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# Obesity and Risk of Thyroid Cancer: Evidence from a Meta-Analysis of 21 Observational Studies

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**Background:** Several studies have evaluated the association between obesity and thyroid cancer risk. However, the results remain uncertain. In this study, we conducted a meta-analysis to assess the association between obesity and thyroid cancer risk.





**Material/Methods:** Published literature from PubMed, EMBASE, Springer Link, Ovid, Chinese Wanfang Data Knowledge Service Platform, Chinese National Knowledge Infrastructure (CNKI), and Chinese Biology Medicine (CBM) were retrieved before 10 August 2014. We included all studies that reported adjusted risk ratios (RRs), hazard ratios (HRs) or odds ratios (ORs), and 95% confidence intervals (CIs) of thyroid cancer risk.

**Results:** Thirty-two studies (n=12 620 676) were included in this meta-analysis. Obesity was associated with a significantly increased risk of thyroid cancer (adjusted RR=1.33; 95% CI, 1.24–1.42;  $I^2=25\%$ ). In the subgroup analysis by study type, increased risk of thyroid cancer was found in cohort studies and case-control studies. In subgroup analysis by sex, both obese men and women were at significantly greater risk of thyroid cancer than non-obese subjects. When stratified by ethnicity, significantly elevated risk was observed in Caucasians and in Asians. In the age subgroup analysis, both young and old populations showed increased thyroid cancer risk. Subgroup analysis on smoking status showed that increased thyroid cancer risks were found in smokers and in non-smokers. In the histology subgroup analyses, increased risks of papillary thyroid cancer, follicular thyroid cancer, and anaplastic thyroid cancer were observed. However, obesity was associated with decreased risk of medullary thyroid cancer.

**Conclusions:** Our results indicate that obesity is associated with an increased thyroid cancer risk, except medullary thyroid cancer.

**MeSH Keywords:** **Meta-Analysis • Obesity • Thyroid Neoplasms**

**Full-text PDF:** <http://www.medscimonit.com/abstract/index/idArt/892035>

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## Background

Thyroid cancer is a common endocrine malignancy that has rapidly increased in global incidence in recent decades [1]. In the United States, the 6.6% average annual increase in thyroid cancer incidence between 2000 and 2009 is the highest among all cancers [1]. Although the death rate of thyroid cancer is relatively low, the rate of disease recurrence or persistence is high, which is associated with increased incurability, morbidity, and mortality [2].

The prevalence of obesity has dramatically increased in the last 2 decades [3]. The diagnosis of obesity is often based on body mass index (BMI), calculated as weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ). The ideal BMI is between 18.5 and 24.9. Being obese is considered as having a BMI of 30.0 or greater [4]. Obesity has long been recognized as a trigger for many diseases, such as hypertension, hypercholesterolemia, diabetes, and insulin resistance. Additionally, during the last decades obesity has been consistently related to the development and progression of different types of cancers. An extensive review published a few years ago estimated that 20% of all cancers might be caused by obesity [5].

The relationship between obesity and risk of thyroid cancer has been studied for more than 10 years. Several studies found obesity to be a risk factor in thyroid cancer, but other studies showed no association between obesity and risk of thyroid cancer. These studies reached conflicting conclusions [6–26]. Two meta-analyses investigated the association between obesity and thyroid cancer risk [27,28], reporting that obesity was associated with thyroid cancer risk. However, recent studies did not confirm this result [23,25,26]. A single study may have insufficient statistical power to detect a slight effect. Furthermore, these 2 meta-analyses did not include all the observational studies. Therefore, in this study we conducted a meta-analysis to assess the association between obesity and thyroid cancer risk.

## Material and Methods

### Publication search

We searched PubMed, EMBASE, Springer Link, Ovid, Chinese Wanfang Data Knowledge Service Platform, Chinese National Knowledge Infrastructure (CNKI), and Chinese Biology Medicine (CBM) databases up to 10 August 2014. References from relevant articles were manually checked for further studies. Combination of the following terms were applied: ‘thyroid cancer’ OR ‘thyroid neoplasms’; ‘obesity’ OR ‘BMI’ OR ‘body mass index’.

### Inclusion criteria and data extraction

We included articles if they met all the following criteria: (1) evaluation of obesity and thyroid cancer risk, (2) using a case-control or cohort design, (3) adjusted risk ratios (RRs), hazard ratios (HRs), or odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Data were extracted by 2 authors independently. If they encountered conflicting evaluations, agreement was reached following a discussion; if they could not reach agreement, another author was consulted to resolve the debate. The following information was extracted from each study: first author, year of publication, study type, ethnicity, age, sex, years of follow-up, sample size, number of cases, covariates, adjusted OR/HR/OR, and the corresponding 95% CI of thyroid cancer risk.

### Statistical analysis

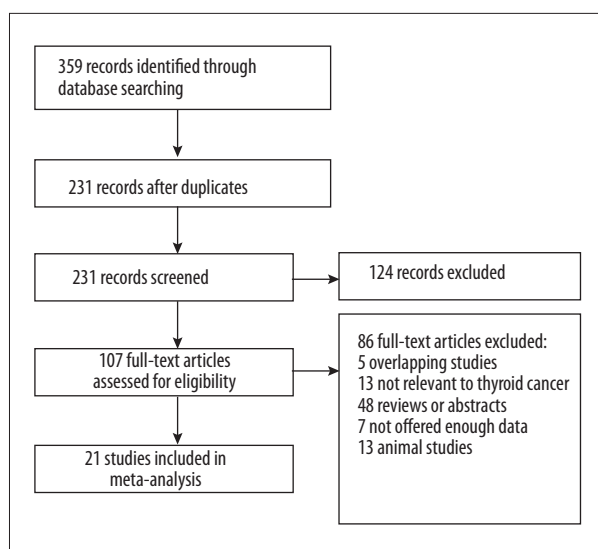
For thyroid cancer risk, we calculated summary RRs and 95% CIs for obesity versus normal weight. The random effects model was utilized. HRs and ORs were regarded as equivalent to RRs. Statistical heterogeneity among studies was evaluated using the  $Q$  and  $I^2$  statistics. For the  $I^2$  metric, we considered low, moderate, and high  $I^2$  values to be 25%, 50%, and 75%, respectively. We did subgroup analyses according to study type, sex, race, pneumonia type, age, smoking status, and histology. Cumulative meta-analysis was also performed. Sensitivity analysis was conducted by excluding 1 study at a time to explore whether the results were driven by 1 large study or by a study with an extreme result. Publication bias was investigated with funnel plots. Egger's test was also used to assess publication bias [29].

All statistical analyses were performed with STATA software (version 12.0, Stata Corporation, College Station, TX, USA). A threshold of  $P < 0.1$  was used to decide whether heterogeneity was present. In other cases,  $P$  values were 2-sided, with a significance level of 0.05.

## Results

### Study characteristics

The process of identifying relevant studies is shown in Figure 1. The initial search produced 359 studies. After exclusion of duplicates and irrelevant studies, 107 potentially eligible studies were selected. After detailed evaluations, 21 studies were selected for final meta-analysis [6–26]. A manual search of reference lists from these studies did not yield any new eligible study. Eleven studies reported 2 cohorts, and finally 32 studies ( $n = 12\,620\,676$ ) were included in this meta-analysis. There



**Figure 1.** Flow diagram of meta-analysis literature search results.

were 24 cohort studies and 8 case-control studies. Table 1 summarizes the main characteristics of these included studies.

### Quantitative data synthesis

The evaluations of the association between obesity and thyroid cancer risk are summarized in Table 2. Obesity was associated with a significantly increased risk of thyroid cancer when compared with normal weight (adjusted RR=1.33; 95% CI, 1.24–1.42;  $I^2=25\%$ ; Figure 2). In the subgroup analysis by study type, increased risk of thyroid cancer was found in cohort studies (RR=1.29; 95% CI, 1.20–1.37;  $I^2=21\%$ ) and case-control studies (OR=1.76; 95% CI, 1.36–2.28;  $I^2=0\%$ ), respectively. In the subgroup analysis according to sex, both obese men (RR=1.26; 95% CI, 1.13–1.40;  $I^2=9\%$ ) and women (RR=1.43; 95% CI, 1.25–1.64;  $I^2=33\%$ ) were significantly at risk of thyroid cancer. When stratified by ethnicity, significantly elevated risk was observed in Caucasians (RR=1.26; 95% CI, 1.18–1.33;  $I^2=9\%$ ) and in Asians (RR=1.54; 95% CI, 1.27–1.86;  $I^2=16\%$ ). In the age subgroup analysis, both young (RR=1.23; 95% CI, 1.13–1.34;  $I^2=0\%$ ) and old populations (RR=1.28; 95% CI, 1.11–1.46;  $I^2=32\%$ ) showed increased thyroid cancer risk. Subgroup analysis on smoking status showed that increased thyroid cancer risks were found in smokers (RR=1.10; 95% CI, 1.02–1.20;  $I^2=0\%$ ) and in non-smokers (RR=1.20; 95% CI, 1.11–1.28;  $I^2=0\%$ ). In the histology subgroup analyses, increased risks of papillary thyroid cancer (RR=1.26; 95% CI, 1.15–1.39;  $I^2=35\%$ ), follicular thyroid cancer (RR=1.29; 95% CI, 1.08–1.53;  $I^2=33\%$ ), and anaplastic thyroid cancer (RR=1.93; 95% CI, 1.23–3.03;  $I^2=0\%$ ) were observed. However, obesity was associated with decreased risk of medullary thyroid cancer (RR=0.50; 95% CI, 0.27–0.97;  $I^2=1\%$ ).

As shown in Figure 3, significant associations were evident with each addition of more data over time. The results showed that

the pooled ORs tended to be stable. A single study involved in the meta-analysis was deleted each time to reflect the influence of the individual data set on the pooled ORs, and the corresponding pooled ORs were not materially altered (Figure 4).

Funnel plot analysis was performed to assess the publication bias of studies. The shape of the funnel plot showed asymmetry (Figure 5). Egger's test found evidence of publication bias ( $P<0.01$ ).

### Discussion

The present meta-analysis, including 12 620 676 subjects from 32 observational studies, explored the association between obesity and thyroid cancer risk. We found that obesity was significantly associated with increased thyroid cancer risk. This result remained significant in various types of studies, such as cohort studies and case-control studies. In addition, obesity was significantly associated with thyroid cancer risk in males and females. Subgroup analyses stratified by ethnicity showed that obese Asians had higher thyroid cancer risk than Caucasians, but it is possible that random error may account for this difference. In fact, only 6 studies investigated the association between obesity and thyroid cancer risk in Asians. Thus, more studies with Asians are needed to validate this result. In addition, Price et al. [30] found that dynamic patterns of change for thyroid hormones were not different in Asian and Western Caucasian women. In the subgroup analysis by age, we found obesity exhibited increased thyroid cancer risk in young and old subjects. Actually, when we limited the meta-analysis to studies that controlled for age, a significant association between obesity and thyroid cancer risk remained (RR=1.30; 95% CI, 1.22–1.40;  $I^2=22\%$ ). This result indicates that the role of obesity was not selective by age. Cigarette smoking is a pro-inflammatory stimulus and an important risk factor for cancer. Several studies explored the interaction between obesity and smoking habits. Our results showed that both smokers and non-smokers had increased thyroid cancer risk. Furthermore, we investigated the association between obesity and different types of thyroid cancer. Obese subjects showed increased risks of papillary thyroid cancer, follicular thyroid cancer, and anaplastic thyroid cancer. Interestingly, there was an inverse association between obesity and medullary thyroid cancer risk. This result indicates that obesity may have a different effect on the pathogenesis and occurrence of thyroid cancer in different histologies. However, why obesity could influence the different histological types of thyroid cancer is still uncertain. Clearly, more studies are needed to elucidate the differential effect of obesity in the various thyroid cancer types.

There were several potential explanations for why obese individuals may have higher risk of thyroid cancer. First, there

**Table 1.** Characteristics of the case-control studies included in this meta-analysis.

First author	Year	Study type	Race	Age	Gender	Years of follow-up	Sample size	No. of Case	Covariate
Samanic 1	2004	Cohort	Caucasian	52	Men	11	3668486	875	Age and calendar year
Samanic 2	2004	Cohort	African	47	Men	12	832214	169	Age and calendar year
Oh	2005	Cohort	Asian	≥20	Men	10	781283	223	Age, smoking status, average amount of alcohol consumed per day, frequency of regular exercise for more than 30 minutes during a week, family history of cancer, and residency area at baseline
Rapp	2005	Cohort	Caucasian	42	Women	9.9	78484	61	Smoking, occupational group at baseline
Engeland 1	2006	Cohort	Caucasian	62	Men	23	963523	778	Age, year of birth, height
Engeland 2	2006	Cohort	Caucasian	58	Women	23	1037424	2268	Age, year of birth, height
Samanic	2006	Cohort	Caucasian	34	Men	19	362552	171	Age, calendar year, smoking status, and relative to normal weight subjects
Guignard 1	2007	Case-control	Caucasian	NA	Men	NA	58	39	Age, year of reference, and ethnic group
Guignard 2	2007	Case-control	Caucasian	NA	Women	NA	354	293	Age, year of reference, ethnic group, number of full-term pregnancies, miscarriages, and irregular menstruations
Suzuki 1	2008	Case-control	Asian	20–79	Men	NA	210	42	Smoking habit, drinking habit, regular exercise, family history of thyroid cancer, past history of thyroid diseases, total non-alcohol energy intake
Suzuki 2	2008	Case-control	Asian	20–79	Women	NA	655	131	Smoking habit, drinking habit, regular exercise, family history of thyroid cancer, past history of thyroid diseases, total non-alcohol energy intake, menopausal status, age at menarche, parity, hormone-replacement therapy
Song	2008	Cohort	Asian	56	Women	9	170481	367	Age, height, smoking status, alcohol intake, physical exercise, and pay level at study entry
Brindel 1	2008	Case-control	Caucasian	<56	Men	NA	33	18	Height, ethnicity, educational level, smoking, interviewer, radiation to head or neck for diagnosis before 15 years old
Brindel 2	2008	Case-control	Caucasian	<56	Women	NA	255	160	Height, ethnicity, educational level, smoking, interviewer, radiation to head or neck for diagnosis before 15 years old, and also for the number of full-term pregnancies and menopausal status among women
Leitzmann	2009	Cohort	Caucasian	62	Women	8	484326	352	Age, sex, physical activity, race, education, smoking status, current alcohol use; and oral contraceptive use among women

**Table 1 continued.** Characteristics of the case-control studies included in this meta-analysis.

First author	Year	Study type	Race	Age	Gender	Years of follow-up	Sample size	No. of Case	Covariate
Meinhold 1	2009	Cohort	Caucasian	43	Men	23	21207	40	Birth year, smoking status, body mass index, number of personal radiographs to the head or neck, cumulative occupational radiation dose, and medical history of benign thyroid conditions
Meinhold 2	2009	Cohort	Caucasian	39	Women	23	69506	242	Birth year, smoking status, body mass index, number of personal radiographs to the head or neck, cumulative occupational radiation dose, and medical history of benign thyroid conditions
Clavel-Chapelon	2010	Cohort	Caucasian	49	Women	13	91909	317	Age, stratified on year of birth, history of goiter or thyroid nodules, smoking status, iodine
Clero	2010	Case-control	Caucasian	18–78	Mixed*	NA	776	554	Ethnicity, educational level, smoking, radiation to head or neck for diagnosis before 15 years old, and also for the number of full-term pregnancies among women
Almquist 1	2011	Cohort	Caucasian	43	Men	12	289866	133	Age, smoking
Almquist 2	2011	Cohort	Caucasian	44	Women	12	288834	255	Age, smoking
Kitahara	2011	Cohort	Caucasian	58	Mixed*	10	848932	1156	Education, race, marital status, smoking, alcohol intake, sex
Kabat	2012	Cohort	Caucasian	44	Women	11	144319	294	Age, education, pack-years of smoking, alcohol intake, history of benign thyroid disease
Marcello	2012	Case-control	Caucasian	34	Mixed	NA	103	115	Age, gender, and ethnicity
Rinaldi 1	2012	Cohort	Caucasian	52	Men	6	150000	58	Center, age, smoking
Rinaldi 2	2012	Cohort	Caucasian	51	Women	6	370000	508	Center, age, smoking
Han 1	2013	Cohort	Asian	51	Men	1	9275	127	Age, smoking status, and TSH levels
Han 2	2013	Cohort	Asian	50	Women	1	8138	140	Age, smoking status, and TSH levels
Farfel 1	2014	Cohort	Caucasian	16–19	Men	48	1145865	437	Year of birth, country of origin, and years of schooling
Farfel 2	2014	Cohort	Caucasian	16–19	Women	16	478445	323	Year of birth, country of origin, and years of schooling
Kitahara 1	2014	Cohort	Caucasian	7–13	Men	39	162632	64	Birth cohort
Kitahara 2	2014	Cohort	Caucasian	7–13	Women	39	158453	171	Birth cohort

\* Information of gender can be extracted. TSH – thyroid stimulating hormone; NA – not available.

is a clinical association between higher serum thyroid-stimulating hormone (TSH) levels and increased risk of malignancy in human thyroid nodules and advanced stage of the disease [31,32]. Some cross-sectional studies in euthyroid subjects demonstrated a positive association between serum TSH and

BMI [33]. Second, leptin levels were higher in thyroid cancer patients compared to healthy subjects in a case-control study [34]. Leptin was also shown to enhance migration of PTC cells [35]. Third, insulin resistance, a common metabolic perturbation in obesity, may play a role in thyroid tumor growth, with



**Table 2.** Main result and subgroup analyses of this meta-analysis.

Characteristics	No. of studies	Test of association				Model	Heterogeneity		
		RR (95% CI)*		Z	P Value		I <sup>2</sup>	P Value	I <sup>2</sup> (%)
All studies	32	1.33	(1.24–1.42)	7.94	<0.00001	R	41.26	0.10	25
Study type									
Cohort study	24	1.29	(1.20–1.37)	7.52	<0.00001	R	28.95	0.18	21
Case-control study	8	1.76	(1.36–2.28)	4.33	<0.0001	R	4.78	0.69	0
Gender									
Male	13	1.26	(1.13–1.40)	4.19	<0.0001	R	6.41	0.89	0
Female	13	1.43	(1.25–1.64)	5.20	<0.00001	R	14.97	0.13	33
Race									
Asian	6	1.54	(1.27–1.86)	4.41	<0.0001	R	5.97	0.31	16
Caucasian	25	1.26	(1.18–1.33)	7.53	<0.00001	R	26.34	0.34	9
Age									
≤50 years	6	1.23	(1.13–1.34)	4.84	<0.00001	R	2.25	0.81	0
>50 years	6	1.28	(1.11–1.46)	3.44	0.0006	R	5.89	0.21	32
Smoking status									
Smoker	3	1.10	(1.02–1.20)	2.41	0.02	R	0.11	0.95	0
Non-smoker	4	1.20	(1.11–1.28)	4.95	<0.00001	R	0.93	0.82	0
Histology									
Papillary thyroid cancer	9	1.26	(1.15–1.39)	4.73	<0.00001	R	12.34	0.14	35
Follicular thyroid cancer	6	1.29	(1.08–1.53)	7.45	0.005	R	7.45	0.19	33
Medullary thyroid cancer	3	0.50	(0.27–0.91)	2.25	0.02	R	2.01	0.37	1
Anaplastic thyroid cancer	3	1.93	(1.23–3.03)	2.85	0.004	R	1.97	0.37	0

\* The multivariable-adjusted RRs with 95% CIs were pooled. RR – risk ratio; CI – confidence intervals; R – random effects model.

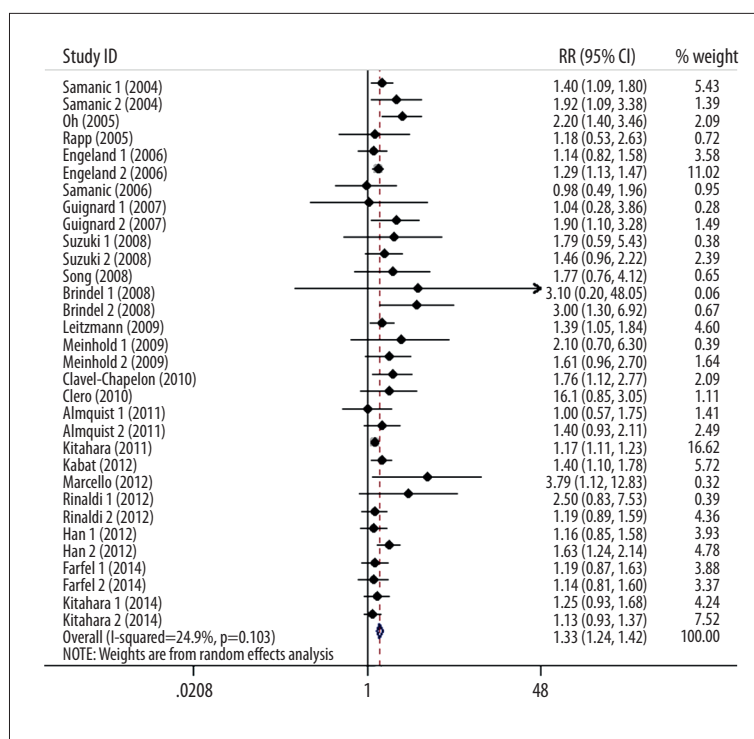
insulin directly binding to insulin receptors or stimulating insulin-like growth factor, estrogen, or other hormones, such as TSH, to enhance the proliferation of thyroid cancer cells [36].

Obesity is a major public health problem worldwide and its prevalence continues to increase [37,38]. The incidence of thyroid cancer has also been increasing in many countries [39,40]. Studies on the positive association between obesity and thyroid cancer will have important implications in the future, because obesity is a modifiable risk factor [41–45]. Future studies on the effects of weight gain or weight loss on altering risk for thyroid cancer are essential.

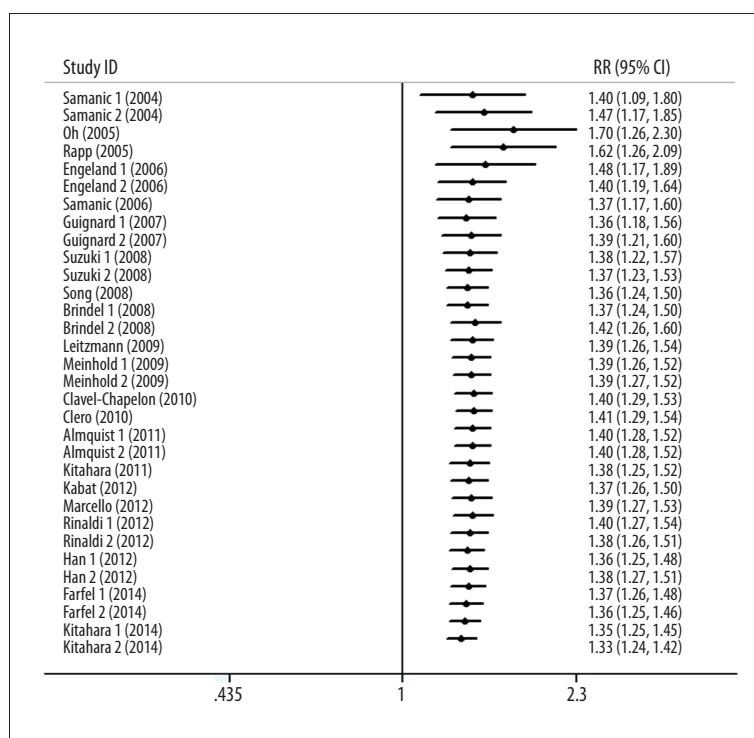
Our result was consistent with 2 previous meta-analyses [27,28]. We also found a significant association between obesity and thyroid cancer risk. However, our study had some

advantages. First, it was the first study of interactions between age, histology, and smoking status specificities and obesity. Second, the methodological issues for meta-analyses, such as one-way sensitivity analysis and cumulative meta-analysis, were well investigated. Third, this meta-analysis included 32 studies (n=12 620 676) and thus was more conclusive and more powerful than previous studies.

Results from one-way sensitivity analysis and cumulative meta-analysis suggest the high stability and reliability of our results. Heterogeneity and publication bias can be important influences on the results of meta-analyses. In our study no significant heterogeneity was observed. Additionally, funnel plots and Egger's tests were used to find potential publication bias. The results indicated that there was significant publication bias. Thus, our results should be interpreted with caution



**Figure 2.** Forest plot for the association between obesity and thyroid cancer risk.

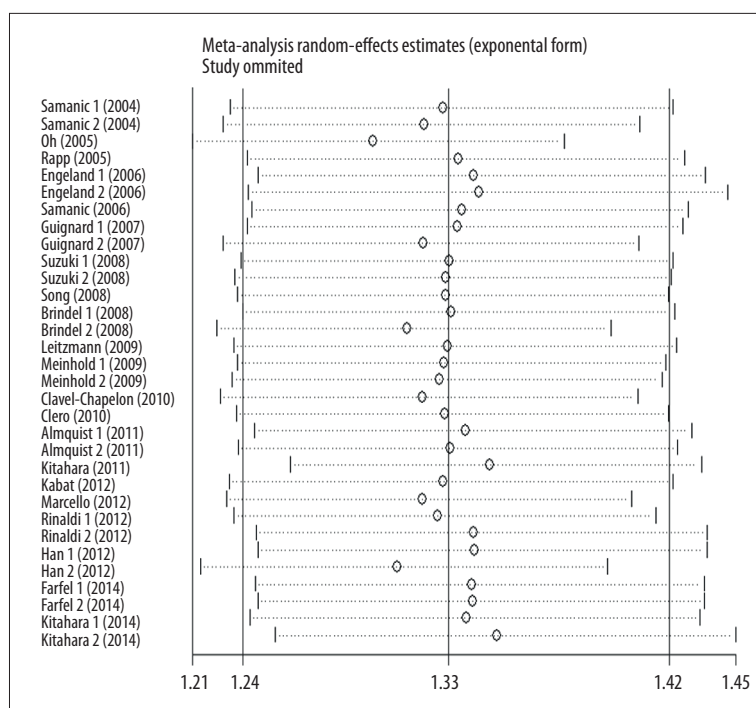


**Figure 3.** Cumulative meta-analysis for the association between obesity and thyroid cancer risk.

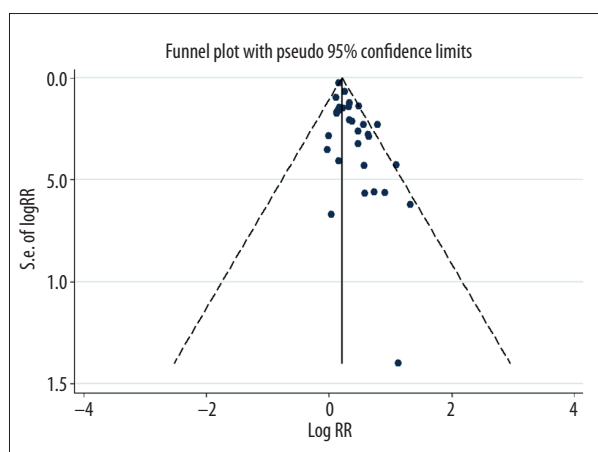
and more studies are needed to confirm the effect of obesity on thyroid cancer risk.

Several limitations need to be addressed. First, the number of published studies was not sufficient for a comprehensive analysis, particularly for Africans. Second, all the studies included

in this meta-analysis used a case-control or cohort design, which are susceptible to recall and selection biases. Third, because this meta-analysis investigated only obesity, we cannot exclude the possibility that the observed associations may be confounded by other lifestyle factors, such as lower physical activity or dietary factors.



**Figure 4.** Sensitivity analysis for the association between obesity and thyroid cancer risk.



**Figure 5.** Begg's funnel plot for publication bias.

## Conclusions

This meta-analysis found a significant association between obesity and thyroid cancer risk, except medullary thyroid cancer. Further studies in more ethnic groups, especially African, are warranted to validate this result.

## Conflicts of interest

None.

## References:

- Jemal A, Bray F, Center MM et al: Global cancer statistics. *Cancer J Clin*, 2012; 61: 69–90
- Tuttle RM, Ball DW, Byrd D et al: Thyroid carcinoma. *J Natl Compr Canc Netw*, 2010; 8: 1228–74
- Baskin ML, Ard J, Franklin F et al: Prevalence of obesity in the United States. *Obes Rev*, 2005; 6: 5–7
- Berrington de Gonzalez A, Hartge P, Cerhan JR et al: Body-mass index and mortality among 1.46 million white adults. *N Engl J Med*, 2010; 363: 2211–19
- Wolin KY, Carson K, Colditz GA: Obesity and cancer. *Oncologist*, 2010; 15: 556–65
- Samanic C, Gridley G, Chow WH et al: Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control*, 2004; 15: 35–43
- Oh SW, Yoon YS, Shin SA: 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*, 2005; 23: 4742–54
- Rapp K, Schroeder J, Klenk J et al: Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. *Br J Cancer*, 2005; 93: 1062–67
- Engeland A, Tretli S, Akslen LA et al: Body size and thyroid cancer in two million Norwegian men and women. *Br J Cancer*, 2006; 95: 366–70
- Samanic C, Chow WH, Gridley G et al: Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control*, 2006; 17: 901–9
- Guignard R, Truong T, Rougier Y et al: Alcohol drinking, tobacco smoking, and anthropometric characteristics as risk factors for thyroid cancer: a countrywide case-control study in New Caledonia. *Am J Epidemiol*, 2007; 166: 1140–49
- Suzuki T, Matsuo K, Hasegawa Y et al: Anthropometric factors at age 20 years and risk of thyroid cancer. *Cancer Causes Control*, 2008; 19: 1233–42
- Song YM, Sung J, Ha M: Obesity and risk of cancer in postmenopausal Korean women. *J Clin Oncol*, 2008; 26: 3395–402



14. Brindel P, Doyon F, Rachédi F et al: Anthropometric factors in differentiated thyroid cancer in French Polynesia: a case-control study. *Cancer Causes Control*, 2009; 20: 581–90
15. Leitzmann MF, Brenner A, Moore SC et al: Prospective study of body mass index, physical activity and thyroid cancer. *Int J Cancer*, 2010; 126: 2947–56
16. Meinhold CL, Ron E, Schonfeld SJ et al: Nonradiation risk factors for thyroid cancer in the US Radiologic Technologists Study. *Am J Epidemiol*, 2010; 171: 242–52
17. Clavel-Chapelon F, Guillas G, Tondeur L et al: Risk of differentiated thyroid cancer in relation to adult weight, height and body shape over life: the French E3N cohort. *Int J Cancer*, 2010; 126: 2984–90
18. Cléro E, Leux C, Brindel P et al: Pooled analysis of two case-control studies in New Caledonia and French Polynesia of body mass index and differentiated thyroid cancer: the importance of body surface area. *Thyroid*, 2010; 20: 1285–93
19. Almqvist M, Johansen D, Björge T et al: Metabolic factors and risk of thyroid cancer in the Metabolic syndrome and Cancer project (Me-Can). *Cancer Causes Control*, 2011; 22: 743–51
20. Kitahara CM, Platz EA, Freeman LE et al: Obesity and thyroid cancer risk among U.S. men and women: a pooled analysis of five prospective studies. *Cancer Epidemiol Biomarkers Prev*, 2011; 20: 464–72
21. Kabat GC, Kim MY, Thomson CA et al: Anthropometric factors and physical activity and risk of thyroid cancer in postmenopausal women. *Cancer Causes Control*, 2012; 23: 421–30
22. Marcello MA, Sampaio AC, Geloneze B et al: Obesity and excess protein and carbohydrate consumption are risk factors for thyroid cancer. *Nutr Cancer*, 2012; 64: 1190–95
23. Rinaldi S, Lise M, Clavel-Chapelon F et al: Body size and risk of differentiated thyroid carcinomas: findings from the EPIC study. *Int J Cancer*, 2012; 131: E1004–14
24. Han JM, Kim TY, Jeon MJ et al: Obesity is a risk factor for thyroid cancer in a large, ultrasonographically screened population. *Eur J Endocrinol*, 2013; 168: 879–86
25. Farfel A, Kark JD, Derazne E et al: Predictors for Thyroid Carcinoma in Israel: A National Cohort of 1,624,310 Adolescents Followed for up to 40 Years. *Thyroid*, 2014; 24: 987–93
26. Kitahara CM, Gamborg M, Berrington de González A et al: Childhood height and body mass index were associated with risk of adult thyroid cancer in a large cohort study. *Cancer Res*, 2014; 74: 235–42
27. Zhao ZG, Guo XG, Ba CX et al: Overweight, obesity and thyroid cancer risk: a meta-analysis of cohort studies. *J Int Med Res*, 2012; 40: 2041–50
28. Peterson E, De P, Nuttall R: BMI, Diet and Female Reproductive Factors as Risks for Thyroid Cancer: A Systematic Review. *PLoS One*, 2012; 7: e29177
29. Egger M, Smith GD, Schneider M et al: Bias in meta-analysis detected by a simple, graphical test. *BMJ*, 1997; 315: 629–34
30. Price A, Obel O, Cresswell J et al: Comparison of thyroid function in pregnant and non-pregnant Asian and western Caucasian women. *Clin Chim Acta*, 2001; 308: 91–98
31. Fiore E, Vitti P: Serum TSH and risk of papillary thyroid cancer in nodular thyroid disease. *J Clin Endocrinol Metab*, 2012; 97: 1134–45
32. McLeod DS, Cooper DS, Ladenson PW et al: Prognosis of differentiated thyroid cancer in relation to serum thyrotropin and thyroglobulin antibody status at time of diagnosis. *Thyroid*, 2014; 24: 35–42
33. Fox CS, Pencina MJ, D'Agostino RB et al: Relations of thyroid function to body weight: cross-sectional and longitudinal observations in a community-based sample. *Arch Intern Med*, 2008; 168: 587–92
34. Hedayati M, Yaghmaei P, Pooyamanesh Z et al: Leptin: a correlated Peptide to papillary thyroid carcinoma? *J Thyroid Res*, 2011; 2011: 832163
35. Cheng SP, Yin PH, Hsu YC et al: Leptin enhances migration of human papillary thyroid cancer cells through the PI3K/AKT and MEK/ERK signaling pathways. *Oncol Rep*, 2011; 26: 1265–71
36. Hursting SD, Lashinger LM, Wheatley KW et al: Reducing the weight of cancer: mechanistic targets for breaking the obesity-carcinogenesis link. *Best Pract Res Clin Endocrinol Metab*, 2008; 22: 659–69
37. Flegal KM, Carroll MD, Kit BK et al: Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA*, 2012; 307: 491–97
38. Ljungvall A, Zimmerman FJ: Bigger bodies. long-term trends and disparities in obesity and body-mass index among U.S. adults, 1960–2008. *Social Science & Medicine*, 2012; 75: 109–19
39. Liang K, He L, Dong W, Zhang H: Risk factors of central lymph node metastasis in cN0 papillary thyroid carcinoma: A study of 529 patients. *Med Sci Monit*, 2015; 21: CLR807–11
40. Pappa T, Alevizaki M: Obesity and Thyroid Cancer: A Clinical Update. *Thyroid*, 2014; 2: 190–99
41. Blumentals WA, Hwu P, Kobayashi N et al: Obesity in hospitalized type 2 diabetes patients: a descriptive study. *Med Sci Monit*, 2013; 19: 359–65
42. Stepień M, Stepień A, Wlazeł RN et al: Obesity indices and adipokines in non-diabetic obese patients with early stages of chronic kidney disease. *Med Sci Monit*, 2013; 19: 1063–72
43. Dong W, Zhang H, Zhang P et al: The changing incidence of thyroid carcinoma in Shenyang, China before and after universal salt iodization. *Med Sci Monit*, 2013; 19: 49–53
44. Singh A, Butuc R, Lopez R: Metastatic papillary thyroid carcinoma with absence of tumor focus in thyroid gland. *Am J Case Rep*, 2013; 14: 73–75
45. Giaginis C, Demetriou N, Alexandrou P et al: Receptor-binding cancer antigen expressed on SiSo cells (RCAS1) expression in human benign and malignant thyroid lesions. *Med Sci Monit*, 2012; 18(4): BR123–29