2.5 Sustained weight loss and cancer risk: illustrative examples

Studies investigating whether weight loss protects against cancer occurrence are limited to a few observational studies on weight reduction in relation to breast cancer incidence and on the impact of intentional weight loss after bariatric surgery on cancer risk in morbidly obese patients.

2.5.1 Studies of weight loss and cancer risk

Few observational studies have been able to assess the impact of weight loss on cancer risk. Women from the Nurses' Health Study who had never used postmenopausal HRT and had lost 10 kg or more sustainably since menopause [duration not reported] had a lower risk of postmenopausal breast cancer than those who maintained their weight since menopause (RR, 0.43; 95% CI, 0.21–0.86) (Eliassen et al., 2006). However, no association was found between short-term (4-year) weight loss and subsequent cancer risk in the same cohort (Rosner et al., 2015). In contrast, regardless of use of postmenopausal HRT, adult weight loss was unrelated to postmenopausal breast cancer risk compared with stable weight in the NIH-AARP study (Ahn et al., 2007), the EPIC-PANACEA study (Emaus et al., 2014), and the Cancer Prevention Study II for the first 5 years of follow-up (Teras et al., 2011); however, in the Cancer Prevention Study II an inverse association was suggested in women who maintained a weight loss of 10 lb [4.5 kg] or more for the next 4 years. Similarly, in the Women's Health Initiative Dietary Intervention Trial, no effect of weight loss on postmenopausal breast cancer risk was found in overweight or obese women (Neuhouser et al., 2015).

[It is important to note that many of the published trials and observational studies were not designed to document weight loss, and weight change may reflect both intentional weight loss (with uncertainty about what exactly the intervention was) and unintentional weight loss (which is potentially illness-induced).]

2.5.2 Studies of bariatric surgery and cancer risk

Several prospective intervention trials or retrospective cohort studies (Christou et al., 2008; Adams et al., 2009; Sjöström et al., 2009; Ward et al., 2014) and reviews (Tee et al., 2013; Maestro et al., 2015) have evaluated the effect of bariatric surgery on cancer risk, comparing the risk of cancer in patients who underwent bariatric surgery with that in an obese control group who did not undergo surgery (Table 2.5). Overall, in most studies the risk of cancer at all sites in obese patients was significantly reduced after bariatric surgery. A 45% decrease in risk of all cancers combined was estimated in a recent meta-analysis (RR, 0.55; 95% CI, 0.41–0.73) (Tee et al., 2013). The extent of the cancer-protective effect of bariatric surgery seems to be more pronounced in women than in men: in the Swedish Obese Subjects study, after a median follow-up of more than 10 years, the relative risk was 0.58 (95% CI, 0.44–0.77) in women and 0.97 (95% CI, 0.62–1.52) in men (Sjöström et al., 2009). Also, there are broadly consistent inverse associations with the subsequent risk of female sex hormone-sensitive cancers, notably endometrial cancer and breast cancer (Adams et al., 2009; Tee et al., 2013; Ward et al., 2014). [However, there were methodological problems in the study designs because of confounding by indication, and failure to adequately capture the extent of body weight reduction after bariatric surgery.]

Studies using population-level registry data (i.e. standardized population cohorts) for comparison purposes have reported an increased incidence of colorectal cancer in obese men who underwent bariatric surgery compared with the expected risk in the general population (Östlund et al., 2010; Derogar et al., 2013). [Because the general population was used as comparator, the median BMI (not reported) would have been considerably less than that for the treatment group, and the observed increase in incidence might reflect the effect of the premature morbidly obese status rather than of the surgery itself. Therefore, any comparison with the general population may be misleading in the evaluation of the effects of bariatric surgery on subsequent cancer risk in obese patients.]

Table 2.5 Studies of obese patients who underwent bariatric surgery and subsequent cancer risk

Reference Location	Study design Mean follow-up (years)	Surgery group	Control group	Cancer site	Surgery cases (cohort) Control cases (cohort)	Relative risk (95% CI)	Adjustments Comments
Men and women							
Christou et al. (2008) Canada	Retrospective hospital-based Maximum, 5.0	Bariatric patients in regional database BMI not available	Diagnosis of "morbid obesity" from hospital records or prescription BMI unknown	All sites[a]	21 (1035) 487 (5746)	0.22 (0.14–0.35)	Age, sex, BMI
Adams et al. (2009) Utah, USA	Retrospective registry 12.5	Roux-en-Y gastric bypass Mean BMI, 44.9	State document applicants with a self-reported BMI > 35 Mean BMI, 47.4	All sites[b]	254 (6596) 477 (9442)	0.76 (0.65–0.89)	Age, sex, BMI Data also reported for the 31 individual cancer sites
				"Obesity-related sites"[c]	104 (6596) 253 (9442)	0.62 (0.49–0.78)	
				Colorectum	25 (6596) 52 (9442)	0.70 (0.43–1.15)	
Women							
Adams et al. (2009) Utah, USA	Retrospective registry Median, 12.5	Roux-en-Y gastric bypass Mean BMI, 44.9	State document applicants with a self-reported BMI > 35 Mean BMI, 47.4	All sites[b]	215 (5654) 412 (7872)	0.73 (0.62–0.87)	Age, BMI
				Breast	25 (5654) 52 (7872)	0.91 (0.67–1.24)	
				Premenopausal breast	49 (5654) 65 (7872)	0.93 (0.63–1.37)	
				Postmenopausal breast	24 (5654) 40 (7872)	0.96 (0.57–1.63)	
				Corpus uteri	14 (5654) 98 (7872)	0.22 (0.13–0.40)	
Sjöström et al. (2009) Sweden	Prospective intervention trial 10.9	Mean BMI, 42.2	Matched using 18 anthropometric, cardiovascular, and biochemical indices Mean BMI, 41.6	All sites[d]	79 (1420) 130 (1447)	0.58 (0.44–0.77)	Age, smoking, weight change, energy intake, and matching Also significantly reduced for melanoma and haematopoietic cancers
Ward et al. (2014) USA	Retrospective clinical data repository Unknown	All female patients with a history of bariatric surgery BMI unknown	All female admissions with an associated diagnosis of obesity BMI unknown	Corpus uteri	424 (103 797) 43 921 (7 328 061)	0.29 (0.26–0.32)	None

Table 2.5 (continued)

Reference Location	Study design Mean follow-up (years)	Surgery group	Control group	Cancer site	Surgery cases (cohort) Control cases (cohort)	Relative risk (95% CI)	Adjustments Comments
Men							
Adams et al. (2009) Utah, USA	Retrospective registry 12.5	Roux-en-Y gastric bypass Mean BMI, 44.9	State document applicants with a self-reported BMI > 35 Mean BMI, 47.4	All sites[b]	39 (942) 65 (1570)	1.02 (0.69–1.51)	Age, BMI
Sjöström et al. (2009) Sweden	Prospective intervention trial 10.9	Mean BMI, 40.6	Matched using 18 anthropometric, cardiovascular, and biochemical indices Mean BMI, 39.2	All sites[d]	39 (590) 39 (590)	0.97 (0.62–1.52)	Age, smoking, weight change, energy intake, and matching Results were not statistically significant for any of the individual cancer sites

[a] Includes colorectum, pancreas, breast, endometrium, kidney, melanoma, myeloma, and non-Hodgkin lymphoma.
[b] Includes 31 cancer sites and “other”.
[c] Includes colorectum, oesophagus (adenocarcinoma), liver, gall bladder, pancreas, postmenopausal breast, corpus and uterus, kidney, non-Hodgkin lymphoma, leukaemia, and multiple myeloma.
[d] Includes colorectum, stomach, liver, pancreas, kidney, bladder, lung and bronchia, haematopoietic system, and melanoma for both sexes, and breast, cervix, and endometrium in women and prostate in men.
BMI, body mass index (in kg/m^2); CI, confidence interval

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