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Obesity and Cancer Risk: a Danish Record-linkage Study

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A cohort of 43 965 obese persons was accrued on the basis of discharge registrations from Danish hospitals, and incidence of cancer in the cohort was compared to that in the Danish population as a whole using indirect standardisation for age and period. Increased incidence was observed for cancer of the uterine corpus independently of age [114 cases, relative risk (RR) = 2.0, confidence interval 1.6–2.4], and for breast cancer in women above the age of 70 (133 cases, RR = 1.2). These findings are consistent with previous studies. In younger women, breast cancer occurred less frequently and ovarian cancer occurred more frequently than expected. Increased incidence was observed for cancers of the oesophagus (26 cases, RR = 1.9) and the liver (58 cases, RR = 1.9), probably reflecting an increased prevalence of excessive alcohol consumption in the cohort. Increased incidence was furthermore observed for cancers of the pancreas (101 cases, RR = 1.7), the prostate (96 cases, RR = 1.3) and the colon (195 cases, RR = 1.2), which may indicate the existence of risk factors which are common to obesity and to these cancers, for example, dietary habits. Kidney cancer was increased in women only. Overall, the incidence of cancer was increased by 16% in the cohort. The results were essentially unchanged by restriction to the subcohort of 8207 persons in whom obesity was the primary discharge diagnosis, and were also similar in the first year of follow-up after hospital discharge. Selection bias is, therefore, not likely to have influenced the results.
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INTRODUCTION

OBESITY IS a common condition, particularly in the economically developed countries. The aetiology of obesity is not well understood, but it is likely that there are heritable as well as environmental (including dietary) components involved [1, 2]. Obesity is a poor state of health, and is associated with excess morbidity and mortality from diabetes, cardiovascular disease and cancer [3, 4] and with overall mortality [5].

In the information on cancer prevention which is distributed to the general public, advice to avoid obesity ranks high. In the material from the Europe Against Cancer campaign, advice to avoid obesity and excessive intake of dietary fat is the third piece of advice given (after avoidance of tobacco smoking and excessive alcohol drinking), and is mentioned before advice on taking care when handling carcinogenic chemicals, and advice to women on having regular cervical cytological examinations. In the material issued by the American Cancer Society, the advice to maintain desirable weight is given after other recommendations regarding smoking, sunlight and ionising radiation, but before advice on specific dietary practices. There have been few systematic attempts to describe the pattern of cancer incidence and mortality in overweight people. Most impressive is the cohort study accrued by the American Cancer Society which describes the pattern of mortality (including cancer mortality) for different categories of relative weight among 750 000 volunteers who completed a questionnaire including questions on height and weight [3, 6]. That study indicated excess mortality from cancers of the colon and rectum, prostate, uterine corpus, uterine cervix, gall bladder and the female breast.

The present study describes the incidence of cancer in a large cohort of overweight men and women in Denmark.

MATERIALS AND METHODS

The present analysis is based on a computerised linkage of three population-based registers in Denmark: the Danish Hospital Discharge Register (DHDR), the Danish Cancer Registry (DCR) [7] and the Danish Register of Deaths (DRD). The DHDR contains information on hospitalisations at nearly all hospital departments in Denmark from 1977 onwards, including the personal identification number, unique to every Danish resident, dates of admission and discharge, and up to 20 discharge diagnoses. All records in the Register from 1977 to 1987 which included a diagnosis of obesity (ICD 277) were extracted. When multiple discharges occurred for the same person, only the first record was retained for the analysis. Using the personal identification numbers, the resulting cohort of persons discharged with a diagnosis of obesity was linked to the DCR and to the DRD to obtain information on cancer incidence and deaths up to 31 December 1987.

The incidence of cancer in the cohort was compared with the incidence in the Danish population as a whole, using indirect

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Table 1. Numbers of persons, person-years and cancer cases in the total cohort of patients with obesity as one of up to 20 diagnoses and in the subcohort of patients with obesity as the primary diagnosis, by sex and time after hospital discharge

Sex	Time after hospital discharge (years)	Number of persons entering interval	Number of person-years	Average duration of follow-up (years)	Number of cancer cases during follow-up
Total cohort					
Men	0–1	14531	13175	0.9	175
	1+	12331	56018	4.5	694
Women	0–1	29434	27082	0.9	286
	1+	25626	125655	4.9	1344
Total	0–1	43965	40257	0.9	461
	1+	37957	181673	4.8	2038
Subcohort with obesity as the primary diagnosis					
Men	0–1	2206	2085	1.0	12
	1+	1974	10460	5.3	58
Women	0–1	6001	5695	1.0	20
	1+	5399	28358	5.3	162
Total	0–1	8207	7780	1.0	32
	1+	7373	38819	5.3	220

standardisation for age and period, both in 5-year intervals [8]. Persons were considered at risk for cancer from the date of first recorded hospital discharge with a diagnosis of obesity to date of death on 31 December 1987. The relative risk (RR) of cancer was estimated as the ratio of the observed numbers of cancer cases to the expected numbers, and 95% confidence intervals (95% CI) and two-tailed P values were calculated [8, 9].

Prior to analysis of the data, in order to reduce the likelihood of selection bias, it was decided to omit from the main analysis the first year of follow-up after hospital discharge, and it was furthermore decided to run a separate analysis on the subset of the cohort members in whom obesity was the first mentioned diagnosis in the record from DHDR. Table 1 gives the full details of the structure of these analyses. The total cohort comprised 43965 persons (14531 men and 29434 women) of whom 37957 contributed at least 1 year of follow-up. The subcohort of patients with obesity as the first diagnosis comprised 8207 persons (2206 men and 6001 women) of whom 7373 contributed at least 1 year of follow-up. The main analysis was based on the 37957 patients who were followed from 1 year after the year of hospital discharge for an average of 4.8 years. In this group, 2038 cases of cancer occurred. Secondary analyses are presented also for the first year of follow-up of the entire cohort (43965 persons followed on average for 0.9 years; 461 cancer cases) and for the subset of cohort members with obesity as the first diagnosis (7373 persons followed for an average of 5.3 years from 1 year after the date of hospital discharge; 220 cancer cases).

Table 2 shows the age distribution of the cohorts. In the entire cohort, the median age was in the fifties among men and in the

Table 2. Age-distribution in the total cohort of patients with obesity as one of up to 20 diagnoses and in the subcohort of patients with obesity as the primary diagnosis, by sex

	Total cohort				Subcohort with obesity as the primary diagnosis			
	Men		Women		Men		Women	
Age	No.	%	No.	%	No.	%	No.	%
0–9	364	2.5	414	1.4	150	6.8	223	3.7
10–19	814	5.6	1081	3.7	501	22.7	663	11.0
20–29	599	4.1	2440	8.3	233	10.6	887	14.8
30–39	1340	9.2	3099	10.5	341	15.5	1280	21.3
40–49	1964	13.5	2945	10.0	324	14.7	868	14.5
50–59	2930	20.2	4369	14.8	303	13.7	775	12.9
60–69	3235	22.3	5641	19.2	205	9.3	630	10.5
70–79	2467	17.0	6512	22.1	121	5.5	508	8.5
80–89	776	5.3	2774	9.4	27	1.2	166	2.8
90+	42	0.3	159	0.5	1	0.0	1	0.0
Total	14531	100.0	29434	100.0	2206	100.0	6001	100.0

sixties in women. In the subcohort of persons with obesity as the first diagnosis, the median age was in the thirties in both men and women.

It should be emphasised that the condition of obesity as indicated in the DHDR has not been verified. The diagnosis of obesity will in most cases have been based only on the physical appearance of the person.

RESULTS

The main analysis is presented in Table 3 for cancer sites for which at least 25 cases were observed. Overall, the relative risk of cancer was increased among the cohort members (RR = 1.16; 95% CI 1.11–1.21). Of the individual types of cancer, a substantially increased incidence was observed for oesophageal cancer (RR = 1.9), liver cancer (RR = 1.9), pancreatic cancer (RR = 1.7), cancer of the uterine corpus (RR = 2.0) and for kidney cancer in women (RR = 2.0). Excess cancer incidence of smaller magnitude and of more marginal statistical significance was furthermore seen for colonic cancer, prostatic cancer, bladder cancer in men, brain cancer in women, secondary and unspecified cancer in women and for leukaemia. An incidence below the expected was observed for lung cancer (RR = 0.8) and for non-melanoma skin cancer in women (RR = 0.8).

Table 4 shows the results of the main analysis alongside the secondary analysis of cancer occurrence in the first year of follow-up of the total cohort, and the analysis of cancer occurrence in the subcohort of patients for whom obesity was the first diagnosis. Comparison between the RRs from the main analysis and from the analysis of the subcohort of patients with obesity as the first diagnosis shows a high degree of similarity, despite the much greater variability of the estimates (and hence reduction in the number of statistically significant associations) brought about by the smaller numbers in the subcohort. Cancer sites which had approximately 2-fold increased incidence in the main analysis (oesophagus, liver, uterine corpus and kidney cancer in women) have very similar estimates based on the subcohort analysis. A few cancer diseases showed a substantially higher excess incidence in the subcohort than in the main analysis: mouth and pharynx (3.0 versus 1.2), pancreas (2.7 versus 1.7) and secondary and unspecified cancer (2.2 versus 1.3). Only for rectal cancer was the RR from the subcohort smaller (0.5) than that from the main analysis (1.1). The former estimate was, however, based on only 4 cases.

Comparison between the main analysis, in which the first year of hospital discharge was ignored, and the analysis of cancer incidence in this first year of follow-up similarly showed close agreement, generally. The only striking exception was brain cancer, which in both men and women was particularly elevated in the first year of follow-up (see also Table 5).

An analysis by age at cancer diagnosis is presented in Table 6 for selected cancer sites. In women, a trend in RR with age was seen for breast cancer, where the incidence is lower than expected in young women and higher than expected in old women. For ovarian cancer, the opposite pattern was seen with an excess incidence in women below the age of 60, while cancer of the uterine corpus was increased in incidence regardless of age. The RRs of prostatic cancer and pancreatic cancer showed decreasing trends with age. The excess risk for prostatic cancer was particularly high in men below the age of 60. The excess incidence of pancreatic incidence was less influenced by age, but was most pronounced in persons in their sixties.

Table 3. Numbers of cases (n) *and relative risks (RR) with* 95% *confidence intervals* (95% *CI) of cancers at different sites in the entire cohort of patients with obesity as one of up to* 20 *diagnoses. The first year of follow-up after hospital discharge is ignored in the analysis*

	Men			Women			Total		
Site	*n*	RR	95% CI	*n*	RR	95% CI	*n*	RR	95% CI
All cancers	694	1.16	1.07–1.25	1344	1.17	1.10–1.23	2038	1.16	1.11–1.21
Mouth and pharynx	22	1.4	0.9–2.1	15	1.1	0.6–1.7	37	1.2	0.9–1.7
Oesophagus	13	1.9	1.0–3.3	13	1.9	1.0–3.2	26	1.9	1.2–2.8
Stomach	30	1.1	0.7–1.5	43	1.1	0.8–1.5	73	1.1	0.9–1.4
Colon	59	1.3	1.0–1.7	136	1.2	1.0–1.4	195	1.2	1.0–1.4
Rectum	33	1.0	0.7–1.4	58	1.2	0.9–1.5	91	1.1	0.9–1.3
Liver	22	1.9	1.2–2.9	36	1.9	1.4–2.7	58	1.9	1.5–2.5
Gallbladder	2	0.5	0.1–1.8	26	1.4	0.9–2.1	28	1.3	0.8–1.8
Pancreas	34	1.8	1.2–2.5	67	1.7	1.3–2.2	101	1.7	1.4–2.1
Lung	99	0.9	0.7–1.0	69	0.8	0.6–1.0	168	0.8	0.7–1.0
Female breast				231	1.0	0.9–1.2	231	1.0	0.9–1.2
Cervix uteri				49	1.2	0.9–1.6	49	1.2	0.9–1.6
Corpus uteri				114	2.0	1.6–2.4	114	2.0	1.6–2.4
Ovary				58	1.1	0.8–1.4	58	1.1	0.8–1.4
Prostate	96	1.3	1.1–1.6				96	1.3	1.1–1.6
Kidney	21	1.2	0.7–1.8	58	2.0	1.5–2.6	79	1.7	1.3–2.1
Bladder	64	1.3	1.0–1.6	35	1.1	0.7–1.5	99	1.2	1.0–1.5
Melanoma	10	1.1	0.5–2.1	22	0.9	0.6–1.4	32	1.0	0.7–1.4
Non-melanoma skin cancer	80	1.0	0.8–1.2	110	0.8	0.6–0.9	190	0.9	0.7–1.0
Brain	8	0.7	0.3–1.4	35	1.5	1.0–2.1	43	1.2	0.9–1.7
Secondary and unspecified cancer	16	1.1	0.6–1.8	49	1.4	1.0–1.9	65	1.3	1.0–1.7
Non-Hodgkin's lymphoma	14	1.3	0.7–2.1	22	1.0	0.6–1.5	36	1.1	0.8–1.5
Leukaemia	23	1.5	0.9–2.2	28	1.2	0.8–1.7	51	1.3	1.0–1.7

Table 4. Numbers of cases (n) *and relative risks (RR) of cancers at different sites in the entire cohort of patients with obesity as one of up to 20 diagnoses (separately for the first year and later periods of follow-up after hosptial discharge) and in the subcohort of patients with obesity as the primary diagnosis (ignoring the first year of follow-up after hospital discharge)*

	Entire cohort				Subcohort	
	Follow-up 1–11 years		Follow-up 0–1 years		Follow-up 1–11 years	
Site	*n*	RR	*n*	RR	*n*	RR
All cancers	2038	1.16*	461	1.21*	220	1.18*
Mouth and pharynx	37	1.2	9	1.3	9	3.0*
Oesophagus	26	1.9*	5	1.7	2	1.7
Stomach	73	1.1	19	1.2	9	1.7
Colon	195	1.2*	31	0.9	17	1.2
Rectum	91	1.1	15	0.8	4	0.5
Liver	58	1.9*	11	1.8	5	1.9
Gall bladder	28	1.3	9	1.8	2	1.0
Pancreas	101	1.7*	19	1.5	14	2.7*
Lung	168	0.8*	43	1.0	20	1.1
Female breast	231	1.0	44	0.9	25	0.8
Cervix uteri	49	1.2	13	1.4	9	1.2
Corpus uteri	114	2.0*	24	1.9*	13	1.8
Ovary	58	1.1	13	1.1	9	1.3
Prostate	96	1.3*	23	1.4	6	1.4
Kidney, men	21	1.2	6	1.4	1	0.7
Kidney, women	58	2.0*	18	3.0*	7	2.2
Bladder	99	1.2*	23	1.2	7	1.0
Melanoma	32	1.0	5	0.7	4	0.8
Non-melanoma skin cancer	190	0.9*	32	0.7*	17	0.8
Brain	43	1.2	30	4.0*	7	1.4
Secondary and unspecified cancer	65	1.3*	7	0.7	10	2.2*
Non-Hodgkin's lymphoma	36	1.1	9	1.3	1	0.3
Leukaemia	51	1.3*	14	1.6	7	1.8

*$P \leq 0.05$.

DISCUSSION

Effects possibly related to hormones

Previous epidemiological studies of obesity in women have repeatedly shown an increased occurrence of cancer of the uterine corpus [6, 10–12], and, in postmenopausal women, of breast cancer [13–15]. The present study replicates these findings exactly, and furthermore shows a decreased incidence of breast cancer in premenopausal women, as has also been reported previously [16–18]. The differential effect of obesity on breast cancer and uterine corpus cancer is likely to be the result of a different response of these tissues to the female sex hormones oestrogen and progesterone [19–21]. The endometrium proliferates in response to oestrogens only in the absence of progesterone (unopposed oestrogens), while the proliferation of the breast tissue is less clearly related to these hormones but is maximal in the luteal phase of the menstrual cycle in the presence of both oestradiol and progesterone. In postmenopausal women, in whom all oestrogens act essentially in the absence of progesterone, unopposed oestrogens formed by aromatisation of androgens in adipose tissue may, therefore, be the mechanism by which the incidence rates of both uterine corpus cancer and breast cancer are increased. Obese premenopausal women frequently have anovulatory cycles, for which reason they may have difficulty in conceiving [22]. In the anovulatory cycle, the normal increase in progesterone in the luteal phase is absent or reduced. Obese women with anovulatory cycles may thus be at increased risk of uterine corpus cancer, possibly due to the increased exposure to unopposed oestrogens, and at decreased risk of breast cancer due to the lower level of exposure to progesterone.

Following the argument outlined above, it might have been expected that the pattern of ovarian cancer would be similar to that of breast cancer because anovulatory cycles would be expected to decrease the incidence of ovarian cancer. The results are in fact quite the opposite, with increased risk in women in their fifties and an expected or lower than expected incidence later in life. Results similar to these have been reported pre-

Table 5. Brain cancer: number or cases (n) *and relative risks (RR) in the entire cohort of patients with obesity as one of up to 20 diagnoses, by sex and time after hospital discharge*

Time after hospital discharge (years)	Men		Women		Total	
	n	RR	*n*	RR	*n*	RR
0–1	12	4.7*	18	3.7*	30	4.0*
1–3	3	0.7	16	1.9*	19	1.5
3–5	4	1.3	9	1.4	13	1.4
5+	1	0.3	10	1.1	11	0.9

Trend for men, women and total, $P < 0.001$. *$P \leq 0.05$.

Table 6. Numbers of cases (n) *and relative risks (RR) of selected cancer sites in the entire cohort of patients with obesity as one of up to* 20 *diagnoses (ignoring the first year of follow-up after hospital discharge), by age*

Site	Age (years) 0–49 n	0–49 RR	50–59 n	50–59 RR	60–69 n	60–69 RR	70–79 n	70–79 RR	80+ n	80+ RR	Trend P value
Breast	17	0.6*	32	0.9	49	1.0	79	1.2	54	1.3*	0.04
			Age 0–59								
Uterine corpus			21	1.7*	34	1.7*	47	2.7*	11	1.5	0.40
Ovary			22	1.7*	13	0.9	18	1.1	5	0.6	0.01
Pancreas			8	1.5	32	2.4*	40	1.6*	21	1.4	0.002
Prostate			7	2.5*	25	1.5*	44	1.3	20	1.1	<0.001

*$P < 0.05$.

viously [23]. It may be possible that the discrepancy between breast cancer and ovarian cancer incidence in younger obese women is due to a different balance between the protective effects of anovulation and the enhancing effects of low parity, the former being the relatively more important effect for breast cancer and the latter being the most important for ovarian cancer. A meta-analysis of studies of parity and breast cancer from the Nordic countries showed a RR of around 1.1–1.3 (depending on age) for nulliparous versus parous women [24], while for ovarian cancer, a cohort study from Norway [25] and a case–control study from England [26] both gave a corresponding RR of 1.7. This may, at least in part, explain the different effects of obesity on these two cancers.

Effects possibly related to alcohol consumption

The increased incidence of oesophageal cancer, liver cancer and, in the subcohort analysis, cancer of the mouth and pharynx is suggestive of a disease pattern related to a high consumption of alcoholic beverages [27]. In Ole Møller Jensen's study of cancer incidence in Danish brewery workers, the cancer sites which were significantly elevated in incidence were oesophagus (RR = 2.1), liver (RR = 1.5), larynx and trachea (RR = 2.0), lung (RR = 1.2), and unspecified organs (RR = 2.2) [28]. In a recent study of cancer incidence in 18 000 alcoholics in Copenhagen, significantly elevated incidence was similarly observed for cancers of the mouth and pharynx (RR = 4.1), oesophagus (RR = 5.3), liver (RR = 3.9), larynx (RR = 3.7), lung (RR = 2.6) and secondary and unspecified cancers (RR = 2.1) (unpublished observations).

There is conflicting evidence for an association between alcohol intake and relative weight [29], although a cross-sectional study in Danish men showed a positive association [30]. In a study in California, alcohol consumption was shown to be associated with abdominal obesity, measured as the waist-to-hip ratio, independently of body mass index [31]. The present data suggest an overrepresentation of drinkers in the cohort, possibly brought about by an association between alcohol drinking and general or abdominal obesity. It is possible also that people with high alcohol consumption have a generally increased morbidity and hospitalisation and are, therefore, preferentially recruited into the cohort. In the latter case, however, it is unlikely that the alcohol-related cancers have contributed to such a selection mechanism, since the risk of alcohol-related cancer is not particularly high in the first year of follow-up.

Effects possibly related to dietary habits

Cancer of the pancreas and cancer of the prostate are diseases for which the aetiologies are poorly characterised, but where an influence of dietary habits is suspected [32, 33]. The incidence of both cancers appears to be substantially increased in the present cohort. A recently published multicentre case–control study of pancreatic cancer aetiology showed no association with body mass index (based on self-reported height and weight or information obtained by proxy interview), but a very strong effect of total caloric intake, particularly caused by a strong effect of carbohydrate intake [34]. Absence of an effect of body mass index was similarly observed in two other case–control studies [35, 36].

An effect of caloric intake without a corresponding effect of body mass index may seem surprising, but in fact it is not clear that a high caloric intake, as estimated from a diet questionnaire, is associated with being overweight [37]. On the other hand, it remains a possibility that pancreatic cancer is associated with obesity but that the case–control methodology failed to detect this due to body weight loss induced by the disease, or a tendency of overweight cases to recall their weight as being lower than its true value. The large American follow-up study of obesity did not have sufficient statistical power to evaluate an association with pancreatic cancer [3], and the possibility remains that the presently observed increased risk of pancreatic cancer is a chance finding.

An increased incidence of prostatic cancer in overweight men has been reported in previous prospective studies [38, 39] and one case–control study [40]. Other case–control studies have not detected any association with body mass index [41–43], and in one of the positive studies, risk tended to be more closely associated with the mass of lean rather than fat tissue [39]. Substantial epidemiological and laboratory evidence point to a possible role of dietary fat, particularly animal fat or saturated fat, in the aetiology of prostatic cancer [44].

As shown in a separate paper [45], the excess incidence of kidney cancer in women is due exclusively to an excess of renal cell carcinoma. Analysis by time after entry into the cohort shows no trend in risk, and the subcohort analysis gave similar results. The presence of an effect of obesity on the occurrence of kidney cancer in women has been suggested in several case–control studies [46–49], and has recently been confirmed in a Danish case–control study (unpublished observations).

Cancer of the colon was associated with body mass index in several previous prospective studies [50–53]; a similar effect does not seem to exist for rectal cancer [50, 53], and has not been observed consistently in case–control studies of colorectal adenomas [54, 55]. Dietary studies suggest that the risk of colon cancer may be enhanced by some aspects of a diet high in meat, fat, protein and total energy, while dietary fibre and vegetables may decrease the risk [56–58]. Furthermore, a protective role of physical activity has been suggested [59].

Miscellaneous

The strangest finding in the present study is the strong association between hospital discharge with a diagnosis of obesity and the risk of brain cancer in the following year. The 4-fold increase in risk is seen in both men and women, and is very unlikely to result from chance alone. The excess risk levels off rapidly after the first year and it is, therefore, not likely that the association reflects a cause-and-effect relationship between obesity and brain cancer development. One might speculate that obesity could be a clinical manifestation of some brain cancers, but we have found no published data to support this idea. Another hypothetical explanation would be that brain cancer patients are often hospitalised for the clinical manifestations of their unrecognised disease without such hospitalisation leading to the correct diagnosis. However, such selection into the cohort of patients with unrecognised cancer does not seem to occur to any appreciable extent for other types of cancer, and we would not expect such a mechanism to apply uniquely to brain cancer. We have no good explanation for the pattern of brain cancer in this cohort.

The higher than expected occurrence of cancers of unknown or unspecified origin in the cohort may possibly be due to a reduced propensity to perform diagnostic or curative surgery in obese patients. The reduced occurrence of non-melanoma skin cancer may reflect a lower prevelance of outdoor occupations or of recreational suntanning in the overweight. Reduced incidence of lung cancer in overweight persons has been reported previously [60, 61]. Smokers tend to be leaner than non-smokers and may, therefore, have a lower probability of being diagnosed as obese. Compared with patients with stomach cancer or colorectal cancer, lung cancer patients have a higher level of resting energy expenditure independently of body weight [62].

CONCLUSION

The present study confirms that obese patients have a somewhat higher risk of cancer than other people. Based on the data and on considerations given above, we may predict that obese women, due to hormonal alterations, are at increased risk of endometrial cancer and postmenopausal breast cancer. Furthermore, it seems clear that obese men are at increased risk of prostatic cancer. There is a suggestion of increased incidences of pancreatic cancer, colon cancer, kidney cancer in women and brain cancer during the first year after hospital discharge, but the aetiological mechanisms for such effects are unclear.

The observed increase in incidence of cancers which are aetiologically related to excessive alcohol intake (mouth and pharynx, oesophagus, liver) is probably not related to obesity itself, and a reduction in weight without reduction in alcohol intake may not be sufficient to reduce these risks.

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