GENERAL REMARKS

This sixteenth Volume of the *IARC Handbooks of Cancer Prevention* series evaluates the cancer-preventive effects of absence of excess body fatness. It is the second Volume since the relaunch of the *IARC Handbooks* series in 2014, and the first Volume on primary prevention in the new series.

The *IARC Handbooks* provide the same rigorous evaluation process as the *IARC Monographs*. They serve national health agencies to inform their preventive strategies for cancer control. To support the World Health Organization Global Action Plan for the prevention and control of noncommunicable diseases, the availability of an international consensus from an independent, specialized agency within the United Nations family provides an authoritative basis for national decision-making, and should facilitate national recommendations and communication with the population at risk.

For this Volume, the Working Procedures of the *IARC Handbooks* have been updated in accordance with the current Preamble of the *IARC Monographs* (IARC, 2006), with definitions of the different types of participants and guidelines for selection of experts and literature searches. In addition, more detailed instructions are given for the scientific review and evaluation criteria. (See the Working Procedures in this Volume.)

Previous evaluations

In 2001, a Working Group of international experts developed Volume 6 of the *IARC Handbooks*, on weight control and physical activity (IARC, 2002). The resulting consensus evaluations are presented in Table 1.

Rationale for a re-evaluation

A re-evaluation of the cancer-preventive effects of avoidance of weight gain was highly desired. The mean body mass index (BMI) of the population has increased dramatically worldwide during the past 40 years (NCD Risk Factor Collaboration (NCD-RisC), 2016). The United Nations High-Level Meeting on Noncommunicable Diseases in September 2011 identified obesity as one of the leading risk factors for chronic diseases, including coronary heart disease, diabetes, and cancer (Beaglehole et al., 2011). Overweight and obesity have been estimated to have accounted for 4.0 million deaths (95% uncertainty interval, 2.7–5.3 million) worldwide in 2015, representing 7.1% (95% uncertainty interval, 4.9–9.6%) of total global mortality (Afshin et al., 2017). In 2014, the overall socioeconomic cost associated with obesity was estimated at US$ 2 trillion globally (Dobbs et al., 2014).

Table 1 Evaluations of *IARC Handbooks* Volume 6 (2002)

Intervention	Humans		Experimental animals		Overall evaluation
	Strength of evidence	Organ site	Strength of evidence	Organ site	
Avoidance of weight gain	*Sufficient*	Colon Breast (postmenopausal) Endometrium Kidney (renal cell) Oesophagus (adenocarcinoma)			Limiting weight gain during adult life, thereby avoiding overweight and obesity, **reduces** the risk of postmenopausal breast cancer and cancers of the colon, uterus (endometrium), kidney (renal cell), and oesophagus (adenocarcinoma).
	ESLE	Breast (premenopausal)			
Intentional weight loss	*Inadequate*		*Sufficient*	(Calorie/dietary restriction) Mammary gland Liver Pituitary gland (adenoma) Colon Skin (non-melanoma) Lymphoma	Weight loss among overweight or obese persons **possibly reduces** risks of these cancers, but no firm conclusion can be drawn because of the sparsity of the epidemiological evidence.
			Limited	Prostate Pancreas	

ESLE, evidence suggesting a lack of effect

Worldwide, it has been estimated that 481 000 new cancer cases (3.6% of all new cases) in adults in 2012 could be attributed to high BMI; the attributable fraction was as high as 9% in women in North America, Europe, and the Middle East (Arnold et al., 2015). This estimation was based on evidence for an association of high BMI with oesophageal adenocarcinoma and cancers of the colon, rectum, pancreas, gall bladder, kidney, postmenopausal breast, corpus uteri, and ovary (Arnold et al., 2015). Taking into account the evaluations of this Volume, which indicate that excess body fatness increases cancer risk at additional sites (a total of 13 cancer sites or subtypes), the fraction of cancer cases worldwide that are attributable to overweight and obesity is even higher than previously estimated.

Content of this *Handbook*

In this Volume, in addition to the identification of target organs for excess body fatness, the following topics have been reviewed when available:

- Sex specificity
- Anthropometric measures of body fatness other than BMI: weight, waist circumference, and waist-to-hip ratio
- Effect of change in BMI or weight over the life-course
- Risk reduction after intentional weight loss
- Effect of excess body fatness on cancer survival in cancer patients, and on recurrence in cancer survivors
- Excess body fatness in children, adolescents, and young adults (age ≤ 25 years) and subsequent cancer risk.

Weight loss

Few data are available on intentional weight loss in humans. Therefore, data in experimental animals provide important information to assess the effect of intentional weight loss. Studies in animals use dietary or calorie restriction to induce a lower weight gain compared with animals fed ad libitum, or to induce weight reduction in obese animals.

For humans, the Working Group considered the data on bariatric surgery as a proxy for the evidence on intentional weight loss. The clinical effectiveness of bariatric surgery for weight loss and improved health has been established (Picot et al., 2009), although risks of complications, reoperation, and death exist.

Impact of physical activity on the assessment of the cancer-preventive effects of absence of excess body fatness

The major contributors to weight gain are excess energy intake and insufficient levels of physical activity, which both lead to chronic positive energy balance. In recent years, new evidence has accumulated on the different types of physical inactivity and on sedentary behaviour as risk factors for cancer. In this *Handbook*, the cancer-preventive effects of absence of excess body fatness were evaluated taking into account potential confounding and/or effect modification by physical activity. Physical activity will be evaluated separately in a future *Handbook*.

A summary of the findings of this Volume has appeared in *The New England Journal of Medicine* (Lauby-Secretan et al., 2016).

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