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# Incident cancer burden attributable to excess body mass index in 30 European countries

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**Excess adiposity is associated with increased risks of developing adult malignancies. To inform public health policy and guide further research, the incident cancer burden attributable to excess body mass index (BMI $\geq$ 25 kg/m$^2$) across 30 European countries were estimated. Population attributable risks (PARs) were calculated using European- and gender-specific risk estimates from a published meta-analysis and gender-specific mean BMI estimates from a World Health Organization Global Infobase. Country-specific numbers of new cancers were derived from Globocan2002. A ten-year lag-period between risk exposure and cancer incidence was assumed and 95% confidence intervals (CI) were estimated in Monte Carlo simulations. In 2002, there were 2,171,351 new all cancer diagnoses in the 30 countries of Europe. Estimated PARs were 2.5% (95% CI 1.5–3.6%) in men and 4.1% (2.3–5.9%) in women. These collectively corresponded to 70,288 (95% CI 40,069–100,668) new cases. Sensitivity analyses revealed estimates were most influenced by the assumed shape of the BMI distribution in the population and cancer-specific risk estimates. In a scenario analysis of a plausible contemporary (2008) population, the estimated PARs increased to 3.2% (2.1–4.3%) and 8.6% (5.6–11.5%), respectively, in men and women. Endometrial, post-menopausal breast and colorectal cancers accounted for 65% of these cancers. This analysis quantifies the burden of incident cancers attributable to excess BMI in Europe. The estimates reported here provide a baseline for future modelling, and underline the need for research into interventions to control weight in the context of endometrial, breast and colorectal cancer.**

Epidemiology

Increased body adiposity, commonly approximated by body mass index (BMI), is an established risk factor for cancer development.[1] Using a standardized dose-response meta-analysis and only including prospective observational studies, the authors recently quantified these risks by gender and major geographical population groups for 20 cancer types.[2] Given the plausibility of the biological explanations,[3] the consistency of associations,[2] the sufficiently long latency times between BMI measurement and cancer occurrence,[2] and the recent demonstrations of risk reversibility in morbidly obese cohorts undergoing bariatric surgery,[4,5] many of these associations are probably causal. Although the increases in risk per 5 kg/m$^2$ increment are modest, the numbers of incident cases attributable to excess BMI might be substantial as the prevalences of overweight and obesity are increasing in many countries.[6,7]

One previous study, reported by Bergström and colleagues,[8] analyzed data from cohort and case-control studies for six cancer types, and calculated the attributable numbers of new cancer cases for the European Union (then nine countries) using the conventional Levin definition of population attributable risk (PAR).[9] This approach may be criticized as it ignores the cases where occurrence would have been delayed in the absence of exposure.[10] Alternative models,[11–15] which incorporate dynamic demographic properties and use a counterfactual approach to estimate avoidable rather than attributable risk, have been developed to overcome this limitation.

**Key words:** body mass index, obesity, cancer risk, meta-analysis, population impact measures
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The aim of this study was to estimate the cancer burden attributable to excess BMI across 30 European countries drawing upon the authors' published meta-analysis.[2] As a prelude to more sophisticated future modelling, this study used the conventional (categorical) approach to derive baseline estimations and associated uncertainties; undertook extensive sensitivity analyses to assess the robustness of these estimates; and compared them with impact measures derived from a counterfactual model (using the PREVENT platform).[15] The rationale for estimating impact is threefold: to inform health policies; to identify research priorities; and form a basis for future modelling of trends and interventions. As a scheme for ranking incident cancer burden due to overweight and obesity exists in the United States,[16] the present study focused on Europe.

## Material and Methods

The steps taken in this analysis are summarized in Figure 1. Gender-specific PARs were calculated per country for each cancer type as described by Levin:[9]

$$\mathrm{PAR} = \frac{P_e(RR-1)}{P_e(RR-1)+1}$$

where $P_e$ is the prevalence of exposure and RR is the relative risk. PAR is defined as the proportion of all cases (exposed and unexposed) that would not have occurred if the exposure had been absent.[17]

Using extracted data from the meta-analysis,[2] calculations were re-run to give Europe-specific adjusted risk estimates for each cancer type by gender. Risk estimates, and their 95% confidence intervals (CIs), were expressed (to 3 decimal places) per 5 kg/m$^2$ increase in BMI.

### Countries and cancer incident cases

The analysis focused on 30 European countries: 27 from the EU (Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom), and three European Free Trade Association countries (Iceland, Norway and Switzerland). The cancers of interest were those for which there was a significant positive association with increasing BMI from the previous meta-analysis.[2] In men, these were: oesophageal adenocarcinoma, thyroid, colon, renal, rectal, and prostate cancers, malignant melanoma, multiple myeloma, leukaemia and non-Hodgkin's lymphoma; and in women were: oesophageal adenocarcinoma, endometrial, gallbladder, renal, thyroid, post-menopausal breast, pancreatic, and colon cancers, leukaemia, multiple myeloma, and non-Hodgkin's lymphoma. Risk estimates for the associations between BMI and lung cancer, squamous cell carcinoma of the oesophagus, and pre-menopausal breast cancer are less than unity but cases from these were not included as "negative" attributions in the models as their estimates are likely to represent confounding (mainly smoking) in the first two cancer types (webfigure in reference 2),[2] and the limitation of BMI as a surrogate of adiposity in the third cancer type.[18]

The numbers of new gender-specific cancer cases per country were extracted from GLOBOCAN2002.[19] GLOBOCAN does not report incident case numbers for colon and rectal cancers separately; oesophageal squamous cell carcinoma and adenocarcinoma separately; and gallbladder cancer. These were estimated from country- and gender-specific proportions for incidences derived from Cancer Incidence in Five Continents vol. VIII (CIV VIII).[20] The CIV VIII does not report incidences for Bulgaria, Cyprus, Greece, Hungary, Luxembourg, and Romania—here incident case numbers were derived using incidences from neighbouring countries of similar socio-cultural and demographic characteristics. For all cancer types, the GLOBOCAN age ranges 15 to 65+ years (*i.e.*, all adult ages) were used except for post-menopausal breast cancer where age range 55+ years was used.

### Risk exposure

Data were extracted on mean BMI and prevalence of excess body weight (overweight and obesity combined) by gender and age from the World Health Organisation (WHO) Global Infobase (which adjusts for differences in inter-survey definitions and representativeness and standardises results to the WHO standard population).[21] For reasonable estimation of causal attribution, exposure to excess BMI was assumed to predate cancer incidence by a lag period of 10 years (*i.e.*, 1992), as this is consistent with cohorts evaluating associations between intentional weight loss and subsequent breast cancer risk;[22–26] is the period required to demonstrate the beneficial effects of bariatric surgery on cancer incidences;[4] and is a typical duration from BMI measurement to incident cancer in the systematic review.[2] We searched the literature and identified 12 surveys from 10 European countries with two or more time-point data, which provided evidence that the upward shifts in mean BMI in Europe over the past two decades were predominantly linear (see supplemental material p1–2). Mean BMI values and their standard deviations (SDs) for 1992 using standard linear regression were extrapolated, and the gender-specific country prevalences of excess body weight (BMI $\geq$ 25 kg/m$^2$), assuming normal BMI distributions, estimated.

The internal validity of the model were tested by comparing the modelled linear trends of mean BMI values with observed survey values for England and the Netherlands, available annually from 1993 to 2007 and 1981 to 2007, respectively, and found good agreement (see supplemental material p3). The proportions of obesity (BMI $\geq$ 30 kg/m$^2$) in the models were compared with those from 17 national datasets (15 countries), and again demonstrated good agreement (see supplemental material p4–5).

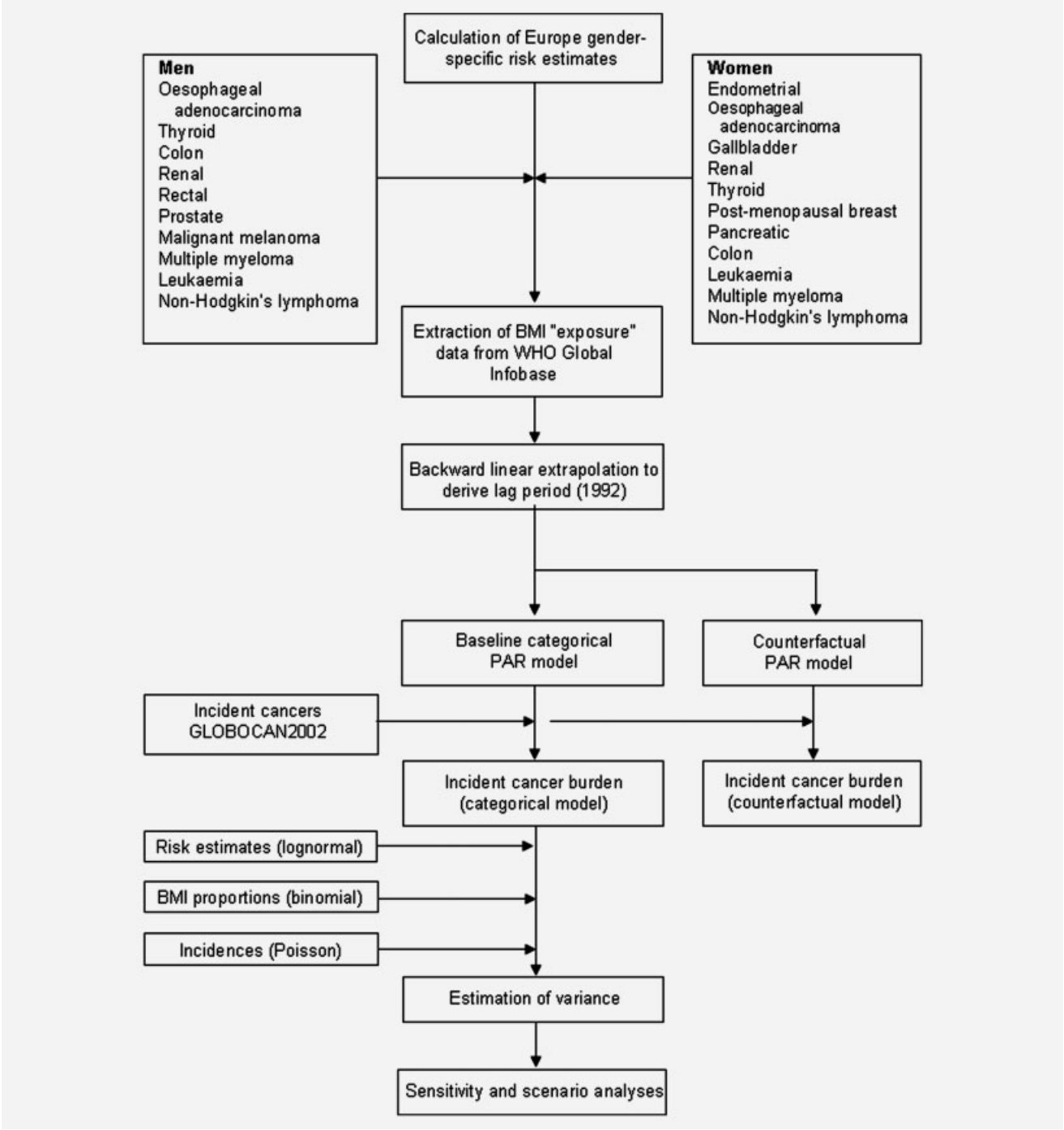


**Figure 1.** Flow diagram of study analysis. BMI, body mass index; WHO, World Health Organisation; PAR, population attributable risk.



### Statistical analysis

BMI was modelled as a simple dichotomous exposure—normal *versus* excess body weight (combined overweight and obesity)—facilitating comparisons with the counterfactual modelling and minimising the complexities of handling weight categories as polytomous outputs.[17] In the absence of consistent fixed reference points in studies from the meta-analysis[2] (*i.e.*, *RR*s were floating), the increased risk due to excess body weight was quantified as the BMI 'distance' between the median of the normal weight population and the median of the excess body weight population for each country by gender. This was then multiplied by the RR per unit kg/m$^2$ increase. The relationship with endometrial cancer was modelled as a polytomous exposure as there is evidence of a threshold effect in risk in the mid-region of the overweight category.[2,27] In this scenario, two excess body weight pseudo

categories—above and below the threshold, respectively, were considered using Miettinen's formula.[17] For all models, the attributable disease burdens[28] were derived by multiplying PARs by the number of new site-specific cancers for 2002.

To determine the uncertainty of the model estimates, we incorporated probability distributions for (i) the prevalence of risk exposure using the sample size of the country-specific surveys to estimate variance (binomial distributions); (ii) our risk estimates and 95% confidence intervals (lognormal distributions); and (iii) cancer incidences (Poisson distributions). Monte Carlo simulations (10,000) were run in R (version 2.7.1, R Foundation, Vienna, Austria, see supplemental material p6–10).

### Sensitivity analyses

The analyses were repeated using a counterfactual approach, where PAR is defined as the percentage reduction in cancer incidence that would take place if exposure to excess weight were reduced to a counterfactual distribution.[29,30] To test the equivalence between the conventional (categorical) and counterfactual (continuous) models, the hypothetical counterfactual distribution was zero exposure (the theoretical minimum risk[30]), using the averaged means $\pm$ SDs of BMI distributions for normal weight categories (BMI $\leq$ 25 kg/m$^2$) across all 30 countries (22.70 $\pm$ 1.17 kg/m$^2$ for men; 22.31 $\pm$ 1.37 kg/m$^2$ for women).

The sensitivity analysis examined the effect of assuming lag periods of 15, 5 and zero years; the effect of using an exponential rather than a linear function to model BMI changes; the effect of excluding cancer types with risk estimates associated with high levels of heterogeneity ($I^2 \geq 70\%$);[31] the effect of an increase in RR estimates of 0.20 per cancer type;[32] and the BMI distribution parameterisation (lognormal, gamma) (see supplemental material p11). Recognizing that in the absence of hormonal replacement therapy (HRT) usage, strengths of BMI associations for post-menopausal breast[33] and endometrial[34] cancer risks are increased—a hypothetical European population with no HRT usage in women was also tested.

We sought to test the scenario of a contemporary (2008) European population recognizing that estimated increases in BMI distributions in some Central European countries may currently be underestimated;[35] that the BMI distribution shifts from a normal to gamma parameterisation as adiposity increases in populations;[36] that in men the wider use of PSA screening nullifies the BMI-cancer association with prostate cancer;[37] and that, in women, HRT usage has declined considerably in many European countries.[38] In all these analyses, the numbers of cancer cases were those for 2002.

## Results

### Europe-specific risk estimates and mean BMI trends

The risk estimates per 5 kg/m$^2$ BMI increase for European studies for the cancer types of interest are listed in Table 1. Severe heterogeneity of studies was noted only for leukaemia in women. BMI-cancer risk associations were linear, except for endometrial cancer, which showed a pivot at BMI 27 kg/m$^2$ (see supplemental material p12). Estimates of RRs were derived from the studies included in the published meta-analysis (search to December 2007),[2] with one recently published study on endometrial cancer[39] added to increase the robustness of the "pivoted" model. For all 30 countries, mean BMI ($\pm$ SD) increased from 25.3 ($\pm$ 4.0) kg/m$^2$ in 1992 (baseline) to 25.9 ($\pm$ 4.1) kg/m$^2$ in 2008 for men (unweighted mean BMI change per 5 years = 0.2 kg/m$^2$); and from 24.8 ($\pm$ 5.1) kg/m$^2$ to 25.4 ($\pm$ 5.2) kg/m$^2$ in women (unweighted mean change per 5 years = 0.2 kg/m$^2$) (see supplemental material p13).

### Population attributable risks and incident burden by country

In 2002, there were 2,171,351 new cancer diagnoses (excluding non-melanoma skin cancers) in the 30 countries—1,170,107 in men and 1,001,244 in women (full details of cancer cases per country in supplemental material p14). Using estimates for prevalences of excess body weight for 1992 (*i.e.*, a ten year lag period), the estimated PARs using the categorical model were 2.5% (1.5–3.6%) of all cancers in men and 4.1% (2.3–5.9%) all cancers in women (Fig. 2) (full details in supplemental material p15–16). The PARs varied between countries; in men, from 1.1% in Romania to 3.5% in the Czech Republic; and in women, from 2.2% in Denmark to 9.4% in Malta. The estimated PARs as a percentage of all obesity-related cancers (515,815 men: 482,494 women) were 5.7% (3.3–8.2%) and 8.5% (4.8–12.2%) for men and women, respectively (supplemental material p17).

The attributable incident cancer burdens by country are summarised in Figure 3 (full details in supplemental material p18–19). For the baseline (1992) model (model A), the estimated number of excess new incident cancer cases for all 30 countries was 70,288 (40,069–100,668): 29,466 (16,940–42,000) in men, and 40,822 (23,129–58,668) in women.

### PARs and incident burden by cancer type

The PARs by cancer types for all 30 countries are summarised in Table 2—these ranged from 2.0% for prostate cancer to 26.7% for oesophageal adenocarcinoma in men, and from 2.6% for colon cancer to 30% for endometrial cancer in women. The largest number of attributable new cancers was for endometrial (16,071 cases) and colorectal (combined men and women: 15,844 cases) cancers (45% combined) followed by post-menopausal breast (8,560 cases) and renal (combined men and women: 8,306 cases) cancers. Notably, the numbers of new cases of oesophageal adenocarcinoma were particular high in the UK relative to the remainder of Europe (946 out of 1,799 in men; 286 out of 489 in women).

### Counterfactual model and other sensitivity analyses

The estimated PARs using the counterfactual method and minimum theoretical risk for all 30 countries were 2.5% and 4.3%, respectively, for men and women. The corresponding attributable incident cancer burdens were 29,388 for men

**Table 1.** Gender-specific estimated risk ratios for European populations by cancer types

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| **Cancer type** | **n*** | **Risk ratio (95% CIs)** | **I2 (%)** | **n*** | **Risk ratio (95% CIs)** | **I2 (%)** |
| **Colorectal** | | | | | | |
| Colon | 9 | 1.209 (1.181, 1.234) | 0% | 6[†] | 1.043 (1.000, 1.101) | 22% |
| Rectum | 9 | 1.091 (1.062, 1.122) | 0% | | NA | |
| Gallbladder | | NA | | 1 | 1.350 (1.249, 1.463) | |
| Leukaemia | 4 | 1.077 (1.001, 1.157) | 23% | 2[†] | 1.135 (1.000, 1.297) | 84% |
| Malignant melanoma | 4 | 1.159 (1.063, 1.264) | 35% | | NA | |
| Multiple myeloma | 3 | 1.086 (1.010, 1.169) | 29% | 2 | 1.113 (1.072, 1.155) | 0% |
| Non-Hodgkin's lymphoma | 5 | 1.057 (1.027, 1.087 | 0% | 5 | 1.103 (1.002, 1.214) | 65% |
| Oesophageal adenocarcinoma | 3 | 1.616 (1.434, 1.820) | 0% | 3 | 1.508 (1.305, 1.743) | 0% |
| Pancreas | | NA | | 5 | 1.137 (1.054, 1.226) | 0% |
| Renal | 5 | 1.214 (1.119, 1.317) | 40% | 6 | 1.327 (1.271, 1.385) | 1% |
| Thyroid | 3[†] | 1.149 (1.000, 1.334) | 31% | 3 | 1.136 (1.055, 1.224) | 5% |
| Prostate | 9 | 1.034 (1.002, 1.068) | 48% | | – | |
| Post-menopausal breast | | – | | 14 | 1.083 (1.027, 1.141) | 57% |
| **Endometrium**[‡] | | | | | | |
| Below 27 kg/m2 | | – | | 11 | 1.221 (1.084, 1.376) | |
| Above 27 kg/m2 | | – | | 11 | 1.729 (1.598, 1.872) | |

All risk estimates are taken from meta-analyses of Europe-specific studies included in the previously published meta-analysis (Ref. 2) – Australian studies (group with European in the original paper) are not included in this definition.
*Number of studies. [†]For thyroid cancer in men, and rectal cancer and leukaemia in women, the lower confidence limits of the estimates for European population studies only, were less than one – if included in the analyses, these would result in meaningless negative new cancer cases attributable to excess body weight. Thus, the lower limit is rounded to unity. [‡]Endometrial cancer was initially treated in the analysis as two "slopes" below and above BMI, 27 kg/m2. Estimates were then combined. Abbreviation: NA, not applicable.

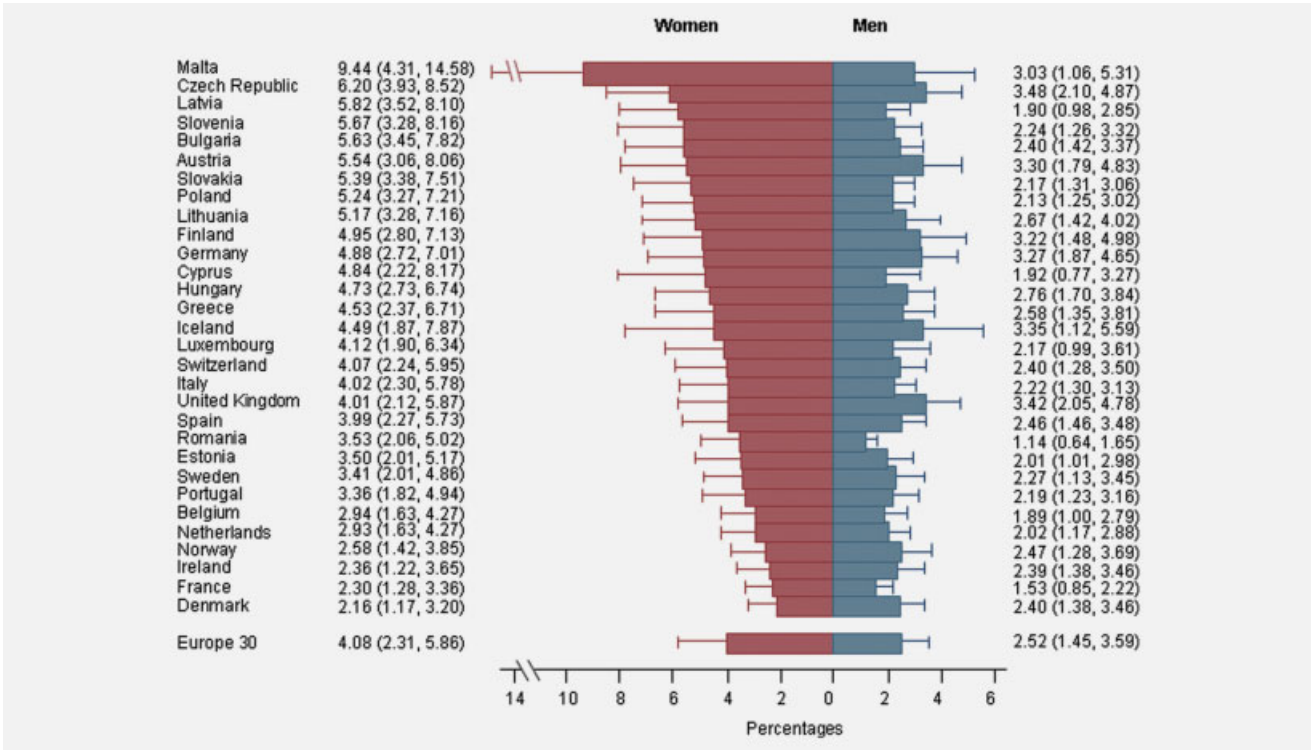


**Figure 2.** Percentages of all cancers attributable to excess body mass index by country.

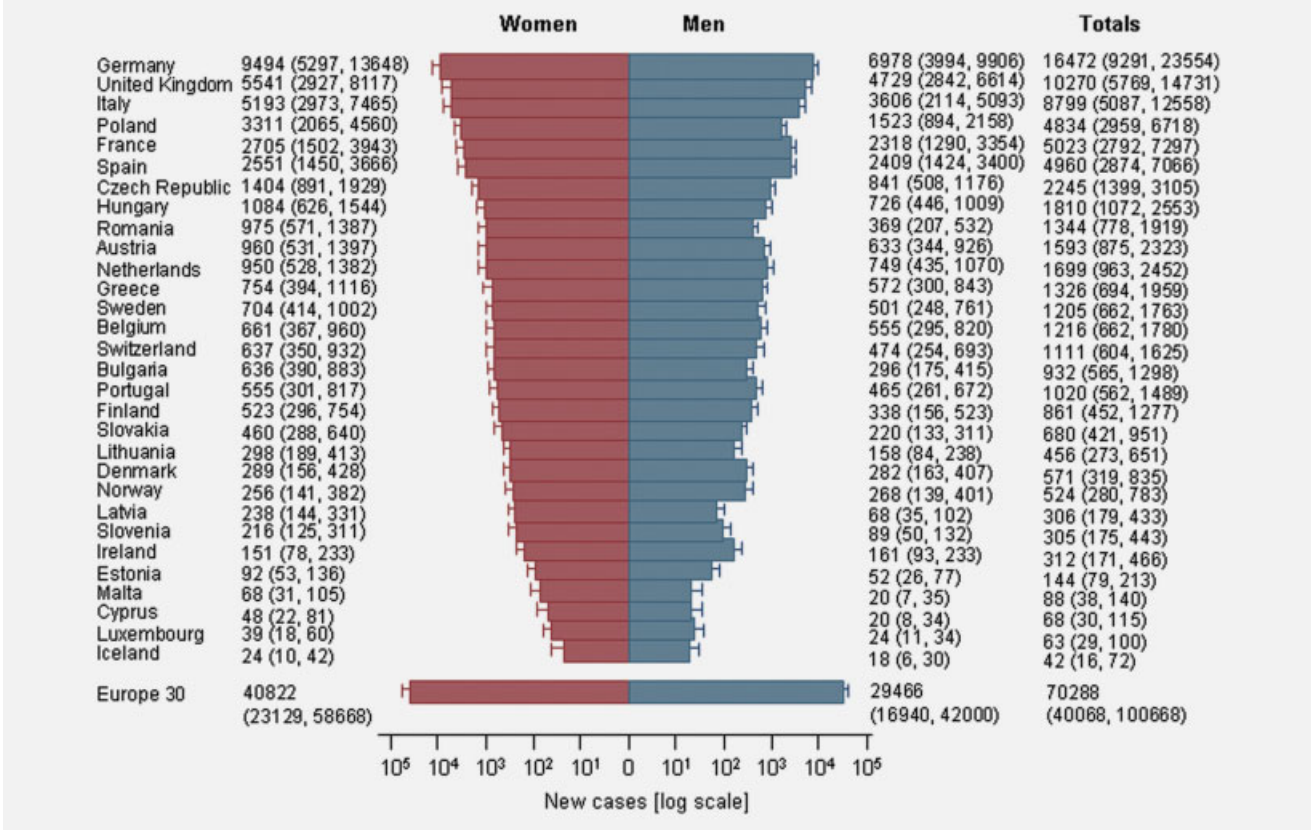


**Figure 3.** Number of new cancer cases attributable to excess body mass index by country.

**Table 2.** Population attributable risks and incident burden by cancer type in 30 European countries (2002)

| | PAR | | Incident cancer burden | | |
|---|---|---|---|---|---|
| **Cancer type** | **Men** | **Women** | **Men** | **Women** | **Men & women** |
| **Colorectal** | | | | | 15844 (11304, 20735) |
| Colon | 10.92 (9.59, 12.24) | 2.57 (0, 5.51) | 10386 (9131, 11643) | 2274 (0, 4890) | 12660 (9131, 16533) |
| Rectum | 5.05 (3.45, 6.67) | – | 3184 (2173, 4202) | – | 3184 (2173, 4202) |
| Gallbladder | – | 18.16 (13.43, 22.81) | – | 2163 (1571, 2764) | 2163 (1571, 2764) |
| Leukaemia | 4.31 (0.09, 8.47) | 7.71 (0, 15.49) | 1387 (35, 2730) | 1801 (0, 3643) | 3188 (35, 6364) |
| Malignant melanoma | 8.52 (3.53, 13.43) | – | 1928 (794, 3050) | – | 1928 (794, 3050) |
| Multiple myeloma | 4.79 (0.56, 8.98) | 6.53 (4.26, 8.82) | 704 (83, 1327) | 836 (537, 1144) | 1540 (620, 2471) |
| Non-Hodgkin's lymphoma | 3.22 (1.57, 4.88) | 5.98 (0.16, 11.79) | 1137 (554, 1725) | 1680 (47, 3343) | 2187 (601, 5068) |
| Oesophageal adenoca. | 26.70 (20.34, 32.82) | 24.46 (15.98, 32.52) | 1799 (1341, 2273) | 489 (301, 698) | 2288 (1642, 2962) |
| Pancreas | – | 7.82 (3.21, 12.39) | – | 2127 (877, 3397) | 2127 (877, 3397) |
| Renal | 11.15 (6.50, 15.72) | 17.06 (14.43, 19.69) | 4520 (2638, 6383) | 3786 (3164, 4427) | 8306 (5802, 10810) |
| Thyroid | 8.02 (0, 16.18) | 7.77 (3.24, 12.26) | 389 (0, 798) | 1035 (428, 1649) | 1424 (428, 2447) |
| Prostate | 1.95 (0.09, 3.81) | – | 4032 (207, 7869) | – | 4032 (207, 7869) |
| Post-menopausal breast | – | 4.87 (1.66, 8.08) | – | 8560 (2920, 14211) | 8560 (2920, 14211) |
| Endometrium | – | 29.98 (25.58, 34.36) | – | 16071 (13652, 18520) | 16071 (13652, 18520) |

More details in the supplemental material pages 15 through 19.
Values for absolute numbers of new cases – where lower limit was a negative number, zero was returned.
Abbreviations: PAR, population attributable risk as a proportion of all cancers; adenoca, adenocarcinoma.

and 43,046 for women (see supplemental material p20–23). The total number of new cases (72,434) is marginally greater than that estimated by the categorical model, but there were high levels of concordance between approaches: the concordance correlation coefficients[40] were 1.00 ($p < 0.0001$) for men and 0.98 ($p < 0.0001$) for women. Other sensitivity analyses are shown in Table 3. The point estimates for attributable burden of new cancers varied only slightly when changing the lag period or assuming an exponential rather than linear increase in BMI. Excluding cancer types with risk estimates associated with high levels of heterogeneity had little effect on estimates. However, results were sensitive to assuming higher RRs (increase by 0.20) for each cancer site; changing the BMI distributions to lognormal or gamma parameterisations; and the hypothetical scenario of no HRT usage in women.

### Contemporary European population

The scenario analyses for a 2008 European population are shown in Table 4. Seven Central European countries (Bulgaria, Estonia, Hungary, Latvia, Lithuania, Poland and Romania) were recorded in the WHO Global Infobase as having no increase in mean BMI through the 2000s. If the mean BMI for these countries increased in line with the gender-specific European average—this had only modest effect on total attribution (model L). In a model with a gamma distribution of BMI, wide usage of PSA screening, and 15% HRT usage (see supplemental material p24–26),[41] the estimated PARs increased to 3.2 (2.1–4.3)% and 8.6 (5.6–11.5)%, respectively, in men and women (model M: 76.5% increase compared with a baseline model). In this model, the largest number of attributable new cancers was for endometrial (33,421), post-menopausal breast (27,770) and colorectal (23,730) cancers—accounting for 65 % of all obesity-related cancers.

## Discussion

### Summary of main findings

This study covered 30 European countries and reported that, in relative terms, 2.5% in men and 4.1% in women, and in absolute terms, over 70,000 new cancer cases were attributable to excess BMI in 2002. The estimates derived from the categorical PAR method were equivalent to those using a counterfactual approach. These estimates are likely to be conservative, as in a scenario analysis of a plausible contemporary (2008) population, the estimated PARs increased a quarter-fold in men and two-fold in women. In this present day scenario, endometrial, breast and colorectal cancers were identified as priorities for research and public health measures. Against the background of rising levels of obesity, incident cancer attributable to excess BMI may be greater in the future.

### Limitations and strengths

The present study has a number of limitations. First, impact measures inherit the problems of the original surveys of risk exposure such as variations in years of survey undertaken, differences in age groups, methods of data collection (*e.g.*, self reported *vs.* measured) and poorly representative sampling of populations. To minimise this potential bias, the authors used WHO standardised BMI prevalence data for each country, and modelled the uncertainty around each country-specific estimate. Second, the assumption that increased cancer risk associated with excess body weight is constant across age groups may be incorrect;[42] or there may be age-dependent combinational effects with other risk factors.[43] However, the authors previously demonstrated that the age of study populations did not influence risk associations (webappendix 7.2 in ref. 2).[2] Third, with the exception of endometrial cancer, the current model assumes that increased risk is linear across the BMI range in a population, whereas by contrast, the association between BMI and all-cause mortality is U-shaped.[42,44,45] Fourth, the underlying models assume causal attribution between excess body weight and cancer risk—yet, there is an absence of evidence that weight reduction decreases cancer incidence. However, analyses of associations between intentional weight loss and cancer risk in prospective cohorts in women[22–25] and men,[26] and the findings of decreased cancer incidence following bariatric surgery in morbidly obese patients,[4] support the hypothesis that there is a reversible effect. Finally, the current analysis considered exposure at a time before the incident cancer and assumed that exposure remains constant thereafter. While this was addressed in the sensitivity analyses and demonstrated only modest shifts in estimates with varying lag periods, there may still be differences in lag periods between women (where hormone-sensitive cancer prevail) and men, as suggested by the differential effects of bariatric surgery on subsequent cancer reduction.[4]

There are several strengths. First, standardized gender-specific estimates from our recent meta-analysis of prospective observational studies were used[2]—estimates which are generally more conservative than where analyses use case-control studies and studies of cancer mortality. Second, the estimates were European-specific. Despite this, there may still be as yet unpublished differences in BMI-cancer risk associations within European populations, just as there are, for example, differences in breast cancer risk for Asian-Pacific populations[2] and Black-American populations.[46] Third, there was broad consistency of association (*i.e.*, homogeneity between studies) for the meta-analyses which underpinned the risk estimates. Fourth, the internal validity of the modelled BMI trends were tested and showed close agreement with published country-specific trends. Fifth, a Monte Carlo approach incorporating uncertainties around relative risks, risk exposures, and cancer incidences was developed. Sixth, the sensitivity analyses demonstrated that the estimates of impact varied most with: relative risk estimation (similar to that shown for deaths attributable to obesity[32]); changes in the shape of BMI distribution; and the prevalence of HRT usage in women; but estimates were not substantially affected by changes in the lag period. Finally, repeating the analyses using an established counterfactual methodology[29] demonstrated similar estimates to those from the categorical model.

**Table 3.** Sensitivity analysis*

| | Men | | | Women | | | Men & women | |
|---|---|---|---|---|---|---|---|---|
| | PAR | No. of cases | Δ† | PAR | No. of cases | Δ† | No. of cases | Δ† |
| Model (baseline) A: 10 lag period (1992) with linear BMI trends | 2.52 (1.45, 3.59) | 29466 (16940, 42000) | | 4.08 (2.31, 5.86) | 40822 (23129, 58668) | | 70288 (40069, 100668) | |
| Model B: 10 lag period (1992) with exponential BMI trends | 2.53 (1.45, 3.59) | 29568 (16992, 42185) | 0.4% | 4.10 (2.32, 5.88) | 41048 (23239, 58883) | 0.6% | 71616 (40231, 101068) | 0.5% |
| Model C: 15 year lag period (1987) with linear BMI trends | 2.35 (1.35, 3.35) | 27506 (15759, 39248) | −7.7% | 3.84 (2.19, 5.52) | 38457 (21894, 55234) | −5.8% | 65963 (37653, 94482) | −6.1% |
| Model D: 5 year lag period (1997) with linear BMI trends | 2.69 (1.54, 3.83) | 31467 (18058, 44817) | 6.8% | 5.87 (4.32, 2.44) | 43218 (24393, 62122) | 5.9% | 74685 (42450, 106939) | 6.3% |
| Model E: no year lag period (2002) | 2.86 (1.64, 4.08) | 33507 (19239, 47713) | 13.7% | 4.56 (2.56, 6.56) | 45661 (25604, 65682) | 11.6% | 79168 (44843, 112295) | 12.6% |
| Model F: baseline excluding risk estimates with high heterogeneity‡ | 2.52 (1.45, 3.59) | 29466 (16940, 42000) | 0% | 3.90 (2.31, 5.50) | 39021 (23177, 55034) | −4.4% | 68487 (40117, 97034) | −2.6% |
| Model G: baseline with 0.20 increase in RR | 6.74 (5.81, 7.68) | 78842 (67960, 89842) | 168% | 8.46 (6.92, 10.02) | 84719 (69323, 100359) | 107% | 163561 (137283, 190201) | 133% |
| Model H: modelling BMI as lognormal distribution (1992) | 2.93 (1.64, 4.21) | 34245 (19198, 49235) | 16.2% | 4.65 (2.52, 6.79) | 46548 (25280, 67945) | 14.0% | 80793 (44478, 117180) | 15.0% |
| Model I: modelling BMI as gamma distribution (1992) | 3.19 (1.83, 4.55) | 37382 (21462, 53255) | 26.9% | 5.48 (3.12, 7.86) | 54868 (31192, 78699) | 34.4% | 92250 (52654, 131954) | 31.2% |
| Model J: hypothetical population with no HRT usage (1992) | – | – | – | 6.00 (3.97, 8.00) | 60028 (39753, 80110) | 47.1% | – | – |

*For all models, the cancer incidences remain those of 2002. †Compared with model A. ‡Excluded leukaemia in women: no exclusions in men. Abbreviations: HRT, hormonal replacement therapy; PAR, population attributable risk as a proportion of all cancers; RR, relative risk.

Table 4. Scenario analysis for a plausible contemporary (2008) European population*

| | Men | | | Women | | | Men & women | |
|---|---|---|---|---|---|---|---|---|
| | PAR | No. of cases | Δ† | PAR | No. of cases | Δ† | No. of cases | Δ† |
| Model K: 2008 European BMI exposures normally distributed | 3.08 (1.77, 4.37) | 35990 (20683, 51189) | | 4.86 (2.72, 6.98) | 48614 (27259, 69925) | | 84604 (47942, 121114) | |
| Model L: European average increases in BMI trends in Central Europe | 3.10 (1.78, 4.40) | 36266 (20828, 51533) | | 4.90 (2.74, 7.04) | 49049 (27446, 70530) | | 85315 (48274, 122063) | |
| Model M: BMI gamma distribution; wide PSA screening usage; 15% HRT usage in population | 3.22 (2.13, 4.29) | 37681 (24925, 50241) | 27.9% | 8.63 (5.62, 11.5) | 86369 (56273, 115183) | 111.6% | 124050 (81198, 165424) | 76.5% |
| **Main cancers in Model M** | | | | | | | | |
| Endometrial cancer | – | – | | 61.4‡ (49.2, 71.7) | 33421 (26803, 39053) | | 33421 (26803, 39053) | |
| Post-menopausal breast cancer | – | – | | 14.8‡ (10.3, 19.2) | 27770 (19367, 36044) | | 27770 (19367, 36044) | |
| Colorectal (colon & rectum) | 13.0‡ (10.9, 15.1) | 20114 (16825, 23413) | | 3.90‡ (0, 8.30) | 3616 (0, 7709) | | 23730 (16825, 31122) | |
| Kidney | 16.8‡ (9.8, 23.5) | 6613 (3878, 9250) | | 25.5‡ (21.4, 29.5 | 5775 (4865, 6701) | | 12388 (8743, 15951) | |

*For all models, the cancer incidences remain those of 2002. †Compared with model A. ‡As a proportion of the given cancer type. Abbreviations: HRT, hormonal replacement therapy; PAR, population attributable risk as a proportion of all cancers; RR, relative risk.

### Comparison with other studies

Published studies have estimated the proportion of cancer deaths attributable to obesity in individual European countries, such as France;[47] or for Europe as a whole (in a global analysis).[48] However, these estimates cannot be used to infer incident cancers as: (i) they are reported against the background of high smoking-attributable cancer deaths (which tend to dilute other attributable factors), and (ii) relative risk for cancer mortality may overinflate those for cancer incidence,[27,49] as increased adiposity may itself unfavourably impact upon cancer treatment selection and outcome. The present results can be more directly compared with the Bergström analysis,[8] which reported population attributable risks of 3% in men and 6% in women, but in that study, there was no differentiation of gender-specific risks and the number of constituent studies meta-analysed was smaller, probably leading to overestimation compared with more contemporary estimates.[1,2,27] The present results are similar to those for the Million Women Study,[27] which estimated 5% of all cancers in UK women to be attributable to combined overweight and obesity (5541 *versus* 6000 new cases annually). Based on a denominator of obesity-related cancers, the World Cancer Research Fund (WCRF)[50] calculated UK population attributable fractions of 18% in men and 16% in women. The equivalent UK estimates (6.9% and 8.0%, respectively) in the present analysis were more conservative, reflecting that the WCRF included relative risks from selected studies (which tends to bias overestimation); assigned high PARs to cancers not included in the present model (for example, pancreas in men); and derived the median of normal weight based on study-specific referent categories rather than population-specific distributions (which biases the normal weight category to the left). With regards to cancer types, for post-menopausal breast cancer, the present Europe-wide estimate is conservative (4.9%) compared with that of 10.2% from an Italian population,[51] in part reflecting that traditionally Italy has a low prevalence of HRT usage.[52] The present PAR estimate for colon cancer in men (10.9%) is less than that of 14.2% estimated from the Health Professional Follow-up study.[53]

### Implications and future studies

The implications of this analysis are threefold. First, the overall size of the incident cancer burden is informative for health policy. For example, it is clear (both in relative and absolute terms) that obesity-related cancer is a greater problem for women than men. By contrast, at a country level, incident cancer burden due to excess BMI is a greater problem in Central European countries like the Czech Republic, whereas it is less of a problem in France. Similarly, obesity-related oesophageal adenocarcinoma seems a substantial problem in the United Kingdom (this country accounts for 54% of new cases across all 30 countries). Ultimately, the relative and absolute numbers need to be placed against the context of other major aetiological factors such as smoking

and alcohol. Martin-Moreno and colleagues[54] recently summarised data on the proportions of cancer incidence attributable to different avoidable factors in Europe and excess body weight ranked third in men (after smoking and alcohol) and second in women (after smoking). This ranking may alter, and in the next decade, as smoking prevalence decreases in some countries,[55] obesity may become the biggest attributable cause of cancer in women. Second, priorities for research in certain malignancies, namely endometrial, breast and colorectal cancers were identified. Finally, while avoidance of weight gain is the ideal, the obesity epidemic increases unabated. With the findings of this study, we may now use a dynamic model such as PREVENT[15] to determine effects of interventions on cancer incidences in a more sophisticated (counterfactual) manner, simultaneously incorporating trends in obesity, length and adherence to interventions, aging populations, and competing risks. Murray and Lopez[56] identified different categories of counterfactual exposure distributions—theoretical, plausible, feasible and cost-effectiveness minimum risks—if there are large differences between plausible/feasible and theoretical minimum risk levels in an intervention modelling, then research into alternative risk reduction strategies and their implementation are indicated. Improvements in modelling will undoubtedly better inform public policy and guide research strategies to prevent the occurrence of large numbers of obesity-related cancers.

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