer).

Conflict of interest

The author declares no conflict of interest.

Table 3 Stomach cancer cases in the UK in 2010 due to intake of salt >6 g daily

Age (years)		Stomach cancer				All cancer[a]		
At exposure	**At outcome**	**Obs.**	**Relative risk**	**Excess attrib. cases**	**PAF (%)**	**Obs**	**Excess attrib. cases**	**PAF (%)**
Men								
19–24	34–39	25	1.49	8	33.0	1792	8	0.5
25–34	40–49	159	1.54	56	35.1	6794	56	0.8
35–49	50–64	828	1.50	277	33.5	37 617	277	0.7
50–64	⩾65	3443	1.43	1041	30.2	108 729	1041	1.0
	All ages	4467		1382	30.9	158 667	1382	0.9
Women								
19–24	34–39	28	1.28	6	22.0	3607	6	0.2
25–34	40–49	95	1.24	18	19.4	13 667	18	0.1
35–49	50–64	361	1.17	53	14.8	41 338	53	0.1
50–64	⩾65	2067	1.13	234	11.3	92 439	234	0.3
	All ages	2577		312	12.1	155 584	312	0.2
All								
19–24	34–39	52		14	27.1	5400	14	0.3
25–34	40–49	254		74	29.2	20 461	74	0.4
35–49	50–64	1189		331	27.8	78 955	331	0.4
50–64	⩾65	5510		1275	23.1	201 167	1275	0.6
	All ages	7044		1694	24.0	314 251	1694	0.5

Abbreviations: attrib. = attributable; Obs. = observed cases; PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

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8.
Cancers attributable to overweight and obesity in the UK in 2010

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In 2002, the International Agency for Research on Cancer Handbook on Weight Control and Physical Activity concluded that overweight and obesity are related to cancers of the colon, endometrium, kidney and oesophagus (adenocarcinomas), as well as postmenopausal breast cancer. Since that report, continuing epidemiological investigation has suggested that other cancers are related to obesity and overweight. In addition to those listed above, the report by the World Cancer Research Fund (WCRF) Panel on Food, Nutrition, Physical Activity, and the Prevention of Cancer (WCRF, 2007) considered that there was convincing evidence for an association with cancers of the pancreas and rectum (as well as colon), and a probable association with cancers of the gall bladder. The fraction of these cancers occurring in 2010 attributable to overweight and obesity in the UK population is estimated in this section.

METHODS

The estimates of risk associated with overweight (BMI $25 < 30\,kg\,m^{-2}$) and obesity (BMI $30+\,kg\,m^{-2}$), relative to a BMI $\leqslant 25\,kg\,m^{-2}$, for the seven cancers, are shown in Table 1. The estimates of relative risk for an increase of $5\,kg\,m^{-2}$ from the meta-analyses by WCRF (2007) have been used for the category 'overweight'. Assuming a constant rate of increase in risk with BMI, the square of this value was taken for the category 'obese'. For postmenopausal breast cancer, WCRF reported that the increase in risk was 8% per BMI increase of $5\,kg\,m^{-2}$ for cohort studies (17 considered) and 13% per BMI increase of $5\,kg\,m^{-2}$ for case–control studies (48 considered). The estimates from the meta-analyses of Bergstrom *et al* (2001) and Renehan *et al* (2008) were almost identical (12% per BMI increase of $5\,kg\,m^{-2}$), and thus this value has been selected.

The latent period, or interval between 'exposure' to overweight/obesity and the appropriate increase in risk of these cancers, is not known. Renehan *et al* (2008) calculated the geometric mean duration of follow-up in the cohort studies available for a meta-analysis of relative risks due to overweight and obesity. The periods ranged from 8.4 years (for breast cancer) to 12.7 years (for gall bladder cancer). We therefore chose to assume that the latency between 'exposure' and outcome would be, on average, 10 years, and thus examine the effects on cancers occurring in 2010 from suboptimal levels of body mass in 2000. The proportion of adults in the age group of 19 – 64 who were overweight or obese in Great Britain in 2000 – 2001 is available from the National Diet and Nutrition Survey (FSA, 2004; Table 4.1). For older adults (aged $\geqslant 65$), we used the values for 2000 from the Health Survey for England (Health and Social Care Information Centre, 2010). The results are shown in Table 2.

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Table 1 Relative risks associated with overweight and obesity

	Relative risks		Excess relative risks	
Cancer (site)	**Overweight**	**Obese**	**Overweight**	**Obese**
Breast (post-menopausal)[a,b]	1.12	1.25	0.12	0.25
Colorectum[c]	1.15	1.32	0.15	0.32
Oesophagus (adenocarcinoma)[c]	1.55	2.40	0.55	1.40
Kidney[c]	1.31	1.72	0.31	0.72
Endometrium[c]	1.52	2.31	0.52	1.31
Gall bladder[c]	1.23	1.51	0.23	0.51
Pancreas[c]	1.14	1.30	0.14	0.30

[a]From Bergstrom *et al* (2001). [b]From Renehan *et al* (2008). [c]From WCRF (2007).

Table 2 Prevalence of overweight and obesity in Great Britain in 2000 – 2001

	Prevalence of overweight and obesity by age group (years)					
BMI	**19 – 24[a]**	**25 – 34[a]**	**35 – 49[a]**	**50 – 64[a]**	**65 – 74[b]**	**⩾75[b]**
Men						
25 < 30 (overweight)	0.25	0.42	0.45	0.46	0.50	0.52
⩾30 (obese)	0.18	0.18	0.25	0.32	0.24	0.17
Women						
25 < 30 (overweight)	0.25	0.28	0.31	0.41	0.41	0.41
⩾30 (obese)	0.14	0.16	0.23	0.22	0.30	0.23

Abbreviations: BMI = body mass index. [a]From the National Diet and Nutrition Survey (ages 19 – 64). [b]From Health Survey for England (ages > 65).

Table 3 Cancer cases diagnosed in 2010 attributable to overweight and obesity in 2000

				Cases attributable to obesity for each cancer																					
Age (years)		Proportion overweight or obese in 2000		Oesophagus (adeno-carcinoma)[a,b]			Gallbladder			Pancreas			Colon-rectum			Breast			Corpus uteri			Kidney		
At exposure	At outcome (+10 years)	Over-weight	Obese	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases	PAF	Obs.	Excess attributable cases
Men																								
19–24	25–34	0.25	0.18	0.28	4	1	0.13	0	0.0	0.08	9	0.7	0.09	133	11.6							0.17	31	5.3
24–34	35–44	0.42	0.18	0.33	27	9	0.16	1	0.2	0.10	67	6.8	0.11	397	42.9							0.21	206	42.4
35–49	45–59	0.45	0.25	0.37	358	134	0.19	24	4.5	0.12	587	71.1	0.13	2921	376.9							0.24	1142	275.9
50–64	60–74	0.46	0.32	0.41	1405	579	0.21	83	17.6	0.14	1771	244.6	0.15	9481	1392.8							0.27	2368	641.7
65–74	75–84	0.50	0.24	0.38	963	589	0.19	59	11.5	0.13	1188	149.2	0.13	6774	905.6							0.25	1418	352.7
⩾75	⩾85	0.52	0.17	0.34	371	227	0.17	22	3.8	0.11	460	50.6	0.12	2388	279.7							0.22	472	104.0
Total (%)		—	—	—	5713	1538 (26.9)		191	37.5 (19.7)		4084	523.1 (12.8)		22 127	3009.4 (13.6)								5697	1422.0 (25.0)
Women																								
19–24	25–34	0.25	0.14	0.25	1	0.2	0.11	1	0.1	0.07	11	0.8	0.08	136	10.2	0.00	634	0.0	0.24	38	9.0	0.15	29	4.3
24–34	35–44	0.28	0.16	0.27	4	1.2	0.13	8	1.0	0.08	53	4.2	0.09	402	34.4	0.00	4012	0.0	0.26	211	55.3	0.17	110	18.4
35–49	45–59	0.31	0.23	0.33	50	16.5	0.16	73	11.6	0.10	437	44.1	0.11	2292	246.8	0.09	15 203	1328.0	0.32	1926	609.2	0.21	554	114.6
50–64	60–74	0.41	0.22	0.35	267	93.0	0.17	198	34.0	0.11	1520	166.9	0.12	6116	715.3	0.10	18 120	1724.3	0.33	3844	1283.9	0.22	1275	282.5
65–74	75–84	0.41	0.30	0.39	320	125.9	0.20	143	28.6	0.13	1374	177.4	0.14	5527	759.3	0.11	7855	881.0	0.38	1570	594.8	0.26	903	231.2
⩾75	⩾85	0.41	0.23	0.36	220	78.5	0.18	86	15.2	0.11	884	100.2	0.12	3283	396.3	0.10	4410	433.4	0.34	605	207.2	0.23	428	97.6
Total (%)		—	—		2819	315.3 (11.2)		509	90.5 (17.8)		4280	493.6 (11.5)		17 787	2162.4 (12.2)		48 385	4366.7 (9.0)		8195	2759.3 (33.7)		3365	748.6 (22.2)
Persons																								
19–24	25–34	—	—		0	1.2		1	0.1		20	1.5		269	21.8		634	0.0		38	9.0		60	9.6
24–34	35–44	—	—		31	10.0		9	1.2		120	11.0		799	77.3		4012	0.0		211	55.3		316	60.8
35–49	45–59	—	—		408	150.4		97	16.1		1024	115.3		5213	623.7		15 203	1328.0		1926	609.2		1696	390.5
50–64	60–74	—	—		1672	672.4		281	51.6		3291	411.5		15 597	2108.1		18 120	1724.3		3844	1283.9		3643	924.2
65–74	75–84	—	—		1283	714.4		202	40.0		2562	326.6		12 301	1664.9		7855	881.0		1570	594.8		2321	
⩾75	⩾85	—	—		591	305.1		108	19.0		1344	150.8		5671			4410			605	207.2		900	
Total (%)		—	—		8532	1853 (21.7)		700	128 (18.3)		8364	1017 (12.2)		39 914	5172 (13.0)		48 385	4367 (9.0)		8195	2759 (33.7)		9062	2171 (24.0)

Abbreviations: Obs = observed cases; PAF = population-attributable fraction. [a]Observed cases are for adenocarcinoma only. [b]Total observed cases (and percentages) are for all oesophageal cancers, and so are greater than the sum of observed cases.

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The number of oesophageal cancers diagnosed in 2010 was partitioned by histological subtype, according to the age- and sex-specific distribution observed in the UK Cancer registries reporting to Cancer Incidence in Five Continents, Volume VIII (Parkin *et al*, 2002). These age-specific proportions were scaled to correspond to the crude proportions observed in the UK registries in 2000–2002 (Curado *et al*, 2007), when adenocarcinomas comprised 69.9% of oesophageal cancers in men and 39.9% in women.

The population-attributable fraction (PAF) was calculated for each sex–age group, corresponding to the level of overweight/obesity 10 years previously, according to the usual formula:

$$\mathrm{PAF} = \frac{(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2)}{1 + [(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2)]}$$

where p_1 is the proportion of population overweight, p_2 the proportion of population obese, ERR_1 the excess relative risk (RR−1) for overweight and ERR_2 the excess relative risk (RR−1) for obesity.

RESULTS

Table 3 shows the calculation of attributable fractions, and corresponding numbers of attributable cases, by age group and sex, for seven cancer types accepted to be causally related to excess body weight, assuming a 10-year latency between the presence of excess body mass and cancer risk.

Table 4 summarises these results. An estimated 17 294 excess in cancer cases occurring in 2010 were due to overweight and obesity (5.5% of all cancers). The sites contributing most to this excess are large bowel (5172) and breast (4194).

Table 4 Numbers and proportion of cases occurring at selected sites attributable to overweight and obesity (UK 2010)

	Excess attributable cases (PAF)		
Cancer	**Male**	**Female**	**Persons**
Oesophagus	1538 (26.9)	315 (11.2)	1853 (21.7)
Gallbladder	381 (9.7)	91 (17.8)	128 (18.3)
Pancreas	523 (12.8)	494 (11.5)	1017 (12.2)
Colorectum	3009 (13.6)	2162 (12.2)	5172 (13.0)
Breast	—	4194 (8.7)	4194 (8.7)
Endometrium	—	2759 (33.7)	2759 (33.7)
Kidney	1422 (25.0)	749 (22.2)	2171 (24.0)
All cancers[a]	6530 (4.1)	10 764 (6.9)	17 294 (5.5)

Abbreviations: PAF = population-attributable fraction (%). [a]Excluding non-melanoma skin cancer.

DISCUSSION

The list of cancers that have been selected as being related to excess body mass (overweight and obesity) is a conservative one. It corresponds to those in the consensus statements of IARC (2002) and WCRF (2007). Needless to say, other studies have identified a large number of other cancers to be associated with excess body mass. In the recent meta-analysis of prospective studies (cohort studies and clinical trials) by Renehan *et al* (2008), there was a positive (statistically significant) association between BMI and cancer of the thyroid, leukaemia, malignant melanoma (men only), non-Hodgkin lymphoma and multiple myeloma. Others have reported significant associations with cancers of the prostate (Bergstrom *et al*, 2001), ovary (Reeves *et al*, 2007; Schouten *et al*, 2008; Lahmann *et al*, 2010) and brain (Benson *et al*, 2008), as well as cancers of the liver (Larsson and Wolk, 2007) and gastric cardia (Calle and Kaaks, 2004).

In common with most reviews, we have chosen to ignore possible differences in risk between men and women, although for some cancers – especially colorectal cancers – a greater effect in men than in women is found in some studies (Calle and Kaaks, 2004; Renehan *et al*, 2008) but not others (Bergstrom *et al*, 2001).

The 10-year 'latency' used to define the relevant time period at which to measure population prevalence of overweight and obesity is somewhat arbitrary. It was based on the average period of follow-up in the large cohort studies from which the estimates of relative risk are derived (as reported by Renehan *et al*, 2008).

Several previous estimates of the fraction of cancer in the UK attributable to overweight and obesity have been published. Bergstrom *et al* (2001) considered a similar range of cancers to those in this paper, but included cancers of the prostate as related to BMI, and excluded oesophageal adenocarcinoma; based on relative risks from their own meta-analyses, they estimated that 2.7% of cancers diagnosed in men and 4.9% in women in the UK in 1995 were related to overweight/obesity during 1983–6. Renehan *et al* (2010) include a much wider range of cancers, as noted earlier, based on their meta-analysis of 2008 (Renehan *et al*, 2008); their estimate of attributable fraction (for 2002, based on overweight/obesity (single category) in 1992 (from WHO)) was 4.01% in women and 3.42% in men. Reeves *et al* (2007) used the results of the Million Women Study to estimate that 5% of cancers in postmenopausal women in 2004 were related to overweight and obesity (based on prevalence in England in the same year), and including nine cancers observed to have a significant trend of increasing risk with increasing BMI (including leukaemia, ovary, multiple myeloma and non-Hodgkin lymphoma, but excluding colorectal cancers). The estimate of the proportion of cancers related to 'body fatness' in the UK in 2002 by WCRF/AICR (2009) is given only for the seven sites analysed in this paper: 18% of the five cancers in men and 16% of the seven in women. This would be equivalent to an overall AF (for all cancers) of 4.2% in men and 8.7% in women. There are several reasons for this larger estimate. WCRF selected 'representative' studies from which to take the relative risks – almost all are in excess of the pooled values from their own meta-analyses. Exposure prevalence was taken from data for the same year as outcome (2002); exposure prevalence would have been lower if prevalence at an earlier period had been used, given the continuously rising trend of overweight and obesity in recent years. Finally, the baseline category (not overweight or obese) was not always $\leqslant 25\,\mathrm{kg\,m^{-2}}$, but for some cancers (breast and pancreas) it was $\leqslant 23\,\mathrm{kg\,m^{-2}}$.

See acknowledgements on page Si.

Conflict of interest

The authors declare no conflict of interest.

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9.

Cancers attributable to inadequate physical exercise in the UK in 2010

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Several studies suggest that regular physical exercise protects against development of breast cancer, large bowel cancer and endometrial cancer, independently of the effect of physical exercise in reducing body weight. The World Cancer Research Fund (WCRF, 2007) summarizes the evidence as 'convincing' for cancers of the colon, and 'probable' for cancers of the breast (in post-menopausal women only) and endometrium (WCRF, 2007).

The evidence that individuals with high levels of physical activity throughout their lives are at lower risk for colon cancer was considered 'sufficient' in the International Agency for Research on Cancer (IARC) evaluation (IARC, 2002), and convincing by WHO/FAO (2003). The relationship between physical exercise and risk of rectal cancer is much less certain (IARC, 2002; Wei *et al*, 2004; Friedenreich *et al*, 2006), although a few studies (e.g., Slattery *et al*, 2003) have shown an inverse association.

In relation to physical activity and risk of breast cancer, IARC (2002) concluded that, although studies have not been entirely consistent, the overall results support a reduction in risk with higher levels of activity. Evidence for a dose – response effect was found in most of the studies that examined the trend. The majority of studies have focused on postmenopausal breast cancer, although there is also some evidence for a protective effect of physical activity on premenopausal disease. In some of the studies, the nature of the physical activity (recreational, occupational, and household) has appeared to be of importance, too.

A recent review and meta-analysis of 13 studies (Voskuil *et al*, 2007) concluded, like WCRF (2007), that physical activity seems to be associated with a reduction in the risk of endometrial cancer, which is independent of body weight.

The Department of Health (2004) target for physical exercise is that everyone should aim to take at least 30 min of physical activity on five or more days of the week. This physical activity should be of at least moderate intensity – similar to brisk walking. Activity can be taken in bouts of 10 – 15 min, allowing for accumulation of activity throughout the day.

In this section, we examine how much cancer of the colon, female breast and endometrium observed in 2010 might be attributed to a deficit in physical activity in the population below this recommended minimum.

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METHODS

Most studies of the effect of physical activity on cancer risk present results in terms of categories of activity (high/medium/low, or as quantiles of the population studied). In order to quantify the effect of change to exercise intensity on the health of the population, risk must be quantified in relation to energy expenditure in MET. (MET means metabolic equivalent, and is used to describe the intensity of activities. One MET is defined as the energy spent sitting quietly (equivalent to (4.184 kJ) per kg per hour), while, for example, moderate activity corresponds to 3 – 6 METs, and vigorous activity to >6 METs. A table showing MET values of different activities is available at http://www.cdc.gov/nccdphp/dnpa/physical/pdf/PA_Intensity_table_2_1.pdf).

At least four recent studies provide estimates of risk of colon cancer in relation to physical activity (adjusted for body mass index) expressed as MET hours: Giovannucci *et al* (1995), Chao *et al* (2004), Friedenreich *et al* (2006) and Wolin *et al* (2007).

At least four recent studies provide estimates of risk of breast cancer in relation to physical activity (adjusted for body mass index) expressed as MET hours: Friedenreich *et al* (2001), Carpenter *et al* (2003), McTiernan *et al* (2003) and Lahmann *et al* (2007).

For each of these studies, the relative risk (RR) per MET-hour per week was estimated by assuming a log-linear relationship between exposure and risk, so that:

$$\text{Relative risk}(x) = \exp\left(\ln\left(\text{risk per unit}\right) \times \text{exposure level}(x)\right)$$

where x is the exposure level (in MET-hours per week).

We used the simple mean of the RR per unit exposure in each study.

The values were as follows:

Post-menopausal breast cancer: RR 0.9955 per MET-hour per week.

Colon cancer: RR 0.9940 per MET-hour per week.

The value for post-menopausal breast cancer in the meta-analysis of WCRF (2007) is very similar – for postmenopausal breast cancer and recreational activity, an RR of 0.97 per 7 MET-hours per week.

As we are concerned with quantifying the effect of a deficit in exercise, we calculate the increase in risk associated with a *decreased* exercise intensity of 1 MET-hour per week as

$$(1/\mathrm{RR}) - 1$$

The values were the following:

0.00457 for post-menopausal breast cancer.
0.00602 for colon cancer.

With respect to endometrial cancer, none of the case–control and cohort studies so far reported provide results with respect to physical activity in comparable units. It is thus not possible to estimate directly the relationship in terms of RR (or ERR) per MET-hour per week. However, in a large case–control study in Sweden, comparable results are given for post-menopausal breast cancer (Moradi *et al*, 2000a) and endometrial cancer (Moradi *et al*, 2000b). The strength of the association between recreational and occupational activity, comparing the lowest with the highest activity categories, is more or less the same for both cancers (RR = 1.3). Therefore, the values per MET-hour per week estimated for breast cancer (as above) have also been used for endometrial cancer.

The latent period, or interval between 'exposure' to an inadequate level of physical activity, and the appropriate increase in risk of these cancers (or, conversely, the duration of exercise required to eliminate the excess risk of a suboptimal level) are not known. For the four cohort studies contributing to the estimate of RR of colon cancer in this analysis (Giovannucci *et al*, 1995; Chao *et al*, 2004; Friedenreich *et al*, 2006; Wolin *et al*, 2007) the mean duration of follow-up was 8.9 years. In the two cohort studies contributing to the estimate for breast cancer (McTiernan *et al*, 2003; Lahmann *et al*, 2007) it was shorter (5.6 years), while in the seven cohort studies in the meta-analysis of endometrial cancer by Voskuil *et al* (2007) mean duration of follow-up was 14.8 years. We chose to assume the same latency for all three of 10 years and thus examine the effects on cancers occurring in 2010 from suboptimal levels of physical activity in 2000.

The minimum target would envisage all those doing less than 30 min, 5 days a week, to move to this minimum (but no increase in exercise levels in those individuals already achieving the target level).

The National Diet and Nutrition Survey (FSA, 2004) provides tables showing reported levels of physical exercise, by age group and sex, for adults aged 19–64 in a sample of households in Great Britain in 2000–2001. There are four categories: moderate exercise of 30 min duration for 5 or more days a week, 1–2 days, 3–4 days and <1 day per week. In all, 36% of men and 26% of women aged 19–64 were already at the target level of at least 30 min moderate physical exercise on at least 5 days a week. For those of age >65, equivalent data were obtained from the Health Survey for England (Health and Social Care Information Centre, 2010) by averaging the values in the surveys of 1997 and 2003. The middle category (1–4 days moderate exercise per week) was split into two (1–2 and 3–4), based on the ratios observed at ages 50–64 in the 2000–2001 National Diet & Nutrition Survey.

The results for all adult age groups (ages 19 and above) are shown in Table 1.

Assuming that exercise of moderate intensity is equivalent to 6 METS, so that 30 min of moderate exercise consumes 3 MET-hours, we estimate the deficit in MET hours below the recommended level of 15 per week (3×5). Thus, for the proportion of the population exercising moderately 3–4 days a week, the deficit is, on average, 4.5 MET-hours per week ($15-[3 \times 3.5]$), for those exercising 1–2 days 10.5 MET-hours per week and for those exercising less than 1 day per week 13.5 MET-hours ($15-[3 \times 0.5]$) per week. These values are shown in the first row of Table 1.

Table 1 Estimated percentage of the population performing physical activity at the level given, in 2000

	% Performing physical activity[a] with specified frequency per week			
Age (years)	**<1 day**	**1 or 2 days**	**3 or 4 days**	**⩾5 days**
Deficit in METs per week	13.5	10.5	4.5	0
Men				
19–24[b]	21	14	17	49
25–34[b]	12	21	21	46
35–49[b]	20	27	19	34
50–64[b]	30	28	18	24
65–74[c]	52.6	20.1	12.9	14.5
⩾75[c]	73.0	11.9	7.6	7.5
All (19+)[d]	28.2	22.9	17.5	31.5
Women				
19–24[b]	20	36	15	29
25–34[b]	14	29	26	30
35–49[b]	21	29	24	25
50–64[b]	24	34	21	22
65–74[c]	57.0	20.1	12.4	10.5
⩾75[c]	81.7	8.7	5.4	4.0
All (19+)[d]	31.6	27.3	19.4	21.5

Abbreviations: METs = metabolic equivalents. [a]Defined as moderate intensity activity of at least 30 min duration. [b]From National Diet and Nutrition Survey, FSA (2004). [c]From Health Survey for England (2009 trend tables), average for 1997 and 2003; the middle physical activity category (1–4 days per week) was split into 1–2 and 3–4 days per week in proportions observed at ages 50–64 in the National Diet and Nutrition Survey, FSA (2004). [d]Based on UK 2000 population.

Population-attributable fractions (PAFs) were calculated for each sex-age group in Table 1 according to the usual formula:

$$\mathrm{PAF} = \frac{(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) + (p_4 \times \mathrm{ERR}_4)}{1 + [(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) + (p_4 \times \mathrm{ERR}_4)}$$

where p_x is the proportion of population in exercise category x and ERR_x the excess RR in exercise category x.

ERR_x is calculated as

$$\{\exp(R_m \times M_x) - 1\}$$

where R_m is the increase in risk for a deficit of 1 MET-hour per week and M_x is the deficit in MET-hours per week (less than 15) in exercise category x.

RESULTS

Table 2 shows the estimated PAF and the number of cases of breast, endometrial and colon cancer 'caused' in 2010 by the deficit in exercise (in 2000), by age group and sex. The excess number of cases is also expressed in terms of cancer as a whole.

An estimated 3.4% of breast cancer cases, 3.8% of endometrial cancer cases and 5.3% of colon cancer cases are attributable to exercising less than the minimum recommended. The 5.3% of colon cancers correspond to 3.3% of large bowel cancers (colon and rectum). This corresponds to 1.0% of all cancer cases, 0.4% in men and 1.7% in women.

DISCUSSION

Although a beneficial effect of physical activity levels on the risk of various cancers has been observed in various individual studies – notably for cancers of the lung, pancreas and prostate – the

Table 2 Cancer cases diagnosed in 2010, attributable to below-target exercise level in 2000

Age (years)		Breast (post-menopausal)			Uterus (endometrium)			Colon			All cancers[a]	
At exposure	At outcome (+10 years)	PAF	Observed cases	Excess attributable cases	PAF	Observed cases	Excess attributable cases	PAF	Observed cases	Excess attributable cases	Observed cases	Excess attributable cases
Men												
19–24	29–34	—	—	—	—	—	—	0.031	58	1.8	1333	1.8
25–34	35–44	—	—	—	—	—	—	0.029	216	6.2	4124	6.2
35–49	45–59	—	—	—	—	—	—	0.038	1451	55.5	22388	55.5
50–64	60–74	—	—	—	—	—	—	0.046	5331	247.3	68043	247.3
65–74	75–84	—	—	—	—	—	—	0.058	4339	250.6	44085	250.6
⩾75	⩾85	—	—	—	—	—	—	0.067	1598	106.9	16064	106.9
Total (%)		—	—	—	—	—	—		13044	668.3 (5.1%)	158667	668.3 (0.4%)
Women												
19–24	29–34	0	582	0	0.032	28	0.9	0.043	60	2.5	2248	3.4
25–34	35–44	0	3857	0	0.028	211	5.9	0.037	236	8.6	8619	14.5
35–49	45–59	0.032	14628	461.7	0.032	1926	60.8	0.042	1301	54.0	31631	576.5
50–64	60–74	0.035	17194	602.8	0.035	3844	134.8	0.046	3914	180.3	54966	917.9
65–74	75–84	0.046	7584	352.4	0.046	1570	73.0	0.061	3873	235.9	35386	661.2
⩾75	⩾85	0.054	4367	237.1	0.054	605	32.8	0.071	2299	163.3	20050	433.3
Total (%)			48385	1654.1 (3.4%)		8195	308.1 (3.8%)		11732	644.7 (5.5%)	155584	2606.9 (1.7%)
Persons												
19–24	29–34		582	0		28	0.9		117	4.3	3582	5.2
25–34	35–44		3857	0		211	5.9		452	14.8	12743	20.7
35–49	45–59		14628	461.7		1926	60.8		2752	109.6	54019	632.1
50–64	60–74		17194	602.8		3844	134.8		9245	427.6	123009	1165.2
65–74	75–84		7584	352.4		1570	73.0		8212	486.4	79472	911.8
⩾75	⩾85		4367	237.1		605	32.8		3897	270.2	36114	540.1
Total (%)			48385	1654.1 (3.4%)		8195	308.1 (3.8%)		24776	1312.9 (5.3%)	314251	3275.2 (1.0%)

Abbreviations: PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

evidence is far from conclusive, and in this section we include only those (colon, post-menopausal breast cancer and endometrial cancer) for which the evidence is considered convincing or probable in the reviews of WRCF (2007) or 'sufficient' by IARC (2002).

There are several probable mechanisms underlying the protective effects of physical activity (McTiernan *et al*, 1998; Quadrilatero and Hoffman-Goetz, 2003). They include modification of levels of metabolic hormones and growth factors, improvement of the anti-tumour immune system, promotion of antioxidant defence and DNA repair. Physical activity may reduce exposure to endogenous oestrogens implicated in breast and endometrial cancer. With respect to colon cancer, physical activity can speed up the transit of food, with reduced exposure to intraluminal carcinogens. Changes to levels of insulin, prostaglandin and bile acids reduce proliferation of mucosal cells.

The current estimate – that around 1% of cancers in the UK may be related to physical inactivity (below a modest aspiration of 30 min five times a week) – is similar to the estimate of Doll and Fau (2003), that less than 1% of cancer deaths are due to physical inactivity. However, the estimates of the proportions of cancers related to inadequate 'physical activity' in the UK in 2002 by WCRF (2009) are substantially higher: 12% of colorectal cancer, 12% of breast cancer and 30% of endometrial cancer. There are several reasons for these larger estimates. WCRF selected 'representative' studies from which to take the RRs; only one (for colon cancer) is referenced to be from their own meta-analyses (WCRF, 2007), where the value (1.33 for more than 150 hours exercise per week *vs* none) is not actually reported. The RR for endometrial cancer, 0.57 for ⩾60 minutes of non-occupational exercise per day compared with <30 min (Schouten *et al*, 2004), is particularly significant. The reference category (optimum physical activity) was different for the three cancers, and in all was higher than the equivalent of 5 × 30 min of moderate exercise per week. Finally, the translation of the exposure prevalence (from the National Diet and Nutrition Survey) to the categories used in the calculation of three different estimates was particularly imaginative.

Using a modelling approach, de Vries *et al* (2010) estimated that, in 2040, 8.7% of colon cancer cases in men and 17.4% in women would be due to suboptimal levels of physical activity during the previous 20 years. The higher percentages than those estimated in the current analysis (4.9% in men and 5.3% in women) are due to several differences in the methods. The main difference is the dichotomizing of the population into 'optimal' and inactive, with RRs from a meta-analysis of leisure-time activity and colon cancer (Samad *et al*, 2005) that suggested substantial risk in inactive individuals *vs* those 'physically active' (1.28 in men, 1.41 in women), which contrasts with the risk of 1.09 in the least active group of Tables 1 and 2 relative to the optimum of 5 × 30 min of moderate exercise per week (substantially less active than the baseline category of Samad *et al*, 2005).

Based on short-term trend data from the Health Survey for England (Health and Social Care Information Centre, 2010), it does seem that, in the period 1997–2009, there has been an increase in the proportion of persons exercising five or more times per week. There is evidence from reviews that interventions to increase individual exercise levels in community, health-care and occupational settings can be successful (Hillsdon *et al*, 2005), although at present there is little review-level evidence of the effectiveness of modifications to the built environment in increasing physical activity in the general population.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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10.
Cancers attributable to exposure to hormones in the UK in 2010

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The International Agency for Research on Cancer (IARC) Monographs on the carcinogenic risk to humans concluded that combined oral oestrogen – progestogen contraceptives are carcinogenic to humans (IARC, 2007). This evaluation was made on the basis of increased risks for cancer of the breast (among current and recent users only), cervix and liver (in populations that are at low risk for hepatitis B viral infection). There is also convincing evidence in humans that these agents confer a protective effect against cancer of the endometrium and ovary.

The IARC (2007) review also concluded that there is sufficient evidence in humans for the carcinogenicity of combined oestrogen – progestogen menopausal therapy in the breast. With respect to endometrial cancer, combined oestrogen – progestogen menopausal therapy was evaluated as carcinogenic when progestogens are taken for <10 days per month, while there was evidence suggesting lack of carcinogenicity in the endometrium when progestogens are taken daily. The risk for endometrial cancer is inversely associated with the number of days per month that progestogens are added to the regimen.

The use of hormonal preparations in the UK has declined dramatically in recent years. According to the data from prescription cost analysis (PCA) on the annual numbers of prescriptions for oestrogens and progestogens dispensed in the community, there has been a marked decline in prescriptions for hormonal preparations in England since 2000 – 1 (http://www.ic.nhs.uk/statistics-and-data-collections/primary-care/prescriptions/prescription-cost-analysis-england–2009).

In this section, the population-attributable fraction (PAF) of cancers diagnosed in women in the UK in 2010 due to current or past use of hormonal preparations is estimated.

METHODS

Prevalence of exposure to hormonal preparations

To examine the changes in use of prescribed agents by age group, data were obtained from the general practice research database (GPRD). The GPRD is the world's largest computerised database of anonymised longitudinal medical records from primary care. Currently data are collected on over 3.4 million active patients from around 450 primary-care practices throughout the UK. Data were abstracted for women, aged 15 to >85 (in 5-year age bands), annually from 1992 to 2009. A list of female sex hormone products were identified and classed into one of the following British National Formulary (BNF) categories:

6.4.1.0 – Oestrogen only hormone replacement therapy (HRT)
6.4.1.1 – Combined oestrogen/progesterone HRT
6.4.1.2 – Progestogens
6.4.1.3 – Tibolone
6.4.1.4 – Raloxifene
7.3.1 – Combined hormonal contraceptives
7.3.2.1 – Oral progestogen-only contraceptives
7.3.2.2 – Parenteral progestogen-only contraceptives
7.3.2.3 – Intra-uterine progestogen-only device
Other – Other female sex hormones.

The information was provided by GPRD as prevalence of women with a prescription per 1000 patients registered at calendar year mid-point, stratified by calendar year, age band and BNF code. As well as prevalence of current (2009) use, the prevalence of ex-users in the same year was estimated, with the simplifying assumption that users do not stop and restart the same preparation. Thus, the prevalence of ex-users of <1 year (Pex(1)) is given by

$$\mathrm{Pex}(1)_{i,a} = [P\mathrm{current}_{i-1,a-1}] - [P\mathrm{current}_{i,a}]$$

where i is the year and a age.

In addition, it was assumed that prescription of progesterone-only preparations in post-menopausal women was accompanied by oestrogens (with each hormone dispensed separately, rather than as a combined preparation), so that prevalence of use of unopposed oestrogens (P(oes)) is given by the difference (P(oes)$-P$(prog)).

Risks of oral contraceptive (OC) use

Breast cancer The Collaborative Group on Hormonal Factors in Breast Cancer (1996) brought together and reanalysed the worldwide epidemiological evidence on the relation between breast cancer risk and use of hormonal contraceptives. Table 1 shows the excess relative risks (ERRs) ($=$relative risk (RR)-1) associated with current and past use of combined (oestrogen plus progesterone) OC preparations. Duration of use, age at first use, and the dose and type of hormone within the contraceptives had little additional effect on breast cancer risk, once recency of use had been taken into account. Hormonal contraceptives containing only progestogens comprised $<3\%$ of the study population, but results

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were broadly similar to those found for combined OCs (an increase in risk for use in the previous 5 years: ERR 0.17; but no evidence of an increase in risk 10 or more years after stopping use); risks are assumed to be the same as for combined contraceptive preparations (Table 1).

Cancer of the cervix uteri Smith *et al* (2003) combined the results from studies published between 1966 and 2002 to examine the relationship between the risk of cancers of the cervix and duration and recency of use of hormonal contraceptives, taking into account potential confounding factors, such as HPV status, sexual partners, screening history, smoking and use of barrier contraceptives. More recently, the International Collaboration of Epidemiological Studies of Cervical Cancer (2007) obtained the original data from 24 studies to conduct a pooled analysis. They found that risk of cervical cancer increased by a factor of 1.07 for each year of use of hormonal contraception (or 1.38 (1.30–1.46) for 5 years use). In ex-users, the excess risk is approximately halved 2–4 years after cessation, and halved again after 5–9 years. There was no significant excess risk 10 years after cessation of use.

Duration of use of contraception, among current users, by age group, is not available from any UK source. In the multicentre study of the International Collaboration (2007), the mean duration of use, in control women, was 6 years. Clearly, the controls for cases of cervix cancer are older women, with a mean age of about 40. Younger women would have had shorter durations of use: we assume 2 years at ages 15–19 and 4 years at ages 20–24, so that the ERRs of current users are as shown in Table 2. For ex-users, we assume a halving of risk after 2–4 years, and halving again at 5–9, as in the International Collaboration Study (2007).

Cancer of the corpus uteri (endometrium) IARC (2007) concluded that there is convincing evidence in humans for a protective effect of combined oral oestrogen–progestogen contraceptives against carcinogenicity in the endometrium. They reviewed four cohort studies and 21 case–control studies reported up to 2003, which consistently showed that the risk for endometrial cancer in women who had taken these medications is approximately halved. The reduction in risk was generally greater with longer duration of use of combined hormonal contraceptives and persisted for at least 15 years after cessation of use. More recently, the EPIC study (Dossus *et al*, 2010) found that women who had ever used OCs had a risk of 0.63 compared with never users, and this was just 0.44 in women who had used OCs for $\geqslant 10$ years.

Schlesselman (1997) conducted a meta-analysis of studies reported up to 1993, and estimated the risk of combined OC use in relation to duration of use, and time since last used. The estimate of RR by duration of use was given by

$$RR_{dur} = \exp\left[-0.023 - 0.493 \times \ln(\text{years} + 1)\right]$$

This is equivalent to a risk of 0.44 for 4 years use, 0.33 for 8 years use and 0.28 for 12 years use.

The estimate of RR by years since last use of combined OCs (recency of use) was given by

$$RR_{rec} = \exp\left[-1.721 + 0.346 \times \ln(\text{years} + 1)\right]$$

This is equivalent to a risk of 0.33 for use within the last 10 years, 0.41 for use within the last 10 years and 0.51 for use within the last 20 years.

Ovarian cancer The IARC (2007) review concluded that women who had ever used combined hormonal contraceptives orally had an overall reduced risk for ovarian cancer, and an inverse relationship was observed with duration of use. The reduced risk appeared to persist for at least 20 years after cessation of use. In the combined analysis by the Collaborative Group on Epidemiological Studies of Ovarian Cancer (Collaborative Group, 2008), the overall reduction in ovarian cancer risk in ever *vs* never users was 27%. Table 3 shows the RRs by duration of use and time since last use.

The effect of combined hormonal contraceptive use on the reduction of risk for ovarian cancer is not confined to any particular type of oral formulation nor to any histological type of ovarian cancer, although it was less consistent for mucinous than for other types in several studies.

Liver cancer Although the IARC (2007) review concluded that combined oral oestrogen–progestogen contraceptives are carcinogenic for the liver, the conclusion was based on a selected group of case–control studies (in populations with 'low prevalence of hepatitis B viral infection and chronic liver disease'), with no cohort studies providing a conclusive result. A more recent meta-analysis of case–control studies (Maheshwari *et al*, 2007) did not obtain a conclusive result based on 12 case–control studies (pooled estimate of ORs 1.57 (95% CI = 0.96–2.54, $P = 0.07$)), or eight studies reporting adjusted ORs (in addition to age and sex) – the pooled estimate was 1.45 (95% CI = 0.93–2.27, $P = 0.11$).

In any case, liver cancer is rare in UK, and there were only some 190 cases below age 50 in UK in 2005; therefore, the number of cases possibly attributable to OC use is trivial.

Table 1 Excess relative risk of breast cancer associated with current and past use of combined OC preparations

Time since cessation of OCs (years)	Excess relative risk of breast cancer
Current use	0.24
1–4	0.16
5–9	0.07
$\geqslant 10$	0

Abbreviation: OC = oral contraceptive.

Table 2 Excess relative risks for cervical cancer in relation to use of OCs, by age

Time since cessation of OCs (years)	Excess relative risk by age group		
	15–19	20–24	25+
Current use	0.14	0.30	0.48
<1	0.14	0.30	0.48
2–4	0.07	0.15	0.24
5–9	—	0.07	0.12
$\geqslant 10$	—	—	0

Abbreviation: OC = oral contraceptive.

Table 3 Risk of ovarian cancer in relation to duration of use, and time since last use of OCs (Collaborative Group, 2008)

Time since use of OCs (years)	Risk of ovarian cancer by duration of use of OCs		
	<5 years	5–9 years	>10 years
<10	0.88	0.52	0.39
10–19	0.85	0.62	0.51
29–29	0.81	0.69	0.60
$\geqslant 30$	0.83	—	—

Abbreviations: OC = oral contraceptive.

Risks of post-menopausal hormone therapy

Breast cancer The magnitude of the risk of postmenopausal hormone therapy for the risk of breast cancer has been quantified based on studies in the USA, Europe and the UK (Collaborative Group, 1997; Writing Group, 2002; Chlebowski *et al*, 2003; Beral, 2003; Bakken *et al*, 2011). In the Million Women Study (Beral, 2003) for example, the RR of breast cancer in current users of HRT was 1.66 (95% CI 1.58–1.75, $P<0.0001$). Incidence was significantly increased for current users of preparations containing oestrogen only (1.30), progestogen only (2.02), oestrogen–progestogen (2.00) and tibolone (1.45). Results varied little between specific oestrogens and progestogens or their doses, or between continuous and sequential regimens. Past users of HRT were, however, not at an increased risk of disease (1.01 (0.94–1.09)). In past users, the risk of breast cancer did not differ significantly from that of never users of HRT, for use that ceased at <5 years, 5–9 years and $\geqslant 10$ years previously, although among women who ceased use of HRT in the previous year, the RR of breast cancer was slightly increased (1.14 (1.01–1.28)). The ERRs are shown in Table 4.

Cancer of the corpus uteri (endometrium) The Million Women Study (Beral *et al*, 2005) found that hormone-replacement therapy containing oestrogen alone increased the risk of endometrial cancer. The RR of endometrial cancer in current users of oestrogen-only HRT was 1.80 (1.19–2.70), while there was no increase in risk in past users (RR 0.97 (0.50–1.87)).

The risk of endometrial cancer was also increased by tibolone. The RR in current users of tibolone was 2.02 (1.58–2.59), while it was 1.23 (0.76–1.99) in past users. Past users had ceased use an average of 2.7 years previously, so that the excess risk in past users of tibolone (0.23) was assumed to last for up to 4 years.

Progestogens, however, counteract the adverse effect of oestrogens on the endometrium, and the effect of continuous combined preparations was a reduction in risk (RR = 0.71), while there was no significant risk (or protection) from use of cyclic preparations (RR = 1.05, 95% CI 0.91–1.22). As the data from GPRD did not distinguish between the proportion of combined oestrogen–progestogen preparations that had been prescribed as continuous combined preparations, or cyclic combined preparations, it was assumed that these were in the ratio of 1:2, as in the Million Women study. An RR for all such preparations was obtained by weighting the RRs of current use (0.75 for continuous, 1.05 for cyclic) accordingly, yielding an RR of 0.95 and an ERR of −0.05 (Table 6). There were no significant differences in risk between current and past users of combined preparations (average time since cessation for women who had taken cyclic preparations was 2.7 years, and that for continuous 1.2 years).

The ERRs used to estimate PAF are shown in Table 5.

Table 4 Excess relative risks of breast cancer in current and past users of HRT

	Excess relative risk of breast cancer	
Preparation	**Current HRT users**	**Past HRT users (<1 year)**
Oestrogen only	0.3	0.06
Oestrogen+progestogen combinations	1	0.21
Progestogens	1.02	0.22
Tibolone	0.45	0.10
Raloxifene hydrochloride	0	0.00
All	0.66	0.14

Abbreviation: HRT = hormone replacement therapy (postmenopausal hormones).

Ovarian cancer The IARC (2007) review concluded that the studies available were inadequate to evaluate an association between ovarian cancer and combined oestrogen–progestogen hormonal therapy. However, more data are now available. In a meta-analysis of eight cohort and 19 case–control studies by Zhou *et al* (2008), ever use of HRT was associated with a 19–24% increase in risk of ovarian cancer, with a greater risk of oestrogen-only therapy compared to oestrogen–progestogen therapy. A more recent meta-analysis of 14 population-based studies found a risk of 1.22 associated with 5 years of use of oestrogen therapy, while in users of combined therapy it was 1.1 (Pearce *et al*, 2009). In the Cancer Prevention II Nutrition Cohort in the USA (Hildebrand *et al*, 2010), current oestrogen use was associated with a risk of 1.70 (for use of $\leqslant 10$ years), while there was no increased risk for users of combined preparations, or in former users of either.

After an average 5.3 years of follow-up in the Million Women Study (Million Women Study Collaborators, 2007), the risk in current users of HRT was 1.20, greater for oestrogen-only (1.34) than for combined (1.14) or other preparations (1.22). The risk in past users was not increased. These values were used to estimate PAF in the UK in 2010.

Attributable fractions

Breast cancer We use the prevalence of current and past use of OC agents, and post-menopausal therapy in 2009 to calculate the excess risk in current users, given the ERRs in Tables 1 and 4. It was assumed that prescription of progestogen-only preparations in post-menopausal women was probably accompanied by oestrogens (with each hormone dispensed separately, rather than as a combined preparation). Total excess risk due to hormonal preparations is obtained by summing the excess risks for current and past users of HRT and OCs.

Cervix cancer With the ERRs in Table 2 and prevalence of current and past use of OCs, total excess risk due to OCs is obtained by summing the excess risks for current and past users (as for breast cancer, above).

Endometrial cancer The protective effect of combined OCs against endometrial cancer is related to duration of use, and, in ex-users, time since last use, as described above. The prevalence of current and past use of OCs in the UK (by age, time since used and duration of use) is not documented. We used data from the Million Women Study (age groups 50–64) (Million Women Study Collaborative Group, 1999), from a study of post-menopausal women in Norfolk (Chan *et al*, 2008), and from a case–control study of pre-menopausal women (aged 36–44) by Roddam *et al* (2007) to estimate the proportions of current and past users of OCs. Prevalence of current and recent (<10 years) ex-users at ages 15–34 was estimated from the GPRD data as described above. With these data, and the equations proposed by Schlesselman (1997), estimates of RR by age, duration of use and time since last use could be made for 2009. These were applied to the estimated

Table 5 Excess relative risks of endometrial cancer in current and past users of HRT

	Excess relative risks of endometrial cancer	
Preparation	**Current HRT users**	**Past HRT users (used HRT within the past 4 years)**
Oestrogen only	0.8	0.00
Oestrogens+progestogen combinations	−0.05	−0.05
Tibolone	1.02	0.23

Abbreviation: HRT = hormone replacement therapy.

numbers of cancers in 2010 to estimate the proportion being prevented by current and past use of combined OCs.

For post-menopausal hormone therapy, the prevalence of use at ages $\geqslant$45 in 2009 was used to calculate the excess risk of endometrial cancer in current users of oestrogen-only preparations, and of tibolone, with an ERR for oestrogen of 0.80 and for tibolone of 1.02 (Table 5). As noted earlier, it was assumed that progestogen-only preparations in post-menopausal women were accompanied by oestrogens (with each hormone dispensed separately, rather than as a combined preparation), so that prevalence of use of oestrogen alone is represented by the difference (oestrogen−progestogen).

Ovarian cancer The prevalence of current and past use of OCs in the UK (by age, time since used and duration of use) was estimated as described for endometrial cancer. With the relevant protective effects from the Collaborative Group study (2008) shown in Table 3, the proportion of cancers being *prevented* by current and past use of OCs in 2010 can be estimated.

For use of post-menopausal hormone therapy, we used the prevalence of use of post-menopausal therapy (ages 45 and over) in 2009 to calculate the excess risk of ovarian cancer in current users of the different preparations, assuming the RRs from the Million Women Study (Million Women Study Collaborators, 2007): oestrogen-only HRT: 1.34, combined preparations: 1.14, others: 1.22 (as usual, also assuming that prescription of progestogen-only preparations in postmenopausal women was accompanied by oestrogens).

RESULTS

Prevalence of exposure to hormonal preparations

Prevalence of use of female sex hormones is greatest in the age group 20–24, when almost 60% of women were receiving a prescription for such agents (Figure 1).

Prescribed hormones in the UK were predominantly combined oestrogen–progesterone OCs, with a smaller proportion of progestogen-only contraceptives, increasing over time. Prevalence of use of contraceptive agents declines with age. The estimated age-specific prevalence, based on prescription data, is very similar to that from the 'Omnibus survey' of 2006–7 (Lader, 2007), reporting prevalence of use of OCs in England as 64% at ages 20–24 and 28% at 35–39. Use of hormonal (non-contraceptive) agents exceeds use of contraceptive agents by age 45–49, and increases to a maximum prevalence in the age group 50–54.

There have been marked changes in use over time. Use of hormonal preparations increased for several years from 1992 to reach a maximum in around 2000, and then declined. The year of maximum use (in terms of women receiving prescriptions) varies with age, from 1997 (ages 45–49), to 2001 (55–59) and 2002 (65–69). Figure 2 shows the prevalence of use of different hormonal agents in women aged 45–69. The changes concern in particular combined oestrogen–progesterone preparations, but use of oestrogen-only agents has also declined.

Attributable fractions

Table 6 summarises the estimates of PAF due to use of OCs and post-menopausal hormone therapy, and the net result of both, on the estimated numbers of cases of breast, cervical, endometrial and ovarian cancers in 2010.

Breast cancer Both post-menopausal hormone therapy and OCs increase the risk of breast cancer. Post-menopausal hormones are estimated to be responsible for 3.2% of breast cancers in 2010, and OCs for 1.1%, so that both sources of hormones together are responsible for 4.3% of breast cancers. Figure 3 shows the estimated fractions that are attributable to hormones, by age group. The excess risk of breast cancer was highest (a 14% excess) in the age ranges with maximum use of contraceptives (20–24) so that the fraction of breast cancer cases attributable to hormones was about 12%.

Cervix cancer The fraction of cervix cancer cases attributable to OCs is 9.7%, with much larger proportions (up to 22%) in younger women (Figure 4).

Endometrial cancer It is estimated that current and past use of OCs is preventing almost 17% of cases of endometrial cancers that would otherwise have occurred.

Because the bulk of post-menopausal hormones are prescribed as combined oestrogen–progestogen preparations, with a small net protective effect (assuming that two-thirds of them are given as continuous combined preparations), the net effect on the risk of endometrial cancer is small. The estimate of the fraction of endometrial cancers attributable to use of post-menopausal

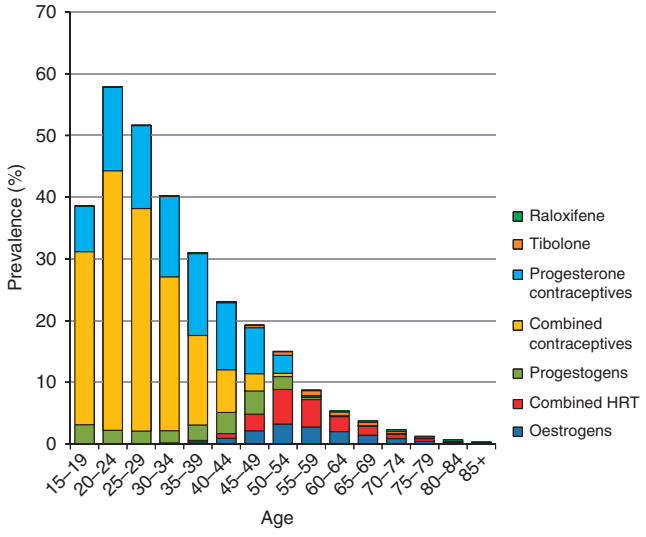

Figure 1 Prevalence (%) of women prescribed hormones, UK 2009.

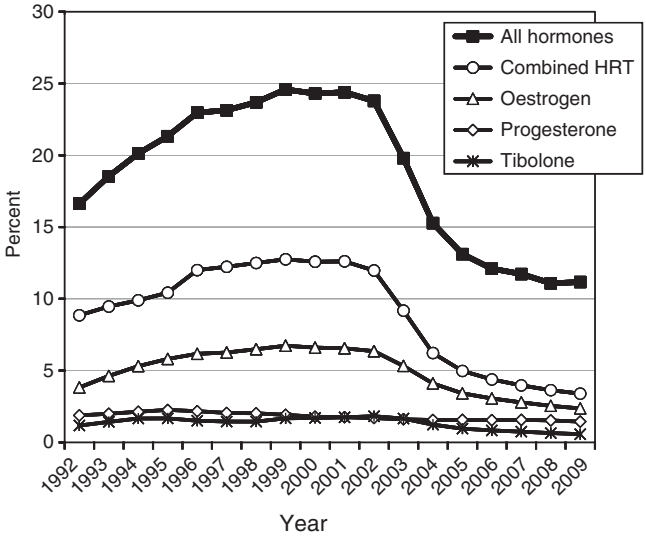

Figure 2 Women aged 45–69 prescribed hormonal agents, 1992–2009.

Table 6 Estimated cases of cancers of the breast, cervix, endometrium and ovary occurring in 2010 attributable to exposure to hormones

		Cases attributable to exposure to hormones, by hormone type					
		HRT		Oral contraceptives		Both	
Cancer and age (years)	Observed cases	Excess attributable cases	PAF (%)	Excess attributable cases	PAF (%)	Excess attributable cases	PAF (%)
Breast							
<40	2018	0	0.0	192	9.5	192	9.5
40–49	6829	376	5.5	343	5.0	719	10.5
50–64	16851	921	5.5	0	0.0	921	5.5
⩾65	22687	235	1.0	0	0.0	235	1.0
All ages	48385	1531	3.2	535	1.1	2067	4.3
Cervix							
<40	1108	0	0.0	203	18.3	203	18.3
40–49	544	0	0.0	54	10.0	54	10.0
50–64	494	0	0.0	4	0.8	0	0.0
⩾65	547	0	0.0	0	0.0	0	0.0
All ages	2691	0	0.0	261	9.7	261	9.7
Corpus uteri (endometrium)							
<40	104	0	0.0	−74	−41.4	−74	−41.4
40–49	454	0	0.1	−283	−38.4	−283	−38.4
50–64	3035	58	1.9	−832	−21.5	−774	−20.3
⩾65	4602	37	0.8	−479	−9.4	−441	−8.7
All ages	8195	95	1.2	−1667	−16.9	−1571	−16.1
Ovary							
<40	445	0	0.0	−94	−17.4	−94	−17.4
40–49	706	7	1.0	−172	−19.6	−165	−18.9
50–64	2004	28	1.4	−282	−12.3	−254	−11.2
⩾65	3665	13	0.4	−156	−4.1	−143	−3.8
All ages	6820	48	0.7	−703	−9.3	−655	−8.8

Abbreviations: HRT = hormone replacement therapy (postmenopausal hormones); PAF = population-attributable fraction.

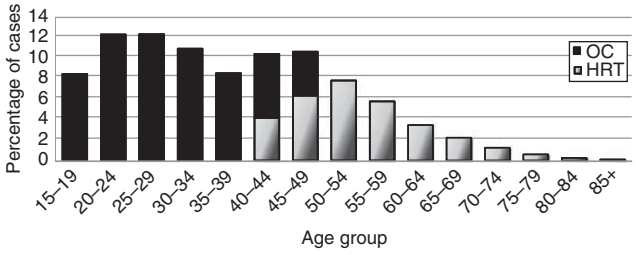

Figure 3 Fraction of breast cancer cases attributable to hormones, by age, UK 2010.

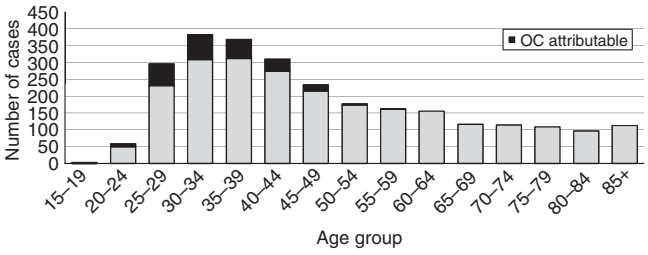

Figure 4 Cervix cancer: total number of cases and those attributable to OC use, UK, 2010.

hormone use is 1.2%, with the highest attributable fraction (2.5%) being in age group 55–59.

Figure 5 illustrates the net effects of OCs and post-menopausal hormones (HRT) by age group.

Ovarian cancer Although there is a small increase in risk of ovarian cancer in post-menopausal women using hormonal preparations (the PAF is 0.7%), this effect is overwhelmed by the longstanding protection provided by current and past use of OCs, which are estimated to be preventing 9.3% of the ovarian cancers that would otherwise have occurred (Table 6).

Figure 6 illustrates the net effects of OCs and post-menopausal hormones (HRT) by age group. Overall in 2010, there would be some 655 fewer cases of ovarian cancer than would have been the

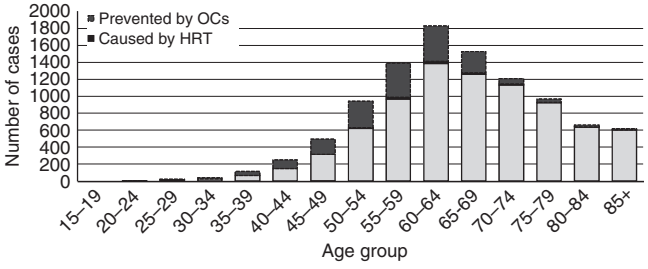

Figure 5 Endometrial cancer: observed cases, including number caused by HRT, and the number estimated to be prevented by current and past use of oral contraceptives (OCs), UK, 2010.

case if there had been no use of exogenous hormones (as OCs or as post-menopausal hormonal therapy).

Summary

Table 7 summarises the results. Overall, a net total of 1675 cancers occurring in 2010 in the UK can be attributed to current or past use of post-menopausal hormonal preparations by women, representing 1.1% of all cancers in women (0.5% for both sexes). However, the net effect of the use of OCs is *protective* – with almost 1600 fewer cancers than would have been the case if they had not been used.

The net effect of hormone use is therefore very tiny – just 102 cases attributable to their use.

DISCUSSION

In this paper, we used the RR of cancer in relation to use of post-menopausal hormones from the Million Women Study (Beral, 2003; Beral *et al*, 2005, Million Women Study Collaborators, 2007) to estimate the likely impact of hormone use on the number of cancer cases at ages >45 in the UK in 2010. This study recorded the use of HRT in women aged 50–64 at the time of enrolment, and followed them for an average of 2.6 years for breast cancer incidence, 3.4 years for incidence of endometrial cancers and 5.3 years for ovarian cancers. For breast cancer, the risk among women who were current users of HRT was 1.66, a result not very different from that observed in the Women's Health Initiative randomised trial for women aged 50–79, in whom the risk of breast cancer in women taking oestrogen plus progesterone was 1.49 after an average 5.6 years of follow-up; the excess relative to the placebo group emerged after 3 years, and continued to widen until the maximum follow-up period of 7 years (Chlebowski *et al*, 2003). The RRs in the EPIC study (Bakken *et al*, 2011) after a mean follow-up of 8.6 years were 1.42 for current users of oestrogen-only and 1.77 for current users of combined preparations. For ovarian cancer, the risks observed in the Million Women Study were very similar to those in the meta-analyses of Zhou *et al* (2008) and Pearce *et al* (2009). With respect to endometrial cancer, however, the EPIC study (Allen *et al*, 2010) found rather higher risks for current users of hormone therapy after 9 years of follow-up than the Million Women Study (2.52 for oestrogen-only HT, 2.96 for tibolone and 1.41 for combined oestrogen–progestogen (although risks differed according to regimen and type of progestogen constituent).

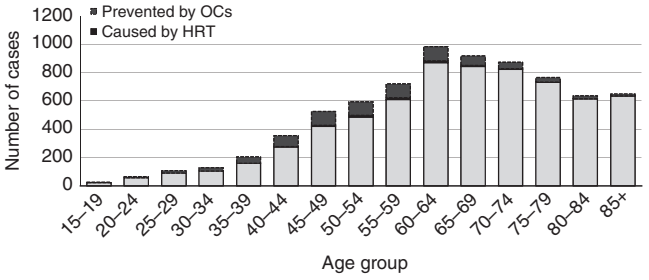

Figure 6 Ovarian cancer: observed cases, including the number caused by HRT and those estimated to be prevented by current and past use of oral contraceptives (OCs), UK, 2010.

As an increased risk of breast and endometrial cancer is observed in past users of at least some hormonal preparations by post-menopausal women, it is important to take this into account, especially as the prevalence of current use has been falling dramatically in the UK since around 2000–1 (Figure 2, Watson *et al*, 2007). In fact, we have no information on prevalence of ex-users in the population, and can only estimate it in terms of the difference in population prevalence from one year to the next, which is surely an underestimate. On the other hand, prevalence of use of hormonal preparations is calculated by dividing the number of women who receive prescriptions for hormonal preparations by the number at risk (in the General Practice Research Database), and this prevalence is assumed to apply to the UK population. In fact, it is possible that many women who receive hormonal preparations have had a hysterectomy, and so would not be at risk of endometrial cancer, so that the attributable fractions for this cancer are overestimated.

Current and recent use of OCs increase the risk of breast and cervical cancer, and decrease the risk of endometrial and ovarian cancer, the latter effects lasting 20 years or more. Although the data on current use of oral contraception should be accurate, information on past use is much less certain, and estimates were based on published data from recent UK studies. The protective effect of OCs is considerably greater with respect to endometrial cancer, as might be expected from the markedly reduced risks in current and past users (IARC, 2007). Pike's (1987) model of the effect of hormones on cancers of the female reproductive organs estimates that 5-year use of oral contraception delays the rise in age-specific incidence of endometrial cancer by 5 years, thus producing lower rates at older ages. On this basis, Key and Pike (1988) predicted that 5-year use of combined OCs beginning at age 28 would produce a 60% reduction in lifetime risk.

It seems that OCs are beneficial not only in preventing unwanted pregnancy but also, on balance, in reducing the numbers of cancers that would otherwise have occurred. For this reason, in the final summary section (Section 16) we include only post-menopausal hormone therapy as a risk factor contributing to cancers in the UK.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

Table 7 Estimated cases of cancer occurring in women in 2010, and the fraction attributable to hormone exposures

	All cancer cases by type of hormone exposure[a]						
		HRT		Oral contraceptives		Both	
Age (years)	Observed cases	Excess attributable cases	PAF (%)	Excess attributable cases	PAF (%)	Excess attributable cases	PAF (%)
<40	8140	0	0.0	228	2.8	228	2.8
40–49	13 667	384	2.8	−58	−0.4	326	2.4
50–64	41 338	1006	2.4	−1109	−2.6	−103	−0.2
⩾65	92 439	285	0.3	−634	−0.7	−349	−0.4
All ages	155 584	1675	1.1	−1573	−1.0	102	0.1

Abbreviations: HRT = hormone replacement therapy (postmenopausal hormones); PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

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11.
Cancers attributable to infection in the UK in 2010

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The infectious agents that have been identified as definitely or probably carcinogenic to humans (Groups 1 and 2A) in the International Agency for Research on Cancer (IARC) monograph series are shown in Table 1. They include hepatitis B (HBV) and C (HCV) viruses, human papillomaviruses (HPV), human immunodeficiency virus (HIV) and T-lymphotropic virus type-1 (HTLV-1), Epstein – Barr virus (EBV) and human herpesvirus 8 (HHV8), and the bacterium *Helicobacter pylori*.

In addition to these associations, there is substantial evidence for a causative relationship between chronic infection with hepatitis C virus (HCV) and non-Hodgkin lymphoma (NHL), an association that has been the subject of several recent systematic reviews (Gisbert *et al*, 2003; Matsuo *et al*, 2004; dal Maso and Franceschi, 2006).

METHODS

Attributable fractions

For most infections, calculation of the population-attributable fraction (PAF) relies on the classic formula for population-attributable risk (Cole and Macmahon, 1971):

$$\mathrm{PAF} = \frac{p(r-1)}{1+p(r-1)}$$

where r represents the relative risk of exposure, and p its prevalence in the population. The formula results in a proportion that is applied to the total number of incident cases in the UK population, to obtain the number of cases that can theoretically be attributed to the factor in that population (PAF). Its application requires identification of data on the prevalence of the exposure to the 'causative' agents in the UK population, as well as the corresponding relative risks. This method is used to estimate the number of cancers due to HBV, HCV, *H. pylori* and HIV (NHL).

For EBV, the prevalence of relevant infection is hard to define, as the virus infects almost everyone in childhood or adolescence and persists in latent form in B-lymphocytes throughout life. Clearly, agents other than EBV are essential co-factors in carcinogenesis, and EBV-attributable cancers are defined as those in which EBV-DNA can be demonstrated in tumour cells.

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For the oncogenic HPVs, it is generally accepted that almost all cancers of the cervix uteri are the result of infection (Walboomers *et al*, 1999), so the AF is 100%. At other sites, the prevalence of infection in normal subjects is hard to define, so use of the classic Cole – MacMahon formula is inappropriate; as for EBV, the HPV-attributable cancers are defined as those in which HPV-DNA can be demonstrated in tumour cells.

RESULTS

Human papillomavirus

IARC (2005) considers that there is convincing evidence that infection with HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 or 66 can lead to cervical cancer. For HPV 16, the evidence further supports a causal role in cancer of the vulva, vagina, penis, anus, oral cavity and oropharynx and a limited association with cancer of the larynx and periungual skin. HPV 18 also shows a limited association with cancer at most of these sites. Evidence for associations of HPV types of genus beta with squamous-cell carcinoma of the skin is limited for the general population. There is some evidence that HPVs are involved in squamous-cell carcinoma of the conjunctiva, but inadequate evidence for a role of HPVs in cancer of the esophagus, lung, colon, ovary, breast, prostate, urinary bladder, and nasal and sinonasal cavities.

With respect to cancer of the cervix, oncogenic HPV may be detected by PCR in virtually all cases of cervix cancer, and it is generally accepted that the virus is necessary for development of cancer, and that all cases of this cancer can be 'attributed' to infection (Walboomers *et al*, 1999).

With respect to squamous-cell cancers of the vulva and vagina, carcinoma of the penis, and anal cancer, published studies do not allow quantification of relative risk and infection prevalence, because they are generally small in size, and usually do not include comparable measurement of prevalence of infection at these sites in normal subjects. In order to estimate attributable fractions, therefore, approximate estimates of the proportion of cancer cases infected with HPV in various series are used.

The prevalence of HPV in vaginal cancer is about 60 – 65% in studies using PCR methodology (Daling *et al*, 2002; IARC, 2005); an overall HPV prevalence of 63% is assumed. About 20 – 50% of vulvar cancers contain oncogenic HPV DNA (Madeleine *et al*, 1997; Herrero and Munoz, 1999), but only the basaloid and warty type that tends to be associated with vulvar intraepithelial

neoplasia is caused by HPV infection (prevalence 75–100%), and only 2–23% of the keratinizing carcinomas harbour HPV (Trimble *et al*, 1996); an overall HPV prevalence of 40% is assumed. For anal cancer, in a large series of cases from Denmark and Sweden, 95% and 83% of cancers involving the anal canal in women and men, respectively, were positive for oncogenic HPV (Frisch *et al*, 1999), and an AF of 90% is assumed. For penile cancer, HPV DNA was found in 30% of 71 cases of penile cancer from Brazil (Bezerra *et al*, 2001) and in 42% of 148 cases from the USA and Paraguay (Rubin *et al*, 2001); the AF is assumed to be 40%.

HPV has a role in the aetiology of a fraction of cancers of the oral cavity and pharynx (Shah, 1998), although the major risk factors are tobacco and alcohol. A review of more than 5000 tumours of the upper aerodigestive tract (Kreimer *et al*, 2005a) found that prevalence of HPV DNA in specimens from Europe was 16.0% (95% CI, 13.4–18.8) for oral cancers, 28.2% (95% CI, 24.4–32.2) for tumours of the oro-pharynx and 21.3% in squamous cell carcinomas (SCCs) of the larynx. However, HPV may not be of aetiological relevance in all such cases. Van Houten *et al* (2001) found that only 45% of DNA-positive cases showed E6 mRNA expression, indicative of viral activity. Kreimer *et al* (2005b) observed that about 50% of head and neck cancers had a high viral load of HPV, and serologic antibodies to HPV16 virus-like particles and HPV16 E6 and E7 proteins were detected in most of these cases. We assume therefore that 8% oral cancers, 14% oropharyngeal cancers and 10.6% laryngeal cancers are HPV-related.

HPV (any type) is estimated to be responsible for 5088 cancers occurring in the UK in 2010 (1.6% of all cancers), comprising 2691 cervix cancers, 1685 cases of ano-genital cancer and 712 cases of upper aerodigestive tract cancer (Table 2).

Table 1 Major human infection-associated malignancies

Malignancy	Agent (group)
Carcinoma	
Bladder	*Schistosoma haematobium* (blood fluke)
Cervix	HPV (papillomavirus)
Liver	HBV (hepadnavirus)
	HCV (flavivirus)
Bile duct	*Opisthorchis viverrini* (liver fluke)
Nasopharynx	EBV (herpesvirus)
Stomach	*Helicobacter pylori* (bacterium)
Lymphoma	
Adult T-cell	HTLV-I (retrovirus)
Burkitt	EBV (herpesvirus)
Hodgkin	EBV (herpesvirus)
Sarcoma	
Kaposi	HHV8 (herpesvirus)

Abbreviations: EBV = Epstein–Barr virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HHV8 = human herpesvirus 8; HPV = human papillomavirus; HTLV-I = human T-cell lymphotropic virus type I. From Mueller *et al* (2005).

Helicobacter pylori

Helicobacter pylori was classified as being carcinogenic for humans in 1994 (IARC, 1994a). It is considered to be causally associated with both carcinoma of the stomach and gastric lymphoma.

Surveys of *H. pylori* show that prevalence gradually increases with age. Several studies have suggested that this represents a birth-cohort effect, with infection becoming progressively less common in recent generations (Banatvala *et al*, 1993; Kosunen *et al*, 1997; Roosendaal *et al*, 1997). In the UK the most comprehensive data on prevalence derive from the serological surveys of 10 000 serum samples collected in England and Wales in 1986 and 1996 (Vyse *et al*, 2002). Prevalence was related to decade of birth and increased from 4% in those born during the 1980s to 30% in those born before 1940; analysis by decade of birth showed no significant difference between samples collected in 1986 and 1996. Estimated prevalence of active infection varied by region and was highest in London.

We estimated prevalence in the UK population in 2000 from the data provided by Vyse *et al* (2002), assuming that prevalence in Scotland and Northern Ireland was the same as that observed in the North of England (Figure 1).

Gastric carcinoma The most satisfactory evidence on the magnitude of the risk is from prospective studies. Retrospective case–control studies are limited in observing *H. pylori* infection after the development of cancer. *H. pylori* tends to disappear as intestinal metaplasia and atrophy develop, so that prevalence of infection may be seriously under-estimated in cases, even if anti-*H. pylori* antibody is used as an indicator of infection. Several case–control studies nested within cohorts have now been published, in which infection is evaluated in cases and controls before the onset of disease. In a meta-analysis by the Helicobacter and Cancer Collaborative Group (2001), including 12 prospective studies yielding 1228 gastric cancer cases, the OR for the association between *H. pylori* infection and the subsequent development of gastric cancer was 2.36 (95% CI 1.98–2.81). Analysing cancers of the gastric cardia, the most proximal portion of the stomach and non-cardia separately, they found no increase in risk for cardia cancers (OR 0.99), while the overall risk for non-cardia cancers was 2.97 (95% CI 2.34–3.77). The risk varied with the interval

Table 2 Estimated numbers of HPV-related cancers, UK (2010)

	Observed cases		HPV-related		
	Male	Female	Male	Female	Excess attributable cases (PAF)
Upper aerodigestive cancers					
Cervix uteri		2691		2691	2691 (100)
Oral cavity	2284	1421	183	114	296 (8.0)
Oropharynx	981	323	138	45	184 (14.1)
Larynx	1803	386	191	40	232 (10.6)
Anogenital cancers					
Anus	364	621	328	559	887 (90.0)
Vulva		1128		451	451 (40.0)
Vagina		251		157	157 (62.5)
Penis	475		190		190 (40.0)
Total (8 sites)	5907	6821	1030	4058	5088 (40.0)

Abbreviations: HPV = human papillomavirus; PAF = population-attributable fraction (%).

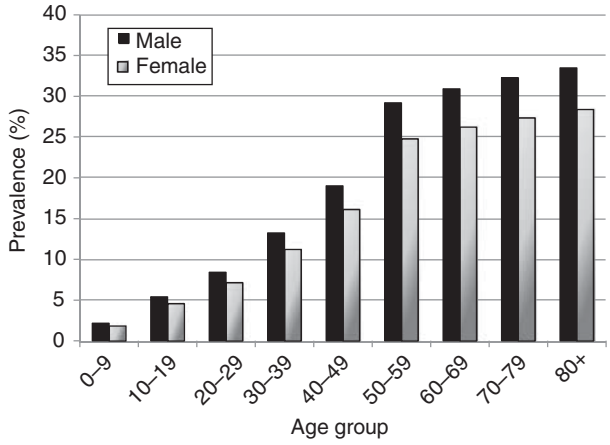

Figure 1 Estimated prevalence of *Helicobacter pylori* in the UK in 2000.

between sample collection and cancer diagnosis (as might be expected, if infection is progressively lost as gastric atrophy develops). The increase in risk was 5.9-fold (95% CI 3.4–10.3) for *H. pylori* positivity 10 years or more prior to diagnosis. The associations were not related to histological type of gastric cancer (intestinal *vs* diffuse) or sex.

The proportion of gastric cancer cases occurring at the cardia, compared with elsewhere in the stomach, can be estimated from cancer registry data from England (2007), and from the results of 11 registries throughout the UK in 1998–2005 (Curado *et al*, 2007). In both sets, a variable proportion of gastric cancer cases (40–65%) are registered without specification of subsite. However, fitting a linear regression model of the proportion of cardia cancers *vs* the proportion of unspecified registrations suggests that mis-specification of site is more or less random. The predicted proportion of cardia cancers (with zero non-specification) is 51.9% in men and 38.9% in women. Age-specific proportions in the UK were estimated based on the distribution by age in England (2007).

With a relative risk of 5.9 and prevalence of infection in 2000 (10 years earlier) as shown in Figure 1, the attributable fraction of non-cardia gastric cancer cases in 2010 is 61% in men and 59% in women. This represents 2231 cases, 29.2% of all stomach cancers in men and 36.0% in women, or 0.7% of all cancers.

Gastric lymphoma One of the two large American cohort studies of *H. pylori* also examined the incidence of gastric NHL and found that these cases showed elevated titres of antibody to *H. pylori* (Parsonnet *et al*, 1994). The relative risk was 6.3 (95% CI 2.0–19.9). Gastric NHL is rather a rare tumour, comprising about 5% of all NHL (Newton *et al*, 1997).

Assuming that 5% of NHL cases in UK are localised to the stomach, there were about 580 new cases in 2010. With a relative risk of 6, and the estimated prevalence of infection in 2000 (Figure 1), 2.8% of NHL cases (327) would be attributable to *H. pylori*.

Epstein–Barr virus

EBV is considered to be a group I carcinogen by IARC (1997), with conclusive evidence with respect to carcinogenicity in Burkitt lymphoma, NHL in immunosuppressed subjects, sino-nasal angiocentric T-cell lymphoma, Hodgkin lymphoma and nasopharyngeal carcinoma. The evidence concerning other cancers for which an association with EBV has been demonstrated (lymphoepithelial carcinomas, gastric adenocarcinoma and smooth muscle tumours in immunosuppressed subjects) was considered to be inconclusive.

EBV and NHL Burkitt lymphoma: Burkitt lymphoma is a rare cancer in UK. There were an estimated 158 new cases in 2010. In North America and Europe, about one-fifth to one-third have demonstrable virus in tumour tissue, or elevated antibody titres to EBV (Lenoir *et al*, 1984; Gutierrez *et al*, 1992). The numbers of EBV-attributable Burkitt lymphoma cases in UK is therefore about 39.

Other NHL: EBV can cause lymphoproliferative diseases in individuals with immune dysfunction (Lenoir and Delecluse, 1989). Lymphomas arising in immunocompromised individuals are relatively rare, except in the case of AIDS, some of which are associated with EBV. The proportion of AIDS-related lymphomas is estimated in the context of HIV-related cancers (below). The proportion of NHLs that occur in immunocompromised individuals, excluding AIDS (hereditary, syndromes, iatrogenic), or are cases of the rare EBV-associated sino-nasal angiocentric T-cell lymphoma, is impossible to estimate. It must be a very small ($<1\%$) fraction of NHLs, so there is no numerical allowance for these cases in the estimates.

EBV and Hodgkin lymphoma Case–control studies generally demonstrate higher titres of anti-EBV antibodies in cases of Hodgkin lymphoma than in controls (Evans and Gutensohn, 1984). In a large prospective study, Mueller *et al* (1989) found that elevated antibody titres precede diagnosis by several years – the actual relative risks (2.6 and 3.7 for IgG and IgA capsid antigens, 4.0 for EBNA and 2.6 for early antigen (diffuse)) and prevalence of raised titres correspond to attributable risks of 30–45%.

Sensitive techniques are able to detect EBV nucleic acids in 25–50% of Hodgkin lymphomas, where it is located in the Reed–Sternberg cells (Weiss *et al*, 1989; Armstrong *et al*, 1992). The association with EBV appears to depend upon age. In the childhood age range about 80% of cases are EBV positive (Weinreb *et al*, 1996), whereas in young adults the proportion is about 15% (Jarrett *et al*, 1991). In older age groups, EBV positivity appears to be relatively high (70–75%) (Jarrett *et al*, 1991; Gledhill *et al*, 1991). In part, this pattern is determined by the frequency of different histological subtypes of Hodgkin lymphoma. The mixed cellularity subtype predominates in childhood, while the nodular sclerosing subtype accounts for the marked peak in young adults. The frequency of EBV positivity is much greater (5–15-fold) in mixed cellularity than in nodular sclerosing Hodgkin lymphoma. Nevertheless, it seems that, even allowing for cell type, age (more childhood cases are EBV positive) and level of socio-economic development are independent predictors of the association (Glaser *et al*, 1997). For the purposes of estimation, the attributable fraction at ages 0–14 is taken to be 80%, 20% at ages 15–44, and 70% at ages >45. Of the UK total of 1709 new cases in 2010, 773, or 45.2% of the total, are estimated to be EBV related.

EBV and nasopharyngeal carcinoma The involvement of EBV in nasopharyngeal cancer (NPC) appears to be with undifferentiated carcinomas of the nasopharynx. In low-risk areas, about 10–25% of NPC is of type 1 (keratinising), which is less often infected. It is assumed that 90% of cases of the estimated 446 NPC cases occurring in the UK in 2010 are infected, a total of 401 cases, or 5.8% of all cancers or of the oral cavity and pharynx.

Summary: EBV EBV is the third most important cancer-causing infection in the UK, responsible for an estimated 1213 cases in 2010 (0.4% of cancers), comprising 773 cases of Hodgkin disease, 401 nasopharyngeal cancers and 39 Burkitt lymphoma cases.

Hepatitis viruses

The role of chronic infection with the viruses of hepatitis B and C in the aetiology of liver cancer is well established (IARC, 1994b). More recently, on the basis of a substantial number of case–control and cohort studies, an association between HCV and NHL

has been demonstrated (Gisbert *et al*, 2003; Matsuo *et al*, 2004; dal Maso and Franceschi, 2006).

Prevalence of hepatitis B surface antigen (HBsAg) positivity and HCV antibodies in the serum of the general population of UK is unknown, as no true random survey results exist. Age-specific prevalence is published for first-time blood donors (subjects found to be positive are obviously excluded from becoming repeat donors), although these are healthy individuals, with a prevalence much lower than the average in the population. An estimate of the prevalence of hepatitis C in adults (aged 15–59), based on a model incorporating all relevant samples, was made for England in 2003 (HPA, 2006); this estimate had not been updated by the end of 2010. These data were assumed for UK, with an estimate of prevalence at ages >60 based on sero-surveys of laboratory samples in England and Wales in the 1990s (Balogun *et al*, 2002).

For hepatitis B, the estimated population prevalence, based on sero-surveys of laboratory samples in England and Wales in 1996 (Gay *et al*, 1999), was used to adjust the observed age–sex-specific prevalence data from blood donors in England in 1995–2008 (HPA, 2009), and further adjusted upwards, to allow for the rather higher prevalence in blood donors in UK, compared with those in England (HPA, 2009).

The estimated prevalences are shown in Figure 2.

HBV and HCV and liver cancer The IARC Monograph (1994b) summarises the results of some 15 cohort studies and 65 case–control studies worldwide, examining the association between seropositivity for HBsAg, indicating chronic infection with HBV, and the risk of hepatocellular carcinoma. The cohort studies yield relative risk estimates of 5.3–148, while the majority of case–control studies yield relative risk estimates between 3 and 30. Some of these studies were able to address potential confounding by aflatoxin, hepatitis C infection, alcohol drinking and tobacco consumption, and the IARC Monograph (1994b) overall evaluation assessed HBV as carcinogenic to humans. A recent meta-analysis by Cho *et al* (2011) found an odds ratio for mono-infection with a HBV of 13.5 for all 47 studies included, and 20.3 for the four studies in low-prevalence areas (such as UK). A relative risk of 20 is assumed in the current analysis.

The magnitude of the risk of liver cancer associated with chronic 'infection' with HCV became evident as the results of studies using second- and third-generation anti-HCV ELISA tests or detection of HCV RNA (by reverse transcription polymerase chain reaction) became available. In a meta-analysis of studies, Donato *et al* (1998) estimated the relative risk in HCV antibody-positive subjects who were HBsAg negative as 17.3. The more recent meta-analysis by Cho *et al* (2011) found an odds ratio of 23.8 in seven studies from low-prevalence countries. We assume a relative risk of 20 for HCV infection.

Assuming relative risks of chronic infection by these viruses of 20, and that joint infection by both HBV and HCV is very rare, we estimate the fraction of liver cancers attributable to the two viruses to be just 15.9% (567 of 3568 cases). This represents 0.18% of cancers in the UK in 2010.

HCV and NHL At least three meta-analyses (Gisbert *et al*, 2003; Matsuo *et al*, 2004; dal Maso and Franceschi, 2006) have been conducted to evaluate the strength of the relationship between HCV and NHL. The most recent of these (dal Maso and Franceschi, 2006) gives a rather lower estimate for the relative risk (2.5) than the earlier studies. However, as it considered all NHL (not just B-cell neoplasms) and took into account differences in age between cases and controls, it is probably the most valid estimate. A recent report pooling the results of seven case–control studies (de Sanjose *et al*, 2008) gave a similar result (odds ratio of 1.8). Using the value of 2.5, and the estimated prevalence of HCV infection in the UK in 2010 (Figure 2), one can estimate the fraction of NHL attributable to HCV as just 0.5% (53 of 11 602 cases).

HIV and HHV8

In 1996, an IARC working group concluded that HIV was carcinogenic to humans, an assessment based on the strong link between infection with the virus and two cancers: Kaposi sarcoma (KS) and NHL (IARC, 1996). These two diseases, along with cancer of the cervix, are considered to be 'AIDS-defining conditions' – that is, a HIV-positive subject with these cancers is considered to have AIDS (CDC, 1992). Subsequently, increased risks for several other cancers have been reported. The most convincing data come from a follow-up of cohorts of HIV-positive subjects, comparing the occurrence of cancers with the number expected in the general population. Such studies suggest increased risks of several cancers, especially Hodgkin disease, anal cancer, seminoma, myeloma, and, less certainly, cancers of the lip, brain and lung (Goedert *et al*, 1998; Frisch *et al*, 2001; Grulich *et al*, 2002).

The evaluation by IARC (1997) considered that the evidence for a role of KSHV/HHV8 in the causation of KS was 'compelling, but as yet limited'. However, it is now generally accepted to be the principal cause of the disease (Boshoff and Weiss, 2001). The effect of HIV is probably through immunosuppression – allowing HHV-8 to escape control and thereby increasing viral load, for example.

HIV/HHV8 and KS Prior to the epidemic of HIV/AIDS, KS was a very rare cancer in the UK. Grulich *et al* (1992) calculated the incidence in England and Wales in 1971–80 as 0.14 per million (same in males and females).

Because of the enormous increase in risk in subjects infected with HIV (1000–5000 times the risk in the general population (Serraino *et al*, 1997)), the increasing incidence of KS was the first obvious manifestation of the AIDS epidemic. Before 1990, up to a third of AIDS cases developed KS at some point (Hoover *et al*, 1993; Lundgren *et al*, 1995). The introduction of antiretroviral therapy (HAART) for treating HIV in adults has caused a decline in the incidence of KS in Western countries (International Collaboration on HIV and Cancer, 2000); in the USA, for example, the incidence of KS in men aged 20–54 in the cancer registries of the SEER program fell from 17.2 per 10^5 in 1990–1 to 2.4 in 2000–2001 (Ries *et al*, 2004).

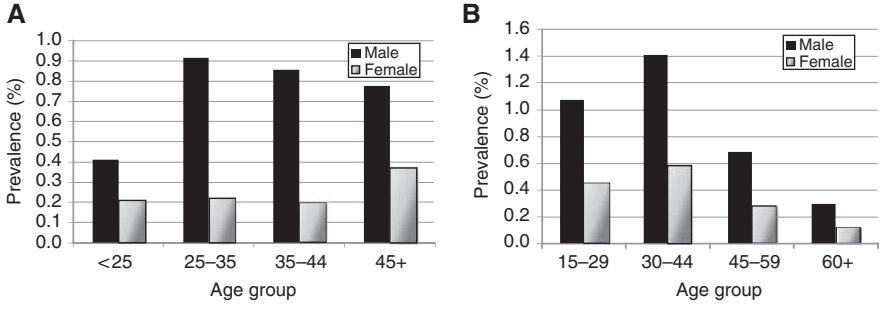

Figure 2 Estimated age- and sex-specific prevalence of carriers of (**A**) HBsAG and (**B**) anti-HCV antibodies in the UK.

The estimated number of KS cases in UK in 2010 is 172. All might be ascribed to infection with HHV-8. Based on the rates in the pre-AIDS era (Grulich *et al*, 1992), the number of cases expected was 10. The difference (162 cases) is considered to be attributable to HIV infection, while all cases of KS are attributable to infection with HHV-8.

HIV and NHL The increased frequency of NHL in AIDS was noted in 1982 (Ziegler *et al*, 1982). Since then, the elevated risk has been confirmed in studies in the United States and Europe (Casabona *et al*, 1991; Beral *et al*, 1991). About 3% of AIDS cases present with a lymphoma, but lymphomas may occur in up to 10% of AIDS cases at some point. Almost all lymphomas in AIDS cases are of B-cell type. The cohort study of Coté *et al*. (1997) estimated the excess risk in AIDS to be about 160 times that in HIV-negative subjects. Risk is highest for high-grade lymphomas; especially diffuse immunoblastic (relative risk = 630) and undifferentiated Burkitt lymphomas (relative risk = 220). Extra nodal lymphomas are more common in AIDS than usual (Beral *et al*, 1991), although it is probably because of the great excess of CNS lymphomas (15-fold increase); other extra nodal lymphomas are not in excess (Coté *et al*. 1997). Males are more commonly affected – but it could be that this is simply because of risk-group differences.

EBV is present in two-thirds of AIDS-related lymphomas (Hamilton–Dutoit *et al*, 1993) and may have an important role in lymphomagenesis (IARC, 1996, 1997). The frequency varies by lymphoma type – it is found in almost all CNS lymphomas, 70–80% of immunoblastic lymphomas and 30–40% of small-cell/Burkitt-type lymphomas.

The availability of HAART in recent years has resulted in a decline in the risk of NHL in HIV-infected individuals; it fell from 0.62% per year in the pre-HAART era (1992–1996) to 0.36% when HAART regimens were widely available (1996–1999) (International Collaboration on HIV and Cancer, 2000). In the USA, cohort studies suggest that the relative risk of NHL in HIV-positive subjects since the introduction of HAART is about 6.5 (Hessol *et al*, 2004; Engels *et al*, 2008), and this figure is used to estimate the attributable fraction.

The overall prevalence of HIV infection in the UK in 2009 was estimated to be 2.89 per 1000 in men aged 15–59 and 1.46 per 1000 in women (HPA, 2010). Prevalence in childhood and those over 60 is much lower: 0.09 and 0.46 per 1000, respectively (HPA, 2010; UK CGHSS, 2006).

Based on these estimated prevalences, and a relative risk of 6.5, only 52 cases of NHL in men and 16 in women (69 total) would have been attributable to HIV in 2010. The numbers seem small, but they are broadly in line with the numbers of cases expected based on observed incidence rates of NHL in HIV-positive subjects in recent years – for example, 1.8 per 1000 in the Swiss cohort in 2002–6 (Polesel *et al*, 2008) and 0.97 in three US states in 1996–2002 (Engels *et al*, 2008). With these rates, 120 cases of NHL would have occurred in HIV-positive subjects in the UK, compared with 11 expected, an excess of 109.

HIV and other cancers *Hodgkin lymphoma*: Several prospective studies suggest that the risk of Hodgkin lymphoma is increased some 10-fold in HIV-infected subjects (Goedert *et al*, 1998; dal Maso *et al*, 2001; Grulich *et al*, 2002). Case series document unusually aggressive disease, including a higher frequency of the unfavourable histological subtypes (mixed cellularity and lymphocyte depleted), advanced stages and poor therapeutic response compared with the behaviour of HD outside of the HIV setting. It is not clear whether most or all of these cases of Hodgkin lymphoma are related to EBV, all of which have already been attributed to infection with this virus. A separate calculation of HIV-attributable cases has not been carried out.

HPV-associated cancers: HPV-associated malignancies – most notably cancer of the cervix uteri and anal cancers – occur frequently in patients with HIV infection and AIDS (Frisch *et al*, 2000). In part, this may simply reflect the lifestyle factors associated with both infections – HIV-positive individuals are more likely to be infected by HPV. On the other hand, HIV may alter the natural history of HPV-associated oncogenesis through loss of immune control, facilitating infection with HPV or enhancing its persistence in cells and therefore increasing the development of squamous intraepithelial lesions (SIL). These cancers have already been attributed to infection with HPV.

HIV infection has been found to be associated with an increased risk of conjunctival SCC in follow-up of cohorts of HIV-positive subjects in the USA (Goedert and Coté, 1995; Frisch *et al*, 2001). With a relative risk of 10, about 1% of cases might be attributable to HIV, given the prevalence of infection in the UK. As only 23 cases of conjunctival cancer were registered in England in 2007, the number of attributable cases is ignored.

Summary: HIV-related cancer In all, 172 cases of KS and 69 cases of NHL were caused by HIV and/or HHV-8 in 2010. Of the KS cases, 162 are attributed to infection with HIV.

Human T lymphotropic virus

The evidence for the causal role of HTLV-1 in acute T-cell leukaemia/lymphoma (ATL) is compelling (IARC, 1996). Prevalence of HTLV infection in UK is available for first-time blood donors (HPA, 2009). Overall, it is 4.7 per 100 000 in men and 10.7 per 100 000 in women, strongly increasing with age. Based on the recorded incidence of ATL (ICD 91.5) in England in 2007, 25 cases would have been expected in the UK population.

Summary

Table 3 summarises the quantification of cancers attributable to infections in the UK in 2010. The estimate is 3925 (2.5% of all cancers) in men and 5820 (3.7% of all cancers) in women. Of the total of 9745, the infectious agents making the largest contribution are HPV (5088 cases, 1.6% of all cancers), *H. pylori* (2559 cases, 0.8%) and EBV (1213 cases, 0.4%).

The cancers for which an infectious aetiology is most important are cervix uteri (2691 cases in 2010), stomach (2231) and the upper aerodigestive tract (mouth, pharynx and larynx – 1113 cases).

DISCUSSION

Worldwide, 17.8% of all cancers are attributable to infections (Parkin, 2006), with a higher percentage in developing countries (26.3%), and an average of 7.7% in developed countries reflecting the higher prevalence of infection with the major causative agents (hepatitis viruses, HPV, *H. pylori*, HIV). The proportion in the UK is around half of the average for developed countries, and very similar to the estimate (3.5%) for the Netherlands (van Lier *et al*, 2008).

The results are dependent on the assumptions made about relative risk, and accuracy of the estimates of prevalence of infection in the general population. For some of the associations – especially in relation to HPV and anogenital cancers – the estimate of attributable fraction was based on the proportion of tumours in which the virus (as viral DNA) could be detected. The reason is mainly that prevalence of infection in the same tissues of normal individuals is usually unknown. This may overestimate attributable fractions, by including some cancer cases in which the presence of the virus was coincidental, without, for example, expressing viral oncoproteins. The estimate of HPV-attributable cancers of the oral cavity, pharynx and larynx attempts

Table 3 Estimated numbers of cancers attributable to different infectious agents, UK 2010

	Estimated number of cancer cases by infectious agent						
Cancer site	**HPV**	***H. pylori***	**EBV**	**HBV and HCV**	**HIV and KSHV**	**HTLV**	**Excess attributable cases (PAF)**
Males							
Oral cavity and pharynx	321		241				562 (0.35)
Larynx	191						191 (0.12)
Stomach		1304					1304 (0.82)
Anus	328						328 (0.21)
Liver				446			446 (0.28)
Kaposi					147		147 (0.09)
External genitalia	190						190 (0.12)
Non-Hodgkin lymphoma		182	31	38	52	12	316 (0.20)
Hodgkin lymphoma			442				442 (0.28)
Total	1030	1486	713	484	200	12	3925
% of all cancer[a]	0.65	0.94	0.45	0.31	0.13	0.01	2.5%
Females							
Oral cavity and pharynx	159		160				319 (0.21)
Larynx	40						40 (0.03)
Stomach		927					927 (0.60)
Anus	559						559 (0.36)
Liver				121			121 (0.08)
Kaposi					25		25 (0.02)
Cervix uteri	2691						2691 (1.73)
External genitalia	608						608 (0.39)
Non-Hodgkin lymphoma		145	9	14	16	13	197 (0.13)
Hodgkin lymphoma			331				331 (0.21)
Total	4058	1072	501	135	41	13	5820
% of all cancers[a]	2.61	0.69	0.32	0.09	0.03	0.01	3.7%
Persons							
Oral cavity and pharynx	480		401				881 (0.28)
Larynx	232						232 (0.07)
Stomach		2231					2231 (0.71)
Anus	887						887 (0.28)
Liver				567			567 (0.18)
Kaposi					172		172 (0.05)
Cervix uteri	2691						2691 (0.86)
External genitalia	798						798 (0.25)
Non-Hodgkin lymphoma		327	39	53	69	24	513 (0.16)
Hodgkin disease			773				773 (0.25)
Total	5088	2559	1213	619	241	24	9745
% of all cancers[a]	1.62	0.81	0.39	0.20	0.08	0.01	3.1%

Abbreviations: EBV = Epstein–Barr virus; *H. pylori* = *Helicobacter pylori*; HBV and HCV = hepatitis B and C viruses; HIV and KSHV = human immunodeficiency virus and human herpesvirus 8/Kaposi sarcoma; HPV = human papillomaviruses; HTLV = human T lymphotropic virus type 1; PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

to compensate for this, by estimating the number of aetiologically relevant infections (expressing E6 and E7 proteins, for example).

The estimate of infection-attributable cancer is a conservative one. Some other associations between infections and human cancers, for which there is reasonable evidence for causality, have not been taken into account. EBV has been detected in several types of cancer, other than those attributed to it in this analysis, with the most suggestive evidence implicating it in the aetiology of gastric cancer (Takada, 2002; Herrmann and Niedobitek, 2003). *Chlamydia trachomatis* infection has been shown to increase the risk of developing SCC of the cervix (Smith *et al*, 2004). In any case, no case of cancer has been attributed to more than one infectious agent, so that the numbers of infection-attributable cases can be calculated for different populations. Thus, for example, the risk of cancer of the cervix uteri may be increased by HIV infection (Frisch *et al*, 2001) as well as *C. trachomatis*, but as all cases are attributed to HPV, none are included as HIV-related cancers. In addition, the estimates of relative risk for those associations accepted as causal that have been used in the calculations are deliberately modest. For example, the relative risk of liver cancer due to infection with hepatitis B is based on measurement of serum HBsAg. However, viral DNA can be found in many liver cancers without evidence of infection based on HBs antigenaemia or antibody to HCV (Paterlini *et al*, 1990). The relative risk of non-cardia gastric cancer in relation to infection with *H. pylori* that was used (5.9) may also be too modest; more sensitive techniques for estimating the presence of *H. pylori* (for example, by detecting bacterial DNA) have much higher relative risks (Mitchell *et al*, 2008), but as the prevalence estimates are based on the presence of anti-*H. pylori* antibody, we use the relative risk estimates based on the same techniques. Accepting that all non-cardia gastric cancers are caused by infection (*H. pylori* and/or EBV) as well as 10% of NHL are caused by HCV (independent of HIV) would not, however, greatly change the overall estimate.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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12.
Cancers in 2010 attributable to ionising radiation exposure in the UK

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The hazards of exposure to some types of ionising radiation were recognized shortly after the discovery of the X-ray in 1895: by 1902 the first radiation-associated cancer was reported in a skin sore and, within a few years, a large number of such skin cancers had been observed. The first report of leukaemia in radiation workers appeared in 1911. Since then there have been many reviews of the health effects of ionising radiation, most notably in the reports of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) (see, for example, UNSCEAR, 2006). The International Agency for Research on Cancer's Monographs on the Carcinogenic Risk to Humans also reviewed the effects of ionising radiation, both in the form of exposure to external γ or X-rays (IARC, 2000) and as α and β particles from internalised radionuclides (IARC, 2001), and all these types of radiation were classified as carcinogenic to humans.

The UK Health Protection Agency (HPA) reviews exposure to ionising radiation among the population of the UK from sources of both natural and artificial origin. A summary of their most recent evaluation is shown in Table 1. Quantitatively, radon was the most important source and contributed about half the total, followed by other sources of natural radiation (cosmic, gamma and internal) contributing about 35%, and medical radiation (which included radiation received during diagnostic procedures, but excluded therapeutic irradiation) at 15%.

In the present report we have estimated the number of cancers attributable to ionising radiation in the population of the UK in 2010. We have considered the sources of exposure included in the HPA's review and, in addition, we have estimated the number of second cancers associated with therapeutic radiation.

METHODS AND RESULTS

Radon

The chemically inert gas radon-222 arises from the uranium-238 present throughout the earth's crust and is a ubiquitous air pollutant. If inhaled, radon itself is mostly exhaled immediately, but its short-lived progeny are solid and tend to deposit on the bronchial epithelium, where they may expose sensitive cells to alpha irradiation. Radon has been classified as carcinogenic to humans (IARC, 2001). Outdoor radon concentrations in the UK are low, but indoor concentrations are higher, especially in houses and other small buildings, and indoor radon at home is the largest source of exposure to natural ionising radiation. Gray *et al* (2009) used information on the distribution of measured radon gas concentrations in UK homes from a nationwide representative survey (Wrixon *et al*, 1988) together with estimates of the percentage increase in the risk of lung cancer per 100 Bq m^{-3} increase in the long-term average radon concentration at home, in people with well-documented smoking histories (Darby *et al*, 2005, 2006) to estimate the burden of fatal radon-induced lung cancer in the UK in 2006.

Table 2a shows the results from Gray *et al* (2009). Table 2b shows the estimated number of cases of lung cancer caused by radon in 2010, based on the number of deaths in Table 2a and the total number of deaths from lung cancer in the UK in 2006 (by age group and sex). It assumes that the fraction of lung cancer cases due to radon is the same as the fraction of lung cancer deaths (that is, that the risk of death from lung cancer in lung cancer patients is the same in radon-induced cases and other cases).

The 1376 cases of lung cancer attributable to residential radon represent 3.4% of the total number of lung cancer cases estimated to have occurred in the UK in 2010 (or 0.4% of all new cancers in 2010). Of these, 57% of the radon-induced cancers occurred in individuals aged 55 – 74 years. Most of the remainder occurred in individuals aged over 75, with 3% at ages <55 (Table 2b). Of the radon-induced lung cancers, 55% were in men. The vast majority of radon-induced lung cancers are caused jointly by radon and active smoking in the sense that the lung cancer could have been avoided by avoiding either exposure; radon alone was estimated to be responsible for only 157 deaths in 2006 (0.5% of lung cancer deaths) (Gray *et al*, 2009). This is equivalent to 182 cases in 2010 (0.45% of lung cancer cases, 0.06% of all cancers).

Medical exposures

Medical exposures to ionising radiation include those for diagnostic (X-rays and nuclear medicine) and therapeutic purposes (radiotherapy). Although we are concerned here with

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Table 1 Summary of the Health Protection Agency's review of the annual exposure of the UK population from all sources of ionising radiation

Source	Average annual dose (μSv)[a]	Total (%)
Natural		
Cosmic	330	12
Gamma	350	13
Internal	250	9.5
Radon[b]	1300	50
Artificial		
Medical (diagnostic only)	410	15
Occupational	6	0.2
Fallout	6	0.2
Discharges	0.9	<0.1
Consumer products	0.1	<0.1
Total (rounded)	2700	100

Based on Hughes *et al* (2005). [a]Throughout this report the term 'dose' is used to indicate 'committed effective dose' unless otherwise specified. 'committed effective dose' is derived by considering the absorbed dose (in joules per kilogram) and then multiplying it by a weighting factor to take account of the type of radiation involved. For sources that do not involve a uniform dose to the whole body, the doses to specific organs are further weighted according to factors recommended by the International Commission on Radiological Protection (ICRP, 2007). [b]Assuming that living for a year in a home with a long-term average radon gas concentration of 20 Bq m^{-3} gives rise to a dose of about 1000 μSv.

Table 2a Lung cancer deaths in 2006 attributable to residential radon exposure in the UK

	Number of deaths		
Age (years)	Males	Females	Total
<35	≈0.5	≈0.5	1
35–54	35	29	64
55–74	312	216	528
⩾75	290	227	517
All ages	637	473	1110

From Gray *et al* (2009).

evaluating the negative consequences – in terms of the number of cancer cases likely to be induced by such radiation – these should be set in the context of the substantial benefits accruing through the management of individual patients.

Diagnostic X-rays Diagnostic X-rays are the largest man-made source of radiation exposure to the general population, contributing about 15% of the total annual dose in the UK from all sources (see Table 1). Although diagnostic X-rays provide great benefits, their use involves a small risk of developing cancer. Berrington de González and Darby (2004) estimated the extent of this risk on the basis of the annual number of diagnostic X-rays undertaken in the UK. They combined data on the frequency of diagnostic X-ray use in 1991–1996, the estimated radiation doses from X-rays to individual body organs, and risk models (based mainly on the Japanese atomic bomb survivors, see UNSCEAR, 2000), with population-based cancer incidence rates from the UK in 1988–92. They estimated the attributable fraction of cases for nine types of cancer, and for all radiation-inducible cancers (i.e., all cancers except lymphomas, multiple myeloma, and chronic lymphocytic leukaemia (CLL)). In their analysis, the cumulative risks (and attributable fractions) were calculated up to age 75. But, under the assumption that radiation-induced cancer risks persist indefinitely, the same population-attributable fractions (PAFs) should be applicable to cases occurring after age 75.

Table 2b Estimated lung cancer cases in 2010 attributable to residential radon in the UK by age and sex

	Number of cases		
Age (years)	Males	Females	Total number (%)
<35	0	1	1 (<0.1)
35–54	20	21	41 (3)
55–74	436	342	778 (57)
⩾75	302	254	556 (40)
All ages	759	618	1376 (100)

Applying the PAFs calculated on the basis of radiation exposure in the mid-1990s to the cancers diagnosed in the UK in 2010 (Table 3) suggests that some 1861 cases, or 0.6% of all cancers, were caused by diagnostic radiation.

Nuclear medicine Small amounts of radiation are received through administration of radio-isotopes for diagnostic or therapeutic purposes. Three surveys of the frequency of different nuclear medicine procedures in the UK and the annual collective dose arising from them have been carried out by the HPA. Based on the most recent survey, which was carried out in 2003–4, the estimated total annual collective dose from diagnostic nuclear medicine procedures was 1620 man Sv, which was approximately 32% higher than at the time of the second survey in 1989, and 67% higher than at the time of the first survey in 1982 (Hart and Wall, 2005). The 2003–4 survey was the first to consider doses from therapeutic nuclear medicine procedures, and the estimated annual collective dose to the UK population from treatment of the three commonest disorders (thyroid carcinoma, thyrotoxicosis and non-toxic goitre) was 742 man Sv. The procedures with the largest contributions to estimated collective dose (>50 man Sv) in 2003–4 are shown in Table 4.

The doses to different organs of the body can be estimated on the basis of the total administered activity for different procedures and conversion factors using estimates of the dose to different organs per unit activity administered. The estimates were taken from publications of the International Commission on Radiological Protection (ICRP, 1988, 1998). Thus, for example, the effective dose of $^{99}Tc^{m}$ phosphates is 5.7×10^{-3} mSv MBq^{-1}, while the dose to the bladder is 4.8×10^{-2} mSv MBq^{-1} (in adults). We may therefore estimate the annual collective bladder dose in UK in 2003–4 as $601 \times (0.048/0.0057)$ or 5061 man Sv.

Organ-specific dose estimates were prepared for 2003–4, 1989 and 1982, with linear interpolation for the intervening years. For years prior to 1982, we assumed the same organ-specific dose profile as in 1982, with a linear diminution in exposure back to zero in 1950, the period around which diagnostic radio isotopes were coming into medical use in UK. For the years 2005–10, we assumed the same organ-specific dose profile as in 2003–4, with the same linear change in exposure as observed in the period 1989–2003/4.

Figure 1 shows the estimated annual collective dose for five specific organs and also the corresponding effective dose to the whole body. These collective doses for the whole population have been converted to average doses for individuals in each age and sex group in the population by multiplying the collective doses by weights proportional to the distribution of exposure in the different age and sex groups, and then dividing by the number of people in the appropriate population at risk. The age and sex distribution of exposures to radioactive isotopes in nuclear medicine is not known; therefore, as a proxy, we assume that it is proportional to the distribution of new cases of cancer in the relevant time period. This is because most investigations occur in the context of chronic disorders (including, very often, suspected

Table 3 Estimated cancer cases in the UK in 2010 by caused by diagnostic radiation

	Males					Females				
	Cumulative risk at ages 0–74 (%)[a]			Number of cases in 2010 at all ages		Cumulative risk at ages 0–74 (%)[a]			Number of cases in 2010 at all ages	
Cancer	Radiation induced	Population	PAF (%)	Observed cases	Excess attributable cases	Radiation induced	Population	PAF (%)	Observed cases	Excess attributable cases
Oesophagus	0.002	0.67	0.3	5713	17	0.002	0.33	0.6	2819	17
Stomach	0.006	1.33	0.5	4467	20	0.005	0.55	0.9	2577	23
Colon-rectum	0.014	1.56	0.9	22 127	199	0.026	1.45	1.8	17 787	319
Liver	0.001	0.18	0.6	2270	13	0.001	0.09	1.1	1298	14
Lung	0.007	5.50	0.1	22 273	28	0.013	2.46	0.5	18 132	96
Female breast	—	—	—	0	0	0.009	6.77	0.1	48 385	62
Bladder	0.034	1.70	2.0	6713	134	0.009	0.56	1.7	2572	43
Thyroid	<0.001	0.06	0.4	602	2	0.001	0.15	0.8	1776	14
Leukaemia (excluding CLL)	0.008	0.60	1.3	3002	40	0.008	0.42	1.9	2182	42
All above	0.072	11.60	0.6	67 167	453	0.074	12.77	0.6	97 528	630
Other radiation-inducible	0.051	8.80	0.6	79 828	462	0.052	8.06	0.6	48 994	316
All cancers[b]	—	—	0.6	158 667	915	—	—	0.6	155 584	946

Abbreviations: CLL = chronic lymphocytic leukaemia; PAF = population-attributable fraction. [a]Cumulative risks, based on exposures in 1991–6, from Berrington de González and Darby (2004). [b]Excluding non-melanoma skin cancer.

Table 4 Nuclear medicine procedures and estimated radiation doses

	Isotope		Average dose per procedure (mSv)	Annual collective dose 2003–4 (man Sv)
Diagnostic				
Bone scan	$^{99}Tc^{m}$	Phosphates	3.0	601
Myocardium	^{201}Tl	Thallous chloride	12.9	209
Myocardium	$^{99}Tc^{m}$	Tetrofosmin	3.1	196
Myocardium	$^{99}Tc^{m}$	Sestamibi	3.7	92
Lung perfusion	$^{99}Tc^{m}$	MAA	0.9	85
Tumours (PET)	^{18}F	FDG	7.0	83
Therapeutic				
Thyroid carcinoma	^{131}I	Iodide	259.0[a]	437
Thyrotoxicosis and goiter	^{131}I	Iodide	29.0[a]	305

Abbreviations: mSv = milli-Sievert; man Sv = man-Sievert. Based on Hart and Wall (2005). [a]Excludes dose to the thyroid.

cancer). The populations in 5-year periods were taken to be equivalent to the census at the mid-year.

Figure 2 shows the estimated average individual effective dose to the whole body, in mSv, in 1982 and 2003–4 for males and females combined.

As we wish to estimate the effect of these estimated annual doses on cancer incidence in 2010, we estimated cumulative dose for specific age groups in 2005, thereby assuming a minimum 5-year latency between exposure and effect, as in BEIR VII (NRC, 2006). Cumulative exposures are small: <1 mSv before age 60, for example, and only about 6.5 mSv (males) and 4 mSv (females) by age 90. To estimate the effects of such radiation for cancers other than leukaemia, we used the cancer risk estimates, expressed as excess relative risks (ERRs) per Sv, from the report of UNSCEAR (2006) as summarised in Table 5.

The ERRs in 2005, together with the estimated doses, were applied to the observed numbers of solid cancer cases in 2010, to obtain the attributable cancers. The total was small – only about 4 excess cases in each sex.

For leukaemia, the relationship between risk and exposure is more complex, as ERR depends not only on dose but also on age at exposure, and time since exposure, and varies by sex. The BEIR

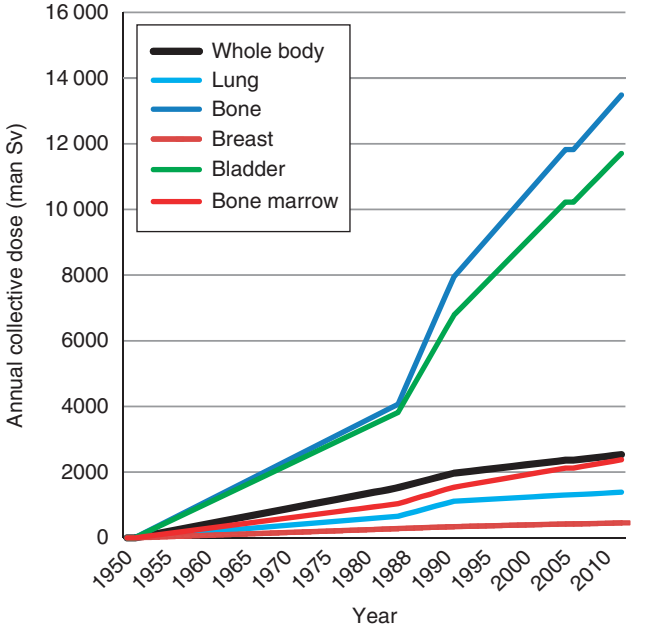

Figure 1 Estimated annual collective doses from nuclear medicine, for five specific organs and for the whole body. The estimate for the whole body is a weighted average of the estimates for specific organs, using the tissue-weighting factors recommended by the ICRP. These were chosen to represent approximately the relative contributions from different organs to the total number of radiation-induced cancers that would arise following uniform irradiation of the whole body (ICRP, 2007).

VII report (NRC, 2006) used a model that expressed ERR as a linear-quadratic function of dose, with allowance for dependencies on sex, age at exposure and time since exposure. The preferred model took the form:

$$\mathrm{ERR} = \beta D(1+\theta D)\exp[\gamma e^{*} + \delta \log(t/25) + \phi e^{*}\log(t/25)]$$

where D is the dose (Sv), t is the time since exposure (years), $e^{*} = (e-30)/10$ for $e<30$, and $=0$ for $e \geqslant 30$, where e is age at exposure in years; $\beta = 1.1$ for males, 1.2 for females; $\gamma = -0.40$ per decade (of age at exposure); $\delta = -0.48$; $\phi = 0.42$; and $\theta = 0.87$.

The model is valid only for the period $\geqslant 5$ years following exposure. Therefore, the formula is used to calculate ERR in each age group, assuming annual doses estimated as described above, starting at those aged 5–9 years in 2010, who would have been first exposed at a mean age of 2.5. The BEIR VII committee (NRC, 2006) dealt with recent exposures by assuming that the excess absolute risk in the period 2–5 years following exposure is equal to that observed 5 years after exposure. Therefore, for the youngest age group (0–4 years), we derived the ERR by assuming that the excess absolute risk was the same as that for children aged 5–9 years who had been exposed at (mean) age 2.5. As exposures are assumed to have been occurring since 1950, we assume that the relative risks in each 5-year age group are multiplicative. That is, the relative risk in children aged 10–14 years in 2010 is the product of that in children exposed for 5 years at (mean) age 7.5 and that in children exposed for 10 years at (mean) age 2.5. As in the BEIR VII report (NRC, 2006), we assumed that the risk of CLL is not influenced by exposure to radiation, so the estimated ERRs were applied to the number of leukaemia cases in the UK, excluding CLL. The proportions of CLL cases among all leukaemia were taken from the published data for England for 2007 (ONS, 2010). We estimate that 7.7 cases of leukaemia in males (0.17% of all leukaemia) and 4.5 in females (0.14% of leukaemia cases) might be attributable to exposures received through nuclear medicine.

Adding the solid cancers and leukaemia cases, the total estimate for cancers attributable to radiation received through nuclear medicine exposures in 2010 is 11.5 in males (0.007% of all cancers) and 7.9 cancers in females (0.005% of all cancers).

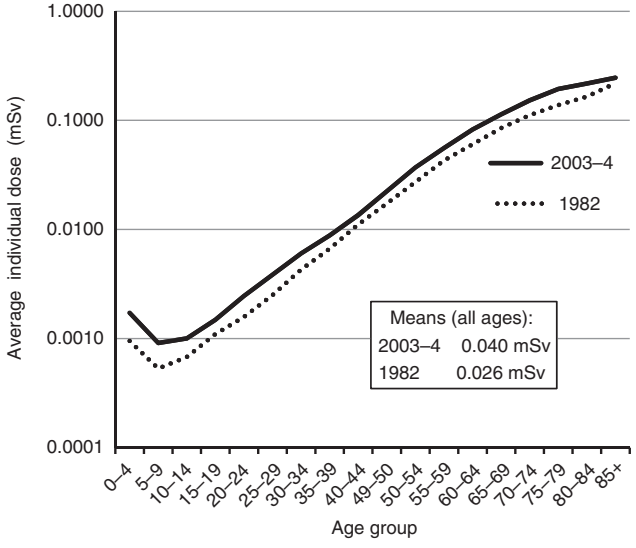

Figure 2 Average individual effective dose to the whole body (mSv), from nuclear medicine practice, 1982 and 2003–4, males and females combined.

Therapeutic radiation Around 3% of the UK population are cancer survivors, with the total number now around 2 million and increasing by 3% per annum (Maddams *et al*, 2009). Many cancer survivors have received radiotherapy, and such treatment usually involves some incidental irradiation of the surrounding normal tissues, thus increasing the risk of a radiation-associated second cancer. Up until now, estimates of the radiation exposure of the UK population have not included exposure from radiotherapy, and the total number of cancers in the UK population associated with past radiation exposure from radiotherapy has not been assessed previously.

Maddams *et al* (2011) have prepared estimates of the cancer burden in the UK in 2007 due to radiotherapy. The method used was based on estimates of the numbers of cancer survivors in the UK at the beginning of 2007 (by cancer site, sex, age and time since diagnosis), the proportion that had received treatment by radiotherapy, and the relative risk of a second cancer associated with previous radiotherapy (from the United States Surveillance Epidemiology and End Results (SEER) programme (Curtis *et al*, 2006)). The methodology for preparing estimates of the number of cancer survivors for England is described in Maddams *et al* (2009); age- and sex-specific population ratios between England and the UK were then used to scale these numbers to a UK level. The radiotherapy proportions from the Thames Cancer Registry were applied to the estimated numbers of cancer survivors in the UK at the beginning of 2007 to provide an estimate of the number who had, and the number who had not, received radiotherapy, by sex, age, cancer site and time since diagnosis (in periods <1, 1–4, 5–9, 10–14, 15–19, 20–35 years). The numbers of second cancers associated with radiotherapy were estimated for 13 cancer sites, based on the risk, relative to the general population (of the SEER registry areas), of developing a second cancer, for intervals <1, 0–4, 5–9 and $10+$ years post diagnosis of the first cancer, for cancer survivors who had received radiotherapy (R_{rt+}) and those who had not (R_{rt-}). The excess risk of cancer due to radiotherapy, relative to the general population (ERR), is then given by

$$\mathrm{ERR} = R_{rt+} - R_{rt-}$$

For each of the 13 cancer sites, the numbers of second cancers expected in the UK during 2010 associated with radiotherapy for a previous cancer were estimated using incidence rates for 2010 in the UK population and the relative risk of a second cancer in cancer survivors. To estimate the total number of second cancers, the numbers estimated to have occurred among survivors of the 13 selected cancer sites were multiplied by the ratio of the number of cancer survivors for all cancers combined to that for just the 13 selected sites combined, by sex, age group and time since diagnosis.

Table 6 shows estimates of the numbers of second cancers (all malignant neoplasms excluding non-melanoma skin cancer) diagnosed in the UK in 2010 among people who had previously been diagnosed with one of the 13 selected sites of the initial cancer.

Table 5 Excess relative risk (% per Sievert)

Excess relative risks (% per Sievert) by cancer and sex																					
Oesophagus		**Stomach**		**Colon**		**Liver**		**Lung**		**Bone**		**Breast**		**Bladder**		**Brain and CNS**		**Thyroid**		**All other solid cancers**	
M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
0.68	0.39	0.44	0.21	1.44	1.21	0.16	0.11	2	4.93	0.19	0.14	—	8.88	2.08	0.73	0.41	0.29	0.16	0.44	3.87	2.4

Abbreviations: CNS, central nervous system; F, female; M, male. Based on United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) Table 71 (2006). Excess relative risk = relative risk − 1.

Table 6 Total numbers of second cancers expected in the UK in 2010, and those associated with the excess risk of cancer due to previous radiotherapy, by site of first cancer (13 selected cancer sites)

First cancer type	Expected number of second cancers[a]	Number (%) associated with radiotherapy for first cancer	
Males			
Oral cavity and pharynx	243	47	(19.3)
Oesophagus	85	8	(9.8)
Stomach	177	1	(0.7)
Colorectal	1751	44	(2.5)
Larynx	391	32	(2.5)
Lung	422	33	(7.7)
Prostate	2006	103	(5.1)
Testes	217	23	(10.8)
Hodgkin lymphoma	218	34	(10.8)
Non-Hodgkin lymphoma	391	2	(0.4)
Total (above 10 sites)	5899	328	(5.6)
Females			
Oral cavity and pharynx	120	20	(16.6)
Oesophagus	45	6	(12.7)
Stomach	74	0	(0.4)
Colorectal	1248	22	(1.7)
Larynx	51	4	(1.7)
Lung	150	8	(5.1)
Breast	7429	626	(8.4)
Cervix uteri	526	90	(17.1)
Corpus uteri	691	61	(8.9)
Hodgkin lymphoma	145	28	(19.2)
Non-Hodgkin lymphoma	286	1	(0.4)
Total (above 11 sites)	10766	866	(8.0)

[a]Second cancers exclude those at the same site as the first, except for oral cavity and pharynx, colorectal and contralateral breast cancers. Also excluded are all leukaemias diagnosed within one year of any first cancer and all second cancers of other sites diagnosed within 5 years of any first cancer.

Table 7 Expected number of second cancers in 2010, by site of second cancer, in survivors of selected primary cancers,[a] and those associated with the excess risk of cancer due to radiotherapy for the initial cancer

Second cancer type[a]	Expected number of second cancers[b]	Number (%) associated with radiotherapy for first cancer	
Males			
Oral cavity and pharynx	179	18	(9.9)
Oesophagus	280	74	(26.3)
Stomach	178	14	(7.7)
Colorectal	836	25	(3.0)
Pancreas	146	3	(2.0)
Larynx	57	4	(7.6)
Lung	859	86	(10.0)
Melanoma of the skin	154	4	(2.8)
Prostate	751	0	(0.0)
Bladder	318	23	(7.2)
Leukaemia	256	0	(0.0)
Other sites	1886	77	(4.1)
All[c]	5899	328	(5.6)
Females			
Oral cavity and Pharynx	132	1	(0.8)
Oesophagus	232	85	(36.6)
Stomach	170	19	(11.0)
Colorectal	1040	48	(4.6)
Pancreas	222	10	(4.4)
Lung	1003	188	(18.8)
Melanoma of the skin	238	43	(17.9)
Breast	3905	129	(3.3)
Cervix	30	2	(7.9)
Corpus uteri	377	35	(9.3)
Ovary	298	12	(4.1)
Bladder	187	15	(7.9)
Leukaemia	218	39	(18.1)
Other sites	2712	240	(8.8)
All[c]	10766	866	(8.0)

[a]Primary cancers as listed in Table 6. [b]Second cancers exclude those at the same site as the first, except for oral cavity and pharynx, colorectal and contralateral breast cancers. Also excluded are all leukaemias diagnosed within one year of any first cancer and all second cancers of other sites diagnosed within 5 years of any first cancer. [c]Excluding non-melanoma skin cancer.

For these 13 sites, we estimate that there would have been 5899 cancers diagnosed in male survivors and 10 766 in female survivors and that, of these, 328 (5.6%) in men and 866 (8.0%) in women were associated with radiotherapy. These second cancers exclude those at the same site as the first, except for cancers of the oral cavity and pharynx, colon–rectum and contralateral breast.

The greatest number of second cancers in the UK in 2010 was among female survivors of breast cancer – 7429 cancers, of which 626 (8.4%) were associated with radiotherapy for the initial breast cancer; these represent 52.4% of the 1194 radiotherapy-associated cancers occurring among survivors of the 13 sites considered. There were also relatively large numbers of cancers occurring among survivors of colorectal cancer (2999: i.e., 1751 in males and 1248 in females) and prostate cancer (2006), although the percentages of these that were associated with radiotherapy were relatively small (2.2% and 5.1%, respectively). Of the second cancers that occurred among survivors of cancer of the oral cavity and pharynx, cervix uteri, and Hodgkin lymphoma, over 15% were estimated to be associated with radiotherapy for the first cancer.

Table 7 summarises the estimated numbers of cancers at different sites occurring in 2010 among the survivors of cancer at any of the 13 selected sites considered, and the numbers of these associated with radiotherapy. The most important among those estimated to be radiation-associated, in terms of numbers of cases, are cancers of the lung (274), oesophagus (159) and female breast (129). In all, 14.7% of second lung cancers were associated with radiotherapy, as were 31.1% of the oesophageal cancers. However, only 3.3% of breast cancers occurring in cancer survivors were radiotherapy-associated.

Table 8 (left-hand columns) shows the distribution of radiotherapy-related second cancers in 2010, in survivors of one of the 13 cancers considered, by age group and sex. The numbers are expressed as a percentage of all second cancers, and as a percentage of all cancers registered in the UK population. It also shows (right-hand columns) the estimated total number of radiotherapy-related second cancers occurring: 430 cases in men (0.26% of all new cancer cases) and 950 cases in women (0.60% of all new cancers).

Other forms of natural background radiation

As noted in Table 1, apart from radon, ionising radiation exposure comes naturally from cosmic rays, followed by terrestrial sources of gamma radiation, and 'internal' emissions.

Cosmic rays are particles that travel through interstellar space. The sun is a source of some of these particles; others come from exploding stars (supernovas). Exposure is increased by air travel at high altitudes.

The amount of terrestrial radiation from rocks and soils varies geographically depending on their local content of uranium.

'Internal' emissions come from radioactive isotopes in food and water and from the human body itself. Exposures from eating and drinking are due in part to the uranium and thorium series of radioisotopes present in food and drinking water. Carbon-14 is present in all living things, and accumulates in the food chain and

Table 8 Expected number of second cancers in the UK in 2010 associated with radiotherapy for a previous cancer, by age and sex

	Among survivors of 13 selected cancers[a]			Among all cancer survivors	
Age group (years)	**Number**	**% of second cancers**	**% of all cancers[b]**	**Number**	**% of all cancers[b]**
Males					
0–34	0	4.7	0.01	1	0.02
35–44	2	9.5	0.05	3	0.08
45–54	9	10.9	0.08	12	0.11
55–64	36	9.0	0.11	45	0.14
65–74	82	6.0	0.16	100	0.19
⩾75	199	4.9	0.33	269	0.44
All ages	328	5.6	0.20	430	0.26
Females					
0–34	0	7.1	0.01	1	0.02
35–44	4	6.4	0.05	6	0.07
45–54	29	6.6	0.15	34	0.18
55–64	137	7.5	0.44	150	0.48
65–74	255	8.7	0.68	277	0.74
⩾75	440	8.0	0.79	482	0.87
All ages	866	8.0	0.55	950	0.60

[a]Primary cancers as listed in Table 6. [b]Excluding non-melanoma skin cancer.

Table 9 Excess incidence of solid cancers in 2010 due to background radiation in the UK

	Males		Females	
Cancer	**Excess attributable cases**	**PAF (%)**	**Excess attributable cases**	**PAF (%)**
Oesophagus	2.4	0.04	0.7	0.03
Stomach	1.2	0.03	0.3	0.01
Colorectum	19.6	0.09	13.5	0.08
Liver	0.2	0.01	0.1	0.01
Lung	27.7	0.12	55.6	0.31
Bone	<0.1	0.01	<0.1	0.01
Female breast	—	—	235.5	0.49
Bladder	9.0	0.13	1.2	0.05
Brain and CNS	0.6	0.02	0.3	0.01
Thyroid	<0.1	0.01	0.3	0.02
All other solid[a]	176.6	0.23	64.2	0.14
All solid[a]	237.3	0.15	371.9	0.24

Abbreviations: CNS = central nervous system; PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

contributes to the internal background dose from ionising radiation.

In estimating the effects of such radiation, we make the simplifying assumption that exposure is uniform throughout the body (rather than concentrated in specific organs), and use the cancer risk estimates, expressed as ERR per unit exposure, from the report of UNSCEAR (2006), as shown in Table 5.

Assuming an average annual dose of 0.93 mSv (Table 1), and a minimum 5-year latency between exposure and the increased risk of solid cancers, the excess incidence of solid cancers (i.e., excluding leukaemias) in the UK in 2010 is shown in Table 9. The total is 609 cases (or 0.2% of all cancers).

For leukaemia, we used the formula for ERR from BEIR described above in the section on Nuclear Medicine to calculate the relative risk in each age group, assuming an annual exposure of 0.93 mSv, starting at those aged 5–9 years in 2010, who would have been first exposed at a mean age of 2.5. For the youngest age group (0–4 years), we assumed that the excess absolute risk was the same as that for children aged 5–9 years who had been exposed at (mean) age 2.5 (see above). As exposure is continuous throughout life (rather than a single exposure to radiation at a given age), we assume that the risks in each 5-year age group are multiplicative (i.e., the risk in children aged 10–14 years in 2010 is the product of that in children exposed for 5 years at (mean) age 7.5 and of that in children exposed for 10 years at (mean) age 2.5). The estimated relative risks were applied to the number of leukaemia cases in the UK, excluding CLL.

We estimate that 316 cases of leukaemia in males (6.8% of all leukaemia) and 245 in females (7.7% of leukaemia cases) might be attributable to background radiation. Of these, 81 cases occurred in children aged <15 years (16.6% of leukaemia cases in this age group).

Adding the solid cancers and leukaemia cases, the total estimate is of 553 radiation-attributable cancers in males (0.35% of all cancers) and 617 cancers in females (0.40% of all cancers).

Summary of results

Table 10 shows the sum of the estimated numbers of cancers resulting from exposure to radon, to other forms of natural background radiation and from man-made sources: diagnostic radiology, radiotherapy and nuclear medicine.

In total, we estimate that approximately 5807 of the cancers diagnosed in the UK in 2010 were the result of such exposures, or around 1.8% of the total.

DISCUSSION

With respect to cancer causation, these calculations suggest that diagnostic radiology is the most important source of ionising radiation in the UK population. Our estimates are based on the work of Berrington de González and Darby (2004), whose estimates may be slightly high as they assumed that the life expectancy of individuals undergoing diagnostic radiology was the same as that of the general population. Any such overestimation is, however, small compared with the likely underestimation due to the application of risks based on exposures 15 years earlier to calculate the attributable fraction of cancers caused by diagnostic radiation occurring in 2010. For solid cancers, radiation-related excess risk starts to appear about 5 years after exposure in

Table 10 Summary of estimated number of cancers in 2010 caused by exposure to ionising radiation, UK

	Excess attributable cases					Total excess attributable cases	PAF (%)
Type of cancer	**Background**	**Radon**	**Diagnostic radiology**	**Radiotherapy**	**Nuclear medicine**	**All radiation**	
Males							
Oesophagus	2	—	17	97	0.0	116	2.0
Stomach	1	—	20	18	0.0	39	0.9
Colon-rectum	20	—	199	33	0.3	252	1.1
Liver	0	—	13	—	0.0	13	0.6
Lung	28	759	28	113	0.5	928	4.2
Breast (female)	—	—	—	—	—	—	—
Bladder	9	—	134	30	1.3	174	2.6
Thyroid	0	—	2	—	0.0	2	0.4
Leukaemia	316	—	40	0	7.7	364	7.8
Other	177	—	462	140	1.6	780	
All[a]	553	759	915	430	11.5	2669	1.7
Females							
Oesophagus	1	—	17	93	0.0	111	3.9
Stomach	0	—	23	21	0.0	44	1.7
Colon—rectum	14	—	319	53	0.0	385	2.2
Liver	0	—	14	—	0.0	15	1.1
Lung	56	618	96	206	0.8	976	5.4
Breast (female)	235	—	62	141	1.9	440	0.9
Bladder	1	—	43	16	0.1	60	2.3
Thyroid	0	—	14	—	0.0	15	0.8
Leukaemia	245	—	42	43	4.5	334	10.4
Other	65	—	316	376	0.5	757	—
All[a]	617	618	945.5	950	7.9	3138	2.0
Persons							
Oesophagus	3	—	34	190	0	227	2.7
Stomach	2	—	44	39	0	84	1.2
Colon—rectum	33	—	518	86	0	637	1.6
Liver	0	—	27	0	0	27	0.8
Lung	83	1376	124	319	1	1905	4.7
Breast (female)	235	—	62	141	2	440	0.9
Bladder	10	—	177	46	1	235	2.5
Thyroid	0	—	17	0	0	17	0.7
Leukaemia	561	—	82	43	12	698	8.9
Other	242	—	778	516	2	1537	0.0
All[a]	1170	1376	1861	1380	19	5807	1.8

Abbreviation: PAF = population-attributable fraction. [a]Excluding non-melanoma skin cancer.

therapeutically irradiated groups (Little, 1993; Weiss *et al*, 1994), while for leukaemia, the increase in risk following exposure certainly starts to appear within 5 years of exposure (Darby *et al*, 1987); therefore, a more appropriate period of exposure would be some 5–10 years earlier (i.e., 2000–5). The use of X-rays – particularly of computerised tomography (CT) scans, which result in higher organ doses of radiation than conventional single-film X-rays – has certainly increased between the period for which Berrington de González and Darby (2004) obtained detailed information on X-ray procedures (1991–6) and 2005. A recent report from the Health Protection Agency (Hart *et al*, 2010) estimated that the per caput dose from diagnostic radiology was about 400 μSv in 2008, compared with about 330 μSv in 1997–8. The increase is due mainly to the increasing use of CT examinations, which by 2008 accounted for 68% of the collective dose from all medical and dental X-ray examinations.

Radiation therapy is probably the second most important source of radiation-associated cancer (about one-quarter of the 5807 radiation-attributable cancers). Maddams *et al* (2011) provide a full discussion of the assumptions and limitations of the estimation, which include the following:

- The total number of survivors in the UK (i.e., the population at risk of a second cancer) is slightly underestimated, as the estimate used includes only those survivors diagnosed up to 35 years previously, although these account for 95% of all survivors.
- The UK prevalence of individuals with a past diagnosis of cancer who have, or have not, received radiotherapy was inferred from the proportions of cancer survivors who are recorded as having received radiotherapy in the database of the Thames Cancer Registry, and it was assumed that these proportions are reasonably representative of the national situation.
- The estimate of the relative risk of second cancers in survivors who had, and had not, received radiotherapy was derived from the experience of cancer patients in the US SEER population between 1973 and 2000. As radiation treatment was not randomised, selection bias could have resulted in differences between treatment groups with regard to other factors that affect second cancer risk – for example, smoking status, the clinical and pathological features of the initial cancer or concomitant disease.
- It was assumed that the nature of radiotherapy treatment for a given cancer was broadly similar in the US and the UK in the same time period (diagnosis of the initial cancer in 1973–2000).
- Estimation was based on data on prevalence and relative risk of radiotherapy for 13 specific cancer types, and the estimate for all cancer survivors involved a further assumption: that the rate of radiation-associated cancers among the sites not considered

(25% of prevalent cancers with past radiotherapy in men, 10% in women) was similar to that among those that were.

In addition, the estimate for 2010 is based on the assumption that the prevalence of cancer at the beginning of 2010 was the same as at the beginning of 2007 (as in Maddams *et al*, 2011). In fact, it is likely that prevalence would have increased somewhat in the intervening 3 years, due to increasing incidence, especially of cancers with a good prognosis (breast, large bowel, prostate), and improvements in survival.

Radiotherapy may also be the cause of some other long-term effects, such as an increased risk of cardiovascular disease. However, any long-term side effects of radiotherapy should always be considered in the context of the considerable benefits in terms of control of symptoms and disease.

The estimated number of cases of lung cancer resulting from exposure to radon includes those cases that are the consequence of both smoking and radon exposure and, since their joint effects are multiplicative (Darby *et al*, 2005), the great majority of such cases occur in smokers, and could be avoided by smoking cessation. Nevertheless, it has been demonstrated that policies requiring basic preventive measures against radon in all new homes throughout the UK would be cost effective and could complement existing policies to reduce smoking (Gray *et al*, 2009). In contrast, policies involving the identification of existing homes with high radon levels are much less cost-effective and can do little to prevent most radon-related deaths, as these are caused by moderate exposure in many homes.

Most exposure to natural background radiation is not, in practice, avoidable. It is a cause of about one in five radiation-induced cancers, almost half of which are leukaemias. Wakeford *et al* (2009) have recently published an estimate of the fraction of childhood leukaemia cases that might be attributable to natural background radiation. The precise result depended on the model used to estimate risk in the UK population, based on the results of the life span study of A-bomb survivors, but it is around 20% (in line with an earlier estimate (Wakeford, 2004)). The result of our rather more simplistic estimation approach (17%) is very similar, despite the assumption that the bone marrow dose of radiation from natural sources is constant throughout life. In fact, the radiation dose to the bone marrow of children – especially from ingested sources – is some 20–40% higher (depending on age) than in adults (Kendall *et al*, 2009), so that our estimates (and those of Wakeford *et al*, 2009) may be a little conservative. In any event, the small contribution of childhood leukaemia to the total of radiation-related cancer means that such adjustments will have almost no effect on the totals in Table 10.

As we describe in the sections related to Methodology, the estimates of population exposure levels (dose) of radiation from the various sources considered rely on many extrapolations and assumptions. Furthermore, we take the conventional view that the relationship between cancer risk and dose at low levels of exposure follows that observed at higher levels, with no threshold effect, although there is very little direct evidence on this point. Despite these limitations, we believe that the overall estimate of around 5000 radiation-induced cancers in the UK (about 2% of the total) is of the correct order of magnitude.

See acknowledgements on page Si.

Conflict of interest

The authors declare no conflict of interest.

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13.
Cancers attributable to solar (ultraviolet) radiation exposure in the UK in 2010

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The evaluation by IARC (1992) concluded that 'There is *sufficient evidence* in humans for the carcinogenicity of solar radiation. Solar radiation causes cutaneous malignant melanoma and non-melanocytic skin cancer. There is *limited evidence* in humans for the carcinogenicity of exposure to ultraviolet (UV) radiation from sunlamps and sun beds'.

In assessing the quantitative contribution of different exposures to cancer in the UK, we are not concerned with non-melanoma skin cancers. This is because there is no agreed method of enumerating such tumours, which may occur at multiple skin sites throughout life, and, because of their generally trivial nature, are in any case under-enumerated in registration systems.

Evaluation of the proportion of total cases of malignant melanoma that is related to solar (UV) exposure poses many problems. Clearly, the method of estimation based on prevalence of exposure and relative risk is inappropriate, given that there is no 'unexposed' population, and the distribution of relevant types of exposure is unknown.

We have therefore estimated the UV-attributable cases occurring in 2010 as the difference between the number observed and those that would have been expected with a theoretical-minimum-risk exposure distribution, based on historical data from UK. These historical data are the estimated incidence rates for the generation of individuals born in 1903, resident in the South Thames region of England.

METHODS

Over the last 30 years, the incidence of malignant melanoma has increased more than for any other common cancer in the UK; in males the age-standardised (European standard) rate rose from 2.5 in 1975 to 14.6 in 2007, and it is projected to be 17.0 in 2010; the female age-standardised rate has increased fourfold – from 3.9 to 15.4 – over the same period, with a projected value of 18.0 in 2010.

The longest series of high-quality incidence data in the UK, with incidence rates from 1960 onwards, is from the South Thames region (Parkin *et al*, 2005). Figures 1 and 2 show the trends in incidence between 1960 and 1997 in males and females, respectively.

We fitted an age-cohort model to the South Thames data to reconstruct age-specific incidence rates for age groups without actual observations, and selected the estimated incidence rates in the cohort born in 1903 as our 'reference', with which to calculate expected numbers of cases in 2010, if solar exposure had been as modest as in the 1903 cohort. Age-standardised incidence rates in this generation are some 10-fold lower in males and 6-fold lower in females than those estimated for 2010, but the disparity is considerably greater in the young than in the elderly (Figure 3).

RESULTS

Table 1 shows the projected numbers of cases of melanoma in the UK in 2010 (6096 in men and 6822 in women), and the number expected in the same year if the rates in the 1903 South Thames cohort had been applied. Overall, some 90% of melanoma cases in men and 82% in women are estimated to be attributed to 'excess' solar irradiation, although the attributable fractions are very much greater at younger ages. The overall attributable fraction (85.9% of melanoma) is equivalent to 3.5% of all new cancer cases in the UK in 2010.

DISCUSSION

With respect to malignant melanoma the evidence for carcinogenicity of solar radiation is derived from various sources. Descriptive studies (in white populations) show a positive association between incidence of and mortality from melanoma and residence at lower latitudes. Studies of migrants suggest that the risk of melanoma is related to solar radiant exposure at the place of residence in early life. The body-site distribution of melanoma favours sites usually exposed to the sun. Evidence from a large number of case–control studies is generally consistent with positive associations with residence in sunny environments throughout life, in early life and even for short periods in early adult life. Positive associations are generally seen between measurements of cumulative sun damage, expressed biologically as microtopographical changes or history of keratoses or non-melanocytic skin cancer, and measures of intermittent exposure to

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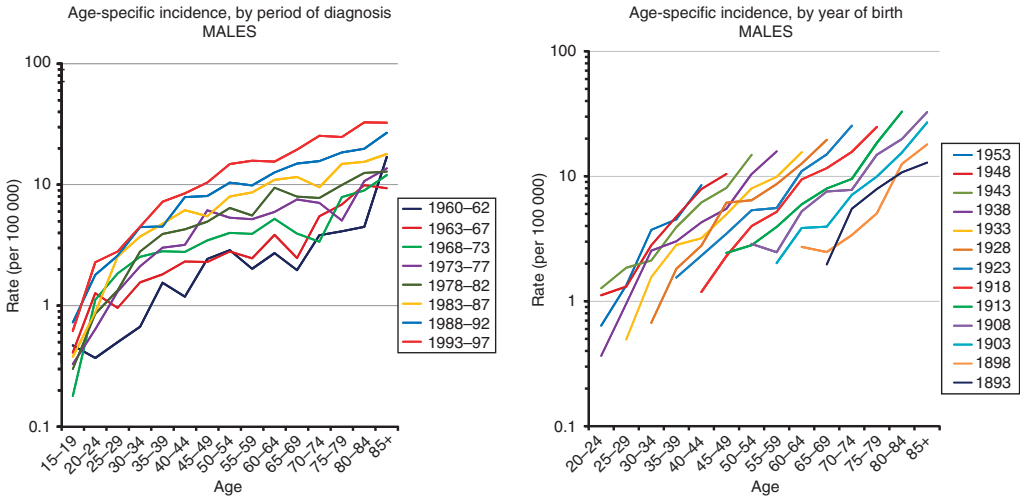

Figure 1 Trends in incidence of malignant melanoma in the South Thames region, 1960–1997, males.

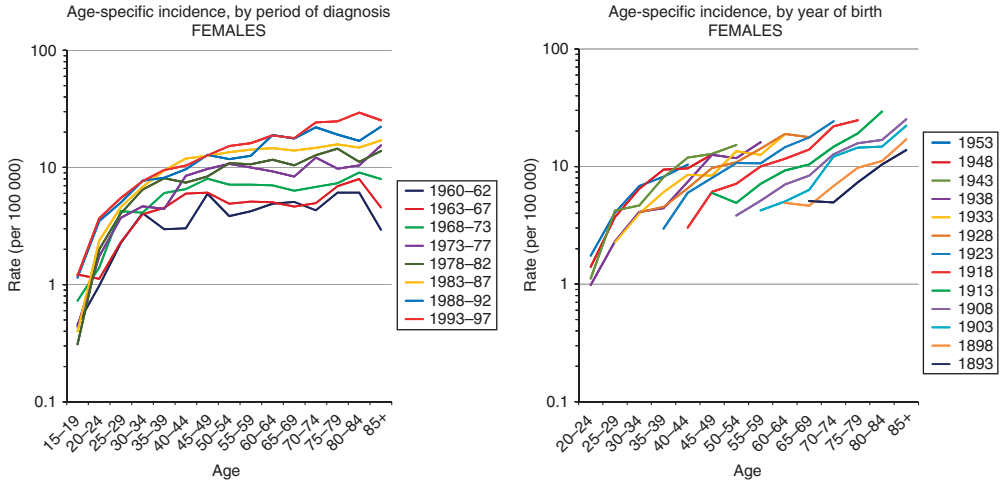

Figure 2 Trends in incidence of malignant melanoma in South Thames region, 1960–1997, females.

the sun (such as particular sun-intensive activities, outdoor recreation or vacations) and with a history of sunburn. In contrast, chronic exposure, as assessed through occupational exposure, appears to reduce the melanoma risk, an observation consistent with the descriptive epidemiology of the condition, which shows lower risks in groups that work outdoors.

Previous evaluations of the proportion of total cases of malignant melanoma that is related to solar (UV) exposure have also relied on the direct method of estimating attributable risk: the difference between observed incidence in the population and incidence in an 'unexposed' reference group. In a widely quoted study, Armstrong and Kricker (1993) used three different estimates of incidence in 'unexposed' populations to compare with the observed rates in Australia:

- The incidence of melanoma at body sites unexposed to the sun (buttocks and (in women) the scalp, from the Queensland Cancer Registry in 1987; Green *et al*, 1993).
- The incidence from areas of lower sun exposure in migrants to Australia.
- A comparison of US Whites and US Blacks, in which the incidence in Blacks was taken as the incidence in unexposed Whites.

In the evaluation of avoidable cancers in the Nordic countries, Winther *et al* (1997) used the crude incidence rates of melanoma at unexposed sites from the above study as the baseline 'unexposed' and estimated attributable fraction in Nordic countries from this study. The IARC's assessment of causes of cancer in France (IARC, 2007) simply took the attributable fraction calculated by Armstrong and Kricker (1993) for Australia as relevant to France in the year 2000. In the evaluation in this section, we chose to use rates from an 'unexposed' reference population that is relevant to UK – the generation born in 1903 in the South Thames region of England.

The pattern of increasing incidence of malignant melanoma in this population over time is a feature of many fair-skinned populations (Lens and Dawes, 2004). In Europe, the increases began first with Scandinavia and the UK and then spread to western, southern and eastern Europe (de Vries *et al*, 2003). The increase has been mainly for thin melanomas (Lipsker *et al*, 1999; Mackie *et al*, 2002). Some of the increase may be due to increased surveillance and early detection, as well as changes in diagnostic criteria, but much of the increase is considered to be real (van der Esch *et al*, 1991) and linked to changes in sun behaviour

(Dennis, 1999; de Vries and Coebergh, 2004; de Vries and Coebergh, 2005). Although the trends observed in South Thames could equally well be related to an increase in risk by period of diagnosis, or by birth cohort, we assume that they are in fact due to changes in exposure to solar UV exposure because of altered patterns of behaviour (in choice of clothing and recreational sunshine), producing an increase in incidence that is cohort-specific. This Edwardian generation almost certainly had little bodily exposure to sunlight in their childhood, and even as young adults opportunities for vacations in sunny climates would have been very limited (Figure 4). Nevertheless, exposure was not zero, so that, even at almost 86%, an estimate of PAF will be something of an underestimate.

In a recent update to its evaluation of the carcinogenicity of UV irradiation, IARC reaffirmed the carcinogenicity of solar radiation, but the classification of the use of UV-emitting tanning devices was raised to Group 1, 'carcinogenic to humans' (El Ghissassi *et al*, 2009). A part of the increase in incidence rates in contemporary UK may well be due to use of sunlamps, but since these devices will almost certainly not have been used by any of the 1903-born

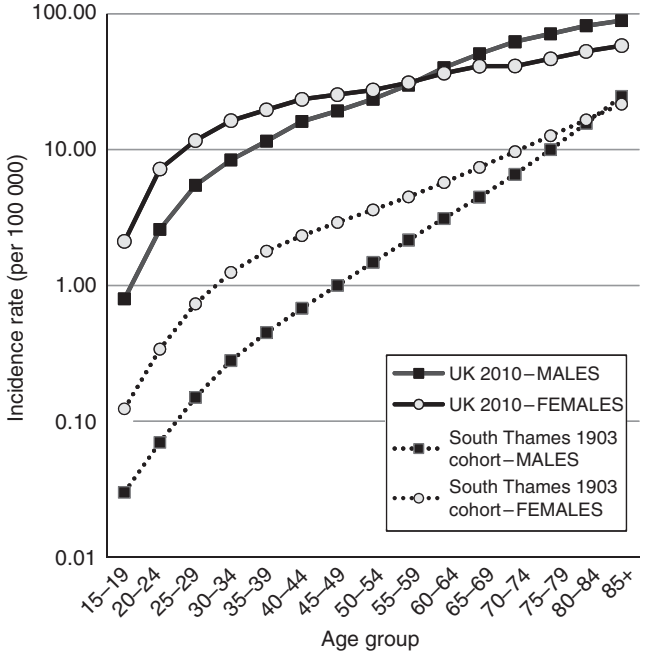

Figure 3 Malignant melanoma: incidence in UK 2010 and South Thames 1903 birth cohort.

Table 1 Malignant melanoma cases diagnosed in 2010, estimated to be due to exposure to solar (ultraviolet) radiation

	Malignant melanoma			All cancer[a]	
Age (years)	**Relative risk**	**Observed cases**	**Excess attributable cases (PAF)**	**Observed cases**	**Excess attributable cases (PAF)**
Males					
<25	33.50	78	75.7 (97.0)	1853	75.7 (4.1)
25–34	32.37	284	275.2 (96.9)	2109	275.2 (13.0)
35–49	21.98	1042	994.6 (95.4)	8359	994.6 (11.9)
50–64	13.88	1717	1593.3 (92.8)	37 617	1593.3 (4.2)
⩾65	6.81	2975	2538.4 (85.3)	108 729	2538.4 (2.3)
Total		6096	5477 (89.8)	158 667	5477.2 (3.5)
Females					
<25	19.31	199	188.7 (94.8)	1646	188.7 (11.5)
25–34	14.18	561	521.4 (92.9)	3284	521.4 (15.9)
35–49	9.72	1551	1391.4 (89.7)	16 877	1391.4 (8.2)
50–64	6.89	1816	1552.4 (85.5)	41 338	1552.4 (3.8)
⩾65	3.69	2695	1965.6 (72.9)	92 439	1965.6 (2.1)
Total		6822	5620 (82.4)	155 584	5619.6 (3.6)
Persons					
<25		277	264 (95.4)	3500	264 (7.6)
25–34		845	797 (94.3)	5393	797 (14.8)
35–49		2593	2386 (92.0)	25 236	2386 (9.5)
50–64		3533	3146 (89.0)	78 955	3146 (4.0)
⩾65		5670	4504 (79.4)	201 167	4504 (2.2)
Total		12 918	11 097 (85.9)	314 251	11097 (3.5)

Abbreviations: PAF, population-attributable fraction (%). [a]Excluding non-melanoma skin cancer.

Figure 4 Holiday makers on the beach around 1919–1921.

generation, the estimate of total UV-attributable cancers based on the differences in incidence rates remains a valid approach.

See acknowledgements on page Si.

Conflict of interest

The authors declare no conflict of interest.

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14.

Cancers attributable to occupational exposures in the UK in 2010

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The International Agency for Research on Cancer (IARC, 2010a) has classified 107 agents, mixtures or exposure circumstances as Group 1 (carcinogenic to humans), many of which are encountered in occupational settings, for example, asbestos and cadmium. An additional 58 agents, mixtures or exposure circumstances have been classified as Group 2A (probably carcinogenic to humans). Those with occupational significance include diesel fumes and benzidine-based dyes (IARC, 2010a). Table 1 (adapted from Siemiatycki *et al*, 2004) shows the most important occupational exposures in these two categories.

A comprehensive analysis of occupational exposures, with quantitative estimates of the cancers attributable to them, has been carried out by Imperial College London and the Health and Safety Laboratory on behalf of the Health & Safety Executive by Rushton *et al* (2007). This analysis has been updated and extended, based on mortality in Britain in 2005 and incidence in 2004 (Rushton *et al*, 2010). Here, we have applied the population-attributable fractions (PAFs) for Great Britain, as estimated in this paper, to the estimated cancer incidence in UK in 2010.

METHODS

The methodology used to estimate PAFs of each cancer is described in the papers by Rushton *et al* (2007, 2010). The carcinogenic agents or exposure circumstances identified for each cancer were those classified by the IARC as Group 1 or 2A carcinogens (IARC, 2010a). Estimation of PAFs requires data on the relative risk of each exposure, and the prevalence in the general population.

Risk estimates were obtained from key studies, meta-analyses or pooled studies, taking into account quality, such as relevance to Britain, sample size, extent of control for confounders, adequacy of exposure assessment, and clarity of case definition. Where possible, risk estimates that had been adjusted for important non-occupational confounding factors, for example, smoking status, were selected. In general, dose–response risk estimates were not available from the epidemiological literature, nor were proportions of those exposed at different levels of exposure over time available for the working population of Britain. However, where possible risk estimates were obtained for an overall 'lower' level and an overall 'higher' level of exposure to the agents of concern.

With respect to the latency between exposure and the elevated risk of cancer, a 'relevant exposure period' was defined. For solid tumours a latency of 10–50 years was assumed; for haematopoietic neoplasms it was 0–20 years.

The proportion of the population exposed to each carcinogenic agent or occupation was obtained from the total number of people employed and the numbers potentially exposed to the carcinogens of interest in each relevant industry/occupation within Britain. If the study from which the risk estimates were obtained was population based, an estimate of the proportion of the population exposed was derived directly from the study data. If the risk estimate was obtained from an industry-based study, national data sources, the CARcinogen EXposure (CAREX) database, the UK Labour Force Survey (LFS) or Census of Employment (CoE) was used to obtain the proportions exposed to the carcinogens concerned in Britain. Adjustment factors were applied to the data to take account of the change in numbers employed and the employment turnover during the 'relevant exposure period'.

The studies from which risk estimates were taken were often mortality studies only and PAFs derived from these were applied to numbers of registrations. The PAFs published by Rushton *et al* (2010) have been applied to the estimated numbers of cancers in the UK in 2010, with the following exceptions:

- We exclude occupationally induced non-melanoma skin cancers, for the reasons stated in the introduction – primarily that enumeration of such tumours is very far from complete (so that including them among the total cancers attributable to different exposures is misleading).
- PAFs due to occupational exposure to environmental tobacco smoke are included with other tobacco-related cancers in Chapter 2 (Parkin, 2011).

RESULTS

Table 2 shows the estimated number of new cancer cases in 2010 for 22 types of cancer, the PAFs (from Rushton *et al*, 2010) and the estimated numbers of cases due to occupational exposures. The

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Table 1 Occupational exposures linked to cancer risk and industries in which exposures can occur

Type of exposure	Industries with possibility for exposure
Aromatic amines	Previously used as intermediates in manufacture of dyes and pigments, textiles, paints, plastics, paper, drugs and pesticides, and as antioxidants in preparation of rubber for tyres and cables
Arsenic	Mining, (copper) smelting, vineyard workers, pesticide production (arsenical pesticides)
Asbestos	Shipbuilding, construction, mining and milling, by-product manufacture, insulating, sheet-metal workers, asbestos cement industry
Benzene	Production, solvents in the shoe production industry, chemical pharmaceutical and rubber industries, printing industry, gasoline additive
Diesel	Transportation workers/drivers, bus drivers, road maintenance, mechanics and garage workers, dock workers
Formaldehyde	Production, pathologists, medical laboratory technicians, plastics, textile and plywood industry
Leather dust	Boot and shoe manufacture and repair
Certain metal compounds (cadmium and cadmium compounds, chromium VI compounds, nickel compounds, iron and steel founding, nickel sulphides and oxides, beryllium)	Iron and steel founding; house painting and paper hanging; smelting, metal founding and welding; occupations that involve manufacture of cadmium oxide, cadmium alloys and cadmium pigments; production of nickel-cadmium batteries; recapture of zinc during zinc refining; chromate production; chromate pigment production; chromium plating; mechanics and those working with iron and metal ware; plumping
Mineral oils	Metal workers; printing industry
Polycyclic aromatic hydrocarbons	Industries with exposure to soots, coal tars, coal-tar pitches, aluminium production (pitch volatiles); e.g. chimney sweeps, coal gasification, coke production, coal-tar distillation, paving and roofing, smelting and metal founders, engine and motor exhausts
Radon	Workers in underground haematite mines
Silica	Mining; stone quarrying; granite production; ceramic and pottery industries; steel production
UV radiation	Outdoor occupations
Vinyl chloride	Production of vinyl chloride and polyvinyl chloride; plastics, rubber and resins manufacturing; car interior workers; furniture makers; transportation workers
Wood dust	Furniture and cabinet-making and construction, logging and sawmill workers, pulp and paper and paperboard industry

Adapted from Siemiatycki *et al* (2004).

Table 2 Estimated fractions of cancer cases in UK, 2010, attributable to occupational exposures

		Observed cases		PAF[a] (%)		Excess attributable cases	
Cancer site	**ICD-10 code**	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**
Nasopharynx	C11	267	178	11	2.5	29	4.5
Oesophagus	C15	5713	2819	3.3	1.1	189	31
Stomach	C16	4467	2577	3	0.3	134	7.7
Liver	C22	2270	1298	0.2	0.1	4.5	1.3
Pancreas	C25	4084	4280	0.02	0.01	0.8	0.4
Sino-nasal[b]	C30–31	279	173	46	20.1	128	35
Larynx	C32	1803	386	2.9	1.6	52	6.2
Lung[c]	C33	22 273	18 132	20.5	4.3	4566	780
Bone	C40–41	362	256	0.04	0.01	0.1	0.0
Mesothelioma[b]	C45	2077	462	97	82.5	2015	381
Soft-tissue sarcoma[b]	C49	867	623	3.4	1.1	29	6.9
Breast (female)	C50	—	48 385	—	4.6	—	2226
Cervix	C53	—	2691	—	0.7	—	19
Ovary	C56	—	6820	—	0.5	—	34
Kidney	C64–66, C68	5697	3365	0.04	0.04	2.3	1.3
Bladder	C67	6713	2572	7.1	1.9	477	49
Eye[b]	C69	210	172	2.9	0.4	6.1	0.7
Brain and CNS	C70–72	2799	1902	0.5	0.1	14	1.9
Thyroid	C73	602	1776	0.12	0.02	0.7	0.4
Non-Hodgkin lymphoma	C82–85, C96	6297	5305	2.1	1.1	132	58
Myeloma	C90	2506	1994	0.4	0.1	10	2.0
Leukaemia	C91–95	4639	3201	0.9	0.5	42	16
All[d]		158 667	155 584	4.9	2.4	7832	3662

Abbreviations: CNS = central nervous system; ICD = International Classification of Diseases; PAF, population-attributable fraction. [a]Rushton *et al* (2010). [b]Number of cases estimated from the UK population (2010) and rates in England in 2008. [c]Lung cancer PAF excludes occupational exposure to environmental tobacco smoke (ETS). [d]Excluding non-melanoma skin cancer.

total is an estimated 11 494 cases (7832 in men and 3662 in women), representing 3.7% of all cancers (excluding non-melanoma skin cancers). The most substantial numbers are lung cancers (exposures due to asbestos, silica, diesel engine exhausts, mineral oils), mesotheliomas (asbestos) and breast cancer, related to shift work that involves circadian disruption (IARC, 2010b).

DISCUSSION

Included in the evaluation of Rushton *et al* (2010) were non-melanoma skin cancers, the calculated PAF of which (4. 6%) was applied directly to the number of registrations in 2004. The latter may have been due to a lack of appreciation by the authors of the incomplete nature of cancer registration for non-melanoma skin cancer. Undercounting of such cancers is a consequence of the relatively trivial nature of the great majority, and many such cancers are treated without hospitalization or, probably, a biopsy. Registration is biased by cell type (basal cell cancers will certainly be undercounted), while some cancers – probably occupationally related ones – may be more completely identified.

Prevalence of exposure in the analysis by Rushton *et al* (2010) was estimated for a period of 10–50 years prior to 2005 for solid tumours, and 0–20 years for haematopoietic neoplasms. If exposure prevalence has been declining, and these latency periods are correct, it is possible that the numbers of attributable cancers for 2010 will be slightly overestimated (because the time since exposure is 5 years longer than for the estimates for 2005).

Several other studies have been carried out to estimate the proportion of cancers in a given population that are possibly the result of exposure to carcinogens in an occupational setting. Doll and Peto (1981) included occupational factors in their evaluation of the quantitative contribution of different factors to cancer mortality in the United States. In addition to the USA, estimates of the effect of occupational exposures on the burden of cancer have been made for the year 2000 for the populations of the Nordic countries (Dreyer *et al*, 1997), Australia (Fritschi and Driscoll, 2006) and France (IARC, 2007). Quantitative estimates of the carcinogenic effect of 11 occupational exposures worldwide in the year 2000 were made by Driscoll *et al* (2005).

These recent studies used a methodology similar to that of Rushton *et al* (2010) – the CAREX (CARcinogen Exposure) database – to provide national estimates of the proportions of workers exposed to different carcinogens and their levels of exposure (Finnish Institute of Occupational Health, 2009), and estimates of the relative risk of different exposures, drawn from literature reviews. There are differences not only in the choice of such studies (and hence of risks associated with occupational exposures, and different levels of exposure), but also in the precise choice of exposures, which can reasonably be considered to be carcinogenic in an occupational setting.

The Nordic study (Dreyer *et al*, 1997) estimated that verified industrial carcinogens will account for approximately 3% of all cancers in men and less than 0.1% of all cancers in women in the Nordic countries around the year 2000, while the French study estimated that 2.5% of cancers in men and 0.3% in women were caused by occupation.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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15.
Cancers attributable to reproductive factors in the UK in 2010

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Reproductive factors influence the risk of cancers of the female genital tract (uterus and ovary) and breast. The following reproductive factors are important in this respect: age at menarche; age at first birth; parity; age at menopause; and duration of breastfeeding. The effects of exogenous hormones are described in Section 10.

Age at menarche

Early age at menarche has been consistently associated with an increased risk of breast and endometrial cancer (Pike *et al*, 2004). Relative risk (RR) for premenopausal breast cancer is reduced by an estimated 7% for each year that menarche is delayed after age 12 years, and by 3% for post-menopausal breast cancer (Clavel-Chapelon, 2002). The effect on risk is through prolongation of the period with relatively high exposure to endogenous oestrogen.

Age at first birth

The younger the woman is when she begins childbearing, the lower her risk of breast cancer (Kelsey *et al*, 1993). The RR of developing breast cancer increases by 3% for each year of delay (Collaborative Group, 2002).

Parity

Increasing parity reduces the risk of breast, endometrial and ovarian cancers (Pike *et al*, 2004). The higher the number of full-term pregnancies, the greater the protection. Compared with nulliparous women, a woman who has at least one full-term pregnancy reduces her risk of breast cancer by around 25% (Layde *et al*, 1989; Ewertz *et al*, 1990) and women with five or more children experience a 50% reduction in risk (Kelsey *et al*, 1993). For endometrial cancer, risk is reduced by 30% for a woman's first birth and by 25% for each successive birth, and later maternal age at last birth has also been shown to reduce the risk (Pike *et al*, 2004). For ovarian cancer, risk in women with four pregnancies is only 40% that in nulliparous women (Ness *et al*, 2002). However, increasing parity increases the risk of cancer of the cervix, independently of any increase in the prevalence of infection with HPV (Munoz *et al*, 2002).

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Age at menopause

Late menopause increases the risk of breast cancer and endometrial cancer (Pike *et al*, 2004). For breast cancer, risk is doubled for a woman with menopause at 55 years compared with less than 45 years (Kelsey *et al*, 1993). For each year that the menopause is delayed, there is an approximate 3% increase in breast cancer risk (Collaborative Group, 1997). Postmenopausal women have a lower risk of breast cancer compared with premenopausal women of the same age, both for natural menopause and for menopause induced through surgery (Collaborative Group, 1997).

Breastfeeding

The role of breastfeeding as a protective factor against the later development of breast cancer has been long suspected (Lane-Claypon, 1926). More recently, this association has been confirmed and the magnitude of the effect estimated as a decrease in risk of 4.3% for every 12 months of breastfeeding (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). For ovarian cancer, the issue is less clear. An early collaborative analysis of case–control studies found a reduced risk in parous women who had ever breastfed compared with those who had never done so (Whittemore *et al*, 1992). Subsequent work suggested that only serous tumours may be so influenced (Jordan *et al*, 2007, 2008). A recent analysis of two US cohort studies (Danforth *et al*, 2007) suggests that each month of breastfeeding reduces the RR by 2% (RR = 0.98 per month, 95% CI 0.97 – 1.00).

Although a woman's reproductive behaviour can influence the risk of cancers of the uterus, ovary and breast, most of the important aspects discussed above are not sensibly considered as targets for preventive interventions.

In this section, therefore, only the cancers attributable to sub-optimal levels of breastfeeding are evaluated.

METHODS

Breastfeeding of infants in Britain is not very common, and is generally not prolonged for more than a few weeks. Surveys of infant feeding in the UK, at 5-yearly intervals since 1975, have been carried out by the Department of Health. The most recent survey (the seventh) was in 2005 (Bolling *et al*, 2007). Table 1 shows the results of these surveys.

Table 1 Percentage of women breastfeeding at given intervals post partum (Great Britain)

Interval post partum	% Women breastfeeding, by year of survey					
	1980	1985	1990	1995	2000	2005
Birth	65	63	62	66	69	76
1 Week	*54*	*52*	*51*	56	55	63
2 Weeks	*51*	*49*	*48*	53	52	60
6 Weeks	*41*	*39*	*39*	42	42	48
4 Months	*27*	*27*	*26*	27	28	34
6 Months	*21*	*20*	*20*	21	21	25
8 Months	*15*	*14*	*14*	15	16	*21*
9 Months	*14*	*13*	*13*	14	13	18

Values in italics have been interpolated.

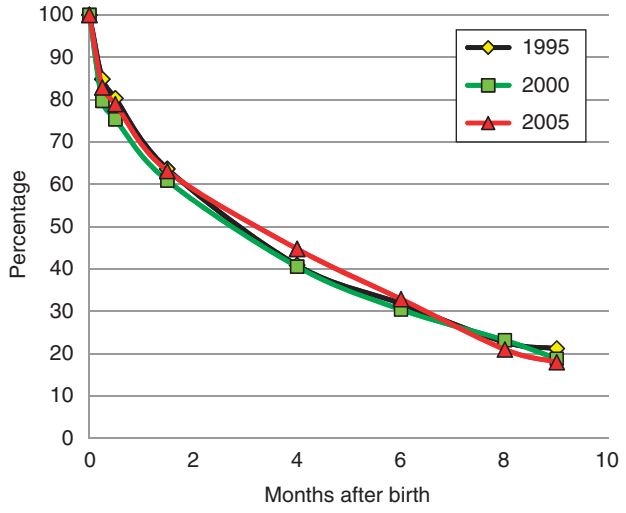

Figure 1 Percent of women continuing breastfeeding, by time since birth.

The values in italics have been interpolated. This seems relatively secure, as the decline in breastfeeding prevalence with time since birth in women who do actually commence seems to be relatively constant (Figure 1).

There is no generally accepted target for breastfeeding. The Global Strategy on Diet, Physical Activity and Health of the World Health Organisation (WHO, 2004) includes a recommendation to 'promote and support exclusive breastfeeding for the first six months of life and promote programmes to ensure optimal feeding for all infants and young children'. Therefore, we have taken as the optimum breastfeeding of all live-born children for six months, with no change to the current pattern after this time. Currently, some 18% of women are breastfeeding to 9 months of age (Table 1).

Table 2 gives information on the birth experience of women in England and Wales in 2008, the most recent year available (Office for National Statistics, 2009).

Table 3 shows the estimated duration of breastfeeding (based on the data of Table 1).

With a change in risk for each month of breastfeeding of −0.366% for breast cancer and −2.0% for ovarian cancer (Collaborative Group on Hormonal Factors in Breast Cancer, 2002; Danforth *et al*, 2007), the actual protection provided by the breastfeeding practices of each generation of women can be estimated (column 1 of Table 4). The breastfeeding practices from

Table 2 Natality of women in England and Wales in 2008, by age/birth cohort

Age (years)	Central birth year	Average number of live-born children	Average age when 50% children had been born	Average year when 50% children had been born
0–4	2006	0	—	—
5–9	2001	0	—	—
10–14	1996	0	—	—
15–19	1991	0.04	13	2004
20–24	1986	0.34	19	2003
25–29	1981	0.80	23	2001
30–34	1976	1.34	26	1999
35–39	1971	1.75	26	1996
40–44	1966	1.90	26	1991
45–49	1961	1.96	27	1985
50–54	1956	2.02	26	1980
55–59	1951	2.04	25	1974
60–64	1946	2.19	25	1968
65–69	1941	2.34	25	1964
70–74	1936	2.40	26	1960
75–79	1931	2.35	27	1956
80–84	1926	2.12	27	1951
⩾85	1921	2.00	27	1946

Table 3 Median and mean duration of breast feeding (Great Britain)

Average	Duration of breastfeeding (months) by year of survey					
	1980	1985	1990	1995	2000	2005
Median	0.60	0.48	0.38	0.84	0.71	1.46
Mean	2.84	2.75	2.71	2.89	2.90	3.50
Mean if all ⩾6 months[a]	6.78	6.75	6.74	6.79	6.78	7.02

[a]Mean if all women could breastfeed their children for 6 months (so prevalence at 6 months is 100%).

Table 1 are assumed to apply to the year in which 50% of the children in a given age group in 2008 would have been born. Since there are no data on breastfeeding practices prior to 1980, the duration of having been breastfed for women in the age groups ⩾55–59 are taken to be the same as in 1980.Table 3 also shows the estimated mean duration of breastfeeding if all women could breastfeed their children for 6 months (so that prevalence at 6 months is 100%), after which the values in Table 1 continue to pertain.

RESULTS

Column 1 of Table 4 shows the decrease in risk of breast and ovarian cancer due to breastfeeding, of women in the UK, by age group, in 2008, and column 2 the decrease in risk if all had been breastfed for a minimum of 6 months. Column 3 shows the excess risk of women in 2008, due to their breastfeeding practice being short of target, and column 4 the population-attributable fraction of breast and ovarian cancer cases by age.

In Table 5, we assume that the RR estimated for 2008 is pertinent for 2010, and show the actual numbers of cancer cases that would be attributable to breastfeeding practices not reaching the optimum level.

In total 2699 cancer cases projected to occur in 2010 (1498 breast cancers, 1201 ovarian cancers) would have been avoided if breastfeeding practice had been at the theoretical 'optimum'. This

Table 4 Effect of breastfeeding on women's risk of breast and ovarian cancer, UK 2008

	Breast cancer				Ovarian cancer			
	1	2	3	4	1	2	3	4
Age (years)	Estimated individual decrease in risk	Target decrease in risk[a]	Excess risk	PAF (%)	Estimated individual decrease in risk	Target decrease in risk[a]	Excess risk	PAF (%)
0–4	—	—	0	—	—	—	0	—
5–9	—	—	0	—	—	—	0	—
10–14	—	—	0	—	—	—	0	—
15–19	0.0005	0.0010	0.001	0.1	0.0026	0.0052	0.003	0.3
20–24	0.0043	0.0086	0.004	0.4	0.0219	0.0443	0.022	2.3
25–29	0.0084	0.0196	0.011	1.1	0.0429	0.1010	0.058	6.1
30–34	0.0140	0.0328	0.019	1.9	0.0718	0.1691	0.097	10.5
35–39	0.0183	0.0429	0.025	2.5	0.0935	0.2212	0.128	14.1
40–44	0.0186	0.0463	0.028	2.8	0.0951	0.2387	0.144	15.9
45–49	0.0195	0.0478	0.028	2.9	0.0997	0.2466	0.147	16.3
50–54	0.0207	0.0495	0.029	2.9	0.1060	0.2550	0.149	16.7
55–59	0.0209	0.0500	0.029	3.0	0.1071	0.2575	0.150	16.8
60–64	0.0225	0.0536	0.031	3.2	0.1149	0.2764	0.161	18.2
65–69	0.0240	0.0573	0.033	3.4	0.1228	0.2953	0.173	19.7
70v74	0.0246	0.0588	0.034	3.5	0.1260	0.3029	0.177	20.2
75–79	0.0241	0.0576	0.033	3.4	0.1233	0.2966	0.173	19.8
80–84	0.0217	0.0519	0.030	3.1	0.1113	0.2676	0.156	17.6
⩾85	0.0205	0.0490	0.028	2.9	0.1050	0.2524	0.147	16.5

Abbreviation: PAF = population-attributable fraction. [a]If all had breastfed for a minimum of 6 months.

Table 5 Cases of breast and ovarian cancer estimated to be due to sub-optimal breast feeding, UK 2010

	Breast				Ovary			
Age (years)	Relative risk	Observed cases	Excess attributable cases	PAF (%)	Relative risk	Observed cases	Excess attributable cases	PAF (%)
0–4	1	2	0	—	1	2	0	—
5–9	1	0	0	—	1	4	2	—
10–14	1	0	0	—	1	6	3	—
15–19	1.0005	4	0	0.1	1.0026	23	0	0.3
20–24	1.0044	32	0	0.4	1.0234	57	1	2.3
25–29	1.0114	167	2	1.1	1.0646	90	5	6.1
30–34	1.0194	548	10	1.9	1.1171	103	11	10.5
35–39	1.0258	1265	32	2.5	1.1639	160	23	14.1
40–44	1.0291	2593	73	2.8	1.1885	278	44	15.9
45–49	1.0298	4236	123	2.9	1.1950	428	70	16.3
50–54	1.0303	4810	141	2.9	1.1999	498	83	16.7
55–59	1.0306	5582	166	3.0	1.2026	623	105	16.8
60–64	1.0329	6459	206	3.2	1.2232	883	161	18.2
65–69	1.0353	6403	219	3.4	1.2448	852	168	19.7
70–74	1.0363	4332	152	3.5	1.2538	828	168	20.2
75–79	1.0355	4058	139	3.4	1.2463	734	145	19.8
80–84	1.0318	3526	109	3.1	1.2134	616	108	17.6
⩾85	1.0299	4367	127	2.9	1.1973	635	105	16.5
All ages		48 385	1498	3.1		6820	1201	17.6

Abbreviation: PAF = population-attributable fraction.

represents 1.7% of cancers in women and 0.9% of all cancer cases in 2010.

DISCUSSION

Though it may be desirable, from the point of view of cancer prevention, to have multiple pregnancies commencing at a young age, there are equally, or more, persuasive reasons to avoid such a lifestyle. It makes no sense, therefore, to prescribe an ideal fertility pattern, against which the number of cancers attributable to a less optimum one can be evaluated. In the IARC calculation of avoidable cancers in France (IARC, 2007), the fertility pattern of 1980 was taken as an ideal against which the excess cases resulting from fertility in 2000 were calculated, although the rationale for this was not explained. The origin of the Doll and Peto (2003) estimate of 15% of UK cancer deaths being attributable to 'reproduction' (and other factors related to the secretion of reproductive hormones) is obscure; the methodology is said to be the same as in their 1981 monograph (Doll and Peto, 1981), although this considers some 46% of the deaths due to cancers of the breast, ovary and uterus (corpus and cervix) as attributable to reproductive and sexual factors, and these cancers are responsible for only 8% of cancer deaths in UK in 2005.

It is reasonable, however, to advocate breastfeeding for a variety of reasons, of which the benefit of cancer protection is one (http://www.breastfeeding.nhs.uk/en/fe/page.asp?n1 = 2). The 'optimum' levels for breastfeeding against which attributable fractions of breast and ovarian cancer have been evaluated are rather artificial, in that it would be impossible for *all* women to breastfeed their infant for 6 months. In the United States, for example, the US Department of Health and Human Services (2005) *Healthy People 2010* objectives for breastfeeding initiation and duration were to increase the proportion of mothers who exclusively breastfeed their infants through age 3 months to 60% and through age 6 months to 25%. Exclusive breastfeeding is defined as an infant receiving only breast milk and no other liquids or solids except for drops or syrups consisting of vitamins, minerals or medicines (WHO, 1991). Clearly, the target for partial breastfeeding may be more ambitious, so that the target may not be so very far from the theoretical optimum, advocated by WHO.

See acknowledgements on page Si.

Conflict of interest

The author declares no conflict of interest.

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16.

The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010

Summary and conclusions

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This chapter summarises the results of the preceding sections, which estimate the fraction of cancers occurring in the UK in 2010 that can be attributed to sub-optimal, past exposures of 14 lifestyle and environmental risk factors. For each of 18 cancer types, we present the percentage of cases attributable to one or all of the risk factors considered (tobacco, alcohol, four elements of diet (consumption of meat, fruit and vegetables, fibre, and salt), overweight, lack of physical exercise, occupation, infections, radiation (ionising and solar), use of hormones, and reproductive history (breast feeding)).

Exposure to less than optimum levels of the 14 factors was responsible for 42.7% of cancers in the UK in 2010 (45.3% in men, 40.1% in women) – a total of about 134 000 cases.

Tobacco smoking is by far the most important risk factor for cancer in the UK, responsible for 60 000 cases (19.4% of all new cancer cases) in 2010. The relative importance of other exposures differs by sex. In men, deficient intake of fruits and vegetables (6.1%), occupational exposures (4.9%) and alcohol consumption (4.6%) are next in importance, while in women, it is overweight and obesity (because of the effect on breast cancer) – responsible for 6.9% of cancers, followed by infectious agents (3.7%).

Population-attributable fractions provide a valuable quantitative appraisal of the impact of different factors in cancer causation, and are thus helpful in prioritising cancer control strategies. However, quantifying the likely impact of preventive interventions requires rather complex scenario modelling, including specification of realistically achievable population distributions of risk factors, and the timescale of change, as well as the latent periods between exposure and outcome, and the rate of change following modification in exposure level.

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In this study, we have estimated the fraction of cancers occurring in the UK in 2010 that can be attributed to sub-optimal past exposures of 14 lifestyle and environmental risk factors. The optimum level of exposure or the theoretical minimum risk exposure distribution for each of the risk factors is summarised in Table 1.

Table 2 provides a summary of the percentage of cancers at each site that can be attributed to the 14 risk factors (the population-attributable fraction (PAF)). The total number of cancer cases (all sites) attributable to each risk factor was obtained by summing the numbers at the individual sites. Cases of different cancers attributable to a single risk factor are additive because each cancer case is assigned to a single ICD category.

However, cancers are caused by multiple factors acting simultaneously, and hence could be prevented by intervening on single or multiple risk factors; for example, some oesophageal cancer cases may be prevented by reducing smoking, alcohol or body weight, increasing the intake of fruits and vegetables, or by combinations of these steps. The percentages presented in Table 2 reflect the effect of removing one cause of cancer independently of other causes. But because cancers have multiple causes, the same cancers can be attributed to more than one cause, so summing the figures in the tables would overestimate the total burden of cancer attributable to the 14 risk factors. Thus, an estimate of the burden of cancer attributable to multiple causes should take into account the overlap between the effects of different carcinogens, which means that, for a specific cancer, the attributable fraction for all risk factors combined will be less than the sum of the PAFs associated with each risk factor.

When risk factors are independent (i.e., they act on different carcinogenic pathways), their effects on relative risks (RRs) will be multiplicative. This is well documented for some factors (for example, the joint effects of tobacco and alcohol), although for most there is a lack of detailed quantitative data on the risks resulting from combined exposure to several risk factors. The hypothesis of the multiplicative effect of RRs is a reasonable one, however, and allows estimation of PAFs from combined exposures. Thus, in Table 2, to obtain the last row (PAF due to all of the exposures), for each cancer, the PAF for the first exposure

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Table 1 Exposures considered, and theoretical optimum exposure level

Exposure	Optimum exposure level
Tobacco smoke	Nil
Alcohol consumption	Nil
Diet	
1 Deficit in intake of fruit and vegetables	$\geqslant$5 servings (400 g) per day
2 Red and preserved meat	Nil
3 Deficit in intake of dietary fibre	$\geqslant$23 g per day
4 Excess intake of salt	$\leqslant$6 g per day
Overweight and obesity	BMI $\leqslant$ 25 kg m^{-2}
Physical exercise	$\geqslant$30 min 5 times per week
Exogenous hormones	Nil
Infections	Nil
Radiation – ionising	Nil
Radiation – solar (UV)	As in the 1903 birth cohort
Occupational exposures	Nil
Reproduction: breast feeding	Minimum of 6 months

(e.g., tobacco smoking) was subtracted from 100%, and the PAF for the second exposure was applied to the remainder (the percentage *not* attributable to smoking). This process was performed sequentially for all relevant exposures, resulting in an estimate of the PAF for all exposures combined.

Exposure to less than optimum levels of the 14 factors was responsible for 42.7% of cancers in the UK in 2010 (45.3% in men, 40.1% in women) – a total of about 134 000 cases.

Tobacco smoking is by far the most important risk factor for cancer in the UK, responsible for 60 000 cases (19.4% of all new cancer cases) in 2010. The relative importance of other exposures differs by sex. In men, deficient intake of fruits and vegetables (6.1%), occupational exposures (4.9%) and alcohol consumption (4.6%) are next in importance, while in women, it is overweight and obesity (because of the effect on breast cancer) – responsible for 6.9% of cancers, followed by infectious agents (3.7%).

SOURCES OF UNCERTAINTY

Results are presented as the estimated percentages of different cancers attributable to specific causes in the UK population of 2010. There are several sources of uncertainty around the estimates. Some of these are quantifiable (e.g., confidence intervals of RRs and exposure prevalence, alternative choice of 'optimal exposure'), while in other cases quantification would be either very difficult (e.g., modelling lag time to provide a biologically-driven estimate of cumulative exposure) or be practically impossible (e.g., using the indirect method to estimate PAFs due to smoking).

Doll and Peto (1981, 2005) provided a 'range of acceptable estimates' for each exposure, to reflect the difference between those for which the risk is certain and well quantified, such as tobacco smoking, and those for which there is considerably more controversy, such as diet. We have not attempted to do so in this section; the uncertainties concerning each exposure are, however, discussed in the relevant sections. Furthermore, as we discuss below, the PAFs should not be used uncritically as a guide to the proportion of cancer cases that can be prevented by interventions.

COMPARISON WITH OTHER STUDIES

Comprehensive estimates of the fractions of cancer cases or deaths attributable to various environmental exposures have been made for world regions (Ezzati *et al*, 2002; Danaei *et al*, 2005), the United States (Danaei *et al*, 2009), France (IARC, 2007) and the Nordic countries (Olsen *et al*, 1997). For the UK, the most widely quoted are possibly those of Doll and Peto (2005), although recently the World Cancer Research Fund/American Institute for Cancer Research published an estimate of cancers attributable to food, nutrition and physical activity in the UK and three other countries (WCRF/AICR, 2009).

The Doll and Peto (2005) estimates relate to deaths from cancer, and the methodology used is that from their 1981 monograph (Doll and Peto, 1981). The estimation method is somewhat variable for the different exposures considered. For example, they attribute to alcohol two-thirds of deaths from alcohol-related cancers (mouth, pharynx, larynx, oesophagus) in men and one-third in women, plus 'a small proportion' of liver cancer deaths. For diet, the fraction is arrived at by summing 'guestimated' fractions by which death rates of different cancers might be reduced by practical dietary means (for example: stomach 90%; breast 50%; cervix 20%).

The WCRF/AICR report (2009), on the other hand, uses estimates of prevalence of exposures to various nutritional factors in the UK, and estimates of RR associated with them, to calculate attributable fractions using the conventional formula. The attributable fractions so derived are generally rather greater than those estimated in this set of papers (Table 3). There are several reasons for this.

First, the WCRF/AICR estimates use current estimates of exposure prevalence applied to numbers of cancer cases in 2002. This is unrealistic. The effects of the exposures considered are not instantaneous, and renouncing alcohol, say, would not reduce one's excess risk to zero immediately. Therefore, in the current exercise, similar to that of IARC (2007) for France, the relevant exposures are taken to be those several years earlier. This is generally 10 years, based on the follow-up periods for which most of the RRs were calculated. However, for some exposures – for example, use of post-menopausal hormones – the risk is raised in current users, but declines rapidly once exposure ceases. As most of the exposures considered have been becoming more prevalent with time, the WCRF/AICR estimates are too high for current cancer cases.

Second, the current estimates make use, whenever they are available, of dose–response summary estimates from meta-analyses by reputable authorities such as IARC, or WCRF itself, in its report 'Food, Nutrition Physical Activity and the Prevention of Cancer' (WCRF/AICR, 2007). The WCRF/AICR estimates use RR estimates from a single study, generally in a different country, to estimate the effects in the UK. This seems highly unlikely to result in a less biased result.

Finally, the current estimates use, whenever possible, per unit exposure risk estimates, and calculate attributable fractions among the proportions of the population with exposures greater or less than an acceptable 'optimum' recommended for the UK. These are dismissed by WCRF/AICR as 'associated with a number of limitations', and their estimates use RRs associated with tertiles of exposure prevalence, and estimate the effect of moving the entire UK population to the lowest tertile of exposure, defined by the study selected for the RR estimate. The baseline exposure varies, therefore, from one cancer to another; for BMI, for example, it is $<25\,\mathrm{kg\,m^{-2}}$ for colorectum, and $<21\,\mathrm{kg\,m^{-2}}$ for breast cancer.

There are a few other, perhaps more minor, points that contribute to the discrepancies: it is obviously not correct to assume all breast cancer is post-menopausal – it is only 80% of the total in UK, so that PAFs for breast cancer related to overweight/obesity are overestimated. The same applies to PAFs for body weight and oesophagus cancer, where only the risk for adeno-carcinomas is increased, and these constitute some 55% of the oesophageal cancers in the UK.

SUMMARY

Figure 1 summarises the estimates of the numbers (and percentages) of incident cancer cases in the UK in 2010 that are

Table 2 Percentage of incident cancer cases in the UK in 2010 due to 14 lifestyle and environmental factors: (a) males and females; (b) persons

	% cancers attributable to risk factor exposure, by cancer site																		
Exposure	**Oral cavity and pharynx**	**Oeso-phagus**	**Stomach**	**Colon–rectum**	**Liver**	**Pancreas**	**Gall-bladder**	**Larynx**	**Lung**	**Meso-thelioma**	**Melanoma**	**Breast**	**Cervix uteri**	**Corpus uteri**	**Ovary**	**Bladder**	**Kidney**	**Leukaemia**	**All[a]**
(a)																			
Males																			
Tobacco	69.5	62.6	26.1	6.6	27.3	26.2	—	79.0	87.3	—	—	—	—	—	—	37.5	29.4	8.4	23.0
Alcohol	37.3	25.3	—	15.5	11.4	—	—	27.3	—	—	—	—	—	—	—	—	—	—	4.6
Fruit and vegetables	57.2	46.6	37.0	—	—	—	—	45.9	8.5	—	—	—	—	—	—	—	—	—	6.1
Meat	—	—	—	24.8	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3.5
Fibre	—	—	—	10.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.4
Salt	—	—	30.9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.9
Overweight and obesity	—	26.9	—	13.6	—	12.8	19.7	—	—	—	—	—	—	—	—	—	25.0	—	4.1
Physical exercise	—	—	—	3.0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.4
Infections	12.3	—	29.2	1.5	19.6	—	—	10.6	—	—	—	—	—	—	—	—	—	—	2.5
Radiation – ionising	—	2.0	0.9	1.1	0.6	—	—	—	4.2	—	—	—	—	—	—	2.6	—	7.8	1.7
Radiation – UV	—	—	—	—	—	—	—	—	—	—	89.8	—	—	—	—	—	—	—	3.5
Occupation	0.6	3.3	3.0	—	0.2	0.02	—	2.9	20.5	97.0	—	—	—	—	—	7.1	—	0.9	4.9
All of the above	92.9	89.7	78.1	56.5	48.6	35.7	19.7	92.8	91.1	97.0	89.8	—	—	—	—	43.5	47.0	16.4	45.3
Females																			
Tobacco	54.9	71.3	15.4	9.9	15.3	31.0	—	79.1	83.6	—	—	—	7.2	—	2.6	34.4	15.0	3.0	15.6
Alcohol	16.9	11.3	—	6.9	5.0	—	—	12.2	—	—	—	6.4	—	—	—	—	—	—	3.3
Fruit and vegetables	53.6	45.1	33.9	—	—	—	—	43.5	9.3	—	—	—	—	—	—	—	—	—	3.4
Meat	—	—	—	16.4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.9
Fibre	—	—	—	14.6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.7
Salt	—	—	12.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.2
Overweight and obesity	—	11.2	—	12.2	—	11.5	17.8	—	—	—	—	8.7	—	33.7	—	—	22.2	—	6.9
Physical exercise	—	—	—	3.6	—	—	—	—	—	—	—	3.4	—	3.8	—	—	—	—	1.7
Post-menopausal hormones	—	—	—	—	—	—	—	—	—	—	—	3.2	0.0	1.2	0.7	—	—	—	1.1
Infections	14.0	—	36.0	3.1	9.3	—	—	10.6	—	—	—	—	100	—	—	—	—	—	3.7
Radiation – ionising	—	3.9	1.7	2.2	1.1	—	—	—	5.4	—	—	0.9	—	—	—	2.3	—	10.4	2.0
Radiation – UV	—	—	—	—	—	—	—	—	—	—	82.4	—	—	—	—	—	—	—	3.6
Occupation	0.2	1.1	0.3	—	0.1	—	—	1.6	4.3	82.5		4.6	0.7	—	0.5	1.9	—	0.5	2.4
Reproduction (breastfeeding)	—	—	—	—	—	—	—	—	—	—	—	3.1	—	—	17.6	—	—	—	1.7
All of the above	85.0	88.2	69.2	51.9	28.0	38.9	17.8	90.9	86.5	82.5	82.4	26.8	100	36.9	20.7	37.1	33.9	13.6	40.1
(b)																			
Persons																			
Tobacco	64.5	65.5	22.2	8.1	23.0	28.7	—	79.0	85.6	—	—	—	7.2	—	2.6	36.7	24.1	6.2	19.4
Alcohol	30.4	20.6	—	11.6%	9.1	—	—	24.6	—	—	—	6.4	—	—	—	—	—	—	4.0
Fruit and vegetables	56.0	46.1	35.8	—	—	—	—	45.4	8.8	—	—	—	—	—	—	—	—	—	4.7
Meat	—	—	—	21.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2.7
Fibre	—	—	—	12.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.5
Salt	—	—	24.0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0.5
Overweight and obesity	—	21.7	—	13.0	—	12.2	18.3	—	—	—	—	8.7	—	33.7	—	—	24.0	—	5.5
Physical exercise	—	—	—	3.3	—	—	—	—	—	—	—	3.4	—	3.8	—	—	—	—	1.0
Post-menopausal hormones	—	—	—	—	—	—	—	—	—	—	—	3.2	0.0	1.2	0.7	—	—	—	0.5
Infections	12.7	—	31.7	2.2	15.9	—	—	10.6	—	—	—	0.0	100	—	—	—	—	—	3.1
Radiation – ionising	—	2.7	1.2	1.6	0.8	—	—	—	4.7	—	—	0.9	—	—	—	2.5	—	8.9	1.8
Radiation – UV	—	—	—	—	—	—	—	—	—	—	85.9	—	—	—	—	—	—	—	3.5
Occupation	0.5	2.6	2.0		0.2	—	—	2.7	13.2	94.4	—	4.6	0.7	—	0.5	5.7	—	0.7	3.7
Reproduction (breastfeeding)	—	—	—	—	—	—	—	—	—	—	—	3.1	—	—	17.6	—	—	—	0.9
All of the above	90.6	89.0	74.9	54.4	41.6	37.3	18.3	92.5	89.2	94.4	85.9	26.8	100	36.9	20.7	41.8	42.3	15.2	42.7

[a]Excluding non-melanoma skin cancer.

Table 3 Comparison of estimate by WCRF/AICR for the UK in 2002, with current estimate for UK 2010

	Population attributable fraction (%)		
	WCRF/AICR (2009)		
Cancer	**Estimate**	**Range**	**Current estimate**
Mouth, pharynx and larynx			
Non-starchy vegetables	34	(2–57)	53
Fruits	17	(0–43)	
Alcoholic drinks	41	(4–67)	29
Total estimate	67	(0–92)	67
Oesophagus			
Non-starchy vegetables	21	(4–40)	46
Fruits	5	(2–9)	
Alcoholic drinks	51	(13–74)	21
Body fatness	31	(11–49)	22
Total estimate	75	(27–93)	67
Stomach			
Non-starchy vegetables	21	(0–41)	36
Fruits	18	(3–33)	
Salt	14	(0–39)	24
Total estimate	45	(0–76)	51
Colon–rectum			
Foods containing fibre	12	(5–18)	12
Red meat	5	(0–21)	21
Processed meat	10	(0–23)	
Alcoholic drinks	7	(0–18)	12
Physical activity	12	(4–20)	3
Body fatness	7	(0–17)	13
Total estimate	43	(0–73)	48
Liver			
Alcoholic drinks	17	(0–79)	9
Gallbladder			
Body fatness	16	(1–30)	18
Pancreas			
Foods containing folate[a]	23	(0–43)	
Body fatness	24	(0–43)	12
Total estimate	41	(0–67)	12
Lung			
Fruits	33	(17–51)	9
Breast			
Alcoholic drinks	22	(10–35)	6
Physical activity	12	(2–22)	3
Body fatness	16	(0–34)	9
Total estimate	42	(7–67)	17
Endometrium			
Physical activity	30	(11–47)	4
Body fatness	38	(27–48)	34
Total estimate	56	(35–72)	36
Prostate			
Foods containing lycopene[a]	20	(0–42)	
Kidney			
Body fatness	19	(12–27)	24
All cancers[b]	26	(6–42)	18

Abbreviations: AICR = American Institute for Cancer Research; WCRF = World Cancer Research Fund. [a]Not evaluated in the current work. [b]Excluding non-melanoma skin cancer.

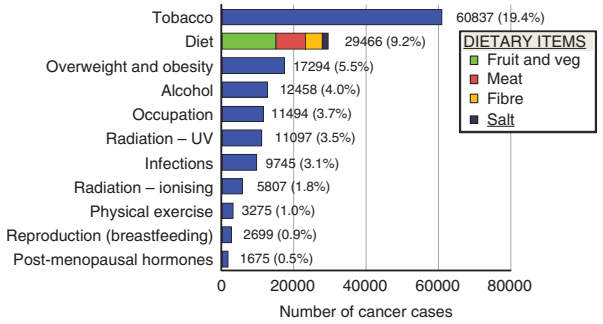

Figure 1 Number and percentage of cancer cases in the UK attributable to different exposures.

attributable to the 14 lifestyle and environmental exposures considered. For the most part these exposures are avoidable (ionising radiation is the exception), especially as for many (the dietary variables, physical exercise, overweight) the 'optimum' exposure represents a relatively modest recommended target. 'Avoidability' is in terms of the proportion of cancer *cases* that might be prevented. If the focus had been on avoidable *deaths*, then other interventions – especially through achieving earlier diagnosis (Richards, 2009) or generalising state-of-the-art treatment (Scottish Executive Health Department, 2001; National Audit Office, 2004) – would contribute to the total.

The four most important lifestyle exposures in Table 2 and Figure 1, tobacco smoking, dietary factors, alcohol drinking and bodyweight, account for 34% of the cancers occuring in 2010 – almost four-fifths of the total from all 14 exposures.

It is clear that tobacco smoking remains by far the most important avoidable cause of cancer in the UK. Reducing the prevalence of smoking has been a consistent public health objective for almost 50 years since the publication of the first report on smoking and health by the Royal College of Physicians (RCP, 1962). The prevalence of cigarette smoking fell substantially in the 1970s and the early 1980s, from 45% in 1974 to 35% in 1982, but the rate of decline then slowed, with prevalence falling by only about one percentage point every 2 years until 1994, after which it levelled out at about 27% before resuming a slow decline in the 2000s (Robinson and Bugler, 2010). The difference in prevalence between men and women has decreased considerably since the 1970s, and by 2008 the difference between men and women was not statistically significant, with 22% of men and 21% of women being current cigarette smokers. The overall reported number of cigarettes smoked per male and female smoker has changed little since the early 1980s. Changes in smoking-related cancer incidence lag several years behind changes in smoking prevalence, so that the current decreases in smoking-related cancer incidence and mortality will slow and eventual stop unless further progress can be achieved in reducing exposure to carcinogens in tobacco smoke.

Although it is currently not possible to pinpoint exactly what constituents of diet are protective against cancer, there is a consensus that diet is an important component of cancer risk. In the current exercise, we examine the likely impact of four components of diet for which the evidence appears to be most persuasive: fruit and vegetables and fibre (protective) and meat and salt (carcinogenic). In combination, deviation from the recommended intake levels is responsible for 9.2% of cancers in 2010 (the individual contributions are 4.7% from deficient fruit and vegetables, 2.7% from consumption of red and processed meat, 1.5% from a deficit of fibre and 0.5% from excess salt).

Excess body weight is the third most common avoidable cause of cancer in the UK, estimated to be responsible for 5.5% of

cancers in 2010 (4.1% in men, 6.9% in women). In the last 15 years there have been significant increases in levels of overweight and obesity, and currently in England, a total of 66% of men and 57% of women have a BMI of $\geqslant 25\,kg\,m^{-2}$: this includes 22% of men and 25% of women who are obese (NHS Information Centre, 2010), defined as a BMI $>30\,kg\,m^{-2}$. Trends among children and young people suggest that we are yet to experience the full health impact of the overweight and obesity epidemic in the UK.

Alcohol consumption is the fourth most important cause of cancer in the UK, and popular belief is that alcohol use is a highly prevalent and growing problem for the UK population. In fact, data from the national General Lifestyle Survey (Robinson and Bugler, 2010) show that the average number of units of alcohol consumed in a week rose in the 1990s to a peak in the period 2000–2002 of around 17 units for men, and 7.5 units for women, but has fallen since that time in both sexes. The proportion of men and women drinking more than the recommended maximum (21 units a week in men and 14 units in women) has also been falling. The fall in consumption occurred among men and women in all age groups, but was most evident among those aged 16–24. It is quite possible, therefore, that the burden of alcohol-related cancers is around its maximum at present, and will fall in future.

Population-attributable fractions provide a valuable quantitative appraisal of the impact of different factors in cancer causation, and are thus helpful in prioritising cancer control strategies. However, they should not be used to indicate the percentage of cancers that can currently be prevented by practical means without reference to the individual sections that discuss some of the uncertainties involved. Furthermore, quantifying the likely impact of preventive interventions requires rather complex scenario modelling, including specification of realistically achievable population distributions of risk factors, and the timescale of change, as well as the latent periods between exposure and outcome, and the rate of change following modification in exposure level (e.g., Soerjomataram *et al*, 2010). Thus, although 50% of colorectal cancer cases diagnosed in the UK in 2010 are attributable to lifestyle (diet, alcohol, physical inactivity and overweight), it has been estimated that only about half of this number is preventable in a reasonable ($\sim$20-year) timescale (Parkin *et al*, 2009).

See acknowledgements on page Si.

Conflict of interest

The authors declare no conflict of interest.

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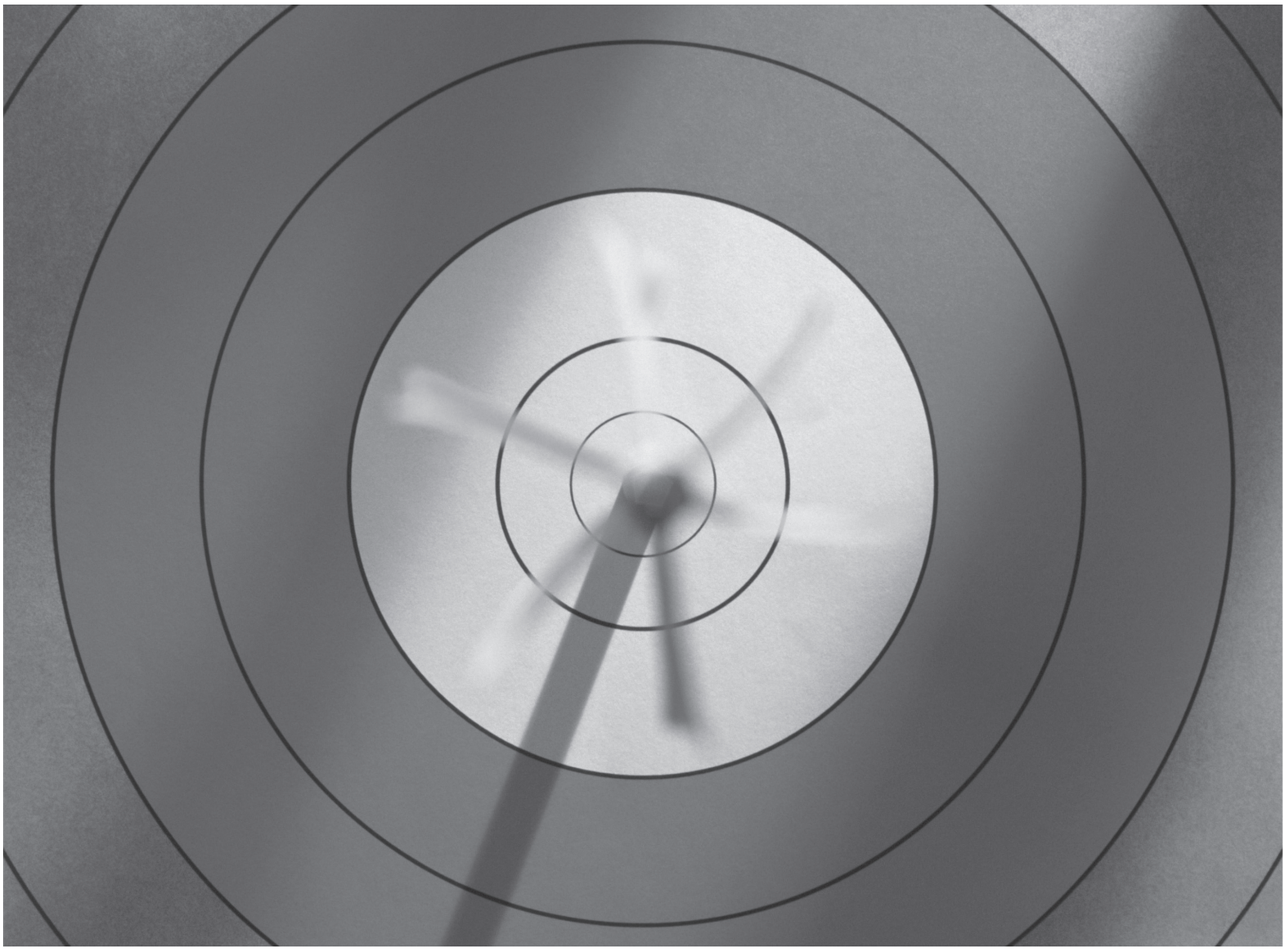

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