Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

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- The result of a five-year examination by a panel of the world’s leading scientists.
- Includes new findings on early life, body fatness, physical activity, and cancer survivors.
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6.1 Body fatness

A key reason for the success of Homo sapiens is our adaptability. Humans have evolved to survive and flourish in almost all environments and circumstances which, during the 250,000 years of our species’ existence, have usually included occasional or regular food scarcity and insecurity. We have built-in defences against starvation: our own stores of fat that are used in times of need.

Food insecurity remains endemic, particularly in Africa and Asia. But many people in the world now have access to more than enough to eat and drink and are also relatively physically inactive (see Chapter 5). As a result, stores of body fat tend to increase. What is now a pandemic of overweight and obesity can be seen as a response to circumstances of plenty. One consequence, in the context of reduction in rates of nutritional deficiencies and infections of childhood and early life, and the ageing of human populations, is an increase in the rates of chronic diseases. These include cancer.

Overall, the Panel judges that evidence on the degree of body fatness and the risk of cancers of a number of sites is strong and generally consistent. The Panel emphasises that the risk of cancer is modified, not only by obesity, as usually defined, but by overweight as well, and even by degrees of body fatness generally regarded as healthy.

The Panel judges as follows:

The evidence that greater body fatness is a cause of adenocarcinoma of the oesophagus, and cancers of the pancreas, colorectum, breast (postmenopause), endometrium, and kidney, is convincing. Greater body fatness is probably a cause of cancer of the gallbladder. There is limited evidence suggesting that greater body fatness is a cause of liver cancer. The evidence that greater abdominal (central) fatness is a cause of colorectal cancer is convincing; and greater abdominal fatness is probably a cause of cancers of the pancreas, breast (postmenopause), and endometrium. By contrast, greater body fatness probably protects against premenopausal breast cancer.

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BODIES FATNESS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
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<tr>
<td>Exposure</td>
<td>Cancer site</td>
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<td>Convincing</td>
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<td>Probable</td>
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<td>Abdominal fatness</td>
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<td>Substantial effect on risk unlikely</td>
<td>None identified</td>
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¹ For oesophageal adenocarcinomas only.
² Directly and indirectly, through the formation of gallstones.

For an explanation of all the terms used in the matrix, please see chapter 3.5.1, the text of this section, and the glossary.
The Panel notes that there is limited evidence suggesting that low body fatness (underweight) is a cause of lung cancer, but residual confounding with smoking and lung disease cannot be ruled out. See Chapter 8 for judgements on physical activity and sedentary ways of life, the energy density of foods and drinks, breastfeeding, other factors, and the risk of weight gain, overweight, and obesity.

Within the remit of this Report, the strongest evidence, corresponding to judgements of ‘convincing’ and ‘probable’, shows that greater body fatness and greater abdominal fatness are causes of cancer of the colorectum; that greater body fatness is additionally a cause of cancers of the oesophagus (adenocarcinoma), pancreas, breast (postmenopause), endometrium, and kidney; and (probably) gallbladder. It also shows that greater abdominal fatness is probably a cause of cancers of the pancreas, breast (postmenopause), and endometrium; but that greater body fatness probably protects against premenopausal breast cancer.

Body fatness and organ mass and composition, commonly assessed by body size measurements, are key factors influencing health and well-being throughout the life course.

The main concern of nutrition science, since its beginnings and until the mid-20th century, has been to protect populations against the consequences of malnutrition in the ‘classic’ sense of the word. That is undernutrition, which increases vulnerability to infectious diseases, especially in infancy and childhood, and results in people who are small and weak, unable to be productive, and with low life expectancy. This remains a central public health priority for middle- and low-income countries.

In the final two decades of the 20th century and into this century, a different and imperative public health nutrition concern has emerged: weight gain, overweight, and obesity. At first, it was generally assumed that societies whose babies are big, whose children grow fast, and whose adults are heavy and tall, were healthy. Compared to societies with inadequate nutrition and poor public health provision, such populations are indeed physically stronger, more productive, have longer lives, and are generally healthier.

This said, since the 1980s, a series of reports based on a rapidly increasing evidence base have concluded that populations of high-income countries, and now also populations of many middle- and low-income countries, are becoming overweight to an extent that is bad for health. These countries are almost exclusively those experiencing social, economic, and nutritional transition. The nutritional transition is characterised by a shift from ‘traditional’ diets that are low in fat and high in fibre to high-energy ‘Western’ diets that are high in fat and low in fibre. It is now generally accepted that obesity, but also overweight short of obesity, increases the risk of a number of major chronic diseases including insulin resistance, hyperlipidaemia, hypertension and stroke, type 2 diabetes, and coronary heart disease, as well as cancers of some sites. In this chapter, the evidence on body fatness and cancer is summarised and judged. Also see Chapter 8.

In this Report, the term ‘body fatness’ refers to the degree of body fatness across the whole range, not only the conventional categories of overweight and obesity.

### 6.1.1 Definitions and patterns

#### 6.1.1.1 Body fatness

Excess energy from food is stored as fat in the body in adipose tissue. The amount of this body tissue varies more from person to person than any other type (such as muscle, bone, or blood). The size and location of these fat stores also vary considerably between populations, people, and over the course of a person's life. Excess body fat is a cause of a number of chronic diseases and reduces life expectancy (also see Chapter 8).

Since the 1980s, typical body compositions have changed, with a worldwide increase in average body fatness and in overweight and obesity. This change is most notable in high-income countries, and in industrial and urban environments in many if not most countries (see chapters 1.1.3 and 1.2.2). In several low-income countries, high levels of body fatness exist alongside undernutrition in the same communities and even in the same families.

Body fatness is difficult to measure directly or accurately. However, because body fatness is the most variable determinant of weight, several weight-based measures are used as markers of body fatness. The most common is the body mass index (BMI), a measure of weight adjusted for height. BMI is calculated as weight in kilograms divided by height in metres squared (kg/m²). In most circumstances, BMI has been shown to be reliably linked to body fatness. But this method does not always provide an accurate measure: unusually muscular and lean people (such as manual workers and power athletes) have a relatively high BMI, even if they have relatively little body fat. See table 6.1.1 and also Chapter 8.

A BMI of between 18.5 and 24.9 is generally regarded as ‘healthy’ or ‘normal’ (healthy or normal body fatness). This is roughly equivalent to 15–20 per cent body fat in adult men and 25–30 per cent in adult women. The ‘underweight’ or ‘thin’ range is a BMI below 18.5 (low body fatness). Above 25 (high body fatness), there are common gradings for overweight, obesity, and extreme (‘morbid’) obesity. The risk of type 2 diabetes and high blood pressure increases with BMI with no clear threshold, but with a marked increase in risk as BMI approaches 25. The ideal average BMI for populations has been estimated to be 21–22.

The principal cut-off points shown in table 6.1.1 have been agreed by the World Health Organization and are based on the risks associated with being underweight, overweight, or obese (see Chapter 8). However, the healthy ranges of BMI vary between populations. The additional cut-off points take this into account and are recommended for reporting purposes, with a view to facilitating international comparisons.

The principal BMI cut-offs are based on data primarily derived from populations of European origin living in high-income countries, so they may not apply globally. Different
BMI cut-off points have been proposed to classify overweight and obesity in different populations, due to different body composition and the relation of BMI to risk in these populations. However, these have not become universally accepted.7 8 A WHO expert consultation on BMI in Asian populations recommended that the principal BMI cut-off points (table 6.1.1) should be retained as the international classification.9 However, it also recommended that additional cut-off points of 23, 27.5, 32.5, and 37.5 kg/m² should be added to the international classification and, for reporting purposes, countries should use all categories (that is, 18.5, 23, 27.5, 30, and 32.5 kg/m²; and in many populations, 35, 37.5, and 40 kg/m²) with a view to facilitating international comparisons. The principal and additional cut-off points are shown in table 6.1.1. At equivalent BMIs, many Asian populations have a higher body fat content, whereas Maori people and Pacific Islanders have more lean tissue and less fat.4 10 11 Many Asian expert groups and health ministries now define the upper limit of 'acceptable' as a BMI of below 23, whereas the equivalent cut-off point for China is 24. It is unlikely that the excess risk in these populations at relatively low BMIs reflects only differences in body fat — there are probably other related metabolic changes, for instance, those induced by fetal and early childhood nutritional differences. WHO has recognised that Asian populations may choose a BMI cut-off of 23 because of the greater susceptibility of these groups of people to type 2 diabetes and perhaps other complications of excess weight gain.9 Mexican people have also been shown to be at greater risk, so Latin American populations may also be considered as more sensitive to the effects of weight gain than white people of European origin.12

### 6.1.1.2 Body fat distribution

Fat is not distributed equally around the body. It accumulates subcutaneously (beneath the skin) around the muscles of the upper arm, buttocks, belly, hips, and thighs. It also accumulates intra-abdominally or viscerally (around the organs). Fat stores can be categorised as 'peripheral' (not around the trunk) or 'abdominal' (also called 'central'). The pattern of fat stores is determined largely by genetic factors, with a typically different pattern in men and women, which tends to change with age. Women tend to store more subcutaneous fat around their hips, buttocks, and thighs than men, producing a body profile known as a ‘pear shape’ (or ‘gynoid’ pattern of fat distribution). Men are more likely to store fat around their abdomen, producing an ‘apple shape’ (or ‘android’ pattern).

The size of peripheral fat stores can be used as a measure of total body fatness, although the proportion of total to abdominal fat varies between people. Waist circumference is a measure that includes both subcutaneous and the more metabolically active intra-abdominal fat stores. The size of intra-abdominal fat stores predicts the risk of chronic diseases, such as metabolic disorders and cardiovascular disease, better than overall indicators of body fatness, such as subcutaneous fat measures or BMI.13 The size of these fat stores also influences several hormone systems, such as insulin, as well as those involved in the body’s response to inflammation, both of which may play a role in cancer processes (box 2.4).14 15

Crude estimates of excess abdominal fat can be made by measuring either waist circumference or by calculating the ratio of this measurement to hip circumference (the ‘waist to hip’ ratio), although this ratio is no longer recommended as a useful indicator of abdominal obesity. Waist circumference is a better single indicator. As is the case for BMI, the cut-off points for excess waist measurements for Asian and Mexican populations are usually lower than those suggested by WHO as suitable for people of European origin. This is because these non-white populations have a greater risk of disease with only modest increases in intra-abdominal fat.

The WHO reference values for waist circumferences of 94 cm (37 inches) in men and 80 cm (31.5 inches) in women (on a population basis) are based on their rough equivalence to a BMI of around 25, whereas waist circumferences of 102 cm (40.2 inches) in men and 88 cm (34.6 inches) in women are equivalent to a BMI of around 30.16 17 For Asian populations, cut-offs for waist circumferences of 90 cm for men and 80 cm for women have been proposed.18

### 6.1.1.3 Adult weight gain

Increases in body weight during adulthood depend mostly on accumulation of fat rather than lean tissue, and therefore any change may better reflect fatness than adult attained weight itself, which is more dependent on lean mass. For this reason, evidence of associations specifically between weight gain in adulthood and cancers was sought.
in the systematic literature reviews that informed the Panel's judgements.

6.1.2 Interpretation of the evidence

6.1.2.1 General
For general considerations that may affect interpretation of the evidence, see chapters 3.3 and 3.5, and boxes 3.1, 3.2, 3.6 and 3.7.

6.1.2.2 Specific
Some considerations specific to body fatness are as follows.

Classification. The system of classifying underweight, ‘normal’ weight, overweight, and degrees of obesity as discrete ranges of BMI, is in general use. However, as shown in this chapter and also Chapter 8, the relationship between body fatness and cancer is continuous across the range of BMI. For this reason, the Panel has chosen to use the term ‘body fatness’ rather than ‘overweight’ or ‘obesity’.

Measurement. BMI is not a perfect marker of body fatness. More precise techniques such as underwater weighing, magnetic resonance imaging, computerised tomography, or dual-energy X-ray absorptiometry are rare in large-scale epidemiological studies due to their difficulty and expense. Abdominal fatness is usually measured either using the waist to hip ratio or the waist circumference alone. There is a lack of consensus on how abdominal fatness is best measured, and measurement error is more likely than for some other anthropometric measures such as height and weight. The currently proposed maximum ‘cut-off’ points for ‘healthy’ waist circumferences (94 cm or 37 inches for men; 80 cm or 31.5 inches for women) and for ‘healthy’ waist to hip ratios (1.0 for men; 0.8 for women) are based almost exclusively on studies of cardiovascular or type 2 diabetes risk in white populations in high-income countries. It is not known whether they can be applied to other ethnic groups or outcomes. The relationship between waist circumference and the size of intra-abdominal fat stores (as opposed to subcutaneous abdominal fat stores) may vary between different ethnic groups. As body fatness tends to increase with age in most populations, and is characteristically higher in women than in men, it is important that studies take into account both age and sex. Measurement of change in weight tends to be more precise than static measures such as weight or BMI.

Reporting bias. Objective measures of height and weight, and therefore BMI, are reliable. However, many studies rely on self-reporting, which is liable to introduce bias. Although reported and actual weights are correlated, weight tends to be under-reported, especially by overweight and obese people. BMIs calculated from self-reported data will therefore tend to be lower than from more objective measures.

6.1.3 Evidence and judgements

The full systematic literature review (SLR) is contained on the CD included with this Report.
There are several general mechanisms through which body fatness and abdominal fatness could plausibly influence cancer risk. For example, increasing body fatness raises the inflammatory response, increases circulating oestrogens, and decreases insulin sensitivity. The physiological effects of obesity are described in more detail in Chapter 8. The effects of body fatness-related hormonal changes and inflammation on cancer processes are detailed in box 2.4. Additional site-specific mechanisms are described with the evidence for each cancer site in the following sections.

6.1.3.1 Body fatness

**Oesophagus**

Three cohort studies and eight case-control studies investigated body fatness (as measured by BMI) and oesophageal adenocarcinomas.

All three cohort studies showed increased risk for the highest body fatness, as measured by BMI, when compared to the lowest (figure 6.1.1); this was statistically significant in both sexes in one study and in men but not women in two others. Effect estimates were 2.58 in men (95% confidence interval (CI) 1.81–3.68; p < 0.001) and 2.06 in women (95% CI 1.25–3.39; p = 0.002); 2.40 in men (95% CI 1.30–4.42) and 1.57 in women (95% CI 0.51–4.84); and 1.76 in men (95% CI 1.03–3.02) and 2.13 in women (95% CI 0.97–4.71). The latter study was adjusted for smoking and alcohol but the other two were not.

Seven case-control studies showed increased risk for the highest body fatness group, as measured by BMI, when...
compared to the lowest (figure 6.1.1). This was statistically significant in five studies,22-24,28,29 and in men but not women in a sixth.25 One study showed non-significant decreased risk.26 Meta-analysis was possible on four case-control studies (all of which showed increased risk), giving an effect estimate of 1.11 (95% CI 1.07–1.15) per kg/m², with moderate heterogeneity (figure 6.1.2). This would produce an increased risk of 55 per cent for each 5 kg/m², assuming a linear relationship, although a curvilinear dose-response relationship cannot be ruled out.

A dose-response relationship is apparent from case-control data (figure 6.1.3). Cohort data show a statistically significant trend in men and are suggestive of a similar trend in women. Studies that investigated body fatness, as measured by BMI, and all types of oesophageal cancer or squamous cell carcinomas showed inconsistent results. Only when results were stratified by cancer type did a consistent pattern emerge, and then only for adenocarcinomas.

An association between body fatness and increased risk of oesophageal adenocarcinoma is consistent, with known geographical and time trends for both BMI and adenocarcinomas. The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

The epidemiology is consistent, with evidence of a dose-response relationship. There is evidence for plausible mechanisms that operate in humans. The evidence that greater body fatness is a cause of oesophageal adenocarcinoma is convincing.

The Panel is aware that since the conclusion of the SLR, two cohort30,31 and five case-control studies32-36 have been published. This new information does not change the Panel judgement (see box 3.8).

Pancreas
Twenty-three cohort studies37-58 and 15 case-control studies59-73 investigated body fatness (as measured by BMI) and pancreatic cancer.

Thirteen cohort studies showed increased risk with increased body fatness,37 38 40 43 44 46 47 49 51 54 55 57 which was statistically significant in four.47 49 54 55 Two studies showed increased risk in both sexes42 50; this was statistically significant in women but not in men in one study,42 and in men but not women in the other.30 One study showed increased risk in both black and white men, which was significant for white men only.56 Two studies showed non-significant increased risk in women and non-significant decreased risk in men.45 52 One study showed statistically significant increased risk in men and non-significant decreased risk in women.39 Three studies showed non-significant decreased risk41 48 53 and one study stated that there was no significant association.58 Meta-analysis was possible on 17 cohort studies, giving a summary effect estimate of 1.14 (95% CI 1.07–1.22) per 5 kg/m², with moderate heterogeneity (figure 6.1.4). Most studies adjusted for smoking, with no apparent difference between people who smoked and those that did not.

Five case-control studies showed increased risk with increased body fatness,62-66 which was statistically significant in one,66 and in men but not women in another study.64 Five studies showed decreased risk,61 64-67 which was statistically significant in one.69 Two studies showed non-significant decreased risk in men and a non-significant increased risk in women.59 72 One study showed a statistically significant increased risk in men and a non-significant decreased risk in women.67 One study showed non-significant decreased
risk in both sexes when interviewed indirectly, a non-significant decreased risk in women when interviewed directly, and a non-significant increased risk in men. One study stated that there was no significant association. Meta-analysis was possible on 13 case-control studies, giving a summary effect estimate of 1.00 (95% CI 0.87–1.15) per 5 kg/m², with high heterogeneity (figure 6.1.4).

A dose-response relationship was apparent from cohort but not case-control data (figure 6.1.5). Although meta-analysis assumes a linear relationship, some cohort studies are suggestive of a curvilinear relationship, though not conclusively so.

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

There is ample epidemiological evidence, which is generally consistent, and there is a dose-response relationship. There is evidence for plausible mechanisms that operate in humans. The evidence that greater body fatness is a cause of pancreatic cancer is convincing.

The Panel is aware that since the conclusion of the SLR, two cohort studies have been published. This new information does not change the Panel judgement (also see box 3.8).

Colorectum
Sixty cohort studies and 86 case-control studies investigated body fatness (as measured by BMI) and cancers of the colon and rectum.

Most of the cohort studies showed increased risk with increased body fatness, and which was statistically significant in approximately half of these studies, which was statistically significant in approximately half of these studies. Relatively few studies showed lower risk with increased body fatness, this was statistically significant in only one. One study showed no effect on risk and three stated that there was no association. Meta-analysis was possible on 28 cohort studies, giving a summary effect estimate of 1.03 (95% CI 1.02–1.04) per kg/m², with moderate heterogeneity (figure 6.1.6). This would produce an increased risk of 15 per cent for each 5 kg/m², assuming a
linear relationship, although a curvilinear dose-response relationship cannot be ruled out.

When stratified according to cancer site, data suggest a larger increased risk and are more consistent for colon cancer (figure 6.1.7) than for rectal cancer (figure 6.1.8), or for colorectal cancer as a whole (figure 6.1.6). A clear dose-response relationship was apparent from cohort data for colorectal cancer (figure 6.1.9).

Because of the abundant prospective data from cohort studies, case-control studies were not summarised.

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

There is abundant and consistent epidemiological evidence with a clear dose response, and evidence for plausible mechanisms that operate in humans. The evidence that greater body fatness is a cause of colorectal cancer is convincing.

The Panel is aware that since the conclusion of the SLR, seven cohort studies and two case-control studies have been published. This new information does not change the Panel judgement (also see box 3.8).
Breast

Forty-three cohort studies, 66 50 122 149-204 156 case-control studies, 60 205-359 and 2 ecological studies, 360 361 investigated body fatness (as measured by BMI) and breast cancer.

Age unspecified


Sixteen cohort studies showed increased risk with increased body fatness, 45 50 152-154 161 162 164 166 168 171 172 179 181 186 188 191 192 201 203 204 which was statistically significant in three, 152 171 179 201 Eight studies showed decreased risk, 161 172 173 184 186 194-197 202 which was statistically significant in two, 173 196-197 Two studies showed no effect on risk. 50 204 Meta-analysis was possible on 16 cohort studies, giving a summary effect estimate of 1.01 (95% CI 1.00–1.02) per 2 kg/m², with moderate heterogeneity (figure 6.1.10).

Forty-seven case-control studies showed increased risk with increased body fatness, 66 208 211 213 215 221 222 224 220 232 235 236 239 240 251 252 254 255 257 260 261 265 267 269 277 278 281 282 285 294-296 298-301 305 306 309 310 313 314 316-319 323-326 329 332 334-337 341 343 344 347-350 352-356 359, this was statistically significant in 226 266 208 211 222 230 232 235 236 239 240 251 252 254 255 257 260 261 265 267 269 277 278 281 282 285 294-296 298-301 305 306 309 310 313 314 316-319 323-326 329 332 334-337 341 343 344 347-350 352-356 359, 4 studies showed no effect on risk, 207 245 278 351; and the remaining 22 showed decreased risk, 205 209 212 214 219 225 228 229 234 238 243 244 259 263 264 270 273 289-292 304 321 322 342 349 which was statistically significant in 4 studies. 214 263 264 291 One of
these studies showed significant increased risk with increased body fatness in Hispanic-American people but no significant decreased risks among white-American people. Meta-analysis was possible on 62 case-control studies, giving a summary effect estimate of 1.02 (95% CI 1.02–1.03) per 2 kg/m², with high heterogeneity (figure 6.1.10).

The two ecological studies showed no consistent association. Postmenopause

Twenty-four cohort studies and 56 case-control studies investigated body fatness, 66 205-208 214 220 224-227 231 233 237 239 241 242 244 246-250 253-259 261-263 268 271 274 275 279-283 286-288 293 295-297 302 304 308 311 315 321 322 327 329 331 333 336-341 345 349 352 357-359 which was statistically significant in seven. Twenty-four cohort studies and 56 case-control studies investigated body fatness, giving a summary effect estimate of 1.03 (95% CI 1.01–1.04) per 2 kg/m², with high heterogeneity (figure 6.1.11). This would produce an increased risk of 8 per cent for each 5 kg/m² increase in body fatness, assuming a linear dose-response relationship cannot be ruled out. Heterogeneity may be explained partially by failure to adjust for hormone replacement therapy (HRT) use. Three major studies that reported results stratified for HRT status all found statistically significant increased risk with increasing body fatness only in women not taking HRT.

Pooled analysis from seven cohort studies (more than 337 000 participants, followed up for up to 11 years, with more than 4300 breast cancer cases) showed a significant increased risk of postmenopausal breast cancer with increased body fatness. The effect estimate was 1.07 (95% CI 1.02–1.11) per 4 kg/m².

Most case-control studies showed increased risk with increased body fatness, giving a summary effect estimate of 1.05 (95% CI 1.05–1.06) per 2 kg/m², with moderate heterogeneity (figure 6.1.12). This would produce an increased risk of 13 per cent for each 5 kg/m², assuming a linear relationship, although a curvilinear dose-response relationship, although a curvilinear dose-response relationship, was significant: in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies, 66 220 227 233 237 241 246-250 253-258 261 262 271 274 275-279-283 286-288 293 295-297 302 308 315 329 333 336-341 345 349 352 357-359 which was statistically significant in approximately half of these studies.
relationship cannot be ruled out. Heterogeneity may be partially explained by differential adjustment between studies.

A dose-response relationship is apparent from cohort and case-control data (figure 6.1.13, figure 6.1.14).

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

There is abundant and consistent epidemiological evidence and a clear dose response, with robust evidence for mechanisms operating in humans. The evidence that greater body fatness is a cause of postmenopausal breast cancer is convincing.

The Panel is aware that since the conclusion of the SLR, one cohort study363 and one case-control study364 have been published. This new information does not change the Panel judgement (also see box 3.8).


Thirteen cohort studies showed decreased risk with increased body fatness,45 149 150 167 170 174-176 184 185 189 191 192 195-198 which was statistically significant in seven.49 150 167 176 184 192 195-198 Four studies showed non-significant increased risk.155 162 188 190 Three studies showed no effect on risk.122

177 178 Meta-analysis was possible on 14 studies, giving a summary effect estimate of 0.94 (95% CI 0.92–0.95) per 2 kg/m², with moderate heterogeneity (figure 6.1.15). This would produce a decreased risk of 15 per cent for each 5 kg/m², assuming a linear relationship, although a curvilinear dose response cannot be ruled out.

Egger’s test for publication bias suggested some over-representation of studies showing a protective effect on premenopausal breast cancer of increasing BMI.

Pooled analysis from 7 cohort studies (more than 337 000 participants, followed up for up to 11 years, with more than 4300 breast cancer cases) showed a significant decreased risk of premenopausal breast cancer with increased body fatness. The effect estimate was 0.89 (95% CI 0.81–0.97) per 4 kg/m².365

Most case-control studies showed decreased risk with increased body fatness,205 206 214 216-218 223-225 231 233 237 239 241 242 247-250 259 262 263 268 281 282 283 284 293 297 302-304 311 312 324-328 330 338-341 349 which was statistically significant in approximately one third of these studies.214 218 223 231 237 250 262 268 303 304 326 327 330
Meta-analysis was possible on 51 case-control studies, giving a summary effect estimate of 0.97 (95% CI 0.96–0.97) per 2 kg/m², with moderate heterogeneity.

A dose-response relationship was apparent from cohort and case-control data.

There is no single, well-established mechanism through which body fatness could prevent premenopausal breast cancer. According to the oestrogen plus progesterone theory, overweight premenopausal women would be more frequently anovulatory and therefore less exposed to endogenous progesterone. However, this theory is not well supported by recent studies, which suggest that natural progesterone could be protective. Normal levels of natural progesterone are likely to be protective and women who are well nourished, or perhaps overnourished, who may become slightly overweight in adulthood, may be protected by their natural fertile condition. Another possible mechanism is that the increased adipose tissue-derived oestrogen levels in overweight children could induce early breast differentiation and eliminate some targets for malignant transformation.

Anovulation and abnormal hormone profiles are commonly associated with obesity. The age-specific pattern of association of breast cancer with BMI, therefore, is largely explained by its relationship with endogenous sex hormone levels.

Breast cancer diagnosed postmenopause is much more common. Therefore, throughout life, a decreased risk of premenopausal breast cancer would be expected to be outweighed by an increased risk of postmenopausal breast cancer (also see chapter 7.10).

There is a substantial amount of consistent epidemiological evidence, with a dose response, but the mechanistic evidence is speculative. Greater body fatness probably protects against premenopausal breast cancer.

The Panel is aware that since the conclusion of the SLR, one cohort and one case-control study have been published. This new information does not change the Panel judgement (also see box 3.8).

**Endometrium**

Twenty-three cohort studies and 2 cross-sectional studies investigated body fatness (as measured by BMI) and endometrial cancer. Three cohort studies and 6 case-control studies investigated BMI measured as a young adult.

Twenty-two cohort studies showed increased risk with increased body fatness, which was statistically significant in 16. One small study showed non-significant decreased risk. Meta-analysis was possible on 15 cohort studies, giving a summary effect estimate of 1.52 (95% CI 1.35–1.72) per 5 kg/m², with high heterogeneity (figure 6.1.17).

Nearly all of the case-control studies showed increased risk with increased body fatness, most of which were statistically significant.
study showed no effect on risk after adjustment for waist circumference, but the unadjusted result showed a statistically significant increased risk. No studies showed decreased risk with increased body fatness. Meta-analysis was possible on 28 case-control studies, giving a summary effect estimate of 1.56 (95% CI 1.45–1.66) per 5 kg/m$^2$, with high heterogeneity (figure 6.1.17). Heterogeneity was predominantly the result of variation in the size of effect, rather than direction of effect.

A dose-response relationship is apparent from cohort and case-control data (figures 6.1.17 and 6.1.18). There was no evidence of effect modification by menopause, smoking, or oestrogen-use status.

Both cross-sectional studies reported an association between higher BMI and increased risk of endometrial cancer. The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

**BMI as a young adult**

All three cohort studies showed increased risk with increased body fatness, which was statistically significant in two. Meta-analysis was possible on all three cohort studies, giving a summary effect estimate of 1.31 (95% CI 1.12–1.54) per 5 kg/m$^2$, with no heterogeneity.

Four case-control studies showed non-significant increased risk with increased body fatness, and two showed non-significant decreased risk. Meta-analysis was possible on all six case-control studies, giving a summary effect estimate of 1.10 (95% CI 0.95–1.27) per 5 kg/m$^2$, with low heterogeneity. A dose-response relationship was apparent from cohort but not case-control data.

There is abundant consistent epidemiological evidence with a clear dose response, and robust evidence for mechanisms operating in humans. The evidence that greater body fatness is a cause of endometrial cancer is convincing.
The Panel is aware that since the conclusion of the SLR, one cohort study and one case control study have been published. This new information does not change the Panel judgement (also see box 3.8).

**Kidney**

Seventeen cohort studies and 20 case-control studies investigated body fatness (as measured by BMI) and kidney cancer.

Fifteen cohort studies showed increased risk with increased body fatness; this was statistically significant in seven studies, and in women but not men in another. Two studies stated that there was no statistically significant association. No cohort studies showed decreased risk. Meta-analysis was possible on seven cohort studies that adjusted for smoking, giving a summary effect estimate of 1.31 (95% CI 1.24–1.39) per 5 kg/m², with low heterogeneity (figure 6.1.19).

Eighteen case-control studies showed increased risk with increased body fatness; this was statistically significant in 14 studies, and in men but not women in another. One study showed no effect on risk and another (where the controls were not drawn from the same population as the cases, making it a relatively low-quality study) showed a non-significant decreased risk. Meta-analysis was possible on two case-control studies that adjusted for smoking and eight unadjusted case-control studies. This gave summary effect estimates of 2.05 (95% CI 1.43–2.92) per 5 kg/m², with low heterogeneity, and 1.42 (95% CI 1.17–1.72) per 5 kg/m², with high heterogeneity, respectively (figure 6.1.19).

A dose-response relationship is apparent from cohort and case-control data (figure 6.1.20).

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 and box 2.4; in addition, laboratory studies point to a potential role for insulin and leptin in renal cell carcinoma.

There is abundant and consistent epidemiological evidence with a dose-response relationship and evidence of plausible mechanisms. The evidence that greater body fatness is a cause of kidney cancer is convincing.

**Gallbladder**

Five cohort studies and seven case-control studies investigated body fatness (as measured by BMI) and gallbladder cancer. Most cohort studies showed increased risk with increased body fatness. For two studies, results for the whole cohort showed statistically significant increased risk. One study reported significant increased risk for women and non-significant increased risk for men, while another reported statistically significant increased risk for women and non-significant decreased risk for men. One study reported a significant increased risk for white men and a non-significant decreased risk for black men. Meta-analysis was possible on four cohort studies, giving a summary effect estimate of 1.23 (95% CI 1.15–1.32) per 5 kg/m², with moderate heterogeneity (figure 6.1.21).

Most case-control studies showed increased risk with increased body fatness, which was
Two studies showed decreased risk.\(^5\)\(^1\)\(^1\)\(^2\)\(^3\) which was statistically significant in one.\(^5\)\(^2\) One study showed no effect on risk in men, but a statistically significant increased risk in women.\(^5\)\(^0\) Meta-analysis was possible on all seven case-control studies,\(^5\)\(^0\)-\(^5\)\(^4\) giving a summary effect estimate of 1.19 (95% CI 0.81–1.75) per 5 kg/m\(^2\), with high heterogeneity. Heterogeneity could be at least partly attributed to differences in the study participants’ ethnicity or sex, or to the number of adjustments made in the study. In addition, there was variation according to whether BMI was derived from direct measurements or self-reports of weight and height, as well as in the outcome measured. For example, one cohort and one case-control study reported biliary tract cancer as opposed to gallbladder cancer specifically, and some studies reported incidence while others reported mortality.

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4). In addition, obesity is a known cause of gallstone formation and having gallstones increases the risk of gallbladder cancer (see chapter 7.7), possibly through bile cholesterol supersaturation leading to cholesterol-based gallstones. High cholesterol in the bile is not necessarily related to dietary cholesterol — it can also be caused by insulin resistance, which can be caused by obesity. Insulin resistance can independently increase cholesterol synthesis in the liver and decrease cholesterol absorption.\(^5\)\(^1\)\(^8\) Bile cholesterol levels are also gender-linked: women excrete more cholesterol in bile than men.

Owing to the link between gallstones and gallbladder cancer, the Panel reviewed the dietary causes of having gallstones, especially in relation to body fatness. BMI increased the risk of having gallstones in a linear fashion.\(^5\)\(^1\)\(^9\) Waist circumference was associated with gallstone risk in men, independently of BMI,\(^5\)\(^2\)\(^0\) and insoluble fibre in the diet showed a protective effect.\(^5\)\(^2\)\(^1\) Gallstone formation is strongly associated with dieting, especially where it involves rapid weight loss — such as seen with very low-energy diets and bariatric surgery.\(^5\)\(^2\)\(^2\)-\(^5\)\(^3\) Rapid weight loss is also a common feature of weight cycling. Weight cycling is associated with obesity and independently associated with gallstones; people who are more severe weight cyclers have a higher risk of gallstones.\(^5\)\(^2\)\(^4\)

There is a substantial amount of generally consistent epidemiological evidence with some evidence of a dose response. There is evidence for several plausible mechanisms. Greater body fatness is a probable cause of gallbladder cancer, directly and also indirectly through the formation of gallstones.

Liver

Six cohort studies\(^4\)\(^2\)-\(^4\)\(^4\)-\(^5\)\(^7\)\(^2\)\(^5\)\(^2\) and two case-control studies investigated body fatness\(^5\)\(^2\)\(^6\)-\(^5\)\(^2\)\(^7\) (as measured by BMI), or obesity, and liver cancer.

Five cohort studies showed increased risk for the highest body fatness group compared to the lowest.\(^4\)\(^2\)-\(^4\)\(^4\)-\(^5\)\(^7\)\(^2\)\(^5\)\(^7\) This was statistically significant in two studies,\(^5\)\(^4\)-\(^5\)\(^7\) and in men but not women in another two.\(^4\)\(^2\)-\(^5\)\(^6\) One cohort study showed a statistically significant increased risk in white men and a significant decreased risk in black men.\(^5\)\(^6\) Effect estimates were 1.68 in women (95% CI 0.93–3.04) and 4.52 in men (95% CI 2.94–6.94);\(^5\)\(^2\)\(^2\) 1.44 in white men (95% CI 1.28–1.61) and 0.68 in black men (95% CI 0.49–0.94);\(^5\)\(^7\) 1.56 in men (95% CI 1.15–2.12);\(^5\)\(^7\) 3.88 in men (95% CI 0.96–15.69);\(^4\)\(^4\) 1.9 in both sexes (95% CI 1.5–2.5);\(^5\)\(^3\) and 1.70 in women (95% CI 0.95–3.05) and 3.60 in men (95% CI 2.08–6.24).\(^5\)\(^5\)

Neither case-control study showed any statistically significant association.\(^5\)\(^2\)\(^6\)\(^2\)\(^7\)

The general mechanisms through which body fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4).

The epidemiological evidence shows some inconsistencies, and the mechanistic evidence is speculative. There is limited evidence suggesting that greater body fatness is a cause of liver cancer.

The Panel is aware that since the conclusion of the SLR, two cohort studies\(^3\)\(^0\)-\(^5\)\(^2\)\(^8\) have been published. This new information does not change the Panel judgement (see box 3.8).

Lung

Twenty-one cohort studies,\(^4\)\(^2\)-\(^5\)\(^7\)\(^4\)-\(^5\)\(^4\)-\(^5\)\(^5\)\(^4\)-\(^5\)\(^7\)\(^3\)\(^3\) 24 case-control studies,\(^5\)\(^4\)-\(^5\)\(^7\)\(^3\)\(^3\) and 1 ecological study\(^5\)\(^7\)\(^4\) investigated body fatness (as measured by BMI) and lung cancer.

Twenty cohort studies showed decreased risk with increased body fatness,\(^4\)\(^2\)-\(^5\)\(^7\)\(^6\) 2.57 88 122 144 529-545; this was statistically significant in 12 studies,\(^4\)\(^2\)-\(^5\)\(^7\)\(^6\) 122 531 533 535 540 542 543 545 and in women but not men in another study.\(^5\)\(^3\)\(^6\) One study showed no effect on risk.\(^1\)\(^4\)\(^4\) Meta-analysis was possible on 14 cohort studies,\(^5\)\(^7\) 88 122 144 530 532 534 535 537 538 540 543-545 giving a summary effect estimate of 0.98 (95% CI 0.98–0.99) per kg/m\(^2\), with high heterogeneity. This would produce a decreased risk of
5 per cent for each 5 kg/m\(^2\), assuming a linear relationship, although a curvilinear dose-response relationship cannot be ruled out. When meta-analysis was restricted to the 10 studies that adjusted for smoking, the effect estimate and CIs remained the same, but with low heterogeneity.\(^{537-538,540,544}\) Heterogeneity was caused by variation in the size but not the direction of the effect.

Begg’s and Egger’s tests suggested publication bias; that is, the smaller the study, the stronger the protective association observed. Smaller studies, with results of weak or no association, appear to have been less likely to be published.

Twenty-two case-control studies showed decreased risk with increased body fatness,\(^{546-560,562-570}\) which was statistically significant in nine.\(^{546,550,551,553,557,563,564,566,567,570}\) Two studies showed increased risk,\(^{561,571}\) which was statistically significant in one.\(^{561}\) Meta-analysis was possible on 10 case-control studies,\(^{546,550,554,555,557,566-568}\) giving a summary effect estimate of 0.98 (95% CI 0.98–0.99) per kg/m\(^2\), with low heterogeneity. The effect estimate was unchanged when three studies that did not adjust for smoking were excluded from the analysis.\(^{546,568,572}\)

The single ecological study showed a non-significant association between increased body fatness and decreased risk.\(^{574}\)

Smoking is the principal cause of lung cancer and may also be associated with lower BMI. There is a high potential for confounding due to cigarette smoking, and residual confounding is therefore possible. In addition, it is possible that people with undiagnosed lung cancer may lose weight, so giving a spurious association (reverse causation).

There is no known mechanism through which greater body fatness could plausibly protect against lung cancer, or through which low body fatness could increase risk.

Although the epidemiological evidence suggests an inverse relationship, this could be caused by confounding by cigarette smoking or reverse causation due to weight loss from undiagnosed cancer. There is limited evidence suggesting that low body fatness is a cause of lung cancer.

### 6.1.3.2 Abdominal fatness

#### Colorectum

Seven cohort studies\(^{87,92,97,115,118,137,142}\) and two case-control studies investigated waist circumference and colorectal cancer. Six cohort studies\(^{82,87,97,115,137,142}\) and four case-control studies investigated waist to hip ratio.

**Waist circumference**

All seven cohort studies showed increased risk with increased waist circumference, which was statistically significant in six.\(^{87,97,115,137,142}\) Meta-analysis was possible on four cohort studies, giving a summary effect estimate of 1.05 (95% CI 1.03–1.07) per 2.5 cm (1 inch), with moderate heterogeneity (figure 6.1.22). Both case-control studies reported increased risk with increased waist circumference.

**Waist to hip ratio**

All six cohort studies showed increased risk with increased waist to hip ratio, which was statistically significant in five.\(^{87,97,115,137,142}\) Meta-analysis was possible on five cohort studies, giving a summary effect estimate of 1.30 (95% CI 1.17–1.44) per ratio increment of 0.1, with moderate heterogeneity (figure 6.1.23). Most case-control studies reported increased risk with increased waist circumference.

Because of the abundant prospective data from cohort studies, case-control studies were not summarised.

The general mechanisms through which body fatness and abdominal fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4). Many of these, such as increased circulating oestrogens and decreased insulin sensitivity, are particularly associated with abdominal rather than overall body fatness.

There is ample, consistent epidemiological evidence with a clear dose response and robust evidence for mechanisms that operate in humans. The evidence that abdominal fatness is a cause of colorectal cancer is convincing.
The Panel is aware that since the conclusion of the SLR, three cohort studies\textsuperscript{311 142 143} have been published. This new information does not change the Panel judgement (see box 3.8).

**Pancreas**

Three cohort studies investigated waist circumference and pancreatic cancer.\textsuperscript{46 74} Two cohort studies investigated waist to hip ratio\textsuperscript{5174} and one investigated patterns of weight gain.\textsuperscript{49}

**Waist circumference**

All three cohort studies showed increased risk with increased waist circumference, which was statistically significant in one. Effect estimates were 1.32 (95% CI 0.73–2.37) per 20 cm (7.9 inches) in women,\textsuperscript{46} 1.74 (95% CI 1.00–3.01) per 20 cm (7.9 inches) in men,\textsuperscript{46} and 1.13 (95% CI 1.01–1.26) per 10 cm (3.9 inches).\textsuperscript{74} The latter study was published after the cut-off date for inclusion in the SLR. However, the Panel was aware of the study and agreed to include it in its consideration of this exposure.

**Waist to hip ratio**

Both cohort studies showed increased risk with increased waist circumference, which was statistically significant in one. Effect estimates were 1.12 (95% CI 0.81–1.55; high versus low)\textsuperscript{51} and 1.24 (95% CI 1.04–1.48) per ratio increment of 0.1.\textsuperscript{74} The latter study was published after the cut-off date for inclusion in the SLR. However, the Panel was aware of the study and agreed to include it in its consideration of this exposure.

**Patterns of weight gain**

The single cohort study showed a statistically significant increased risk with a self-reported tendency to abdominal (central) weight gain, when compared to peripheral weight gain. The effect estimate was 1.45 (95% CI 1.02–2.07).\textsuperscript{48}

The general mechanisms through which abdominal fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4). Many of these, such as increased circulating oestrogens and decreased insulin sensitivity, are particularly associated with abdominal rather than overall body fatness.

There is a substantial amount of epidemiological evidence, generally consistent, and there is evidence for plausible mechanisms. Abdominal fatness is a probable cause of pancreatic cancer.

**Breast (postmenopause)**

Eight cohort studies\textsuperscript{157 159 170 174 180 187 199 575–577} and three case-control studies\textsuperscript{207 242 304} investigated waist circumference and postmenopausal breast cancer. Eight cohort studies\textsuperscript{157 159 163 170 174 180 187 199 199 575–576} and eight case-control studies\textsuperscript{241 242 247 248 297 304 308 321} investigated waist to hip ratio.

**Waist circumference**

All eight cohort studies showed increased risk with increased waist circumference, which was statistically significant in two.\textsuperscript{157 180 199} Meta-analysis was possible on four cohort studies,\textsuperscript{159 170 575–577} giving a summary effect estimate of 1.05 (95% CI 1.00–1.10) per 8 cm (3.1 inches), with no heterogeneity.

All three case-control studies showed increased risk with increased waist circumference, which was statistically significant in two.\textsuperscript{207 242}

**Waist to hip ratio**

Six cohort studies showed increased risk with increased waist to hip ratio,\textsuperscript{157 159 163 170 174 180 187 199 575} which was statistically significant in four.\textsuperscript{163 170 187 199 575} Two studies showed non-significant decreased risk.\textsuperscript{189 576} Meta-analysis was possible on five cohort studies, giving a summary effect estimate of 1.19 (95% CI 1.10–1.28) per ratio increment of 0.1, with moderate heterogeneity (figure 6.1.24).

Five case-control studies showed increased risk with increased waist to hip ratio,\textsuperscript{242 247 297 308 321} which was statistically significant in three.\textsuperscript{242 297 308} Three studies showed non-significant decreased risk.\textsuperscript{241 248 304} Meta-analysis was possible on seven case-control studies, giving a summary effect estimate of 1.07 (95% CI 1.00–1.14) per ratio increment of 0.1, with moderate heterogeneity (figure 6.1.24).

The general mechanisms through which abdominal fatness could plausibly influence cancer risk are outlined in 6.1.3 (also see box 2.4). Many of these, such as increased circulating oestrogens and decreased insulin sensitivity, are particularly associated with abdominal rather than overall body fatness.

There is a substantial amount of epidemiological evidence but some inconsistency. There is robust evidence for mechanisms that operate in humans. Abdominal fatness is a probable cause of postmenopausal breast cancer.
Endometrium

One cohort study\(^1\) and four case-control studies\(^4\) investigated waist circumference and endometrial cancer. One cohort study\(^1\) and six case-control studies\(^3\) investigated waist to hip ratios.

Waist circumference

The single cohort study showed a statistically significant increased risk for the highest waist circumference group when compared to the lowest. The effect estimate was 4.2 (95% CI 2.8–6.2).\(^1\)

All four case-control studies showed statistically significant increased risk for the highest waist circumference group when compared to the lowest.\(^4\) Three studies adjusted for BMI.\(^4\)

Waist to hip ratio

The single cohort study showed a statistically significant increased risk for the highest waist circumference group when compared to the lowest. The effect estimate was 1.33 (1.18–1.51).\(^1\)

All four case-control studies showed statistically significant increased risk for the highest waist circumference group when compared to the lowest.\(^4\) Three studies adjusted for BMI.\(^4\)

There is a substantial amount of generally consistent epidemiological evidence, but limited prospective data. There is evidence for plausible mechanisms. Greater abdominal fatness is a probable cause of cancer of the endometrium.

6.1.3.3 Adult weight gain

Breast (postmenopause)

Seven cohort studies\(^1\) and 17 case-control studies\(^2\) investigated adult weight gain and postmenopausal breast cancer.

All seven cohort studies showed increased risk with increasing amounts of weight gained in adulthood, which was statistically significant in two.\(^1\) Two cohort studies stratified results according to whether or not participants were using HRT. Both studies showed a statistically significant increased risk in women not using HRT. Studies of weight gain and premenopausal breast cancer showed no overall effect on risk.

The full SLR is contained on the CD included with this Report.

Thirteen case-control studies showed increased risk with increasing amounts of weight gained in adulthood, which was statistically significant in two.\(^2\) No studies reported significant decreased risk. Meta-analysis was possible on six case-control studies, giving a summary effect estimate of 1.05 (95% CI 1.04–1.07) per 5 kg (11 lbs) gained, with high heterogeneity (figure 6.1.26).
Heterogeneity may be explained by failure to separate postmenopausal participants using HRT.

There is ample, consistent epidemiological evidence from both cohort and case-control studies. A dose response was apparent from case-control and cohort studies. Adult weight gain is a probable cause of postmenopausal breast cancer.

6.1.4 Comparison with previous report

The previous report used different terminology. It concluded that the evidence that ‘high body mass’ was a cause of cancer of the endometrium was convincing, and that high body mass was probably a cause of cancers both of the breast (postmenopause) and the kidney. In the previous report, the evidence that high body mass was a cause of cancers of the colon and gallbladder was judged to be possible. Since that time, several cohort studies and other epidemiological and other evidence have greatly strengthened the evidence on body fatness, and specifically on overweight and obesity. Also, the distinction between adenocarcinomas and squamous cell carcinomas has identified a clear relationship between body fatness and adenocarcinomas of the oesophagus. The previous report did not make any judgements specifically on abdominal fatness.

The previous report did not include judgements on body fatness and pancreatic cancer, although it did conclude that high energy intake was a possible cause of this cancer. It also noted data from correlation and animal studies suggesting that high energy intake might increase the risk of cancer in general, without making any judgement.

6.1.5 Conclusions

The Panel concludes:

The evidence that greater body fatness is a cause of cancers of various sites is more impressive now than it was in the mid-1990s.

The evidence that greater body fatness is a cause of cancers of the oesophagus (adenocarcinoma), pancreas, colorectum, breast (postmenopause), endometrium, and kidney is convincing. Greater body fatness is probably a cause of gallbladder cancer, both directly, and indirectly through the formation of gallstones. There is also limited evidence suggesting that greater body fatness is a cause of liver cancer. The evidence that abdominal fatness is a cause of colorectal cancer is convincing; and abdominal fatness is probably a cause of cancers of the pancreas, breast (postmenopause), and endometrium. By contrast, greater body fatness probably protects against cancer of the breast diagnosed before the menopause. The Panel notes that there is limited evidence suggesting that low body fatness (underweight) is a cause of cancer of the lung, but residual confounding with smoking and lung disease cannot be ruled out. See chapters 7.4 and 7.10, and Chapter 8 for discussion of the role of energy density in weight gain, overweight, and obesity.