

ABSENCE OF EXCESS BODY FATNESS

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2.2.19 Cancer of the thyroid

Cancer of the thyroid includes a variety of histological types, ranging from the most common group of differentiated cancers (papillary carcinoma and follicular carcinoma) to medullary carcinoma and anaplastic (undifferentiated) carcinoma. Globally, thyroid cancer incidence has been increasing during the past three decades; incidence rates in women are generally 2–3 times those in men. Known risk factors include exposure to radiation for all thyroid cancers, and iodine deficiency for follicular carcinoma.

In 2001, the Working Group of the *IARC Handbook on weight control and physical activity* ([IARC, 2002](#)) concluded that the evidence of an association between avoidance of weight gain and thyroid cancer was *inadequate*. The 2007 WCRF review did not draw any conclusions about body fatness and thyroid cancer risk ([WCRF/AICR, 2007](#)).

(a) Cohort studies

The evidence from cohort studies since 2000 includes 15 publications (excluding analyses that were later updated and analyses based on fewer than 100 incident cases), including a large pooled analysis of 22 cohorts ([Kitahara et al., 2016](#)). [Table 2.2.19a](#) presents results from these studies for BMI at baseline, with comments on findings according to other measures of body fatness, such as weight changes over the life-course, waist circumference, or waist-to-hip ratio.

In general, the evidence from cohort studies supports a positive association between BMI and thyroid cancer, with most studies reporting a significantly increased risk at the highest versus lowest category of BMI and/or a significant dose-response relationship. However, in those studies that provided estimates for women and men separately, inconsistent findings were observed across studies. [Almquist et al. \(2011\)](#) found no association between BMI and thyroid cancer in

either sex, but a positive trend across BMI quintiles in women only ($P_{\text{trend}} = 0.02$). In a Norwegian population-based cohort, [Engeland et al. \(2006\)](#) observed no association in men, but a positive association in women; the estimated relative risk for BMI ≥ 30 kg/m² compared with the reference BMI of 18–24.9 kg/m² was 1.29 (95% CI, 1.13–1.46). In the Radiologic Technologists Study in the USA ([Meinhold et al. \(2010\)](#)), no association was observed in men, whereas the association in women was also positive (RR, 1.74; 95% CI, 1.03–2.94). A systematic review, including 11 studies, estimated the relative risk of thyroid cancer for obese compared with normal-weight individuals to be 1.53 (95% CI, 0.89–2.64) in men and 1.57 (95% CI, 1.13–2.19) in women ([Schmid et al., 2015](#)). Another systematic review ([Zhang et al., 2014](#)), including 16 cohort studies, estimated an overall relative risk of thyroid cancer of 1.29 (95% CI, 1.20–1.37) in relation to obesity, with similar risk estimates in men and in women [the Working Group noted that this study provided limited information]. A pooled analysis by [Kitahara et al. \(2016\)](#) of 22 cohorts including 2296 incident cases found a modest positive association between baseline BMI and thyroid cancer risk overall, and the association was stronger in men (RR per 5 kg/m², 1.17; 95% CI, 1.06–1.28) than in women (RR per 5 kg/m², 1.04; 95% CI, 1.00–1.09).

A total of four studies assessed the association between body fatness and thyroid cancer risk by histological subtype ([Engeland et al., 2006](#); [Kabat et al., 2012](#); [Rinaldi et al., 2012](#); [Kitahara et al., 2016](#)). The association with BMI was similar for the papillary and follicular histological subtypes.

In the only study that assessed BMI at younger ages ([Kitahara et al., 2016](#)), thyroid cancer risk was similar for BMI in young adulthood (RR per 5 kg/m², 1.13; 95% CI, 1.02–1.25) and BMI later in adult life (RR per 5 kg/m², 1.06; 95% CI, 1.02–1.10); a positive association was also reported with BMI gain in adult life (RR per 5 kg/m², 1.07; 95% CI, 1.00–1.15), after adjustment for BMI.

Two studies assessed anthropometric measures of body fatness other than BMI. In the pooled analysis by [Kitahara et al. \(2016\)](#), a weaker positive association was found with waist circumference (RR per 5 cm, 1.03; 95% CI, 1.01–1.05) than with BMI (RR per 5 kg/m², 1.06; 95% CI, 1.02–1.10). In the EPIC cohort ([Rinaldi et al., 2012](#)), associations with waist circumference and waist-to-hip ratio were similar to those observed with BMI.

(b) Case-control studies

Six informative case-control studies were identified that evaluated the association between BMI and thyroid cancer, including two larger pooled analyses ([Table 2.2.19b](#)). One study ([Cléro et al., 2010](#)) that combined two of the five studies but that did not offer additional information was excluded. In two studies, the total number of cases in men was less than 50 ([Guignard et al., 2007](#); [Suzuki et al., 2008](#)); therefore, only data for women are reported. Two studies ([Guignard et al., 2007](#); [Xu et al., 2014](#)) were restricted to papillary carcinomas.

Overall, there appeared to be an association between elevated current BMI (in adulthood) and the occurrence of thyroid cancer. There was some indication that this relationship was stronger in women than in men. [However, this may reflect small case numbers in the studies, especially in men, related to the low prevalence of the disease.] Two of the studies evaluated the associations between BMI at age 18 years ([Brindel et al., 2009](#)) and at age 20 years ([Suzuki et al., 2008](#)) and thyroid cancer, and noted some evidence for an association with thyroid cancer occurrence.

Table 2.2.19a Cohort studies of measures of body fatness and cancer of the thyroid

| Reference Cohort Location Follow-up period | Total number of subjects Sex Incidence/mortality | Exposure categories | Exposed cases | Relative risk (95% CI) | Covariates | Comments |
|--|--|--|--|--|---|--|
| Samanic et al. (2004) United States Veterans cohort USA 1969–1996 | 4 500 700 Men Incidence or mortality | Obesity Non-obese Obese Non-obese Obese | White men: 811 64 Black men: 156 13 | 1.00 1.40 (1.09–1.81) 1.00 1.92 (1.09–3.40) | Age, calendar year | Obesity defined as discharge diagnosis of obesity: ICD-8: 277; ICD-9: 278.0 Cancers diagnosed within 1 yr of obesity diagnoses were excluded from the study In White men only, higher risk of adrenal thyroid cancer |
| Oh et al. (2005) Korea National Health Insurance Corporation cohort Republic of Korea 1992–2002 | 781 283 Men | BMI < 18.5 18.5–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [P _{trend}] | 3 72 70 53 28 – | 0.82 (0.20–3.34) 1.00 1.52 (1.07–2.14) 2.00 (1.38–2.89) 2.23 (1.40–3.55) – | Age, smoking, alcohol consumption, exercise, family history of cancer, area of residence | |
| Engeland et al. (2006) Norwegian population- based cohort Norway 1972–2003 | 963 523 Men Incidence 1 037 424 Women Incidence | BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P _{trend}] BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P _{trend}] | 2 412 322 42 30 1187 710 341 | 0.47 (0.12–1.87) 1.00 1.12 (0.97–1.30) 1.14 (0.82–1.56) [0.005] 0.68 (0.47–0.98) 1.00 1.08 (0.98–1.20) 1.29 (1.13–1.46) [0.001] | Age Age | Association was similar for age 50–74 yr Association was similar for age 20–49 yr and stronger for age 50–74 yr (57% increased risk). Somewhat stronger associations for follicular carcinoma vs papillary carcinoma |
| Samanic et al. (2006) Swedish Construction Worker Cohort Sweden 1971–1999 | 362 552 Men Incidence | BMI 18.5–24.9 25–29.9 ≥ 30 [P _{trend}] | 89 73 9 | 1.00 1.24 (0.90–1.71) 0.98 (0.49–1.96) [0.48] | Age, calendar year, smoking | |

Table 2.2.19a (continued)

| Reference Cohort Location Follow-up period | Total number of subjects Sex Incidence/mortality | Exposure categories | Exposed cases | Relative risk (95% CI) | Covariates | Comments |
|---|--|--|--|--|---|--|
| Song et al. (2008) Female public servants Republic of Korea 1994–2003 | 170 481 Women | BMI < 18.5 18.5–20.9 21–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 per 1 kg/m ² | 3 40 89 115 93 59 11 | 0.35 (0.11–1.10) 0.78 (0.52–1.16) 1.00 1.05 (0.79–1.41) 1.08 (0.80–1.47) 1.02 (0.72–1.45) 0.70 (0.35–1.40) 1.02 (0.98–1.04) | Age, height, smoking, alcohol consumption, exercise, SES | |
| Clavel-Chapelon et al. (2010) E3N cohort (female teachers) France 1990–2005 | 91 909 Women | BMI < 18.5 18.5–22 22–25 25–30 ≥ 30 [P _{trend}] | 3 99 129 62 24 | 0.35 (0.11–1.12) 1.00 1.39 (1.07–1.81) 1.18 (0.86–1.63) 1.76 (1.12–2.76) [0.005] | Age, year of birth, history of benign thyroid conditions, smoking, iodine | Large body shape (Sørensen's silhouette) at baseline and at age 35–40 yr, but not at age 20–25 yr, associated with increased risk |
| Leitzmann et al. (2010) NIH-AARP cohort USA 1995–2003 | 484 326 Men and women Incidence | BMI 18.5–24.9 25–29.9 ≥ 30 [P _{trend}] | 107 153 92 | 1.00 1.27 (0.99–1.64) 1.39 (1.05–1.85) [0.007] | Age, sex, physical activity, race/ ethnicity, education level, smoking, alcohol consumption, OC use | For WC, positive association in men but not in women. For waist-to-hip ratio, null association in either sex |
| Meinhold et al. (2010) Radiologic Technologists Study USA 1983–2006 | 21 207 Men Incidence 69 506 Women Incidence | BMI 18.5–24.9 25–29.9 30–34.5 ≥ 35 [P _{trend}] BMI < 18.5 18.5–24.9 25–29.9 30–34.5 ≥ 35 [P _{trend}] | 13 15 9 2 6 144 44 26 16 | 1.00 0.89 (0.42–1.90) 1.91 (0.80–4.56) 2.14 (0.60–7.67) [0.11] 0.96 (0.42–2.18) 1.00 0.90 (0.64–1.27) 1.41 (0.92–2.16) 1.74 (1.03–2.94) [0.04] | Year of birth, smoking, radiation exposure, history of benign thyroid conditions | |

Table 2.2.19a (continued)

| Reference Cohort Location Follow-up period | Total number of subjects Sex Incidence/mortality | Exposure categories | Exposed cases | Relative risk (95% CI) | Covariates | Comments |
|--|---|--|----------------------------|--|---|---|
| Almquist et al. (2011) 7 population-based cohorts Austria, Norway, and Sweden 2006–2016 | 289 866 Men Incidence | BMI, quintiles Q1 Q2 Q3 Q4 Q5 [<i>P</i> _{trend}] | 23 35 20 29 26 | 1.00 1.41 (0.83–2.39) 0.77 (0.42–1.41) 1.09 (0.63–1.89) 1.00 (0.57–1.77) [0.61] | Age, smoking | |
| | 288 834 Women Incidence | BMI, quintiles Q1 Q2 Q3 Q4 Q5 [<i>P</i> _{trend}] | 41 37 51 59 67 | 1.00 0.84 (0.54–1.31) 1.10 (0.73–1.68) 1.22 (0.81–1.84) 1.40 (0.93–2.09) [0.02] | Age, smoking | |
| Kabat et al. (2012) Women’s Health Initiative USA 1993–2011 | 144 319 Women Incidence | BMI < 25 25– < 30 30–35 ≥ 35 [<i>P</i> _{trend}] | 92 99 71 32 | 1.00 1.06 (0.79–1.42) 1.40 (1.00–1.94) 0.97 (0.62–1.50) [0.39] | Age, age at first pregnancy, education level, smoking, alcohol consumption, exercise, history of benign thyroid conditions | Waist-to-hip ratio and weight change, null association. Similar associations for papillary carcinoma and follicular carcinoma |
| Rinaldi et al. (2012) EPIC cohort Europe 1992–2009 | 343 765 Women Incidence | BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}] | 3 290 145 66 4 | 0.27 (0.09–0.84) 1.00 1.12 (0.91–1.38) 1.19 (0.89–1.59) [0.042] | Age, centre, smoking | Only 58 incident cases identified in men (results not presented). Similar findings for papillary carcinoma only. WC and waist-to-hip ratio both positively associated with risk |
| Bhaskaran et al. (2014) Clinical Practice Research Datalink United Kingdom 1987–2012 | 5.24 million Men and women Incidence | BMI per 5 kg/m ² | 941 | 1.09 (1.00–1.19) | Age, sex, year, diabetes, alcohol consumption, smoking, SES | Similar association in never- smokers |

Table 2.2.19a (continued)

| Reference Cohort Location Follow-up period | Total number of subjects Sex Incidence/mortality | Exposure categories | Exposed cases | Relative risk (95% CI) | Covariates | Comments | |
|---|---|-------------------------|------------------|---------------------------|---|--|---|
| Kitahara et al. (2016) Pooled analysis of 22 cohorts Asia, Australia, Europe, and North America 1979–2009 | 578 922 | BMI | | | Age, alcohol consumption, physical activity, race/ethnicity, marital status, education level, smoking | WC less associated. Similar associations for papillary carcinoma and follicular carcinoma | |
| | Men | 15–18.4 | 2 | 0.66 (0.16–2.67) | | | |
| | Incidence | 18.5–24.9 | 191 | 1.0 | | | |
| | | 25–29.9 | 327 | 1.23 (1.02–1.47) | | | |
| | | ≥ 30 | 129 | 1.35 (1.07–1.71) | | | |
| | | per 5 kg/m ² | | 1.17 (1.06–1.28) | | | |
| | 774 373 | BMI | | | | | Similar associations for WC. Similar associations for papillary carcinoma and follicular carcinoma |
| | Women | 15–18.4 | 29 | 0.86 (0.59–1.24) | | | |
| | Incidence | 18.5–24.9 | 995 | 1.0 | | | |
| | | 25–29.9 | 615 | 1.02 (0.93–1.14) | | | |
| | ≥ 30 | 356 | 1.05 (0.92–1.19) | | | | |
| | per 5 kg/m ² | | 1.04 (1.00–1.09) | | | | |
| | BMI at baseline | | | 1.06 (1.02–1.10) | | | |
| | per 5 kg/m ² | | | 1.13 (1.02–1.25) | | | |
| | BMI in young adulthood | | | 1.07 (1.00–1.15) | | | |
| | per 5 kg/m ² | | | | | | |
| | BMI gain in adult life | | | | | | |
| | per 5 kg/m ² | | | | | | |

BMI, body mass index (in kg/m²); CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; OC, oral contraceptive; SES, socioeconomic status; WC, waist circumference; yr, year or years

Table 2.2.19b Case-control studies of measures of body fatness and cancer of the thyroid

| Reference Study location Period | Total number of cases Sex Source of controls | Exposure categories | Exposed cases | Odds ratio (95% CI) | Adjustment for confounding | Comments |
|---|---|---|---------------------------|--|---|---|
| Dal Maso et al. (2000) Pooled analysis of 12 case-control studies China, Greece, Italy, Japan, Norway, Sweden, Switzerland, and USA | Men: 417 Women: 2056 Population and hospital | BMI, tertiles T1 T2 T3 [<i>P</i> _{trend}] | NR | Men: 1.0 0.8 (0.6–1.1) 1.0 (0.8–1.4) [0.71] | Age, history of radiation exposure | |
| Guignard et al. (2007) New Caledonia 1993–1999 | Women: 279 Population | BMI <18.5 18.5–24.99 25.0–29.9 30.0–34.9 ≥ 35.0 [<i>P</i> _{trend}] | 7 80 87 61 41 | 0.99 (0.35–2.80) 1.00 1.18 (0.75–1.86) 1.92 (1.14–3.22) 1.85 (1.02–3.35) [0.01] | Age, reference year, ethnicity, smoking, number of full- term pregnancies, miscarriages, and irregular menstruations | Papillary and follicular carcinomas only The risk was greater in women aged > 50 yr Data for men NR because of the low number of cases |
| Suzuki et al. (2008) Japan 2001–2005 | Women: 131 Hospital | Current BMI, tertiles 15.4–20.4 20.4–22.9 22.9–37.0 [<i>P</i> _{trend}] BMI at age 20 yr, tertiles 14.9–19.2 19.3–21.1 21.2–33.4 [<i>P</i> _{trend}] | 31 51 49 | 1.00 1.01 (0.59–1.74) 1.48 (0.86–2.57) [0.141] | Age, smoking habits, drinking habits, regular exercise, family history of thyroid cancer, past history of thyroid diseases, total non-alcohol energy intake, referral pattern to the hospital, menopausal status, age at menarche, parity, HRT use | Papillary and follicular carcinomas only Null associations with BMI or weight change since age 20 yr Data for men NR because of the low number of cases |

Table 2.2.19b (continued)

| Reference Study location Period | Total number of cases Sex Source of controls | Exposure categories | Exposed cases | Odds ratio (95% CI) | Adjustment for confounding | Comments |
|---|---|--|--|--|---|--|
| Brindel et al. (2009) French Polynesia 1979–2004 | Men: 23 Women: 177 Population; matched by date of birth and sex | BMI before diagnosis < 18.5 18.5–24.9 25.0–29.9 30.0–34.9 ≥ 35.0 < 18.5 18.5–24.9 25.0–29.9 30.0–34.9 ≥ 35.0 BMI at age 18 yr < 18.5 18.5–24.9 25.0–29.9 ≥ 30.0 < 18.5 18.5–24.9 25.0–29.9 ≥ 30.0 | Men: 0 7 11 2 3 Women: 7 74 44 25 27 Men: 1 16 3 2 Women: 26 117 32 5 | – 1.0 5.9 (0.8–40.8) 3.1 (0.2–42.1) 3.2 (0.3–39.2) 0.8 (0.3–2.4) 1.0 3.5 (1.7–7.4) 1.2 (0.6–2.6) 3.0 (1.3–7.1) 0.05 (0.0–1.0) 1.0 0.8 (0.1–6.3) 4.8 (0.2–113) 0.6 (0.3–1.2) 1.0 3.7 (1.6–8.4) 1.2 (0.3–5.2) | Height, ethnicity, education level, smoking, interviewer, radiation to head or neck before age 15 yr In women, also adjusted for number of full-term pregnancies, menopausal status | |
| Xu et al. (2014) Pooled analysis Germany, Italy, USA 1993–2013 | Men: 557 Women: 1360 Hospital | BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}] | 35 581 422 319 | 0.82 (0.52–1.30) 1.00 1.67 (1.38–2.03) 3.91 (3.02–5.05) [0.001] | Age, sex, race/ ethnicity, study centre | Papillary carcinoma only. Body fat percentage (calculated by the formula of Deurenberg) also associated with increased risk, overall and by sex |

Table 2.2.19b (continued)

| Reference Study location Period | Total number of cases Sex Source of controls | Exposure categories | Exposed cases | Odds ratio (95% CI) | Adjustment for confounding | Comments |
|---|---|-------------------------------|------------------|------------------------|---|--|
| Xhaard et al. (2015) France 2005–2010 | Men and women: 761 Population | BMI | All: | | Stratified by sex, region, and age and adjusted for education level, ethnicity, smoking status, family history of thyroid cancer, and number of pregnancies (in women only) | No differences in risk were observed when restricting to papillary carcinomas (<i>n</i> = 676 cases) |
| | | < 18.5 | 52 | 1.00 | | |
| | | 18.5–24.9 | 496 | 1.15 (0.77–1.71) | | |
| | | 25–29.9 | 138 | 1.23 (0.77–1.96) | | |
| | | ≥ 30 | 72 | 1.56 (0.92–2.66) | | |
| | | [<i>P</i> _{trend}] | | [0.09] | | |
| | | BMI | Women: | | | |
| | | < 18.5 | 45 | 1.00 | | |
| | | 18.5–24.9 | 384 | 1.25 (0.82–1.90) | | |
| | | 25–29.9 | 102 | 1.50 (0.89–2.51) | | |
| ≥ 30 | 65 | 1.78 (1.01–3.14) | | | | |
| [<i>P</i> _{trend}] | | [0.03] | | | | |

BMI, body mass index (in kg/m²); CI, confidence interval; HRT, hormone replacement therapy; NR, not reported; yr, year or years

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