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Research Article

# Cancers Potentially Preventable through Excess Weight Reduction in Germany in 2010

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**Keywords**
Overweight · Obesity · Cancer incidence · Population-attributable risk · Germany

**Abstract**
***Objective:*** In order to quantify the preventive potential of body weight reduction in Germany, population-attributable risks (PARs) were estimated for 13 cancer types. ***Methods:*** PARs were calculated using body weight prevalence from a nationwide survey from 1998, cancer incidence estimates for 2010 from cancer registry data and relative risk estimates from published meta-analyses. Three counterfactual scenarios were evaluated: reducing BMI to maximally 21 kg/m$^2$ (main analysis) and weight reductions among overweight and obese persons of 5% and 10%. ***Results:*** An estimated 9% of all incident cancer cases in Germany – 40,748 cases – could be attributed to excess body weight in 2010. The highest proportions were estimated for endometrial cancer (48%) and oesophageal adenocarcinoma (48% for women, 46% for men). The largest case numbers were estimated for postmenopausal breast (9,081 cases), colorectal (8,002 cases among men, 3,297 cases among women) and endometrial cancer (5,468 cases). The additional counterfactual scenarios suggested that weight reductions of 5% and 10% could prevent 5,572 cases and 11,427 cases, respectively. ***Conclusions***: In Germany there is a considerable preventive potential for cancers associated with excess body weight. Efforts to prevent further weight gain and encourage weight loss should be promoted.



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## Introduction

Excess body weight is associated with many types of cancer [1–3] as well as with other diseases such as type 2 diabetes, hypertension and cardiovascular diseases [4–6]. Regarding its etiologic role in carcinogenesis, it has been hypothesized that excess body weight may act through various pathways: increased lipids and lipid signalling, heightened inflammatory responses, insulin resistance and adipokine dysregulation [7, 8].

In Europe, country-level self-reported obesity prevalence varies greatly, ranging from 9 to 23% among women and 9 to 27% among men, with the prevalence in Germany lying slightly above the European average [10]. A nationwide survey of German adults with measured height and weight (which tend to yield higher BMI than self-reports [11]) indicated that 60% of German adults were at least overweight and that 23% were obese [12].

The proportion of overweight and obese people worldwide has increased over recent decades [13], and increasing trends can be observed across Europe and in Germany as well [14].

Meanwhile, the prevalence of other important cancer risk factors, in particular tobacco and alcohol consumption, has decreased in European countries [14–16]. Given these trends, the relative burden of overweight- and obesity-associated cancers is likely to rise [17].

To address differences both in risk factor prevalence and temporal trends in prevalence it is important to perform country-specific analyses of disease burden. Up to now, only one study has estimated the health burden and costs attributable to overweight/obesity for Germany, using German BMI prevalence data and relative risks derived from a large US study [18]. This study considered various diseases related to excess body weight and focused on cancer mortality instead of cancer incidence, providing a limited picture of the cancer burden caused by excess body weight. Apart from that, two other European studies [19, 20] have estimated overweight-attributable cancer incidence for Germany, but these used non-representative prevalence data and indirect cancer incidence estimates from the International Agency for Research on Cancer. The German Cancer Research Center (DKFZ) recently published an article about the cancer burden of overweight and obesity in Germany [21]. Their results correspond generally to our estimates. For some cancer types their results are somewhat lower, due to differences in the reference exposure category and relative risks.

To obtain more precise estimates taking into account a realistic latency period between risk factor exposition and cancer diagnosis, we estimated the cancer incidence attributable to overweight/obesity in Germany in 2010 for 13 different cancer types using representative prevalence data on excess body weight from a nationwide survey from 1998, national estimates of cancer incidence from German cancer registries as well as relative risk estimates from published meta-analyses. We evaluated three counterfactual scenarios: reduction of all BMI above 21 to 21 kg/m$^2$ as well as weight reductions among overweight or obese persons of 5 and 10%. The latter two scenarios were chosen in order to evaluate more realistic goals for the reduction of excess body weight in Germany.

## Material and Methods

Analyses of population-attributable risks (PARs) are based on the assumption of a causal relationship between the exposure (excess body weight) and outcome (cancer). Therefore, PARs were calculated for cancer types for which the International Agency for Research on Cancer (IARC) deemed an association with overweight/obesity to be convincing [1, 2]. The following cancer types were included (according to ICD-10 classification): oesophagus (C15, only adenocarcinoma; morphology codes see table 1), gastric cardia (C16.0), colon (C18), rectum (C19–C20), liver (C22), gallbladder (C23), pancreas (C25), postmenopausal breast (C50), endometrium (C54–C55), ovary (C56), kidney (C64), thyroid (C73) and multiple myeloma (C90). Calcula-

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**Table 1.** Summary risk estimates per 5kg/m$^2$ increase in BMI by cancer sites and sex obtained from meta-analyses [27–30]

| Cancer type | Men | | Women | |
|---|---|---|---|---|
| | no. of included studies | RR* (95% CI) | no. of included studies | RR* (95% CI) |
| Oesophageal adenocarcinoma[§] | 5 | 1.52 (1.33–1.74) | 3 | 1.51 (1.30–1.74) |
| Gastric cardia | 7 | 1.32 (1.07–1.64) | 7 | 1.32 (1.07–1.64) |
| Colon | 24 | 1.30 (1.25–1.36) | 20 | 1.12 (1.06–1.17) |
| Rectum | 17 | 1.09 (1.06–1.13) | 14 | 1.02 (0.99–1.05) |
| Liver | 19 | 1.37 (1.23–1.53) | 19 | 1.37 (1.23–1.53) |
| Gallbladder | 12 | 1.09 (1.03–1.15) | 12 | 1.09 (1.03–1.15) |
| Pancreas | 14 | 1.13 (1.04–1.22) | 15 | 1.10 (1.04–1.16) |
| Breast (postmenopausal) | – | – | 29 | 1.13 (1.09–1.17) |
| Endometrium | – | – | 28 | 1.54 (1.47–1.61) |
| Ovary | – | – | 24 | 1.08 (1.04–1.12) |
| Kidney | 9 | 1.24 (1.17–1.32) | 10 | 1.33 (1.25–1.42) |
| Thyroid | 4 | 1.32 (1.04–1.59) | 3 | 1.14 (1.05–1.22) |
| Multiple myeloma | 7 | 1.12 (1.06–1.18) | 6 | 1.11 (1.08–1.15) |

No. = Number; RR = relative risk; CI = confidence interval.
*per 5 kg/m$^2$ increase in BMI.
[§]Morphology codes: 8140–8141, 8143–8145, 8190–8231, 8260–8263, 8310, 8401, 8480–8490, 8550–8551, 8570–8574, 8576 [53].

tions required information from three sources: i) the distribution of BMI in 1998 from a national, representative survey of adults in Germany, ii) cancer incidence rates for 2010 estimated from German cancer registry data and iii) risk estimates for the association between BMI and the included cancer types. PARs were calculated for men and women ≥35 years of age living in Germany in the year 2010.

*Distribution of BMI in Germany*

The distribution of BMI in the German population was obtained from the German National Health Interview and Examination Survey conducted by the Robert Koch Institute between 1997 and 1999 (GNHIES98). The study methods have been fully reported elsewhere [22, 23]. Briefly, the survey, which is conducted approximately every 10 years, covered a nationwide sample of the population in Germany aged 18–79 years and aimed to describe the health status and health behaviour of adults living in Germany. A total of 7,124 people took part in examinations and/or completed a validated questionnaire about relevant health issues. Anthropometric measurements were conducted by trained staff according to a standardized procedure with calibrated instruments. The current analyses refer to subjects ≥23 years old who took part in the examinations (n = 5,931). BMI was calculated as weight in kilograms divided by height in meters squared (kg/m$^2$). We mapped the distribution of BMI from the GNHIES98 survey to cancer incidence in 2010 to emulate the average follow-up time of 12 years in the prospective studies included in the selected meta-analyses (e.g. [24]). To achieve this, we added 12 years to the age at assessment of GNHIES98 participants. Furthermore, participants identified as having died through the end of December 2009 [25] were excluded from calculations.

*Cancer Incidence in Germany*

Cancer incidence in Germany for the year 2010 was obtained from estimates by the German Centre for Cancer Registry Data at the Robert Koch Institute. These annual national incidence calculations depend on the estimated completeness of each registry in the network providing nationwide coverage since 2009. Completeness estimates are based on mortality/incidence ratios and well established registries fulfilling defined quality criteria as a reference region [26]. For 2010 the estimated total number of incident cancer cases of 489,976 are based on 461,808 notified cases transmitted by the registries through the end of 2015. Age-, sex- and site-specific incidence rates were estimated using these data. PARs were calculated for the 13

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cancer types mentioned above. In 2010 there were an estimated 201,511 incident cases of the considered cancer types in the German population aged ≥35 years.

Regular incidence estimates for Germany are generally limited to 3-digit ICD-10 codes. Figures for oesophageal adenocarcinoma and gastric cardia tumours were calculated using age- and sex-specific proportions of these tumours among all registered oesophageal and gastric tumours in regions with registration completeness ≥ 90%. Furthermore, menopausal status at diagnosis is not indicated in the available cancer registry data. Therefore, we defined all breast cancer cases before the age of 50 years as premenopausal and all others as postmenopausal.

*Relative Risks*

Relative Risk (RR) estimates concerning the association between overweight/obesity and each cancer type were derived from meta-analyses [27–30]. The meta-analyses were identified via PubMed using the following MeSH-terms: (overweight OR obesity) AND (oesophageal/gastric/colorectal/liver/gallbladder/pancreas/breast/endometrial/ovary/kidney/thyroid/multiple myeloma cancer OR neoplasm) AND meta-analysis. The search was limited to human studies as well as to papers written in English or German. To assess the quality of the identified meta-analyses, we used the AMSTAR-Score [31], a tool to assess the methodological quality of systematic reviews by an 11-item questionnaire. Meta-analyses were eligible for selection if they reported risk estimates for incident cancer with BMI as a continuous variable and included only prospective observational studies predominantly from Europe and North America. If more than one meta-analysis was eligible, the one deemed of best quality according to the AMSTAR-Score was selected. Table 1 displays the number of included studies in the selected meta-analyses and the RRs used to calculate the PARs.

*Statistical Analysis*

PARs were calculated according to the method of Tseng et al. [32], which is based on the formula from Bruzzi et al [33]. The original formula from Bruzzi et al. [33] requires knowledge of the risk factor distribution among cases. The method described by Tseng et al. [32] can be used to estimate this based on population-wide risk factor prevalence, e.g. based on representative surveys, combined with adjusted RR estimates and incidence data.

The original PAR formula from Bruzzi et al. [33] and the method from Tseng et al. [32] both assume a categorical risk factor. Since the categorization of BMI can lead to spurious results [34], we extended the previously published methods to accommodate a continuous-scale risk factor by replacing instances of summation with integration. Specifically, the equation by Tseng et al. [32] to determine the BMI-adjusted RR for age group *j* ($RR_{*j}$ for age groups 35–44, 45–54, 55–64, 65–74 and 75+ years) was changed from

$$RR_{*j} = \frac{R_{(w)j} \cdot p_{.j}}{R_{(w)0} \cdot p_{.0}} \cdot \left[\frac{\sum_{i=0}^{k} p_{i0} \cdot RR_{i*}}{\sum_{i=0}^{k} p_{ij} \cdot RR_{i*}}\right] \qquad (1)$$

to

$$RR_{*j} = \frac{R_{(w)j} \cdot p_{.j}}{R_{(w)0} \cdot p_{.0}} \cdot \left[\frac{\int_0^{\infty} dBCCG(x)_0 \cdot RR(x)\, dx}{\int_0^{\infty} dBCCG(x)_j \cdot RR(x)\, dx}\right] \qquad (2),$$

where $R_{(w)j}$ is the age group-specific incidence rate; $p_{.j}$ is the proportion of the population in age group j; RR(x) is the confounder-adjusted RR at a BMI of x; $dBCCG(x)_j$ is the density of the age group- and sex-specific, 3-parameter Box-Cox Cole and Green model, fitted to the GNHIES98 survey data using the gamlss package for R [35] at a BMI of x; and dx indicates integration over BMI. Equation 2 from Tseng et al. [32] was changed from

$$p_{(c)i} = \frac{\sum_{j=0}^{l} RR_{ij} \cdot p_{ij}}{\sum_{i=0}^{k} \sum_{j=0}^{l} RR_{ij} \cdot p_{ij}} \qquad (3)$$

to

$$p_{(c)i} = \frac{\sum_{j=0}^{l} RR_{*j} \cdot RR(x) \cdot dBCCG(x)_j}{\sum_{j=0}^{l} \int_0^{\infty} RR_{*j} \cdot RR(x) \cdot dBCCG(x)_j\, dx} \qquad (4),$$

where $p(c)_i$ is the proportion of cases exposed at a BMI of x and other parameters are as described above. Finally, Equation 1 was changed from

$$PAR = 1 - \sum_{i=0}^{k} \frac{p_{(c)i}}{RR_{i*}} \quad (5)$$

to

$$PAR = 1 - \int_{0}^{\infty} \frac{p_{(c)i}}{RR(x)} dx \quad (6).$$

To determine RR(x), the following algorithm was used: for BMI ≤ 21 kg/m$^2$, RR was defined as 1. For BMI between 21 and 40 kg/m$^2$, the cancer-specific RR per unit increase in BMI (rr) was raised to the power of (BMI – 21). For all BMI of 40 and above, the RR at a BMI of 40 was used. Thus, a BMI of 21 kg/m$^2$ and below was considered to confer zero excess cancer risk, and risk did not continue to increase above a BMI of 40 kg/m$^2$:

$$RR(x) = \begin{cases} 1, & x \le 21 \\ rr^{x-21}, & 21 < x < 40 \\ rr^{19}, & x \ge 40 \end{cases} \quad (7).$$

Separate PARs were calculated for each of three counterfactual scenarios. For the first counterfactual scenario (main analysis), we calculated PARs based on a weight reduction for all individuals with a BMI > 21 kg/m$^2$ to a value of 21 kg/m$^2$. For the two additional scenarios, we calculated PARs based on weight reductions of 5% and 10% among overweight and obese persons (i.e., BMI ≥ 25 kg/m$^2$). The two latter scenarios reflect the magnitude of weight reduction recommended by the WHO in order to help prevent overweight-related diseases [1].

To examine how uncertainty in the RRs and survey data could affect PAR estimates, we conducted simulation analyses with 5,000 repetitions. RR estimates were sampled assuming independent log-normal distributions based on the published point estimates and the standard errors derived from published 95% confidence intervals (95% CI). Due to the complex sampling design of the surveys, a fully appropriate resampling technique with which we could incorporate uncertainty in the risk factor distribution was not identified. Instead, we sampled from the multivariate normal distribution of parameters from the fitted 3-parameter Box-Cox Cole and Green model to obtain simulated risk factor distributions. We present the 2.5th and 97.5th percentile PAR estimates calculated with these simulated relative risks and risk factor prevalence for our main analysis.

## Results

Risk factor prevalence for the years 1997–1999 are based on data from 2,798 men and 3,133 women from the GNHIES98 survey, with a weighted average age at interview of 44.2 ± 0.3 (mean ± SE) and 47.0 ± 0.3 years, respectively. The mean BMI was 27.1 ± 0.1 kg/m$^2$ for men and 26.6 ± 0.1 kg/m$^2$ for women. Among men, 50.3% were overweight and 19.3% obese, whereas 31.1% of women were overweight and 23.0% obese. About 93.2% of men and women had a BMI > 21 kg/m$^2$. Table 2 gives an overview of the BMI distribution in the German population according to sex and age group.

Table 3 provides the PAR estimates for 2010 by cancer type for the main analysis. Overall, 10.5% of all new cancer cases in 2010 among women and 6.7% among men can be attributed to excess body weight, corresponding to 23,654 and 17,094 cases, respectively. Among women, PAR was highest for endometrial cancer with 48.1% (95% CI 43.8–52.2%) and oesophageal adenocarcinoma with 47.8% (95% CI 32.7–60.0%) followed by kidney (34.4%; 95% CI 27.5–40.7%) and gastric cardia cancer (34.4%; 95% CI 8.7–54.4%). Among men, 45.7% (95% CI 33.1–56.8%) of oesophageal adenocarcinomas, 36.9% (95% CI 25.2–46.8%) of liver cancer, 32.8% (95% CI 8.6–51.8%) of gastric cardia cancer and 31.6% (95% CI 27.0–35.9%) of colon cancer were attributable to excess body weight. Overall, 40,748 new cancer cases in 2010 were attributable to overweight and obesity – 8.5% of all new cases that year.

**Table 2.** Estimated distributions of body mass index (BMI) in Germany in 1998 by sex and age group

| Age group at examination, years | Age group in 2010, years | Men, % (95% CI) | | | Women, % (95% CI) | | |
|---|---|---|---|---|---|---|---|
| | | normal weight* | overweight* | obese* | normal weight* | overweight* | obese* |
| 23–32 | 35–44 | 11.6 (10.2–13.2) | 9.8 (8.5–11.3) | 2.2 (1.6–3.0) | 13.8 (12.3–15.4) | 3.6 (3.0–4.3) | 2.3 (1.7–3.0) |
| 33–42 | 45–54 | 8.6 (7.4–9.9) | 13.2 (11.9–14.5) | 4.9 (4.0–5.9) | 13.4 (12.1–14.8) | 5.8 (4.9–6.8) | 4.2 (3.4–5.2) |
| 43–52 | 55–64 | 4.8 (3.9–5.8) | 10.5 (9.3–11.8) | 4.6 (3.9–5.5) | 7.5 (6.5–8.6) | 6.0 (5.1–7.1) | 4.6 (3.9–5.5) |
| 53–62 | 65–74 | 2.9 (2.4–3.6) | 10.4 (9.2–11.8) | 4.9 (4.0–5.9) | 5.6 (4.8–6.5 | 7.4 (6.6–8.3) | 5.7 (4.9–6.6) |
| 62+ | 75+ | 2.2 (1.7–2.9) | 6.4 (5.5–7.4) | 2.7 (2.1–3.4) | 4.2 (3.4–5.2) | 8.3 (7.2–9.5) | 6.2 (5.1–7.6) |
| Overall (23+) | | 30.1 (27.9–32.4) | 50.3 (48.2–52.3) | 19.3 (17.7–21.0) | 44.4 (42.2–46.8) | 31.1 (29.5–32.8) | 23.0 (20.9–25.1) |

CI = Confidence interval.
*Normal weight is defined as a BMI of 18.5 to <25 kg/m$^2$; overweight as ≥25 to <30 kg/m$^2$ and obesity as ≥30 kg/m$^2$.

**Table 3.** Estimated population attributable risk (PAR %) for 13 cancer types associated with excess body weight (BMI above 21 kg/m$^2$) in Germany in 2010

| Cancer type | Men | | Women | |
|---|---|---|---|---|
| | PAR % (95% CI) | estimated absolute no. | PAR % (95% CI) | estimated absolute no. |
| Oesophageal adenocarcinoma | 45.7 (33.1–56.8) | 951 | 47.8 (32.7–60.0) | 203 |
| Gastric cardia | 32.8 (8.6–51.8) | 1,199 | 34.4 (8.7–54.4) | 440 |
| Colon | 31.6 (27.0–35.9) | 6,522 | 15.3 (8.8–21.8) | 3,071 |
| Rectum | 11.3 (7.1–15.2) | 1,480 | 2.7 (–1.3–6.6) | 226 |
| Liver | 36.9 (25.2–46.8) | 2,142 | 9.3 (–104.6–72.9) | 223 |
| Gallbladder | 11.4 (4.2–18.3) | 64 | 11.8 (4.2–19.0) | 180 |
| Pancreas | 16.0 (5.9–25.2) | 1,292 | 12.9 (5.6–20.2) | 1,075 |
| Breast (postmenopausal) | – | – | 15.4 (11.2–19.6) | 9,081 |
| Endometrium | – | – | 48.1 (43.8–52.2) | 5,468 |
| Ovary | – | – | 9.8 (5.2–14.3) | 756 |
| Kidney | 26.1 (19.4–32.6) | 2,451 | 34.4 (27.5–40.7) | 1,995 |
| Thyroid | 30.8 (7.6–49.4) | 481 | 13.8 (6.0–21.1) | 523 |
| Multiple myeloma | 14.6 (8.0–20.7) | 511 | 13.8 (9.9–17.8) | 414 |
| Total | 6.7 | 17,094 | 10.5 | 23,654 |

PAR = Population attributable risk; CI = confidence interval; no. = number.

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**Table 4.** Estimated population attributable risk (PAR %) for 13 cancer types after 5% and 10% reduction in weight among overweight and obese people in Germany in 2010

| Cancer type | 5% weight reduction | | | | 10% weight reduction | | | |
|---|---|---|---|---|---|---|---|---|
| | men | | women | | men | | women | |
| | PAR % | Est. abs. no. | PAR % | Est. abs. no. | PAR % | Est. abs. no. | PAR % | Est. abs. no. |
| Oesophageal adenocarcinoma | 6.0 | 125 | 5.3 | 23 | 12.5 | 260 | 11.2 | 48 |
| Gastric cardia | 4.7 | 172 | 4.3 | 55 | 9.7 | 355 | 8.8 | 112 |
| Colon | 4.6 | 949 | 2.1 | 422 | 9.4 | 1 940 | 4.3 | 863 |
| Rectum | 1.8 | 236 | 0.4 | 33 | 3.6 | 471 | 0.8 | 67 |
| Liver | 5.2 | 302 | 1.3 | 31 | 10.6 | 615 | 2.7 | 65 |
| Gallbladder | 1.8 | 10 | 1.7 | 26 | 3.7 | 21 | 3.4 | 52 |
| Pancreas | 2.5 | 204 | 1.8 | 150 | 5.0 | 409 | 3.7 | 308 |
| Breast (postmenopausal) | – | – | 2.1 | 1,238 | – | – | 4.3 | 2,535 |
| Endometrium | – | – | 5.3 | 602 | – | – | 11.2 | 1,273 |
| Ovary | – | – | 1.4 | 108 | – | – | 2.8 | 216 |
| Kidney | 3.9 | 366 | 4.2 | 244 | 7.9 | 742 | 8.8 | 510 |
| Thyroid | 4.5 | 70 | 1.8 | 68 | 9.1 | 142 | 3.7 | 140 |
| Multiple myeloma | 2.3 | 81 | 1.9 | 57 | 4.7 | 165 | 3.9 | 117 |
| Total | 1.0 | 2,515 | 1.4 | 3,057 | 2.0 | 5,120 | 2.8 | 6,307 |

PAR = Population attributable risk; Est. abs. no. = estimated absolute numbers.

With a PAR of 15.4% (95% CI 11.2–19.6%), 9,081 cases of postmenopausal breast cancer were attributable to overweight and obesity. With 8,002 cases, colorectal cancer accounted for the highest absolute number of attributable cases among men.

The two additional counterfactual scenarios revealed that, if weight could be reduced by 5% or 10% among overweight and obese persons, the mean BMI would shift from 26.8 kg/m$^2$ to 25.9 kg/m$^2$ and 25.0 kg/m$^2$ respectively. An estimated 5,572 cancer cases (5% weight reduction) or 11,427 cases (10% weight reduction) could be prevented in the German population aged ≥35 years. This corresponds to 1.2% or 2.4% of all new cancer cases in 2010 (table 4). The PAR estimates for a 10% weight reduction are three to four times smaller than the PARs for the main analysis.

## Discussion

Our analyses indicate that about 9% of all new cancer cases in 2010 among adults in Germany aged ≥35 years were attributable to excess body weight. This corresponds to 40,750 cases that might have been preventable had BMI in the population 12 years prior not exceeded 21 kg/m$^2$. Postmenopausal breast, endometrial and colon cancer accounted for 75% of the total attributable cases among women, whereas colon, kidney and liver cancer accounted for 65% among men. Women seem to have a higher overall PAR, with 10.5% versus 6.7% among men. The higher PAR and attributable cases among women are likely due to postmenopausal breast, endometrial and ovarian cancers, which are strongly associated with excess body weight. Other studies investigating BMI and cancer incidence also estimated an overall PAR for women nearly twice as high as for men [20, 36]. Hence, excess body weight seems to be a greater issue for women than for men regarding cancer, while other risk factors like tobacco or alcohol consumption seem to have the greatest influence among men.

The counterfactual scenarios involving weight reductions of 5% and 10% among overweight and obese persons revealed that these more modest weight reductions could have prevented 5,572 or 11,427cancer cases (1.2% or 2.4% of all new cancer cases) in 2010. These are probably more realistic estimates of the preventable proportion of the current cancer burden due to excess body weight than assuming a theoretical cap of BMI at 21 kg/m$^2$. To achieve a maximum BMI of 21 kg/m$^2$ in the German population, men and women who had a BMI above 21 kg/m$^2$ at the time of the GNHIES98 survey would have had to reduce their weight on average by 21%. Instead, the prevalence of obesity in Germany since then has generally increased, predominantly among young adults [12, 37]. Therefore, measures to reduce or prevent further increases in BMI are relevant for Germany, and young men and women appear to be a population group at higher risk.

In comparisons with other studies, our PAR estimates show both similarities as well as some considerable differences. The World Cancer Research Fund published estimates in 2009 for the UK and the US that are very similar to our estimates [38]. Renehan and colleagues [20] published estimates for Europe in 2010 that are much lower than our estimates, especially for those cancer types for which we estimated a high PAR (oesophageal, endometrial and renal cancer). These differences might be due to different BMI distributions in the populations as Renehan and colleagues [20] used data on prevalence of excess body weight from the WHO Global Infobase and on cancer incidence from GLOBOCAN 2002. Lehnert and colleagues [18] estimated population-attributable fractions for cancer mortality in the German population using BMI prevalence data from the German Health Interview and Examination Survey (DEGS1) and the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe) and RR estimates from a cohort study of US adults. Their estimates are considerably lower for oesophageal, gastric, cervix uteri and kidney cancer but largely the same for the other cancer types. As noted, however, those investigators addressed cancer mortality as opposed to incidence, which hampers a direct comparison of these PAR estimates.

Tobacco and alcohol consumption have large detrimental effects on population health, including large PARs for lung, laryngeal and renal cancers [39, 40]. Previous estimates for the German adult population, using methods similar to those used here, showed that tobacco has the greatest PAR for organs of the upper aerodigestive tract (UADT) [39]. Alcohol showed a smaller overall PAR by itself, but high PARs were seen for cancers of the UADT in combination with tobacco [40]. Table 5 provides an overview of PAR estimates for these risk factors regarding cancer types affected by excess body weight. For some common cancer sites (colon-rectum, liver, breast and endometrium) overweight and obesity account for more cases than tobacco or alcohol consumption. Regarding men, the PAR for colorectal cancer is about 10% for both tobacco and alcohol, whereas the PAR for excess body weight is 24%. Concerning breast cancer among women aged 35 years and older, the PAR for overweight/obesity is nearly twice as high as for alcohol (13 vs. 7%). Overweight and obesity should therefore not be underestimated as cancer risk factors, especially considering the increasing obesity prevalence and decreasing tobacco and alcohol consumption in Germany and in other countries.

### *Limitations and Strengths*

The present analysis has a number of limitations. First, BMI might not always be an accurate measure for general adiposity and excess body weight, as it does not differentiate between body fat and fat-free mass. Waist-to-hip ratio (WHR) and waist circumference (WC) are alternative measures of excess body weight, but recent studies showed only limited evidence that WHR or WC are better predictors of cancer risk than BMI [8]. Thus, we used BMI as an approximation of general adiposity as it is an accepted indicator for and the most widely used measure of the degree of overweight and obesity [1].

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**Table 5.** Comparison of population attributable risk (PAR) estimates for excess body weight, tobacco [39] and alcohol [40] in German

| Cancer type | PAR in % (95% CI) | | | | | |
|---|---|---|---|---|---|---|
| | excess body weight* | | tobacco# | | alcohol* | |
| | men | women | men | women | men | women |
| Colon / rectum | 23.7[a] | 11.6[a] | 9.8 (6.3–13.4) | 5.0 (2.6–7.4) | 9.7 (3.6–15.8) | –2.9 (–7.6–1.5) |
| Liver | 36.9 (25.2–46.8) | 9.3 (–104.6–72.9) | 24.9 (16.0–33.5) | 18.0 (5.44–33.6) | –4.9 (–26.6–15.5) | –12.1 (–30.8–5.0) |
| Breast | –[b] | 12.9[a,c] | –[b] | –[b] | –[b] | 6.6 (4.9–8.4) |
| Ovary | NA | 9.8 (5.2–14.3) | NA | 9.3 (2.6–15.8) | –[b] | –[b] |
| Pancreas | 16.0 (5.9–25.2) | 12.9 (5.6–20.2) | 18.3 (15.0–21.7) | 12.1 (10.1–14.1) | –[b] | –[b] |
| Kidney | 26.1 (19.4–32.6) | 34.4 (27.5–40.7) | 22.3 (15.5–28.6) | 5.8 (0.3–11.2) | –[b] | –[b] |
| Overall PARs§ | 6.7 | 10.5 | 22.8 | 7.9 | 3.4 | 2.0 |

*PAR based on cancer incidence from 2010.
#PAR based on cancer incidence from 2008.
§ Overall PARs include all associated cancer types, not just those included in the table.
[a]Proportions were re-calculated and therefore CIs are lacking.
[b]Not calculated due to insufficient evidence for causal association between cancer type and risk factor.
[c]Proportion recalculated for women aged 35 years and older, still considering elevated risk for postmenopausal women only.

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A second limitation is the use of BMI from one time point. At least for colorectal and postmenopausal breast cancer, (large) weight gain in adulthood increases cancer risk and dynamic weight change seems to be a more sensitive indicator of adiposity than BMI measured at one point in time [41, 42].

Third, in calculating PAR for postmenopausal breast cancer, age was used as a proxy for menopausal status as we lacked any data on menopausal status at diagnosis in the cancer registry data. Other analyses have obtained consistent estimates when comparing clinically defined menopausal status with an aged-based cut-off [43].

Fourth, the decision that a BMI of 21 kg/m$^2$ confers zero excess risk may be arbitrary and might only be of theoretical value. However, it reflects the population BMI recommended by the World Health Organization for achieving lowest weight-related health risks [44]. Furthermore, there seems to be no excess cancer mortality risk for underweight persons (BMI < 18 kg/m$^2$) [45]. In Germany, only 2.3% of women and 0.7% of men are underweight.

Fifth, PARs were calculated with the general assumptions that BMI directly causes cancer and that reducing BMI reduces cancer risk. Although based on observational studies, various meta-analyses and reviews have demonstrated a positive association between cancer risk and BMI [29, 41, 43, 46]. In addition, plausible biological mechanisms linking overweight and obesity with carcinogenesis have been identified [7, 8]. The weight of this evidence sufficed to deem the association convincing [1–3]. Nevertheless, it remains unknown whether effective interventions to decrease body weight in adult populations will reduce cancer incidence [43]. Some support for the effectiveness of interventions comes from prospective cohorts investigating intentional weight loss and cancer risk [47, 48], as well as from findings of reduced cancer incidence after bariatric surgery in morbidly obese patients [49].

Sixth, nationwide obesity prevalence data based on anthropometric measurements are only recorded about every 10 years in Germany. Under consideration of a 12-year lag time between BMI measurement and cancer incidence, the most recent prevalence data come from 1998, corresponding to cancer incidence in 2010.

Finally, there are indications for associations between excess body weight and cancer types that were not considered in the present estimates, such as aggressive prostate cancer or male breast cancer [2]. Thus, our results may have underestimated the full impact of excess body weight on cancer incidence.

To our knowledge, this is the first study quantifying the preventable proportion of the incidence of 13 different cancer types attributable to excess body weight in Germany under multiple counterfactual scenarios using age- and sex-specific BMI estimates from a nationwide survey as well as cancer incidence from German cancer registries. These aspects allow representative PAR estimates for the German population. Moreover, height and weight were measured in a standardized way, thereby increasing accuracy and consistency compared to self-reported data. From a public health perspective, the focus on incident cases allows a more complete view of the cancer burden caused by excess body weight than a focus on cancer mortality. Preventing cancer incidence not only prevents cancer death but also prevents the loss of quality of life as well as the increased health care resources that go along with a cancer diagnosis.

The two additional counterfactual scenarios illustrate the impact of weight reduction by simulating a shift of the BMI distribution from a mean of 27 kg/m$^2$ to a mean of 26 kg/m$^2$ (5% reduction) or 25 kg/m$^2$ (10% reduction). These likely reflect more realistic scenarios than assuming a theoretical minimum risk with a maximum BMI of 21 kg/m$^2$. However, even the BMI achieved with a 10% reduction among overweight and obese people, would still lie above the range of population average BMI recommended by the WHO [44].

Despite the weight reduction recommendations of the WHO, there is little evidence thus far of progress in the German population. In fact, BMI has increased over recent decades among adults [12, 37] as well as among children, the latter having plateaued at a high level in recent years [50, 51]. Due to the potentially long delay before weight-related cancer develops, the burden of cancer associated with excess body weight is likely to grow further. The increasing rates of overweight-associated oesophageal adenocarcinoma in the last 20 years in various western societies, compared to decreasing rates of tobacco- and alcohol-related oesophageal squamous cell carcinoma [52, 53], indicate the growing importance of excess body weight.

## Conclusions

In Germany there is a considerable preventive potential regarding cancers associated with excess body weight. For some cancers, the proportion attributable to excess body weight, measured as BMI, exceeds that attributable to tobacco or alcohol consumption. Even a modest weight reduction of 5% in overweight and obese persons might prevent over 5,000 cases per year. In light of increasing BMI and decreasing tobacco and alcohol consumption in the German population, both the absolute and the relative impact of overweight and obesity on cancer incidence is increasing. Efforts to prevent weight gain and encourage weight loss for overweight and obese persons at all ages should be promoted.

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## Disclosure Statement

The authors declare that they have no conflicts of interest.

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