Anthropometric factors and thyroid cancer risk by histological subtype: pooled analysis of 22 prospective studies

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Financial disclosures: This work was supported in part by the Intramural Research Program of the National Cancer Institute, National Institutes of Health.

Conflicts of interest: None

ABSTRACT

Background: Greater height and body mass index (BMI) have been associated with an increased risk of thyroid cancer, particularly papillary carcinoma, the most common and least aggressive subtype. Few studies have evaluated these associations in relation to other, more aggressive histologic types or thyroid cancer-specific mortality.

Methods: In this large pooled analysis of 22 prospective studies (833,176 men and 1,260,871 women), we investigated thyroid cancer incidence associated with greater height, body mass index (BMI) at baseline and young adulthood, and adulthood BMI gain (difference between young-adult and baseline BMI), overall and separately by sex and histological subtype using multivariable Cox proportional hazards regression models. Associations with thyroid cancer mortality were investigated in a subset of cohorts (578,922 men and 774,373 women) that contributed cause of death information.

Results: During follow-up, 2,996 incident thyroid cancers and 104 thyroid cancer deaths were identified. All anthropometric factors were positively associated with thyroid cancer incidence: HRs (95% CIs) for height (per 5 cm)=1.07 (1.04-1.10), BMI (per 5 kg/m^2)=1.06 (1.02-1.10), waist circumference (per 5 cm)=1.03 (1.01-1.05), young-adult BMI (per 5 kg/m^2)=1.13 (1.02-1.25), and adulthood BMI gain (per 5 kg/m^2)=1.07 (1.00-1.15). Associations for baseline BMI and waist circumference were attenuated after mutual adjustment. Baseline BMI was more strongly associated with risk in men compared with women (P-interaction=0.04). Positive associations were observed for papillary, follicular, and anaplastic, but not medullary, thyroid carcinomas. Similar, but stronger, associations were observed for thyroid cancer mortality.

Conclusion: Our results suggest that greater height and excess adiposity throughout adulthood are associated with higher incidence of most major types of thyroid cancer, including the least common but most aggressive form, anaplastic carcinoma, and higher thyroid cancer mortality. Potential underlying biological mechanisms should be explored in future studies.

INTRODUCTION

Although thyroid cancer only accounts for approximately 2% of all cancers diagnosed worldwide (1), the incidence of thyroid cancer, particularly papillary thyroid carcinoma, has increased dramatically in many countries over the past few decades (2). This pattern appears to reflect the enhanced ability to detect very small thyroid tumors, but some of the increase may be attributable to changes in the prevalence of lifestyle and environmental risk factors (3). Exposure to ionizing radiation during childhood and adolescence, which is the only established modifiable risk factor, does not appear to have contributed importantly to these trends (4, 5). Among other possible contributing factors includes the rising prevalence of obesity (6, 7).

Greater body mass index (BMI), a measure of total adiposity, has been associated with an increased risk of thyroid cancer in several observational studies (6, 8-14), with some exceptions (15-18). Most of these studies also showed positive associations with greater height. While the underlying biological mechanisms remain speculative, studies utilizing other anthropometric measures or the same measures at different periods during life could provide additional clues. Compared with BMI, waist circumference more directly measures the amount of central adipose tissue, the metabolic consequences of which include insulin resistance and inflammation (19). However, associations of waist circumference with thyroid cancer risk have been examined in only three studies, with conflicting results (14, 15, 20). BMI specifically in young adulthood has been associated with an increased risk of thyroid cancer in some studies (6, 10, 11, 15) but not others (8, 21). Few studies have evaluated associations for specific histological subtypes apart from papillary carcinoma, which is the least aggressive and increasingly predominant subtype.

We compiled individual-level data from 22 prospective cohort studies from North America, Europe, Australia, and Asia to comprehensively evaluate height, baseline and young-adult BMI, adulthood BMI gain (difference between young-adult and baseline BMI), and waist circumference in relation to risk of thyroid cancer and major histologic subtypes.

METHODS

Study population

Cohorts participating in the National Cancer Institute Cohort Consortium were eligible to join a pooled study of anthropometric factors and thyroid cancer risk if the baseline year occurred on or after 1970 and the study ascertained height and weight information (22-43). **Table 1** provides a brief description of the included cohorts and their acronyms. Full cohort data were available from 20 cohorts. CSDLH and NLCS used a case-cohort approach, providing data from all incident thyroid cancer cases and a random sample of participants from the full cohort. Height and weight were self-reported in most cohorts, but measured in MCCS, SMHS, SWHS, most of EPIC (89%), and most of SISTER (>99%). Information on waist circumference was ascertained in 15 cohorts (AARP, BCDDP, COSM, CPSII, CSDLH, CTS, EPIC, IWHS, MCCS, NYUWHS, SISTER, SMC, SMHS, SWHS, WLH), having been measured by someone other than the participant in six of these cohorts (EPIC (89%), MCCS, NYUWHS, SISTER, SMHS, SWHS), and data on young-adult weight (recalled for ages 17-21 by participants) was assessed in 10 of the cohorts (AARP, AHS, COSM, CPSII, IWHS, MCCS, PLCO, SMC, VITAL, WLH). We calculated baseline and young-adult body mass index (BMI) as kg/m^2. BMI gain was defined as baseline BMI minus young-adult BMI. Information on covariates, including education, marital status, alcohol consumption, smoking, physical activity level, and history of benign thyroid disease were self-reported. We formatted these data uniformly across studies using standard units and category cut-points prior to analysis. Each study received approval from its respective institutional review board.

From a total of 2,281,345 eligible study participants, we excluded participants without follow-up time (n=19,953), whose age at study exit was implausible (>110 years) (n=65), who were younger than 18 or older than 85 years of age at baseline (n=7,286), who reported having had a previous diagnosis of cancer at baseline (n=102,116) as well as anyone with missing data on height or weight (n=55,703). Participants with BMI values of less than 15 kg/m^2 (n=1,717) and greater than or equal to 60 kg/m^2 (n=458) were also excluded. The final sample consisted of 2,094,047 individuals (833,176 men and 1,260,871 women) from 22 prospective cohort studies.

Thyroid cancer follow-up

Participants were followed baseline questionnaire completion date to any first primary cancer diagnosis other than non-melanoma skin cancer, loss-to-follow-up, death, or cohort-specific administrative end date, whichever occurred first. Cancer diagnoses were identified through linkages to local, state, or national cancer registries (AARP, AHS, COSM, CSDLH, CTS, IWHS, MCCS, NLCS, SMC, WLH, VITAL), self-report verified through medical record confirmation (PHS, PLCO, SISTER, USRT, WHS), or a combination of approaches (BCDDP, CPSII, EPIC, NYUWHS, SMHS, SWHS). Participants were classified as cases if the first primary cancer diagnosed during follow-up was malignant thyroid cancer (International Classification of Disease for Oncology, Third Edition [ICD-O-3], topography code C73 or the equivalent). Histological subtypes of thyroid cancer were further classified using ICD-3 morphology codes or the equivalent (papillary: 8050, 8260, 8340-8344, 8350, 8450-8460; follicular: 8290, 8330-8335; medullary: 8345, 8510-8513; anaplastic: 8020-8035) (44).

While not an original objective of the current study, we additionally evaluated anthropometric factors in relation to thyroid cancer mortality among the subset of the cohorts that additionally provided information on cause of death (AARP, AHS, BCDDP, COSM, CPSII, CTS, IWHS, MCCS, NYUWHS, PHS, PLCO,

SMC, USRT, VITAL, WHS, and WLH), including 1,353,295 study subjects (578,922 men and 774,373 women). Thyroid cancer deaths were defined using ICD-9 code 193 and ICD-10 code C73.

Statistical analysis

We estimated cohort- and sex-specific hazard ratios (HRs) and 95% confidence intervals (CIs) using Cox proportional hazards regression models with attained age in years as the underlying time metric and adjusted for known or potential thyroid cancer risk factors, including race (White, Black, Asian, other), smoking status (never, former, current), education (high school or less, some college/post-high school training, college graduate), marital status (married/living together, divorced/separated, widowed, single/never married), physical activity level (cohort-specific tertiles), and alcohol intake (0-9, 10-19, 20+ grams of ethanol per day). Data from the CSDLH and NLCS cohorts were analyzed separately using a case-cohort approach (45). Between-study heterogeneity was evaluated using the I^2 index, with a value of 0% indicating none and higher values indicating increasing heterogeneity (46). Full-cohort data from 20 prospective studies were then aggregated to estimate pooled multivariable-adjusted HRs and 95% CIs in models additionally stratified by cohort, with anthropometric factors modeled categorically and continuously. We found no evidence of non-linear relationships between any of the exposures examined in relation to thyroid cancer incidence or mortality based on restricted cubic spline models with automatic stepwise selection of up to four knots. *P*-values for log-linear relationships were based on Wald tests corresponding to continuous values of the exposure. The aggregate data were also used to evaluate effect modification, specifically by sex, geographical area, race/ethnicity, age at the time of report for height and weight, and age at thyroid cancer diagnosis, and smoking status, and to examine associations by histology. We conducted interaction tests by comparing the fit of a model including a cross-product term between the exposure and effect modifier to one without using the likelihood ratio test. To evaluate effect modification by age at diagnosis, we treated exposures as time-varying by splitting person-time for

each participant by category of attained age and evaluating the fit of a model with the cross-product term between exposure and attained age category to one without. We observed no evidence of violation of the proportional hazards assumption.

RESULTS

A general description of the studies is shown in **Table 1**. During an average 10.4 years of follow-up, we identified 2,996 first primary thyroid cancer cases (695 men and 2,301 women). We classified 2,182 (73%) as papillary, 418 (14%) as follicular, 100 (3%) as medullary, and 53 (2%) as anaplastic. The mean age at baseline was 57 years and the mean age at thyroid cancer diagnosis during follow-up was 62 years (range: 25-92).

In the subset of cohorts that contributed cause of death information, we identified 104 thyroid cancer deaths (53 men and 51 women).

Study- and sex-specific HRs and 95% CIs for continuous values of height (per 5 cm increase), baseline BMI (per 5 kg/m^2 increase), waist circumference (per 5 cm increase), young-adult BMI (per 5 kg/m^2 increase), and BMI gain (per 5 kg/m^2 increase) are shown in **Supplementary Figures 1-5**. Significant between-cohort differences were observed for the associations for baseline BMI (I^2=41.1%) and young-adult BMI in women (I^2=59.0%) and waist circumference in men (I^2=58.9%). Heterogeity remained after individually excluding the two largest cohorts, AARP and EPIC.

Pooled results

In the aggregate dataset of 20 cohorts, increases in risk of thyroid cancer were observed for greater values (on a continuous scale, per 5 cm or 5 kg/m^2) of height (HR=1.07, 95% CI: 1.04-1.10), baseline BMI (HR=1.06, 95% CI: 1.02-1.10), waist circumference (HR=1.03, 95% CI: 1.01-1.05), young-adult BMI

(HR=1.13, 95% CI: 1.02-1.25), and adulthood BMI gain (HR=1.07, 95% CI: 1.00-1.15) (**Table 2**). The risk of thyroid cancer generally increased across categories of baseline height, BMI, and waist circumference, as well as young-adult BMI. Adult BMI gain of 5.0-9.9 kg/m^2 was associated with a statistically significant 23% increased risk (95% CI: 6-42%) compared with a BMI gain of 0-4.9 kg/m^2, but the risk for a BMI gain of ≥10 kg/m^2 was not significantly different from unity. Positive associations for height, baseline BMI, waist circumference, and young-adult BMI were observed in both men and women. The association for baseline BMI was significantly stronger for men versus women (*P*-interaction=0.04). The association for adulthood BMI gain was restricted to men (HR for men=1.23, 95% CI: 1.07-1.41), but not significantly modified by sex (*P*-interaction=0.12).

The HRs for BMI (per 5 kg/m^2 increase) were attenuated after restricting the analysis to subjects with measured values, although the sample size was substantially reduced (based on 743 cases, HR=1.01, 95% CI: 0.93-1.10); this attenuation was restricted to men (HR=0.76, 95% CI: 0.57-1.03; HR for women=1.03, 95% CI: 0.95-1.13). The HRs for height (per 5 cm) did not materially change (data not shown). As observed previously (14), the HRs for height and BMI in EPIC did not materially change after excluding self-reported values (data not shown). Adjusting for history of benign thyroid conditions from the subset of studies with this information yielded similar results (data not shown). HRs and 95% CIs for height in models unadjusted for BMI were similar to adjusted models in the overall study population, in men, and in women: 1.07 (1.04-1.10), 1.05 (0.99-1.11) and 1.07 (1.04-1.11), respectively.

HRs for waist circumference (per 5 cm increase**)** and BMI (per 5 kg/m^2 increase**)** were both attenuated after mutual adjustment (HR for waist=1.02, 95% CI: 0.98-1.06; HR for BMI=1.01, 95% CI 0.92-1.12); similar findings were observed by sex (data not shown). No consistent pattern in the association between waist circumference (per 5 cm increase) and thyroid cancer was observed in models stratified by baseline

BMI: HRs (95% CIs) for BMI <25.0, 25.0-29.9, and ≥30 kg/m^2 were 1.01 (0.96-1.07), 1.05 (0.99-1.12), and 1.02 (0.96-1.08), respectively.

Results from models of waist-to-hip ratio, available for 50.7% of the entire sample, suggested a non-significant linear association with thyroid cancer risk (data not shown in tables). The HRs (95% CIs) per 0.1 difference were 1.05 (0.97-1.14) overall, 1.06 (0.88-1.28) for men, and 1.05 (0.96-1.14) for women. These results are consistent with results from models of waist circumference.

We found that the positive association for adulthood BMI gain (per 5 kg/m^2) was restricted to participants whose young-adult BMI was 18.5-22.4 (HR=1.16, 95% CI: 1.05-1.29). HRs (95% CIs) per 5 kg/m^2 of BMI gain within the categories of young-adult BMI <18.5, 22.5-24.9, and ≥25 kg/m^2 were 0.95 (0.76-1.19), 1.02 (0.86-1.21), and 0.99 (0.84-1.16), respectively.

Differences by demographic factors and smoking status. Significant differences were observed for the association of height and thyroid cancer risk by race (stronger for Blacks and Asians), baseline age (stronger for younger ages), and age at thyroid cancer diagnosis (stronger for younger ages) (**Supplementary Table 1**). Other differences observed, although not statistically significant, including stronger associations for baseline and young-adult BMI and BMI gain among individuals who were older at baseline, stronger associations for waist circumference in U.S.-based studies and in Whites, and stronger associations for BMI gain in Asians than Whites or Blacks and never smokers (**Supplementary Table 1**). In women, no significant differences were observed by age at thyroid cancer diagnosis (before versus after age 55, a proxy for age at menopause; data not shown).

Differences by histology. Significant positive associations were observed for papillary carcinoma with height and young-adult BMI, follicular carcinoma with height and baseline BMI, and anaplastic

carcinoma with baseline BMI and BMI gain in adulthood (**Table 3**). Inverse associations for baseline BMI, waist circumference, and BMI gain with risk of medullary carcinoma did not materially change after excluding the first two years of follow-up (data not shown). Sex modified some of the histology-specific associations. Papillary carcinoma was associated with baseline BMI only in men and height only in women, but these differences were not statistically significant (*P*-interactions=0.08 and 0.47, respectively). Inverse associations for medullary carcinoma with baseline BMI, waist circumference, and BMI gain were observed only in women, but this sex difference was significant only for baseline BMI (*P*-interactions=0.02, 0.30, 0.27, respectively). The association for baseline BMI and anaplastic thyroid cancer was stronger in women versus men (*P*-interaction=0.03). However, the results for medullary and anaplastic thyroid cancer were based on relatively few cases (no more than 92 and 42, respectively, in any given model).

Thyroid cancer mortality. We found that greater height, baseline BMI, waist circumference, young-adult BMI, and adulthood BMI gain were associated with increased risk of thyroid cancer mortality; results from continuous models (per 5-unit increases) of baseline BMI (HR=1.29, 95% CI: 1.07-1.55), waist circumference (HR=1.22, 95% CI: 1.10-1.36), and young-adult BMI (HR=1.56, 95% CI: 1.13-2.15) were statistically significant (**Supplementary Table 2**). The patterns in risk overall and by sex were similar to those observed for thyroid cancer incidence, but the associations were generally stronger in magnitude. No significant differences were observed by sex.

DISCUSSION

In this comprehensive pooled analysis of 22 prospective cohort studies from North America, Europe, and Asia, we found that height, baseline BMI, waist circumference, young-adult BMI, and adulthood BMI gain were each positively associated with incidence of total thyroid cancer. These associations were independent of smoking and other factors associated with thyroid cancer risk. The association for

baseline BMI was stronger in men compared with women. Some other differences in risk by population subgroup were observed (e.g., stronger associations for baseline BMI in U.S. studies and in whites). Risk patterns were similar for papillary, follicular, and anaplastic carcinoma. None of the anthropometric factors examined were associated with risk of medullary carcinoma, but the confidence intervals were wide. These associations were stronger in magnitude for thyroid cancer mortality compared with incidence.

Compared to most other cancer sites, the associations we observed for height (per 5 cm increase) and BMI (per 5 kg/m^2 increase) with incidence of total, papillary, and follicular thyroid cancer were similar in magnitude (47-50). However, the associations of BMI with anaplastic thyroid cancer in women (HR=1.66) and thyroid cancer mortality in men (HR=1.47) and men and women combined (HR=1.29) were stronger and more comparable with cancers that have consistently been linked with obesity, including esophageal adenocarcinoma and endometrial and kidney cancers (50).

Few observational studies have collected information on anthropometric measures other than height and weight. BMI is a widely-used measure of adiposity but provides no information on the amount of lean versus fat mass or central versus peripheral body fat (51). Waist circumference and weight gain are more direct measures of central (visceral) adiposity and body fat mass, respectively. In the current study, we found positive associations for waist circumference (but not independent of baseline BMI), young-adult BMI, and adulthood BMI gain with thyroid cancer risk. These results suggest an important role of excess total (as opposed to central) adiposity across the lifespan on thyroid cancer incidence. Prospective studies that directly evaluate pre-diagnostic levels of biomarkers of insulin resistance, inflammation, estrogen, and other metabolic disturbances related to total adiposity may provide some insight regarding possible underlying mechanisms (52-54).

While the likelihood of thyroid nodule detection and thyroid cancer diagnosis could conceivably be greater for individuals with an underlying thyroid condition, our results did not change after adjusting for

a history of benign thyroid conditions. In cross-sectional studies, a greater BMI has been associated with higher thyroid cancer prevalence among individuals with screen-detected thyroid nodules (55) and increased tumor aggressiveness among overweight and obese papillary thyroid cancer patients (56, 57). In a previous case-control study, greater BMI was associated with risk of thyroid cancers less than and greater than 10 mm in size (9). Taken together, these observations suggest that surveillance biases do not fully account for associations observed between excess adiposity and thyroid cancer in this and other studies.

Consistent with most previous studies, adult height was positively associated with thyroid cancer risk in both men and women. Taller height in adolescence has also been associated with risk of thyroid cancer in adulthood (58). This relationship could be explained by higher circulating levels of insulin-like growth factor-I (IGF-I) in taller individuals (59). A higher serum concentration of IGF-I was associated with increased risk of differentiated thyroid cancer in the European Investigation into Cancer and Nutrition cohort (60). Other potential explanations for the positive association for height include the larger size of the thyroid gland (and, thus, greater number of cells with the potential to undergo malignant transformation) and greater likelihood of nodule detection via palpation.

Due to relatively small sample sizes, very few previous studies have shown associations between anthropometric factors and risk of specific histological sub-types of thyroid cancer apart from papillary thyroid carcinoma, the most common form of the disease. A previous large prospective study in Norway showed that baseline BMI was positively associated with risk of total thyroid cancer and papillary, follicular, and anaplastic sub-types and an inverse association with medullary thyroid cancer (12). An inverse association between BMI and medullary thyroid cancer risk was also reported in a pooled analysis of 14 case-control studies (67 cases) (61). Also consistent with our results, the Norwegian study showed a stronger association of BMI with follicular and anaplastic compared with papillary thyroid cancer (12).

The incidence of papillary thyroid cancer has increased dramatically in several countries over the past three to four decades (2). The rising prevalence of obesity in these countries has been proposed as one potential explanation (6). While our results are consistent with this hypothesis, they also suggest that the strength of this association is relatively weak, particularly for women. Several other factors influence thyroid cancer incidence trends, including changing clinical practices with regard to screening and diagnosis and changing prevalence of other thyroid cancer risk factors. Based on results from the current study, we would expect that increasing rates of obesity would, if anything, have a weak impact on population-level changes in papillary thyroid cancer incidence.

Overall, our results suggest that greater adiposity and taller height are associated with increased risk of thyroid tumors that arise from the follicular, but not parafollicular, cells of the thyroid (62). Excess weight and weight gain may be particularly important for risk of more aggressive tumors, as suggested by the relatively strong associations we observed for BMI and BMI gain with anaplastic thyroid cancer and thyroid cancer mortality. This hypothesis is supported by a recent study examining the effect of an obesity-inducing high-fat diet on thyroid carcinogenesis using a $Thrb^{PV/PV}/Pten^{+/-}$ mouse model, which found that such a diet increased thyroid tumor cell proliferation and induced anaplastic changes, as well as increased serum leptin levels (63). Although anaplastic thyroid cancer is uncommon, median survival after diagnosis is low; thus, improving our understanding of the etiology of this malignancy is particularly important.

Major strengths of this pooled analysis include the prospective study design, wide variability in the included studies, and the large sample size which allowed for a detailed investigation by race, smoking, geography, baseline age, and age at diagnosis, as well as histology. To the best of our knowledge, this is the first study evaluating the association between anthropometric factors and thyroid cancer mortality. All of the included studies collected information on potential confounders, including education, smoking,

alcohol intake, physical activity, which allowed us to control for these possible sources of confounding using a standardized approach.

Limitations of our study include the use of mostly self-reported, as opposed to measured, anthropometric factors, and the lack of information on body weight during follow-up. However, measurement error was most likely non-differential by case status, which would have attenuated the associations. We lacked information on thyroid tumor size, which could have helped distinguish smaller, less aggressive thyroid cancers from those that are clinically relevant. However, we found, in the subset of cohorts for which we received cause of death information, stronger associations for height and excess weight with thyroid cancer mortality compared with incidence. These results suggest that biological factors related to taller height and greater adiposity at baseline (generally mid-to-older adulthood) and young adulthood influence the development of more aggressive forms of thyroid cancer. Despite the large sample size, some of our results, particularly in subgroup analyses, may be due to chance. While the large number of studies contributing to our pooled analysis allowed for an evaluation of the consistency of the associations across different study populations, our results should be interpreted cautiously and in consideration of the difference in the range of values of the anthropometric factors across populations and the between-study heterogeneity observed for some factors.

In summary, greater height, excess weight early in life, and, among men, excess weight in mid-to-older adulthood were associated with increased incidence of total thyroid cancer and most major thyroid cancer subtypes, including anaplastic thyroid cancer. Baseline BMI and waist circumference and young-adulthood BMI were more strongly associated with thyroid cancer mortality compared with incidence, providing further support that these factors influence risk of more aggressive or clinically-relevant forms of thyroid cancer. Future research is needed to understand the possible underlying biological

mechanisms. More broadly, our results support efforts to achieve and maintain a healthy weight throughout life to minimize risks of cancer and other major chronic diseases.

ACKNOWLEDGMENTS

COSM and SMC: These cohorts are supported by the Swedish Research Council, the Swedish Cancer Foundation, and by Strategic Funds from Karolinska Institutet, Stockholm, Sweden

CPS-II: The American Cancer Society funds the creation, maintenance, and updating of the Cancer Prevention Study-II (CPS-II) cohort.

CTS: The CTS is supported by grant R01 CA77398 from the National Cancer Institute. The collection of cancer incidence data used in the CTS is supported by the California Department of Public Health (CDPH) as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the NCI's SEER program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's (CDCP) National Program of Cancer Registries, under agreement U58DP003862-01 awarded to the CDPH. The ideas and opinions expressed herein are those of the author(s) and endorsement by the CDPH, NCI, and CDCP or their contractors and subcontractors is not intended nor should be inferred.

EPIC: The authors are grateful to the support of the World Cancer Research Fund (2009/92). The coordination of EPIC is financially supported by the European Commission (DG-SANCO) and the International Agency for Research on Cancer. The national cohorts are supported by Danish Cancer Society, Denmark; Ligue Contre le Cancer, France; Institut Gustave Roussy, France; Mutuelle Generale de l'Education Nationale, France; Institut National de la Sante et de la Recherche Medicale, France; Deutsche Krebshilfe, Germany, Deutsches Krebsforschungszentrum and Federal Ministry of Education and Research, Germany; Hellenic Health Foundation, Greece; Italian Association for Research on Cancer; National Research Council, Italy; Dutch Ministry of Public Health, Welfare and Sports, the Netherlands; Netherlands Cancer Registry, the Netherlands; LK Research Funds, the Netherlands; Dutch Prevention Funds, the Netherlands; Dutch ZON (Zorg Onderzoek Nederland), the Netherlands; World Cancer Research Fund, London, UK; Statistics Netherlands, the Netherlands; European Research Council, Norway; Health Research Fund, Regional Governments of Andalucia, Asturias, Basque Country, Murcia (project no. 6236) and Navarra, ISCIII RETIC (RD06/0020/0091), Spain; Swedish Cancer Society, Sweden; Swedish Scientific Council, Sweden; Regional Government of Skane and Vasterbotten, Sweden; Cancer Research United Kingdom; Medical Research Council, United Kingdom; Stroke Association, United Kingdom, British Heart Foundation, United Kingdom; Department of Health, Food Standards Agency, United Kingdom; and Wellcome Trust; United Kingdom. We thank Bertrand Hemon for his precious help with the EPIC database. The principle investigators and funders corresponding to each of the EPIC centers that contributed cases were Kim Overvad, Anne Tjonneland (Denmark); Francoise Clavel-Chapelon (France); Heiner Boeing, Rudolf Kaaks (Germany); Antonia Trichopoulou (Greece);Vittorio Krogh, Domenico Palli, Paolo Vineis, Salvatore Panico, Rosario Tumino (Italy); Eiliv Lund (Norway); Antonio Agudo, Maria Jose Sanchez, J.Ramón Quirós, Carmen Navarro, Aurelio Barricarte, Miren Dorronsoro (Spain); Mattias Johansson, Jonas Manjer (Sweden); H. Bas Bueno-de-Mesquita, Petra H. Peeters (The Netherlands); Timothy Key, Nick Wareham (UK); The coordination of European Prospective Investigation into Cancer and Nutrition is financially supported by the European Commission (DG-SANCO) and the International Agency for Research on Cancer. The national cohorts are supported by the French National Cancer Institute (L'Institut National du Cancer; INCA); Grant Number: 2009-139; Ligue contre le Cancer, Institut Gustave Roussy, Mutuelle Générale de l'Education Nationale, Institut National de la Santéet de la Recherche Medicale (INSERM) (France);

German Cancer Aid; German Cancer Research Center (DKFZ); German Federal Ministry of Education and Research; Danish Cancer Society; Health Research Fund (FIS) of the Spanish Ministry of Health (RTICC (DR06/0020/0091); the participating regional governments from Asturias, Andalucía, Murcia, Navarra and Vasco Country and the Catalan Institute of Oncology of Spain; Cancer Research UK; Medical Research Council, UK; the Stroke Association, UK; British Heart Foundation; Department of Health, UK; Food Standards Agency, UK; the Wellcome Trust, UK; the Hellenic Health Foundation; Italian Association for Research on Cancer; Compagnia San Paolo, Italy; Dutch Ministry of Public Health, Welfare and Sports; Dutch Ministry of Health; Dutch Prevention Funds; LK Research Funds; Dutch ZON (Zorg Onderzoek Nederland); World Cancer Research Fund (WCRF); Statistics Netherlands (The Netherlands); Swedish Cancer Society; Swedish Scientific Council; Regional Government of Skane, Sweden; Nordforsk—Centre of Excellence programme.

IWHS: The authors thank the study participants. IWHS is funded by a grant from the National Cancer Institute (R01 CA39742).

Melbourne Collaborative Cohort Study: This study was made possible by the contribution of many people, including the original investigators and the diligent team who recruited the participants and who continue working on follow-up. We would also like to express our gratitude to the many thousands of Melbourne residents who continue to participate in the study. This work was supported by infrastructure from Cancer Council Victoria and grants from the National Health and Medical Research Council of Australia 209057 and 251533.

PHS: This study is supported by grants from the National Cancer Institute (CA-34933, CA-40360, and CA-097193) and from the National Heart, Lung, and Blood Institute (HL-26490 and HL-34595), National Institutes of Health, Bethesda, MD, USA.

The Sister Study is supported by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences (ZO1-ES-044005). Support for data collection and study and data management are provided by Social & Scientific Systems, Inc., and Westat, Inc., Durham, NC, USA. Aimee D'Aloisio, Sandra Halverson, Dan Scharf, and David Shore helped prepare the data for this analysis.

The SWHS and SMHS are supported in part by research grants from the National Cancer Institute (R37 CA070867 , UM1 CA182910, R01 CA082729, and UM1 CA173640]. The authors thank participants and research staff members of the studies for their contribution.

USRT: The authors thank the study participants and Jerry Reid of the American Registry of Radiologic Technologists for their continued support of this study; Diane Kampa and Allison Iwan of the University of Minnesota for study management and data collection; and Jeremy Miller at Information Management Services, Inc., for biomedical computing support.

VITAL: Emily White was supported by the grant K05-CA154337 (National Cancer Institute and Office of Dietary Supplements).

AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 04/22/2014.

2. Kilfoy BA, Zheng T, Holford TR, Han X, Ward MH, Sjodin A, Zhang Y, Bai Y, Zhu C, Guo GL, Rothman N, Zhang Y 2009 International patterns and trends in thyroid cancer incidence, 1973-2002. Cancer Causes Control 20:525-531.

3. Enewold L, Zhu K, Ron E, Marrogi AJ, Stojadinovic A, Peoples GE, Devesa SS 2009 Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. Cancer Epidemiol Biomarkers Prev 18:784-791.

4. Ito Y, Nikiforov YE, Schlumberger M, Vigneri R 2013 Increasing incidence of thyroid cancer: controversies explored. Nat Rev Endocrinol 9:178-184.

5. Neta G, Rajaraman P, Berrington de Gonzalez A, Doody MM, Alexander BH, Preston D, Simon SL, Melo D, Miller J, Freedman DM, Linet MS, Sigurdson AJ 2013 A prospective study of medical diagnostic radiography and risk of thyroid cancer. Am J Epidemiol 177:800-809.

6. Kitahara CM, Platz EA, Beane Freeman LE, Hsing AW, Linet MS, Park Y, Schairer C, Schatzkin A, Shikany JM, Berrington de González A 2011 Obesity and thyroid cancer risk among U.S. men and women: a pooled analysis of 5 prospective studies. Cancer Epidemiol Biomarkers Prev 20:464-472.

7. Kitahara CM, Linet MS, Beane Freeman LE, Check DP, Church TR, Park Y, Purdue MP, Schairer C, Berrington de González A 2012 Cigarette smoking, alcohol intake, and thyroid cancer

risk: a pooled analysis of five prospective studies in the United States. Cancer Causes Control 23:1615-1624.

8. Dal Maso L, La Vecchia C, Franceschi S, Preston-Martin S, Ron E, Levi F, Mack W, Mark SD, McTiernan A, Kolonel L, Mabuchi K, Jin F, et al. 2000 A pooled analysis of thyroid cancer studies. V. Anthropometric factors. Cancer Causes Control 11:137-144.

9. Guignard R, Truong T, Rougier Y, Baron-Dubourdieu D, Guénel P 2007 Alcohol drinking, tobacco smoking, and anthropometric characteristics as risk factors for thyroid cancer: a countrywide case-control study in New Caledonia. Am J Epidemiol 166:1140-1149.

10. Suzuki T, Matsuo K, Hasegawa Y, Hiraki A, Kawase T, Tanaka H, Tajima K 2008 Anthropometric factors at age 20 years and risk of thyroid cancer. Cancer Causes Control 19:1233-1242.

11. Brindel P, Doyon F, Rachédi F, Boissin JL, Sebbag J, Shan L, Chungue V, Bost-Bezeaud F, Petitdidier P, Paoaafaite J, Teuri J, de Vathaire F 2009 Anthropometric factors in differentiated thyroid cancer in French Polynesia: a case-control study. Cancer Causes Control 20:581-590.

12. Engeland A, Tretli S, Akslen LA, Bjørge T 2006 Body size and thyroid cancer in two million Norwegian men and women. Br J Cancer 95:366-370.

13. Oh SW, Yoon YS, Shin SA 2005 Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. J Clin Oncol 23:4742-4754.

14. Rinaldi S, Lise M, Clavel-Chapelon F, Boutron-Ruault MC, Guillas G, Overvad K, Tjønneland A, Halkjaer J, Lukanova A, Kaaks R, Bergmann MM, Boeing H, et al. 2012 Body size and risk of differentiated thyroid carcinomas: findings from the EPIC study. Int J Cancer 131(6):E1004-14.

15. Kabat GC, Kim MY, Thomson CA, Luo J, Wactawski-Wende J, Rohan TE 2012 Anthropometric factors and physical activity and risk of thyroid cancer in postmenopausal women. Cancer Causes Control 23:421-430.

16. Iribarren C, Haselkorn T, Tekawa IS, Friedman GD 2001 Cohort study of thyroid cancer in a San Francisco Bay area population. Int J Cancer 93:745-750.

17. Samanic C, Gridley G, Chow WH, Lubin J, Hoover RN, Fraumeni JF Jr 2004 Obesity and cancer risk among white and black United States veterans. Cancer Causes Control 15:35-43.

18. Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, Diem G, Oberaigner W, Weiland SK 2005 Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. Br J Cancer 93:1062-1067.

19. Tchernof A, Després JP 2013 Pathophysiology of human visceral obesity: an update. Physiol Rev 93:359-404.

20. Kitahara CM, Platz EA, Park Y, Hollenbeck AR, Schatzkin A, Berrington de González A 2012 Body fat distribution, weight change during adulthood, and thyroid cancer risk in the NIH-AARP Diet and Health Study. Int J Cancer 130:1411-1419.

21. Clavel-Chapelon F, Guillas G, Tondeur L, Kernaleguen C, Boutron-Ruault MC 2010 Risk of differentiated thyroid cancer in relation to adult weight, height and body shape over life: the French E3N cohort. Int J Cancer 126:2984-2990.

22. Schatzkin A, Subar AF, Thompson FE, Harlan LC, Tangrea J, Hollenbeck AR, Hurwitz PE, Coyle L, Schussler N, Michaud DS, Freedman LS, Brown CC, et al. 2001 Design and serendipity in establishing a large cohort with wide dietary intake distributions: the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol 154:1119–1125.

23. Alavanja MC, Sandler DP, McMaster SB, Zahm SH, McDonnell CJ, Lynch CF, Pennybacker M, Rothman N, Dosemeci M, Bond AE, Blair A 1996 The Agricultural Health Study. Environ Health Perspect 104:362–369.

24. Schairer C, Byrne C, Keyl PM, Brinton LA, Sturgeon SR, Hoover RN 1994 Menopausal estrogen and estrogen-progestin replacement therapy and risk of breast cancer (United States). Cancer Causes Control 5:491–500.

25. Orsini N, Bellocco R, Bottai M, Pagano M, Michaelsson K, Wolk A 2008 Combined effects of obesity and physical activity in predicting mortality among men. J Intern Med 264:442–451.

26. Calle EE, Rodriguez C, Jacobs EJ, Almon ML, Chao A, McCullough ML, Feigelson HS, Thun MJ 2002 The American Cancer Society Cancer Prevention Study II Nutrition Cohort: rationale, study design, and baseline characteristics. Cancer 94:500-511.

27. Rohan TE, Soskolne CL, Carroll KK, Kreiger N 2007 The Canadian Study of Diet, Lifestyle, and Health: design and characteristics of a new cohort study of cancer risk. Cancer Detect Prev 31:12-17.

28. Bernstein L, Allen M, Anton-Culver H, Deapen D, Horn-Ross PL, Peel D, Pinder R, Reynolds P, Sullivan-Halley J, West D, Wright W, Ziogas A, et al. 2002 High breast cancer incidence rates among California teachers: results from the California Teachers Study (United States). Cancer Causes Control 13:625–635.

29. Riboli E, Hunt KJ, Slimani N, Ferrari P, Norat T, Fahey M, Charrondière UR, Hémon B, Casagrande C, Vignat J, Overvad K, Tjønneland A, et al 2002 European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutrition 5:1113-1124.

30. Folsom AR, Kaye SA, Sellers TA, Hong CP, Cerhan JR, Potter JD, Prineas RJ 1993 Body fat distribution and 5-year risk of death in older women. JAMA 269: 483–487.

31. Giles GG, English DR 2002 The Melbourne Collaborative Cohort Study. IARC Sci Publ 156: 69–70.

32. van den Brandt PA, Goldbohm RA, van 't Veer P, Volovics A, Hermus RJ, Sturmans F 1990 A large-scale prospective cohort study on diet and cancer in The Netherlands. J Clin Epidemiol 43:285-295.

33. Toniolo PG, Levitz M, Zeleniuch-Jacquotte A, Banerjee S, Koenig KL, Shore RE, Strax P, Pasternack BS 1995 A prospective study of endogenous estrogens and breast cancer in postmenopausal women. J Natl Cancer Inst 87:190–197.

34. Sesso HD, Gaziano JM, VanDenburgh M, Hennekens CH, Glynn RJ, Buring JE 2002 Comparison of baseline characteristics and mortality experience of participants and nonparticipants in a randomized clinical trial: the Physicians' Health Study. Controlled Clinical Trials 23:686-702.

35. Prorok PC, Andriole GL, Bresalier RS, Buys SS, Chia D, Crawford ED, Fogel R, Gelmann EP, Gilbert F, Hasson MA, Hayes RB, Johnson CC, et al 2000 Design of the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. Controlled Clinical Trials 21:273S-309S.

36. D'Aloisio AA, Baird DD, DeRoo LA, Sandler DP 2010 Association of intrauterine and early-life exposures with diagnosis of uterine leiomyomata by 35 years of age in the Sister Study. Environ Health Perspect 118:375–381.

37. Wolk A, Larsson SC, Johansson JE, Ekman P 2006 Long-term fatty fish consumption and renal cell carcinoma incidence in women. JAMA 296:1371–1376.

38. Cai H, Zheng W, Xiang YB, Xu WH, Yang G, Li H, Shu XO 2007 Dietary patterns and their correlates among middle-aged and elderly Chinese men: a report from the Shanghai Men's Health Study. Br J Nutr 98:1006-1013.

39. Zheng W, Chow WH, Yang G, Jin F, Rothman N, Blair A, Li HL, Wen W, Ji BT, Li Q, Shu XO, Gao YT 2005 The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. Am J Epidemiol 162:1123-1131.

40. Freedman DM, Ron E, Ballard-Barbash R, Doody MM, Linet MS 2006 Body mass index and all-cause mortality in a nationwide US cohort. Int J Obes (Lond) 30:822–829.

41. White E, Patterson RE, Kristal AR, Thornquist M, King I, Shattuck AL, Evans I, Satia-About a J, Littman AJ, Potter JD 2004 VITamins and Lifestyle cohort study: study design and characteristics of supplement users. Am J Epidemiol 159:83–93.

42. Rexrode KM, Lee IM, Cook NR, Hennekens CH, Buring JE 2000 Baseline characteristics of participants in the Women's Health Study. J Womens Health Gend Based Med 9:19–27.

43. Weiderpass E, Braaten T, Magnusson C, Kumle M, Vainio H, Lund E, Adami HO 2004 A prospective study of body size in different periods of life and risk of premenopausal breast cancer. Cancer Epidemiol Biomarkers Prev 13:1121–1127.

44. Egevad L, Heanue M, Berney D, Fleming K, Ferlay J 2007 Chapter 4: Histological groups. In: Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P (eds) Cancer Incidence in Five Continents. IX. IARC Press; Lyon, France, pp. 61-66.

45. Barlow WE, Ichikawa L, Rosner D, Izumi S 1999 Analysis of case-cohort designs. J Clin Epidemiol 52:1165-1172.

46. Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, Botella J 2006 Assessing heterogeneity in meta-analysis: Q statistic or I^2 index? Psychological Methods 11:193-206.

47. Green J, Cairns BJ, Casabonne D, Wright FL, Reeves G, Beral V; Million Women Study collaborators 2011 Height and cancer incidence in the Million Women Study: prospective cohort, and meta-analysis of prospective studies of height and total cancer risk. Lancet Oncology 12:785-794.

48. Kabat GC, Kim MY, Hollenbeck AR, Rohan TE 2014 Attained height, sex, and risk of cancer at different anatomic sites in the NIH-AARP Diet and Health Study. Cancer Causes Control 25:1697-1706.

49. Sung J, Song YM, Lawlor DA, Smith GD, Ebrahim S 2009 Height and site-specific cancer risk: A cohort study of a Korean adult population. Am J Epidemiol 2009;170:53-64.

50. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M 2008 Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 371:569-578.

51. Han JM, Kim TY, Jeon MJ, Yim JH, Kim WG, Song DE, Hong SJ, Bae SJ, Kim HK, Shin MH, Shong YK, Kim WB 2013 Obesity is a risk factor for thyroid cancer in a large, ultrasonographically screened population. Eur J Endocrinol 168:879-886.

52. Trésallet C, Seman M, Tissier F, Buffet C, Lupinacci RM, Vuarnesson H, Leenhardt L, Menegaux F 2014 The incidence of papillary thyroid carcinoma and outcomes in operative patients according to their body mass indices. Surgery 156:1145-1152.

53. Kim HJ, Kim NK, Choi JH, Sohn SY, Kim SW, Jin SM, Jang HW, Suh S, Min YK, Chung JH, Kim SW 2013 Associations between body mass index and clinic-pathological characteristics of papillary thyroid cancer. Clin Endocrinol (Oxf) 78:134-140.

54. Willett WC, Dietz WH, Colditz GA 1999 Guidelines for healthy weight. N Engl J Med 341:427-434.

55. Pazaitou-Panayiotou K, Polyzos SA, Matzoros CS 2013 Obesity and thyroid cancer: epidemiologic associations and underlying mechanisms. Obes Rev 14:1006-1022.

56. Di Cristofano A 2013 Obesity and thyroid cancer: is leptin the (only) link? Endocrinology 154:2567-2569.

57. De Pergola G, Silvestris F 2013 Obesity as a major risk factor for cancer. J Obes 291546.

58. Kitahara CM, Gamborg M, Berrington de González A, Sørensen TI, Baker JL 2014 Childhood height and body mass index were associated with risk of adult thyroid cancer in a large cohort study. Cancer Res 74:235-242.

59. Crowe FL, Key TJ, Allen NE, Appleby PN, Overvad K, Grønbaek H, Tjønneland A, Halkjaer J, Dossus L, Boeing H, Kröger J, Trichopoulou A, et al. 2011 A cross-sectional analysis of the associations between adult height, BMI and serum concentrations of IGF-I and IGFBP-1 -2 and -3 in the European Prospective Investigation into Cancer and Nutrition (EPIC). Ann Hum Biol 38:194-202.

60. Schmidt JA, Allen NE, Almquist M, Franceschi S, Rinaldi S, Tipper SJ, Tsilidis KK, Weiderpass E, Overvad K, Tjønneland A, Boutron-Ruault MC, Dossus L, et al. 2014 Insulin-like growth factor-I and risk of differentiated thyroid carcinoma in the European Prospective Investigation into Cancer and Nutrition. Cancer Epidemiol Biomarkers Prev 23:976-985.

61. Negri E, Ron E, Franceschi S, La Vecchia C, Preston-Martin S, Kolonel L, Kleinerman RA, Mabuchi K, Jin F, Wingren G, Hallquist A, et al 2002 Risk factors for medullary thyroid carcinoma: a pooled analysis. Cancer Causes Control 13:365-372.

62. Ron E, Schneider AB 2006 Thyroid cancer. In: Schottenfeld D, Fraumeni JF (eds) Cancer Epidemiology and Prevention, 3rd edition. Oxford University Press, New York City, NY, pp. 975-994.

63. Kim WG, Park JW, Willingham MC, Cheng SY 2013 Diet-induced obesity increases tumor growth and promotes anaplastic change in thyroid cancer in a mouse model. Endocrinology 154:2936-2947.

Table 1. Description of the studies included in the pooled analysis of anthropometric factors and thyroid cancer risk

Cohort name	Cohort acronym	Geographic location	Study design	Participants		Thyroid cancer cases		Study period	Years of follow-up, mean (SD)	Age at baseline, mean (SD)	Baseline BMI ≥30 (%)
				Men	Women	Men	Women				
NIH-AARP Diet and Health Study 22)	AARP	U.S.	Cohort	304,592	195,251	260	327	1995-2006	9.1 (2.9)	62.0 (5.4)	22
Agricultural Health Study (23)	AHS	U.S.	Cohort	38,383	27,458	33	55	1993-2008	12.7 (2.5)	47.2 (12.4)	22
Breast Cancer Detection Demonstration Project (24)	BCDDP	U.S.	Cohort	----	38,140	----	35	1987-1997	8.2 (1.7)	61.7 (8.0)	13
Cohort of Swedish Men (25)	COSM	Sweden	Cohort	43,500	----	21	----	1998-2008	9.3 (2.5)	60.6 (9.7)	10
Cancer Prevention Study-II (26)	CPSII	U.S.	Cohort	72,589	80,997	87	129	1992-2009	12.2 (3.9)	63.0 (6.4)	15
Canadian Study of Diet, Lifestyle, and Health[a] (27)	CSDLH	Canada	Case-cohort	4,100	4,268	23	73	1991-2010	9.9 (4.9)	61.2 (13.1)	10
California Teachers Study (28)	CTS	U.S.	Cohort	----	104,442	----	277	1995-2010	12.9 (4.0)	51.9 (13.5)	14
European Prospective Investigation Into Cancer and Nutrition (29)	EPIC	Europe (multiple sites)	Cohort	146,430	341,073	67	540	1991-2010	11.0 (2.8)	51.3 (9.9)	14
Iowa Women's Health Study (30)	IWHS	U.S.	Cohort	----	37,957	----	67	1986-2005	16.4 (5.5)	62.2 (4.2)	19
Melbourne Collaborative Cohort Study (31)	MCCS	Australia	Cohort	15,687	22,335	12	35	1990-2009	14.9 (4.1)	55.1 (8.7)	21
Netherlands Cohort Study[b] (32)	NLCS	Netherlands	Case-cohort	2,269	2,389	23	52	1986-2003	14.9 (4.3)	61.4 (4.2)	7
New York University Women's Health Study (33)	NYUWHS	U.S.	Cohort	----	13,306	----	48	1985-2007	18.7 (5.2)	50.6 (8.7)	13
Physicians' Health Study (34)	PHS	U.S.	Cohort	28,350	----	51	----	1981-2009	18.1 (8.4)	55.3 (9.7)	6
Prostate, Lung, Colorectal, and Ovarian Cancer Screening Study (35)	PLCO	U.S.	Cohort	71,068	69,990	50	93	1993-2006	8.4 (2.8)	63.1 (5.4)	24
Sister Study (36)	SISTER	U.S.	Cohort	----	48,167	----	81	2003-2012	3.7 (1.3)	55.5 (9.0)	30
Swedish Mammography Cohort (37)	SMC	Sweden	Cohort	----	36,375	----	16	1998-2008	9.7 (2.1)	62.3 (9.2)	11
Shanghai Men's Health Study (38)	SMHS	China	Cohort	61,394	----	26	----	2001-2009	5.4 (1.4)	55.4 (9.7)	3
Shanghai Women's Health Study (39)	SWHS	China	Cohort	----	74,861	----	163	1996-2009	10.8 (1.9)	52.6 (9.1)	5
U.S. Radiologic Technologists Study (40)	USRT	U.S.	Cohort	13,317	49,395	19	119	1994-2006	8.9 (1.5)	47.9 (8.5)	16
VITamins and Lifestyle Study (41)	VITAL	U.S.	Cohort	31,497	31,310	23	69	2000-2009	7.4 (2.0)	60.9 (7.3)	25
Women's Health Study (42)	WHS	U.S.	Cohort	----	38,946	----	101	1993-2010	14.7 (3.9)	54.7 (7.0)	18
Swedish Women's Lifestyle and Health Study (43)	WLH	Sweden	Cohort	----	44,211	----	21	1991-2006	14.8 (1.7)	40.2 (5.8)	6
Overall				**833,176**	**1,260,871**	**695**	**2,301**	**1981-2012**	**10.4 (4.0)**	**56.7 (10.3)**	**17**

[a] Subcohort selected from a full cohort of 34,291 men and 39,618 women
[b] Subcohort selected from a full cohort of 58,279 men and 62,573 women

Table 2. Hazard ratios (HRs) and 95% confidence intervals (CIs) for thyroid cancer according to anthropometric factors

	Men			**Women**			**Total**		
	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI
Height (cm)[b,c]									
M 122-169/W 122-149	67	0.87	0.64-1.18	32	0.73	0.50-1.07	99	0.79	0.63-1.00
M 170-174/W 150-154	119	1.00	Reference	174	1.00	Reference	305	1.00	Reference
M 175-179/W 155-159	192	1.18	0.94-1.48	335	**1.23**	**1.03-1.48**	557	**1.21**	**1.05-1.40**
M 180-184/W 160-164	158	1.07	0.84-1.37	564	**1.21**	**1.02-1.44**	790	**1.20**	**1.05-1.37**
M 185-189/W 165-169	68	1.02	0.76-1.39	488	**1.24**	**1.04-1.48**	598	**1.19**	**1.03-1.38**
M 190-244/W 170-244	35	1.35	0.92-1.98	388	**1.41**	**1.17-1.69**	452	**1.38**	**1.18-1.61**
Per 5 cm	*639*	*1.05*	*1.00-1.11*	*1,981*	***1.08***	***1.04-1.12***	*2,801*	***1.07***	***1.04-1.10***
Baseline BMI (kg/m^2)[d]									
15.0-18.4	2	0.66	0.16-2.67	29	0.86	0.59-1.24	32	0.78	0.55-1.10
18.5-24.9	191	1.00	Reference	995	1.00	Reference	1,313	1.00	Reference
25.0-29.9	327	**1.23**	**1.02-1.47**	615	1.02	0.93-1.14	980	1.05	0.96-1.14
30.0-59.9	129	**1.35**	**1.07-1.71**	356	1.05	0.92-1.19	500	1.09	0.98-1.22
Per 5 kg/m^2	*649*	***1.17[g]***	***1.06-1.28***	*1,995*	*1.04[g]*	*1.00-1.09*	*2,825*	***1.06***	***1.02-1.10***
Waist circumference (cm)[e]									
M 52-79/W 52-69	15	1.31	0.73-2.36	185	0.97	0.80-1.16	200	0.99	0.84-1.18
M 80-89/W 70-79	59	1.00	Reference	357	1.00	Reference	416	1.00	Reference
M 90-99/W 80-89	114	1.18	0.85-1.62	292	1.06	0.91-1.24	406	1.08	0.94-1.24
M 100-109/W 90-99	70	1.26	0.88-1.81	171	**1.25**	**1.04-1.51**	243	**1.25**	**1.06-1.48**
M 110-189/W100-189	37	1.50	0.98-2.30	94	1.13	0.90-1.44	132	1.22	1.00-1.49
Per 5 cm	*295*	*1.04*	*0.98-1.10*	*1,099*	***1.02***	***1.00-1.05***	*1,397*	***1.03***	***1.01-1.05***
Young-adult BMI (kg/m^2)[d]									
15.0-18.4	32	1.04	0.71-1.52	113	1.21	0.98-1.50	145	1.17	0.97-1.40
18.5-22.4	159	1.00	Reference	360	1.00	Reference	519	1.00	Reference
22.5-24.9	96	1.28	0.99-1.65	82	1.01	0.79-1.28	178	1.13	0.95-1.34
25.0-59.9	66	1.34	1.00-1.80	62	**1.50**	**1.14-1.96**	128	**1.40**	**1.15-1.70**
Per 5 kg/m^2	*353*	***1.18***	***1.01-1.40***	*617*	*1.10*	*0.96-1.25*	*970*	***1.13***	***1.02-1.25***
Adulthood BMI gain (kg/m^2)[f]									
<0	20	0.79	0.49-1.29	56	1.11	0.82-1.50	76	1.01	0.79-1.30
0-4.9	156	1.00	Reference	245	1.00	Reference	401	1.00	Reference
5.0-9.9	143	**1.30**	**1.03-1.65**	223	**1.20**	**1.00-1.44**	366	**1.23**	**1.06-1.42**
≥10.0	34	1.27	0.86-1.86	93	1.09	0.85-1.39	127	1.13	0.92-1.39
Per 5 kg/m^2	*353*	***1.23***	***1.07-1.41***	*617*	*1.02*	*0.94-1.11*	*970*	*1.07*	*1.00-1.15*

Bolded: P-value <0.05

[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status and stratified by cohort

[b] Additionally adjusted for baseline BMI (per 5 kg/m^2)

[c] Restricted to height values between 122-244 cm

[d] Restricted to BMI values between 15.0-59.9 kg/m^2

[e] Restricted to waist circumference values between 52-189 cm

[f] Additionally adjusted for young-adult BMI (per 5 kg/m^2)

[g] *P*-interaction (by sex)= 0.04

Table 3. Sex-specific hazard ratios (HRs) and 95% confidence intervals (CIs) for thyroid cancer and histological subtypes according to anthropometric factors

	Papillary			Follicular			Medullary			Anaplastic		
	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI
Men												
Height (per 5 cm)[b,c]	396	1.02	0.95-1.10	131	1.09	0.97-1.23	29	1.16	0.90-1.50	19	1.11	0.81-1.51
Baseline BMI (per 5 kg/m^2)[d]	402	**1.15**	**1.02-1.29**	132	1.17	0.95-1.44	31	1.25[g]	0.80-1.93	19	0.85[h]	0.45-1.63
Waist circumference (per 5cm)[e]	198	1.04	0.97-1.11	62	1.02	0.90-1.15	12	0.99	0.74-1.32	7	0.80	0.53-1.20
Young-adult BMI (per 5 kg/m^2)[d]	238	**1.27**	**1.05-1.54**	81	0.90	0.61-1.31	12	1.17	0.47-2.94	12	1.33	0.56-3.17
Adulthood BMI gain (per 5 kg/m^2)[f]	238	**1.24**	**1.05-1.46**	81	1.24	0.92-1.66	12	0.97	0.43-2.22	12	1.12	0.51-2.46
Women												
Height (per 5 cm)[b,c]	1,663	**1.08**	**1.04-1.12**	248	**1.15**	**1.04-1.26**	61	0.95	0.78-1.16	23	1.21	0.89-1.66
Baseline BMI (per 5 kg/m^2)[d]	1,676	1.01	0.96-1.06	249	1.13	1.00-1.28	61	0.65[g]	0.47-0.91	23	**1.66[h]**	**1.23-2.23**
Waist circumference (per 5cm)[e]	802	1.01	0.98-1.04	139	1.07	1.00-1.15	35	0.84	0.71-0.99	9	1.22	0.96-1.56
Young-adult BMI (per 5 kg/m^2)[d]	481	1.10	0.95-1.27	100	1.15	0.84-1.59	16	0.58	0.20-1.70	7	1.43	0.51-4.04
Adulthood BMI gain (per 5 kg/m^2)[f]	481	1.03	0.94-1.14	100	1.01	0.81-1.25	16	0.41	0.19-0.86	7	2.13	1.20-3.78
Total[i]												
Height (per 5 cm)[b,c]	2,059	**1.07**	**1.03-1.10**	379	**1.13**	**1.04-1.21**	90	1.02	0.87-1.20	42	1.17	0.94-1.46
Baseline BMI (per 5 kg/m^2)[d]	2,078	1.03	0.98-1.08	381	**1.14**	**1.02-1.26**	92	0.80	0.62-1.03	42	**1.43**	**1.09-1.89**
Waist circumference (per 5cm)[e]	1,000	1.01	0.98-1.04	201	1.06	1.00-1.13	47	0.87	0.76-1.01	16	1.07	0.86-1.32
Young-adult BMI (per 5 kg/m^2)[d]	719	**1.16**	**1.03-1.30**	181	1.03	0.80-1.32	28	0.86	0.44-1.69	19	1.38	0.71-2.67
Adulthood BMI gain (per 5 kg/m^2)[f]	719	1.08	0.99-1.17	181	1.09	0.92-1.30	28	0.59	0.34-1.00	19	**1.60**	**1.01-2.54**

Bolded: P-value <0.05

[a] Adjusted for age (used as time metric), alcohol intake (0-9, 10-19, 20+ grams of ethanol per day), physical activity level (cohort-specific tertiles), race (White, Black, Asian, other), marital status (married/living together, divorced/separated, widowed, single/never married), education (high school or less, some college/post-high school training, college graduate), and smoking status (never, former, current) and stratified by cohort

[b] Additionally adjusted for baseline BMI (per 5 kg/m^2)

[c] Restricted to height values between 122-244 cm

[d] Restricted to BMI values between 15.0-59.9 kg/m^2

[e] Restricted to waist circumference values between 52-189 cm

[f] Additionally adjusted for young-adult BMI (per 5 kg/m^2)

[g] *P*-interaction (by sex)= 0.02

[h] *P*-interaction (by sex)= 0.03

[i] Additionally adjusted for sex

Supplementary Table 1. Hazard ratios (HRs) and 95% confidence intervals (CIs) for thyroid cancer by demographic factors and smoking status

	Height (per 5 cm)			**Baseline BMI (per 5 kg/m^2)**			**Waist circumference (per 5 cm)**			**Young-adult BMI (per 5 kg/m^2)**			**Adulthood BMI gain (per 5 kg/m^2)**		
	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI
Geographical area															
U.S.	1,902	**1.07**	**1.03-1.10**[b]	1,924	**1.09**	**1.04-1.14**[b]	733	**1.05**	**1.02-1.08**[b]	877	**1.13**	**1.01-1.26**	877	**1.08**	**1.00-1.17**
Europe	810	**1.06**	**1.00-1.11**	834	1.03	0.95-1.11	508	1.03	0.99-1.07	110	1.15	0.86-1.54	110	0.94	0.72-1.21
China	189	**1.24**	**1.08-1.42**	189	0.80	0.64-1.01	189	**0.91**	**0.83-0.99**	---	---	---	---	---	---
Australia	47	0.99	0.79-1.24	47	1.15	0.86-1.55	47	1.01	0.88-1.14	46	1.20	0.76-1.89	46	1.06	0.75-1.49
Race															
White	2,466	**1.06**	**1.03-1.10**[b]	2,490	**1.07**	**1.03-1.12**	1,155	**1.04**	**1.01-1.06**[b]	928	**1.13**	**1.01-1.25**	928	1.07	1.00-1.16
Black	46	**1.22**	**1.04-1.43**	46	0.88	0.66-1.17	13	1.01	0.82-1.23	21	1.03	0.54-1.96	21	0.83	0.52-1.31
Asian	220	**1.23**	**1.09-1.39**	220	0.90	0.74-1.11	197	**0.91**	**0.83-0.99**	11	1.29	0.44-3.76	11	**2.69**	**1.43-5.04**
Baseline age															
<50	846	**1.08**	**1.02-1.14**[b]	858	1.05	0.97-1.13	438	1.04	1.00-1.08	71	0.93	0.63-1.38	71	1.10	0.81-1.51
50-59	1,013	**1.08**	**1.03-1.14**	1,022	1.04	0.97-1.10	482	1.03	0.99-1.07	379	1.12	0.95-1.31	379	1.00	0.90-1.12
60+	942	**1.06**	**1.01-1.11**	945	**1.09**	**1.02-1.17**	477	1.03	0.99-1.07	520	**1.16**	**1.01-1.33**	520	**1.13**	**1.02-1.25**
Age at diagnosis/ study exit															
<50	372	**1.10**	**1.01-1.19**[b]	379	1.04	0.93-1.15	179	1.04	0.98-1.11	100	1.03	0.76-1.39	100	1.15	0.90-1.47
50-59	794	1.05	1.00-1.11	801	1.03	0.95-1.11	384	1.01	0.96-1.05	187	1.18	0.95-1.46	187	1.01	0.86-1.19
60-69	1,018	**1.08**	**1.03-1.14**	1,025	1.06	0.99-1.13	436	1.03	0.99-1.07	435	1.11	0.95-1.29	435	1.06	0.95-1.17
70+	617	1.05	0.99-1.11	620	**1.11**	**1.02-1.21**	252	1.03	0.97-1.09	379	1.13	0.95-1.34	379	1.13	1.00-1.27
Smoking status															
Never	1,578	**1.08**	**1.04-1.13**	1,594	1.06	1.00-1.11	810	1.03	0.99-1.06	480	1.10	0.94-1.28	480	**1.12**	**1.02-1.24**
Former	900	1.04	0.99-1.09	905	1.05	0.98-1.12	410	1.02	0.98-1.06	398	1.12	0.96-1.31	398	1.02	0.90-1.14
Current	259	**1.14**	**1.04-1.25**	262	1.04	0.90-1.20	157	1.03	0.96-1.11	72	1.11	0.78-1.58	72	0.94	0.71-1.26

Bolded= P-value <0.05 (Wald test)

[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status and stratified by cohort

[b] *P*-interaction <0.05

Supplementary Table 2. Hazard ratios (HRs) and 95% confidence intervals (CIs) for thyroid cancer mortality according to anthropometric factors

	Men			**Women**			**Total**		
	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI	No. cases	HR[a]	95% CI
Height (cm)[b,c]									
M 122-169/W 122-149	5	0.87	0.30-2.51	2	1.57	0.30-8.19	7	0.97	0.40-2.39
M 170-174/W 150-154	11	1.00	Reference	5	1.00	Reference	16	1.00	Reference
M 175-179/W 155-159	11	0.68	0.29-1.57	5	0.80	0.23-2.78	16	0.72	0.36-1.44
M 180-184/W 160-164	19	1.31	0.62-2.77	15	1.20	0.43-3.36	34	1.21	0.66-2.22
M 185-189/W 165-169	5	0.77	0.27-2.23	13	1.23	0.43-3.36	18	0.99	0.49-1.98
M 190-244/W 170-244	2	0.82	0.18-3.73	11	1.63	0.55-4.85	13	1.30	0.60-2.79
Per 5 cm	*53*	*1.05*	*0.87-1.27*	*51*	***1.26***	***1.04-1.54***	*104*	*1.14*	*1.00-1.31*
Baseline BMI (kg/m^2)[d]									
15.0-18.4	0		n.e	1	2.02	0.27-15.37	1	1.43	0.19-10.51
18.5-24.9	15	1.00	Reference	15	1.00	Reference	30	1.00	Reference
25.0-29.9	18	0.83	0.41-1.67	17	1.50	0.74-3.03	35	1.09	0.66-1.80
30.0-59.9	20	**2.43**	**1.19-4.99**	18	**2.72**	**1.33-5.56**	38	**2.55**	**1.54-4.22**
Per 5 kg/m^2	*53*	***1.47***	***1.10-1.96***	*51*	*1.20*	*0.93-1.54*	*104*	***1.29***	***1.07-1.55***
Waist circumference (cm)[e]									
M 52-79/W 52-69	1		n.e	4	1.28	0.27-6.00	5	2.16	0.48-9.70
M 80-89/W 70-79	0	1.00	Reference	3	1.00	Reference	3	1.00	Reference
M 90-99/W 80-89	7		n.e	8	3.39	0.89-12.95	15	**4.59**	**1.31-16.11**
M 100-109/W 90-99	7		n.e	7	**5.52**	**1.37-22.29**	14	**7.62**	**2.12-27.35**
M 110-189/W100-189	4		n.e	4	**5.71**	**1.19-27.46**	8	**8.60**	**2.18-33.86**
Per 5 cm	*19*	*1.19*	*0.99-1.44*	*26*	***1.24***	***1.08-1.41***	*45*	***1.22***	***1.10-1.36***
Young-adult BMI (kg/m^2)[d]									
15.0-18.4	4	2.53	0.76-8.45	4	0.88	0.30-2.63	8	1.37	0.61-3.04
18.5-22.4	8	1.00	Reference	17	1.00	Reference	25	1.00	Reference
22.5-24.9	9	2.45	0.94-6.40	3	0.77	0.22-2.62	12	1.45	0.72-2.91
25.0-59.9	12	**5.04**	**2.03-12.50**	5	2.60	0.95-7.13	17	**3.54**	**1.88-6.66**
Per 5 kg/m^2	*33*	***1.76***	***1.19-2.61***	*29*	*1.30*	*0.74-2.27*	*62*	***1.56***	***1.13-2.15***
Adulthood BMI gain (kg/m^2)[f]									
<0	2	0.47	0.10-2.27	5	2.69	0.80-9.05	7	1.22	0.49-3.00
0-4.9	16	1.00	Reference	7	1.00	Reference	23	1.00	Reference
5.0-9.9	9	0.84	0.37-1.94	11	1.96	0.75-5.10	20	1.15	0.63-2.12
≥10.0	6	2.15	0.81-5.72	6	2.47	0.81-7.55	12	1.95	0.94-4.04
Per 5 kg/m^2	*33*	*1.43*	*0.97-2.11*	29	1.16	0.80-1.68	*62*	*1.23*	*0.94-1.60*

Bolded: P-value <0.05

[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status and stratified by cohort

[b] Additionally adjusted for baseline BMI (per 5 kg/m^2)

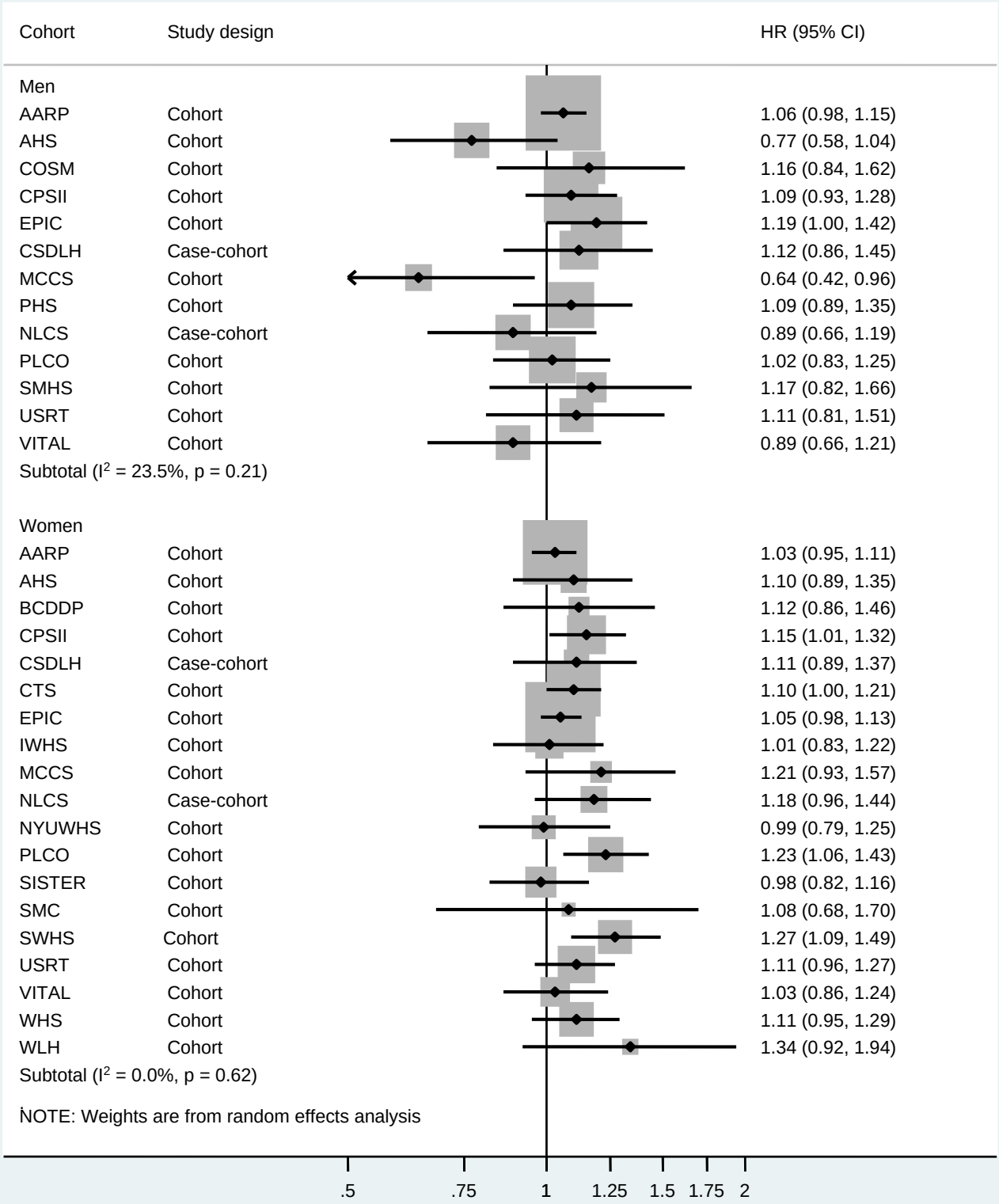
[c] Restricted to height values between 122-244 cm

[d] Restricted to BMI values between 15.0-59.9 kg/m^2

[e] Restricted to waist circumference values between 52-189 cm

[f] Additionally adjusted for young-adult BMI (per 5 kg/m^2)

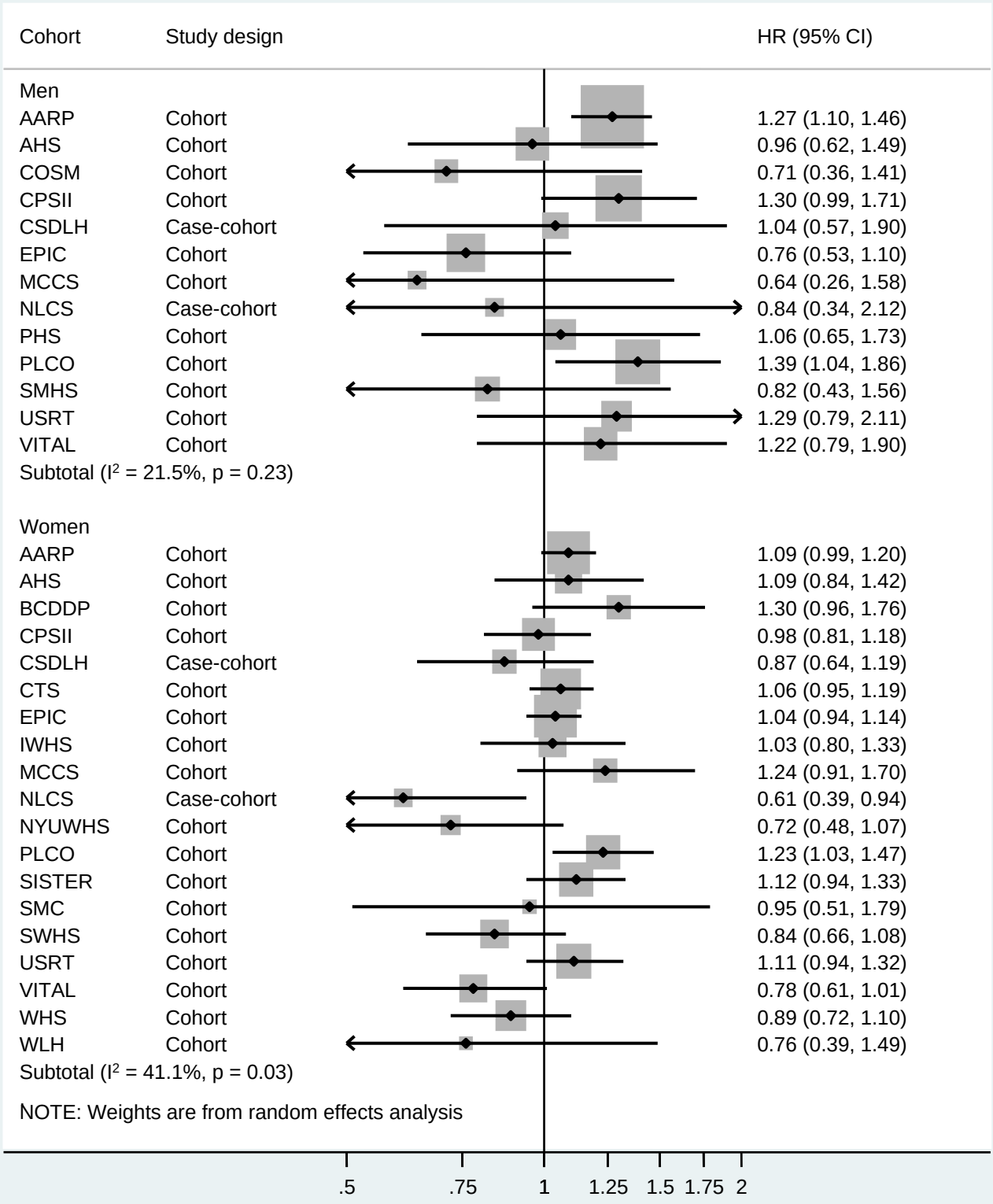
Supplementary Figure 1. Hazard ratios (HRs)[a,b] and 95% confidence intervals (CIs) for a 5 cm increase in height and thyroid cancer, by sex and cohort



[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, baseline BMI, and smoking status

[b] Restricted to height values between 122-244 cm

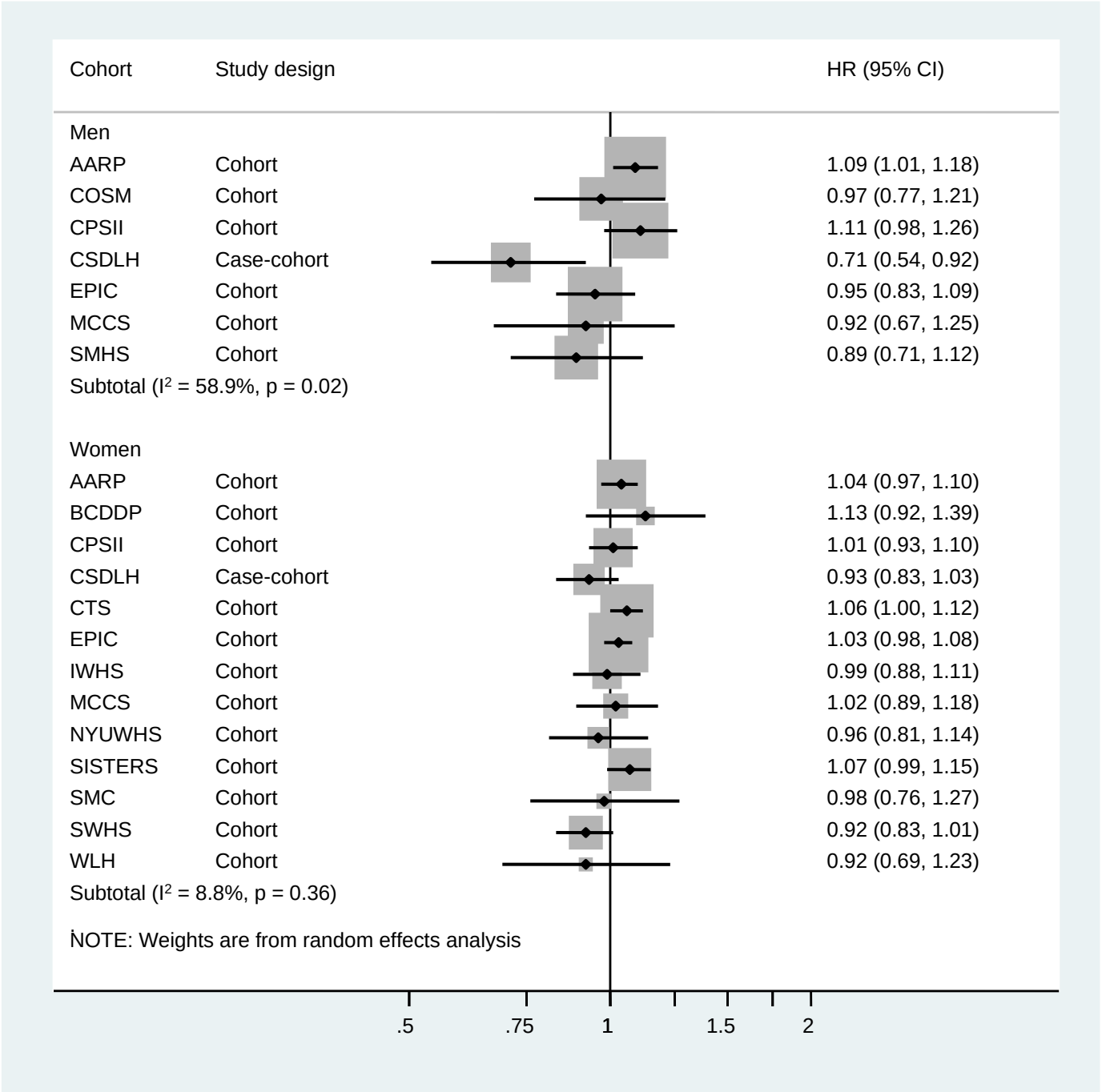
Supplementary Figure 2. Hazard ratios (HRs)[a,b] and 95% confidence intervals (CIs) for a 5 kg/m^2 increase in BMI and thyroid cancer, by sex and cohort



[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status

[b] Restricted to BMI values between 15.0-59.9 kg/m^2

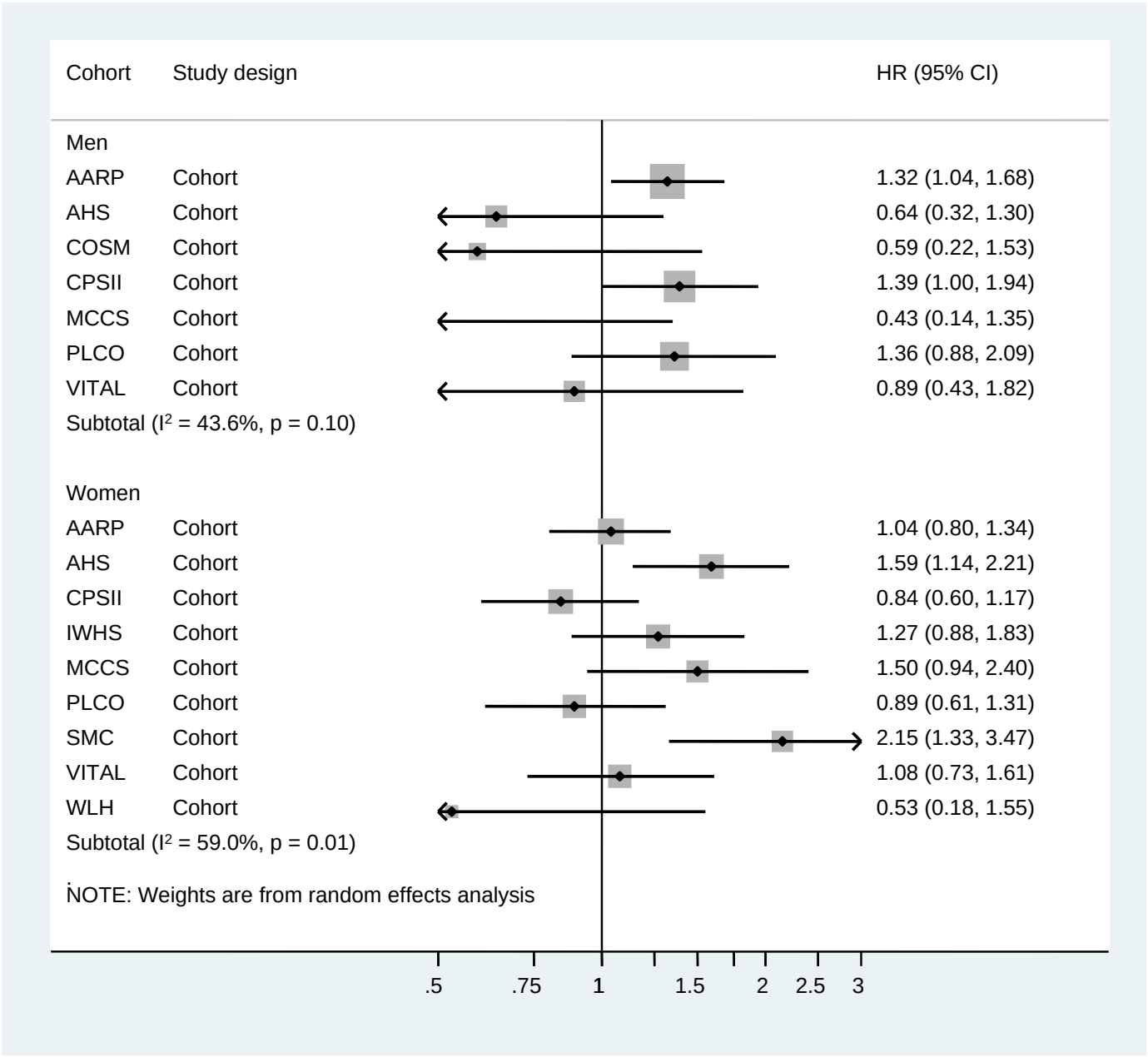
Supplementary Figure 3. Hazard ratios (HRs)[a,b] and 95% confidence intervals (CIs) for a 5 cm increase in waist circumference and thyroid cancer, by sex and cohort



[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status

[b] Restricted to waist circumference values between 52-189 cm

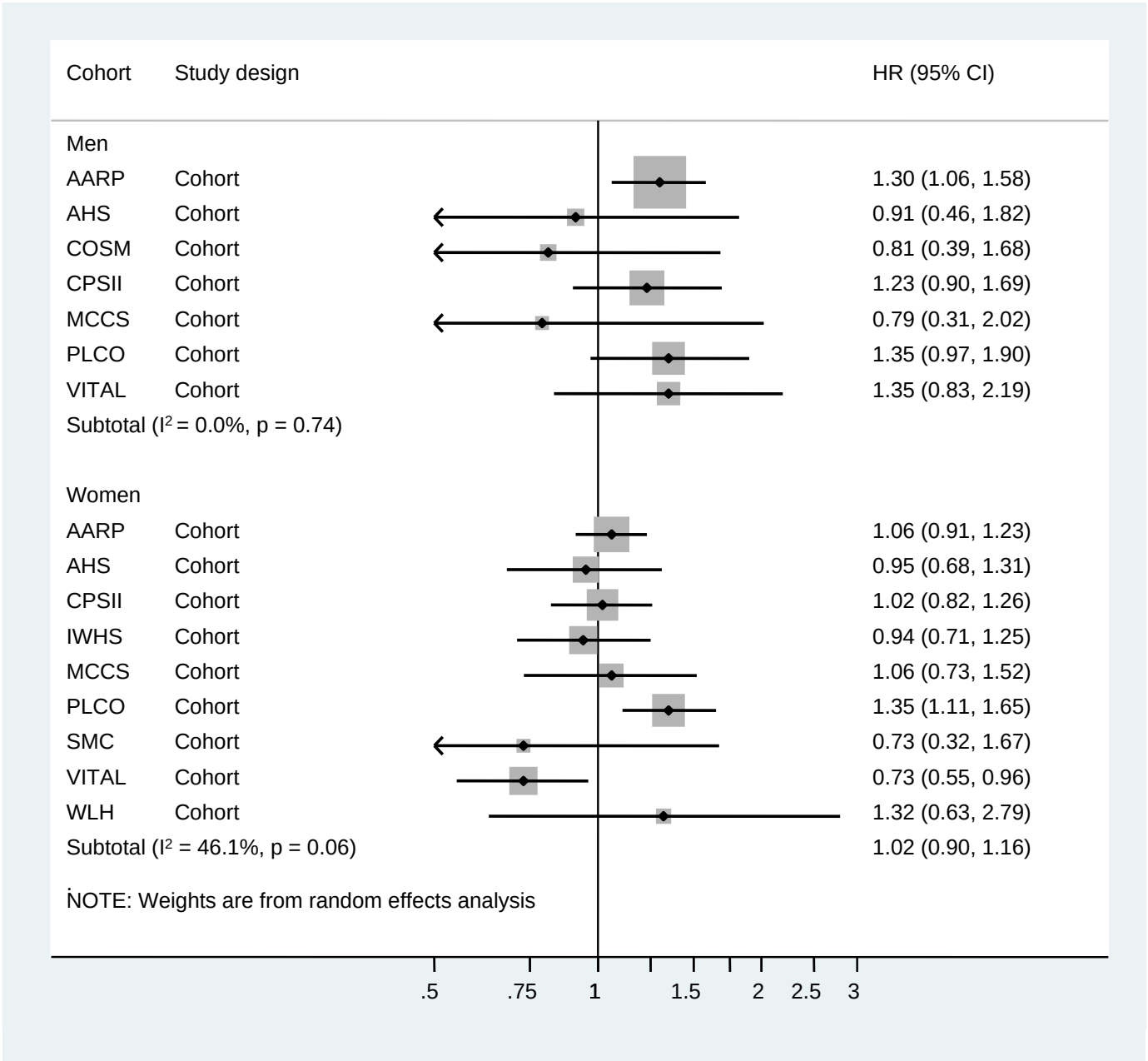
Supplementary Figure 4. Hazard ratios (HRs)[a,b] and 95% confidence intervals (CIs) for a 5 kg/m^2 increase in young-adult BMI and thyroid cancer, by sex and cohort



[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, and smoking status

[b] Restricted to BMI values between 15.0-59.9 kg/m^2

Supplementary Figure 5. Hazard ratios (HRs)[a] and 95% confidence intervals (CIs) for a 5 kg/m^2 gain in BMI during adulthood and thyroid cancer, by sex and cohort



[a] Adjusted for age (used as time metric), sex, alcohol intake, physical activity level, race, marital status, education, smoking status, and young-adult BMI (per 5 kg/m^2)