

## BODY FATNESS AND WEIGHT GAIN AND THE RISK OF CANCER

| WCRF/AICR GRADING |                                     | DECREASES RISK                  |   | INCREASES RISK     |   |
|-------------------|-------------------------------------|---------------------------------|---|--------------------|---|
|                   |                                     | Exposure                        | Cancer site   | Exposure           | Cancer site   |
| STRONG EVIDENCE   | Convincing                          |                                 |   | Adult body fatness | Oesophagus (adenocarcinoma) 2016 <sup>1</sup><br>Pancreas 2012 <sup>1</sup><br>Liver 2015 <sup>2</sup><br>Colorectum 2017 <sup>1</sup><br>Breast (postmenopause) 2017 <sup>1,3</sup><br>Endometrium 2013 <sup>4,5</sup><br>Kidney 2015 <sup>1</sup> |
|                   |                                     |                                 |   | Adult weight gain  | Breast (postmenopause) 2017 <sup>3</sup>  |
|                   | Probable                            | Adult body fatness              | Breast (premenopause) 2017 <sup>1,3</sup>   | Adult body fatness | Mouth, pharynx and larynx 2018 <sup>1</sup><br>Stomach (cardia) 2016 <sup>2</sup><br>Gallbladder 2015 <sup>2,7</sup><br>Ovary 2014 <sup>2,5,8</sup><br>Prostate (advanced) 2014 <sup>1,9</sup>  |
|                   |                                     | Body fatness in young adulthood | Breast (premenopause) 2017 <sup>3,6</sup><br>Breast (postmenopause) 2017 <sup>3,6</sup> |                    |   |
| LIMITED EVIDENCE  | Limited – suggestive                |                                 |   | Adult body fatness | Cervix (BMI ≥ 29 kg/m <sup>2</sup> ) 2017 <sup>2,5</sup>  |
| STRONG EVIDENCE   | Substantial effect on risk unlikely | None identified                 |   |                    |   |

- 1 Conclusions for adult body fatness and cancers of the following types were based on evidence marked by body mass index (BMI), waist circumference and waist-hip ratio: mouth, pharynx and larynx; oesophagus (adenocarcinoma); pancreas; colorectum; breast (pre and postmenopause); prostate (advanced); and kidney.
- 2 Conclusions for adult body fatness and cancers of the following types were based on evidence marked by BMI: stomach (cardia), gallbladder, liver, ovary and cervix (BMI ≥ 29 kg/m<sup>2</sup>).
- 3 Evidence for the link between body fatness, weight gain and breast cancer is presented separately for the risk of pre and postmenopausal breast cancer because of the well-established effect modification by menopausal status.
- 4 The conclusion for adult body fatness and endometrial cancer was based on evidence marked by BMI (including BMI at age 18 to 25 years), weight gain, waist circumference and waist-hip ratio.
- 5 There is no evidence of effect modification by menopausal status for body fatness and the risk of endometrial, ovarian or cervical cancer so the evidence for all women (irrespective of menopausal status) is presented together.
- 6 Evidence for body fatness in young adulthood and breast cancer (pre and postmenopause) comes from women aged about 18 to 30 years and includes evidence marked by BMI.
- 7 Adult body fatness may act indirectly, through gallstones, or directly, either after gallstone formation or in their absence, to cause gallbladder cancer. It is not yet possible to separate these effects.
- 8 The effect of adult body fatness on the risk of ovarian cancer may vary according to tumour type, menopausal hormone therapy use and menopausal status.
- 9 The effect of adult body fatness on the risk of prostate cancer was observed in advanced, high-grade and fatal prostate cancers.

Summary of CUP dose–response meta-analyses of adult body fatness and the risk of cancer

| Cancer                                 | Measure                  | Total no. of studies | No. of studies in meta-analysis | No. of cases | Risk estimate (95% confidence intervals [CI]) | Increment           | I <sup>2</sup> (%) | Conclusion <sup>1</sup>              | Date of CUP cancer report <sup>2</sup> |
|--|--------------------------|----------------------|---------------------------------|--------------|---|---------------------|--------------------|--------------------------------------|--|
| Oesophagus (adenocarcinoma)            | BMI                      | 9                    | 9                               | 1,725        | 1.48 (1.35–1.62)                              | 5 kg/m <sup>2</sup> | 37                 | Convincing: Increases risk           | 2016                                   |
|  | Waist circumference      | 2                    | 2                               | 335          | 1.34 (1.17–1.52)                              | 10 cm               | 10                 |                                      |  |
|  | Waist-hip ratio          | 3                    | 3                               | 380          | 1.38 (1.10–1.73)                              | 0.1 unit            | 27                 |                                      |  |
| Pancreas                               | BMI (cancer incidence)   | 30                   | 23                              | 9,504        | 1.10 (1.07–1.14)                              | 5 kg/m <sup>2</sup> | 19                 | Convincing: Increases risk           | 2012                                   |
|  | BMI (cancer mortality)   | 30                   | 7                               | 8,869        | 1.10 (1.02–1.19)                              | 5 kg/m <sup>2</sup> | 61                 |                                      |  |
|  | Waist circumference      | 5                    | 5                               | 949          | 1.11 (1.05–1.18)                              | 10 cm               | 0                  |                                      |  |
|  | Waist-hip ratio          | 4                    | 4                               | 1,047        | 1.19 (1.09–1.31)                              | 0.1 unit            | 11                 |                                      |  |
| Liver                                  | BMI                      | 15                   | 12                              | 14,311       | 1.30 (1.16–1.46)                              | 5 kg/m <sup>2</sup> | 78                 | Convincing: Increases risk           | 2015                                   |
| Colorectum                             | BMI                      | 57                   | 38                              | 71,089       | 1.05 (1.03–1.07)                              | 5 kg/m <sup>2</sup> | 74                 | Convincing: Increases risk           | 2017                                   |
|  | Waist circumference      | 13                   | 8                               | 4,301        | 1.02 (1.01–1.03)                              | 10 cm               | 0                  |                                      |  |
|  | Waist-hip ratio          | 6                    | 4                               | 2,564        | 1.02 (1.01–1.04)                              | 0.1 unit            | 17                 |                                      |  |
| Breast (postmenopause) <sup>3</sup>    | BMI                      | 156                  | 56                              | 80,404       | 1.12 (1.09–1.15)                              | 5 kg/m <sup>2</sup> | 74                 | Convincing: Increases risk           | 2017                                   |
|  | Waist circumference      | 27                   | 11                              | 14,033       | 1.11 (1.09–1.13)                              | 10 cm               | 0                  |                                      |  |
|  | Waist-hip ratio          | 29                   | 18                              | 15,643       | 1.10 (1.05–1.16)                              | 0.1 unit            | 60                 |                                      |  |
| Endometrium <sup>4</sup>               | BMI                      | 34                   | 26                              | 18,717       | 1.50 (1.42–1.59)                              | 5 kg/m <sup>2</sup> | 86                 | Convincing: Increases risk           | 2013                                   |
|  | BMI (age 18 to 25 years) | 8                    | 7                               | 3,476        | 1.42 (1.22–1.66)                              | 5 kg/m <sup>2</sup> | 79                 |                                      |  |
|  | Weight gain              | 5                    | 5                               | 1,971        | 1.16 (1.10–1.22)                              | 5 kg                | 66                 |                                      |  |
|  | Waist circumference      | 4                    | 4                               | 1,641        | 1.13 (1.08–1.18)                              | 5 cm                | 71                 |                                      |  |
|  | Waist-hip ratio          | 5                    | 5                               | 2,330        | 1.21 (1.13–1.29)                              | 0.1 unit            | 0                  |                                      |  |
| Kidney                                 | BMI                      | 28                   | 23                              | 15,575       | 1.30 (1.25–1.35)                              | 5 kg/m <sup>2</sup> | 39                 | Convincing: Increases risk           | 2015                                   |
|  | Waist circumference      | 3                    | 3                               | 751          | 1.11 (1.05–1.19)                              | 10 cm               | 0                  |                                      |  |
|  | Waist-hip ratio          | 4                    | 3                               | 751          | 1.26 (1.18–1.36)                              | 0.1 unit            | 0                  |                                      |  |
| Mouth, pharynx and larynx <sup>5</sup> | BMI                      | 20                   | 20                              | 796          | 1.15 (1.06–1.24)                              | 5 kg/m <sup>2</sup> | –                  | Probable: Increases risk             | 2018                                   |
| Stomach (cardia)                       | BMI                      | 10                   | 7                               | 2,050        | 1.23 (1.07–1.40)                              | 5 kg/m <sup>2</sup> | 56                 | Probable: Increases risk             | 2016                                   |
| Gallbladder <sup>6</sup>               | BMI                      | 11                   | 8                               | 6,004        | 1.25 (1.15–1.37)                              | 5 kg/m <sup>2</sup> | 52                 | Probable: Increases risk             | 2015                                   |
| Ovary <sup>4,7</sup>                   | BMI                      | 26                   | 25                              | 15,899       | 1.06 (1.02–1.11)                              | 5 kg/m <sup>2</sup> | 55                 | Probable: Increases risk             | 2014                                   |
| Prostate (advanced) <sup>8</sup>       | BMI                      | 24                   | 23                              | 11,149       | 1.08 (1.04–1.12)                              | 5 kg/m <sup>2</sup> | 19                 | Probable: Increases risk             | 2014                                   |
|  | Waist circumference      | 5                    | 4                               | 1,781        | 1.12 (1.04–1.21)                              | 10 cm               | 15                 |                                      |  |
|  | Waist-hip ratio          | 4                    | 4                               | 1,781        | 1.15 (1.03–1.28)                              | 0.1 unit            | 0                  |                                      |  |
| Cervix <sup>4,9</sup>                  | BMI                      | 10                   | 9                               | 5,144        | 1.02 (0.97–1.07)                              | 5 kg/m <sup>2</sup> | 69                 | Limited – suggestive: Increases risk | 2017                                   |
| Breast (premenopause) <sup>3</sup>     | BMI                      | 128                  | 37                              | 16,371       | 0.93 (0.90–0.97)                              | 5 kg/m <sup>2</sup> | 55                 | Probable: Decreases risk             | 2017                                   |
|  | Waist circumference      | 6                    | 6                               | 2,423        | 0.99 (0.95–1.04)                              | 10 cm               | 0                  |                                      |  |
|  | Waist-hip ratio          | 11                   | 11                              | 3,465        | 1.06 (0.98–1.16)                              | 0.1 unit            | 27                 |                                      |  |

Summary of published pooled analyses of body mass index and the risk of oesophageal adenocarcinoma

| Publication             | Increment           | RR<br>(95% CI)      | I <sup>2</sup> (%) | No. of studies               | No. of cases |
|-------------------------|---------------------|---------------------|--------------------|------------------------------|--------------|
| Me-Can [107]            | 5 kg/m <sup>2</sup> | 1.78<br>(1.45–2.17) | –                  | 7 cohort                     | 114          |
| BEACON Consortium [108] | 1 kg/m <sup>2</sup> | 1.09<br>(1.06–1.12) | 76                 | 2 cohort,<br>10 case-control | 1,897        |

# Summary of published pooled analyses of body mass index and the risk of pancreatic cancer

| Publication   | Increment/<br>contrast                     | RR<br>(95% CI)                   | I <sup>2</sup> (%) | No. of studies               | No. of<br>cases    |
|---|--|----------------------------------|--------------------|------------------------------|--------------------|
| Pooling Project of Prospective Studies on Diet and Cancer [142] | 5 kg/m <sup>2</sup>                        | 1.14<br>(1.07–1.21)              | –                  | 14 cohort                    | 2,135<br>diagnoses |
| National Cancer Institute pooled analysis [144]                 | 5 kg/m <sup>2</sup>                        | 1.08<br>(1.03–1.14)              | 0                  | 7 cohort                     | 2,454<br>diagnoses |
| Asia-Pacific Cohort Studies Collaboration [145]                 | 5 kg/m <sup>2</sup>                        | 1.02<br>(0.83–1.25)              | –                  | 39 cohort                    | 301<br>deaths      |
| Pancreatic Cancer Cohort Consortium (PanScan) [143]             | BMI > 35 vs<br>18.5–24.9 kg/m <sup>2</sup> | 1.55<br>(1.16–2.07) <sup>1</sup> | –                  | 12 cohort,<br>1 case-control | 2,095<br>diagnoses |

# Summary of published pooled analyses of waist circumference and the risk of pancreatic cancer

| Publication   | Contrast  | RR (95% CI)                       | I <sup>2</sup> (%) | No. of studies (cohort) | No. of cases |
|---|---|-----------------------------------|--------------------|-------------------------|--------------|
| Pooling Project of Prospective Studies on Diet and Cancer [142] | Highest vs lowest                                 | 1.16 (0.92–1.46)                  | 10                 | 7                       | 743          |
|   | Highest vs lowest (additionally adjusted for BMI) | 1.04 (0.73–1.47)                  | 26                 |                         |              |
| Pancreatic Cancer Cohort Consortium (PanScan) [143]             | Highest vs lowest                                 | 1.23 (0.94–1.62)<br>ptrend = 0.04 | –                  | 6                       | 812          |

# Summary of published pooled analyses of waist-hip ratio and the risk of pancreatic cancer

| Publication   | Contrast  | RR (95% CI)      | I <sup>2</sup> (%) | No. of studies (cohort) | No. of cases |
|---|---|------------------|--------------------|-------------------------|--------------|
| Pooling Project of Prospective Studies on Diet and Cancer [142] | Highest vs lowest                                 | 1.35 (1.03–1.78) | 0                  | 6                       | 552          |
|   | Highest vs lowest (additionally adjusted for BMI) | 1.34 (1.00–1.79) | 0                  |                         |              |
| Pancreatic Cancer Cohort Consortium (PanScan) [143]             | Highest vs lowest                                 | 1.71 (1.27–2.30) | –                  | 6                       | 750          |

## Summary of published pooled analyses of body mass index and the risk of liver cancer

| Publication                                     | Increment/contrast  | RR<br>(95% CI)   | No. of<br>studies<br>(cohort) | No. of<br>cases  |
|---|---|------------------|-------------------------------|------------------|
| Asia-Pacific Cohort Studies Collaboration [165] | ≥ 25 vs 18.5–22.9 kg/m <sup>2</sup>                                       | 1.27 (0.93–1.74) | 44                            | 420 deaths       |
| Prospective Studies Collaboration [163]         | 5 kg/m <sup>2</sup>   | 1.47 (1.26–1.71) | 57                            | 422 deaths       |
| Asia-Pacific Cohort Studies Collaboration [145] | 30–60 vs 18.5–24.9 kg/m <sup>2</sup>                                      | 1.10 (0.63–1.91) | 39                            | 744 deaths       |
|   | 5 kg/m <sup>2</sup>   | 1.11 (0.63–1.91) |                               |                  |
| European cohorts [164]                          | Highest vs lowest quintile (median)<br>BMI 31.3 vs 20.7 kg/m <sup>2</sup> | 1.92 (1.23–2.96) | 7                             | 266<br>diagnoses |

# Summary of published pooled analyses of body mass index and the risk of postmenopausal breast cancer

| Publication  | Increment/contrast                   | RR (95% CI)      | No. of studies (cohort) | No. of cases    |
|--|--------------------------------------|------------------|-------------------------|-----------------|
| The Metabolic Syndrome and Cancer Project (Me-Can) [253]                       | ≥ 31.7 vs ≤ 20 kg/m <sup>2</sup>     |                  | 6                       |                 |
|  | Incidence                            | 0.87 (0.71–1.07) |                         | 1,106 diagnoses |
|  | Mortality                            | 0.92 (0.66–1.27) |                         | 219 deaths      |
| Asia-Pacific Cohort Studies Collaboration (APCSC) [145]                        | Mortality                            |                  | 35                      | 324 deaths      |
|  | 30–60 vs 18.5–24.9 kg/m <sup>2</sup> | 1.63 (1.13–2.35) |                         |                 |
|  | 5 kg/m <sup>2</sup>                  | 1.19 (1.03–1.38) |                         |                 |
| The Australia and New Zealand Diabetes and Cancer Collaboration (ANZDCC) [254] | 1 SD                                 | 1.06 (1.01–1.12) | 10                      | 1,323 diagnoses |



# Summary of published pooled analyses of waist circumference and the risk of postmenopausal breast cancer

| Publication  | Increment | RR (95% CI)      | No. of studies | No. of cases    |
|--|-----------|------------------|----------------|-----------------|
| The Australia and New Zealand Diabetes and Cancer Collaboration (ANZDCC) [254] | 1 SD      | 1.06 (1.01–1.12) | 10 cohort      | 1,323 diagnoses |

# Summary of published pooled analyses of waist-hip ratio and the risk of postmenopausal breast cancer

| Publication  | Increment | RR (95% CI)      | No. of studies | No. of cases |
|--|-----------|------------------|----------------|--------------|
| The Australia and New Zealand Diabetes and Cancer Collaboration (ANZDCC) [254] | 1 SD      | 1.06 (0.95–1.07) | 10 cohort      | 1,323        |

Summary of published pooled analyses of body mass index and the risk of kidney cancer

| Publication  | Increment/contrast                         | RR (95% CI)      | No. of studies (cohort) | No. of cases  |
|--|--|------------------|-------------------------|---------------|
| Asia-Pacific Cohort Studies Collaboration [145]              | BMI ≥ 30 vs 18.5–24.9 kg/m <sup>2</sup>    | 1.59 (0.78–3.24) | 39                      | 93 deaths     |
|  | 5 kg/m <sup>2</sup>                        | 1.20 (0.86–1.66) |                         |               |
| Metabolic Syndrome and Cancer Project – Me-Can project [317] | BMI 31.7 vs 21.5 kg/m <sup>2</sup> (men)   | 1.51 (1.13–2.03) | 7                       | 592 diagnoses |
|  | BMI 31.7 vs 20.0 kg/m <sup>2</sup> (women) | 2.21 (1.32–3.70) | 7                       | 263 diagnoses |
| Prospective Studies Collaboration [163]                      | 5 kg/m <sup>2</sup>                        | 1.23 (1.06–1.43) | 57                      | 422 deaths    |

Summary of published pooled analysis [97] of body mass index and the risk of head and neck cancer

| Publication                  | No. of cases | HR (95% CI)<br>Obese (≥30.0)<br>vs. 21 to <23<br>kg/m <sup>2</sup> | HR (95% CI)<br>Underweight (15.0<br>to 20.9) vs. 21.0<br>to <23 kg/m <sup>2</sup> | HR (95% CI)<br>per 5 kg/m <sup>2</sup> | P <sub>trend</sub> |
|------------------------------|--------------|--|---|--|--------------------|
| All                          | 3,760        | 0.85 (0.76–0.96)   | 1.28 (1.11–1.46)  | 0.94 (0.90–0.98)                       | 0.003              |
| People who have never smoked | 796          | 1.40 (1.08–1.81)   | 1.17 (0.85–1.61)  | 1.15 (1.06–1.24)                       | 0.0006             |
| People who smoke             | 1,508        | 0.58 (0.47–0.72)   | 1.30 (1.08–1.57)  | 0.76 (0.71–0.82)                       | <0.0001            |
| People who used to smoke     | 1,367        | 0.96 (0.79–1.18)   | 1.24 (0.94–1.63)  | 0.99 (0.93–1.06)                       | 0.79               |

# Summary of published pooled analysis [97] of body mass index and the risk of cancers of the mouth, pharynx and larynx in people who have never smoked

| Cancer site   | Increment   | No. of cases | HR (95% CI)      | P <sub>trend</sub> |
|---|---|--------------|------------------|--------------------|
| Oral cavity   | per 5 kg/m <sup>2</sup> BMI in people who have never smoked | 298          | 1.10 (0.97–1.25) | 0.14               |
| Oral cavity and pharyngeal (not otherwise specified) combined |   | 93           | 1.36 (1.11–1.66) | 0.003              |
| Oropharyngeal   |   | 241          | 0.98 (0.84–1.14) | 0.77               |
| Hypopharyngeal  |   | 22           | 0.96 (0.55–1.67) | 0.88               |
| Laryngeal   |   | 142          | 1.42 (1.19–1.70) | 0.0001             |

# Summary of other pooled analyses of body mass index and the risk of mouth, pharynx, larynx cancer

| Publication  |   | Increment/contrast  | RR (95% CI)                   | P <sub>trend</sub> | No. of cases    | No. of cases  |
|--|---|---|-------------------------------|--------------------|-----------------|---------------|
| Asia-Pacific Cohort Studies Collaboration [145]                            | Oropharyngeal and laryngeal combined, mortality | 5 kg/m <sup>2</sup>   | 0.66 (0.46–0.95) <sup>1</sup> | –                  | 39 cohort       | 159 deaths    |
|  | Upper aerodigestive tract, mortality            | 5 kg/m <sup>2</sup>   | 0.78 (0.62–0.98) <sup>1</sup> | –                  |                 | 388 deaths    |
| International Head and Neck Cancer Epidemiology (INHANCE) Consortium [332] | Oral cavity                                     | BMI ≥ 35 kg/m <sup>2</sup> vs BMI 18.5–24.9 kg/m <sup>2</sup>   |                               |                    | 15 case-control |               |
|  |   | Men   | 0.65 (0.40–1.10) <sup>2</sup> | <0.01              |                 | 1,516         |
|  |   | Women   | 0.92 (0.50–1.60) <sup>2</sup> | <0.01              |                 | 935 diagnoses |
|  | Oropharyngeal                                   | BMI ≥ 35 kg/m <sup>2</sup> vs BMI 18.5–24.9 kg/m <sup>2</sup>   |                               |                    |                 |               |
|  |   | Men   | 0.48 (0.30–0.70) <sup>2</sup> | <0.01              |                 | 1,733         |
|  |   | Women   | 0.35 (0.20–0.70) <sup>2</sup> | <0.01              |                 | 564 diagnoses |
|  | Hypopharyngeal                                  | BMI 30.0–34.9 kg/m <sup>2</sup> vs BMI < 18.5 kg/m <sup>2</sup> |                               |                    |                 |               |
|  |   | Men   | 0.24 (0.10–0.50) <sup>2</sup> | 0.10               |                 | 412           |
|  |   | Women   | 0.24 (0.10–0.80) <sup>2</sup> | <0.01              |                 | 96 diagnoses  |
|  | Laryngeal                                       | BMI ≥ 35 kg/m <sup>2</sup> vs BMI 18.5–24.9 kg/m <sup>2</sup>   |                               |                    |                 |               |
|  |   | Men   | 0.77 (0.40–1.40) <sup>2</sup> | <0.01              |                 | 1,503         |
|  |   | Women   | 0.27 (0.10–0.80) <sup>2</sup> | <0.01              |                 | 237 diagnoses |

## Summary of published pooled analysis [97] of waist circumference and the risk of head and neck cancer

| Publication                         | No. of cases | HR (95% CI)<br>Highest vs lowest | RR (95% CI)<br>per 5 cm) <sup>1</sup> | P <sub>trend</sub> |
|-------------------------------------|--------------|----------------------------------|---------------------------------------|--------------------|
| <b>All</b>                          | 1,931        | 1.08 (0.93–1.25)                 | 1.04 (1.03–1.05)                      | < 0.0001           |
| <b>People who have never smoked</b> | 441          | 1.51 (1.09–2.08)                 | 1.07 (1.01–1.14)                      | 0.022              |
| <b>People who smoke</b>             | 706          | 0.80 (0.62–1.04)                 | 1.04 (1.02–1.05)                      | < 0.0001           |
| <b>People who used to smoke</b>     | 745          | 1.21 (0.94–1.55)                 | 1.06 (1.01–1.11)                      | 0.01               |

## Summary of published pooled analysis [97] of waist-hip ratio and the risk of head and neck cancer

| Publication                         | No. of cases | HR (95% CI)<br>Highest vs lowest | RR (95% CI)<br>per 0.1 unit) <sup>1</sup> | P <sub>trend</sub> |
|-------------------------------------|--------------|----------------------------------|---|--------------------|
| <b>All</b>                          | 1,677        | 1.30 (1.12–1.50)                 | 1.07 (1.05–1.09)                          | < 0.0001           |
| <b>People who have never smoked</b> | 382          | 1.23 (0.89–1.69)                 | 1.06 (0.93–1.11)                          | 0.2013             |
| <b>People who smoke</b>             | 577          | 1.38 (1.09–1.75)                 | 1.08 (1.04–1.12)                          | 0.0017             |
| <b>People who used to smoke</b>     | 685          | 1.25 (0.98–1.59)                 | 1.10 (1.01–1.21)                          | 0.0351             |