Trends in Oncology Vol 5 Issue 1 2023
DOI: 10.37155/2717–5278–0501–4

Original Research Article

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Meta-analysis of the Incidence of Thyroid Nodules in China and a Survey on the Incidence of Thyroid Nodules in Fuyu County, Heilongjiang Province

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Fund: Outstanding Youth Project of Harbin Medical University Cancer Hospital (JCQN2018-04)

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How to cite: Rui Xie, Guo-Cheng Liu, Hong-Yu Li, Xin Qu, Bing-Shuo Liu , Hong-Tao Hu. Meta-analysis of the Incidence of Thyroid Nodules in China and a Survey on the Incidence of Thyroid Nodules in Fuyu County, Heilongjiang Province.[J]. *Trends in Oncology*,2023, vol. 5(iss. 1). DOI: 10.37155/2717-5278-0501-4

Abstract: Objective: This study aimed to understand the incidence of thyroid nodules in China through a meta-analysis and analyze the epidemiology of thyroid nodules in the adult population of Fuyu County, Heilongjiang Province, providing assistance for clinical diagnosis and treatment. **Methods:** We searched the China National Knowledge Infrastructure (CNKI), Wanfang Data, and VIP databases to collect literature published from 2010 to 2021 on the incidence of thyroid nodules in China. Stata 15.1 software was used to estimate the prevalence, and subgroup analyses were performed for age, gender, and blood pressure factors. We also analyzed the health examination data of 10,911 adults in Fuyu County from 2016 to 2020, gathered during the Harbin Medical University Cancer Hospital's precision poverty alleviation program "Healthy Prosperity Tour." The prevalence of thyroid nodules in the study population was calculated based on thyroid ultrasound results, and statistical analysis was conducted using SPSS 26.0 software. **Results:** The meta-analysis included a total of 330 studies. The results showed that the overall incidence of thyroid nodules in China was 34.7% [95% *CI* (32.9%, 36.5%)]. The incidence in males was 30.1% [95% *CI* (28.2%, 32.1%)], and in females, it was 40.1% [95% *CI* (27.8%, 42.4%)]. The total incidence of thyroid nodules in the three northeastern provinces (Heilongjiang, Jilin, and Liaoning) was 34.8% [95% *CI* (23.3%, 46.2%)], with a male incidence of 33.2% and a female incidence of 44.5%. The survey in Fuyu County revealed an overall incidence of 48.8% (5322/10911) for thyroid nodules. The female incidence was 53.3% (3937/7390), significantly higher than the male incidence of 39.3% (1385/3521), with statistically significant differences. Logistic regression analysis showed that the final factors included in the regression model were gender and age ($P < 0.05$), while blood pressure had no significant impact on thyroid nodules ($P > 0.05$). **Discussion:** The incidence of thyroid nodules in China is relatively high,

1. Methods

with a significantly higher incidence in females than males, increasing with age. The incidence of thyroid nodules in Fuyu County is higher than in Heilongjiang Province, the three northeastern provinces, and the national average, warranting increased attention.

Thyroid nodules refer to scattered lesions caused by localized abnormal growth of thyroid cells, and they are a common disorder of the endocrine system[1]. Over 95% of thyroid nodules are benign, and surgical treatment is generally unnecessary[2]. In the absence of thyroid dysfunction, most patients do not exhibit significant clinical symptoms. Currently, high-resolution ultrasound examination is the preferred method for assessing thyroid nodules, and ultrasound can also assist in distinguishing between benign and malignant thyroid nodules. Neck ultrasound examination is recommended for all thyroid nodule patients.

With the widespread application of ultrasound technology and increased awareness of personal health, the detection rate of asymptomatic thyroid nodules has generally increased[3]. The incidence of thyroid nodules is gradually rising, possibly related to factors such as high mental stress, fast-paced lifestyles, lack of exercise, and changes in dietary structure. It is worth noting that there is an issue of over-treatment for thyroid nodules in China[4]. Patients with thyroid nodules should choose scientific treatment methods, undergo regular follow-ups, and avoid blind treatment. In this study, a meta-analysis was conducted on the reported incidence of thyroid nodules in various provinces and cities nationwide, analyzing the overall incidence of thyroid nodules in the country. By comparing the incidence of thyroid nodules in Fuyu County, Qiqihar City, Heilongjiang Province, with the nationwide meta-analysis results, reliable evidence is provided for the prevention and treatment of thyroid nodules.

Keywords: Thyroid nodules; Incidence rate; Meta-analysis; Ultrasound examination

1. Methods

1.1 Study Subjects

We selected the adult population who underwent thyroid color Doppler ultrasound examinations during the rural health check-ups organized by the Harbin Medical University Cancer Hospital's precision poverty alleviation program "Healthy Prosperity Tour" in Fuyu County, Qiqihar City, Heilongjiang Province, from 2016 to 2020 as the study subjects. A total of 10,911 individuals with complete health examination data were included, comprising 3,521 males and 7,390 females. The age distribution ranged from 18 to 94 years (see Figure 1), with an average age of (58.4±11.2) years. The grouping criteria for individuals with hypertension were defined as follows: systolic blood pressure ⩾ 140 mmHg or diastolic blood pressure ⩾ 90 mmHg.

1.2 Instruments and Methods

The subjects were positioned in a supine posture with elevated shoulders, tilting their heads backward to fully expose the anterior neck area. The ultrasound examinations were conducted by experienced clinical ultrasound physicians using the UMT-500 model ultrasound diagnostic device manufactured by Shenzhen Mindray Bio-Medical Electronics Co., Ltd.

1.3 Thyroid Nodule Diagnostic Criteria

The diagnostic criteria for thyroid nodules were referenced from the "Guidelines for the Diagnosis and Treatment of Thyroid Nodules and Differentiated Thyroid Cancer" developed by the Chinese Medical Association Endocrinology Society[1].

1.4 Search Strategy

Literature was retrieved through the China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform (Wangfang Data), and VIP databases. The search term used was (Thyroid Nodules), and the search was conducted in June 2021. The publication date was restricted to articles published between 2010 and 2021.

1.5 Literature Selection

Inclusion Criteria: (1) Studies focused on the population of thyroid nodules in mainland China. (2) Data including the incidence rate of thyroid nodules. (3) The diagnostic method for thyroid nodules involved the use of an ultrasound diagnostic device. (4) Published in core journals.

Exclusion Criteria: (1) Data with errors or incompleteness. (2) Duplicate publications. (3) Studies with the same study population. (4) Conference papers or review articles.

Literature was rigorously screened based on the inclusion and exclusion criteria. The initial screening was conducted based on titles and abstracts, followed by a secondary screening involving a thorough reading of the full texts to exclude literature that did not meet the criteria. Two evaluators independently assessed the included literature. In cases of divergent opinions, discussions were held, or a third evaluator was consulted to make the final decision on inclusion.

1.6 Data Extraction

Two evaluators independently extracted relevant data and cross-checked their findings. In case of discrepancies, a third researcher reassessed the data. Excel spreadsheets were used to organize and extract information from the literature. The extracted information from the literature primarily included the first author, publication year, total number of cases included, number of cases with thyroid nodules, gender distribution, age distribution, blood pressure, and geographical region.

1.7 Statistical Methods

Meta-analysis was performed using Stata 15.1 software. Rates and 95% confidence intervals were calculated, and forest plots were generated. A funnel plot was used to assess publication bias. I^2 analysis was employed to evaluate heterogeneity among the included study results. If statistical heterogeneity was present between studies ($I^2 > 50\%$), a random-effects model was used for analysis; otherwise, a fixed-effects model was applied. Sensitivity analysis was conducted to assess the robustness of the results concerning heterogeneity. A significance level of $P < 0.05$ indicated statistical significance. Statistical analyses were performed using the SPSS 26.0 software package. χ^2 tests were used for the comparison of detection rates, and single-factor logistic regression analysis was employed for factor analysis. A significance level of $P < 0.05$ indicated statistical significance.

2. Results

2.1 Incidence of Thyroid Nodules in Fuyu County

Among the 10,911 individuals surveyed, 5,322 cases were detected with thyroid nodules, resulting in a total incidence rate of 48.8% (5,322/10,911). The incidence rate in females was 53.3% (3,937/7,390), significantly higher than the incidence rate in males of 39.3% (1,385/3,521), and this difference was statistically significant ($\chi^2 = 185.46$, $P < 0.05$).

The incidence rates of thyroid nodules in different age groups were as follows: 28.5% in the 18-39 age group, 44.8% in the 40-59 age group, and 54.8% in the 60 and above age group. There were significant differences in the incidence rates of thyroid nodules among different age groups in the total population, showing an increasing trend with age ($\chi^2 = 211.60$, $P < 0.05$). The incidence rate in individuals with high blood pressure was 49.8%, higher than the incidence rate in those with normal blood pressure (47.3%), and this difference was statistically significant ($\chi^2 = 6.753$, $P < 0.05$). See Table 1.

2.2 Logistic Regression Analysis of Risk Factors for Thyroid Nodules

Multivariable logistic regression analysis was conducted, incorporating gender, age, and blood pressure as covariates based on the statistically significant differences identified through χ^2 tests. The dependent variable was the presence or absence of thyroid nodules. The final factors included in the regression model were gender and age ($P < 0.05$), while blood pressure showed no significant impact on thyroid nodules ($P > 0.05$). See Table 2.

2.3 Literature Characteristics

Initially, a total of 11,131 articles were identified through the literature search. Following the inclusion and exclusion criteria, as well as the initial screening based on titles and abstracts, 453 articles were selected for full-text reading. After the secondary screening, a total of 330 articles were included in the study (see Figure 2). The cumulative sample size was 2,165,080 individuals, with 651,435 cases of thyroid nodules identified. The surveyed locations spanned 30 provinces and cities, including Beijing, Shanghai, Heilongjiang, Jiangsu, Hainan, Xinjiang, among others.

2.4 Meta-analysis of the Incidence of Thyroid Nodules in Mainland China

The results of the meta-analysis revealed significant heterogeneity among the studies ($I^2 = 100.0\%$, $P < 0.05$), and therefore, a random-effects model was employed. The combined results indicated that the incidence of thyroid nodules in mainland China was 34.7% [95% *CI* (32.9%, 36.5%)].

2.5 Subgroup Analysis, refer to Table 3 and Table 4

2.5.1 Subgroup Analysis by Gender

In the national population, the incidence of thyroid

nodules in males was 30.1% [95% *CI* (28.2%, 32.1%)], while in females, it was 40.1% [95% *CI* (27.8%, 42.4%)]. Among the population in the three northeastern provinces, the incidence of thyroid nodules in males was 33.2% [95% *CI* (27.1%, 39.4%)], and in females, it was 44.5% [95% *CI* (38.2%, 50.9%)].

2.5.2 Subgroup Analysis by Age

In the age groups < 18 years, 18-39 years, 40-59 years, and ⩾ 60 years, the incidence of thyroid nodules was 11.8% [95% *CI* (10.1%, 13.5%)], 24.1% [95% *CI* (22.2%, 26.0%)], 40.0% [95% *CI* (36.5%, 43.4%)], and 54.3% [95% *CI* (51.0%, 57.6%)], respectively. The incidence of thyroid nodules in the national population showed an increasing trend with age.

2.5.3 Subgroup Analysis by Region

The provinces with the highest incidence rates of thyroid nodules were Hainan Province at 74.0% [95% *CI* (71.9%, 76.1%)], Shanghai at 53.8% [95% *CI* (48.1%, 59.4%)], and Jiangxi Province at 52.5% [95% *CI* (49.5%, 55.4%)]. The province with the lowest incidence rate was Guizhou Province at 12.3% [95% *CI* (0.3%, 24.3%)].

In the three northeastern provinces (Heilongjiang, Jilin, and Liaoning), the overall incidence rate of thyroid nodules was 34.8% [95% *CI* (23.3%, 46.2%)]. The incidence rate in Heilongjiang Province was 37.6% [95% *CI* (29.0%, 46.1%)], in Jilin Province it was 23.0% [95% *CI* (10.3%, 35.6%)], and in Liaoning Province it was 37.6% [95% *CI* (10.9%, 64.3%)].

2.6 Publication Bias and Sensitivity Analysis

Analysis of funnel plots for each group revealed the presence of publication bias. However, after conducting sensitivity analysis by excluding the influence of the combined effect values for each individual study, the results did not show significant changes.

3. Discussion

Meta-analysis, also known as "synthesis analysis," is a statistical method for systematically quantitatively synthesizing previous research results[5]. Currently, meta-analysis is widely used in the medical field and is an important research method in evidence-based medicine, providing a solid basis for evidence-based decision-making. In this study, a total of 330 epidemiological studies related to thyroid nodules were included, with a cumulative sample size of 2,165,080 individuals, including 651,435 cases of thyroid nodules. The research samples covered 30 provinces and cities in China, providing a comprehensive overview of the incidence of thyroid nodules nationally and in various regions.

The results of this Meta-analysis indicate that the national incidence rate of thyroid nodules is 34.7%. The incidence rate among females nationwide is 40.1%, while among males, it is 30.1%. The incidence of thyroid nodules in females is significantly higher than in males. In the three northeastern provinces (Heilongjiang, Jilin, and Liaoning), as well as in each individual province, the incidence rate among females is higher than that among males, with Liaoning Province having the highest incidence among females. The results of the health examination in Fuyu County also show that the incidence rate among females remains higher than among males. Female gender is identified as one of the risk factors for thyroid nodules. This may be attributed to the influence of estrogen on the occurrence of thyroid nodules, or it could be related to the increased demand for thyroid hormones during menstrual, pregnancy, and lactation periods in females. It has been reported that pregnancy is associated with the enlargement of pre-existing thyroid nodules and the formation of new thyroid nodules[6]. A nationwide cross-sectional study indicates that iodine deficiency, iodine excess, subclinical hypothyroidism, and positive thyroid autoantibodies are prevalent among reproductive-age women in China[7], and these factors may contribute to the higher susceptibility of females to thyroid nodules.

Subgroup analysis based on different age groups reveals that the incidence of thyroid nodules gradually increases with age in the overall population. The highest incidence of thyroid nodules is observed in the elderly population aged 60 and above. This may be associated with age-related degenerative changes in the thyroid, leading to compensatory nodular hyperplasia in the thyroid[8]. Kwong et al. reported that as individuals age, the incidence of thyroid nodules increases, but the risk of these nodules being malignant decreases[9]. Data shows that the incidence of thyroid nodules is higher in middle-aged and elderly women. This demographic group should be considered a priority for the prevention and treatment of thyroid nodules.

Subgroup analysis based on different provinces in

China reveals significant differences in the incidence of thyroid nodules. Hainan Province, Shanghai City, and Jiangxi Province have the highest incidence rates of thyroid nodules, with Hainan Province having the highest rate (74.0%). It is noteworthy that the inclusion of two studies from Hainan Province involves different years and focuses on the prevalence of thyroid nodules in centenarians, potentially introducing publication bias[10,11]. Guizhou Province has the lowest incidence rate of thyroid nodules. The incidence rate of thyroid nodules in Heilongjiang Province (37.6%) is higher than the national average (34.7%), and the incidence among females (45.5%) is significantly higher than among males (34.7%). A study by Tian C et al.[12] indicates that the incidence of thyroid nodules in Heilongjiang Province is 36.88%, with a higher prevalence among middle-aged and elderly women, aligning closely with the findings of this study.

The results of the physical examinations in Fuyu County reveal a significantly higher incidence rate of thyroid nodules (48.8%) compared to Heilongjiang Province (37.6%), the three northeastern provinces (34.8%), and the national average (34.7%). Both males (39.3%) and females (53.3%) in Fuyu County also exhibit higher incidence rates compared to national averages for males (30.1%) and females (40.1%). The incidence rates of thyroid nodules in different age groups (18-39 years: 28.5%; 40-59 years: 44.8%; ⩾ 60 years: 54.8%) are also higher than the national averages (18-39 years: 24.1%; 40-59 years: 40.0%; ⩾ 60 years: 54.3%). Fuyu County is located in the western part of Heilongjiang Province, characterized by a temperate continental monsoon climate with distinct seasonal changes and cold winters. The dietary habits in the northeastern region are characterized by high oil and salt intake, consumption of red meat, and large quantities of pickled foods. Residents also tend to have a high alcohol intake, and overall physical activity levels are relatively low[13]. Wang Y et al. reported that daily iodine intake exceeding 5g in iodized salt increases the risk of thyroid nodules. However, regular physical exercise and higher education levels can reduce the risk associated with excessive iodized salt intake[14]. To mitigate the risk of thyroid nodules, it is recommended for local residents to optimize their dietary structure and improve their lifestyle. In recent years, the air quality in the northeastern region has gradually improved, but pollution in heavy industrial areas remains significant[15]. These factors may contribute to the high incidence of thyroid nodules in Fuyu County. Therefore, Fuyu County is considered an area with a high prevalence of thyroid nodules, and it is essential to enhance awareness, conduct regular medical examinations, provide medical education to residents, assess the risk of thyroid nodule malignancy in a timely manner, and offer appropriate and correct treatment to avoid over-treatment. This approach holds significant importance for improving the residents' quality of life and alleviating economic pressure.

In this study, the Meta-analysis included research with the advantages of large sample sizes, extensive distribution, and comprehensive age ranges. The physical examination data from Fuyu County were obtained by experienced senior doctors in our hospital, using the same equipment, ensuring the reliability and authenticity of the examination data. However, there are limitations in this study:

The physical examination data from Fuyu County are specific to precision poverty alleviation information, lacking information on the overall population's educational level, lifestyle habits, urinary iodine levels, body mass index, and other indicators.

(1) The Meta-analysis included studies from diverse regions, but there is heterogeneity and publication bias among the studies, which may have some impact on the overall results.

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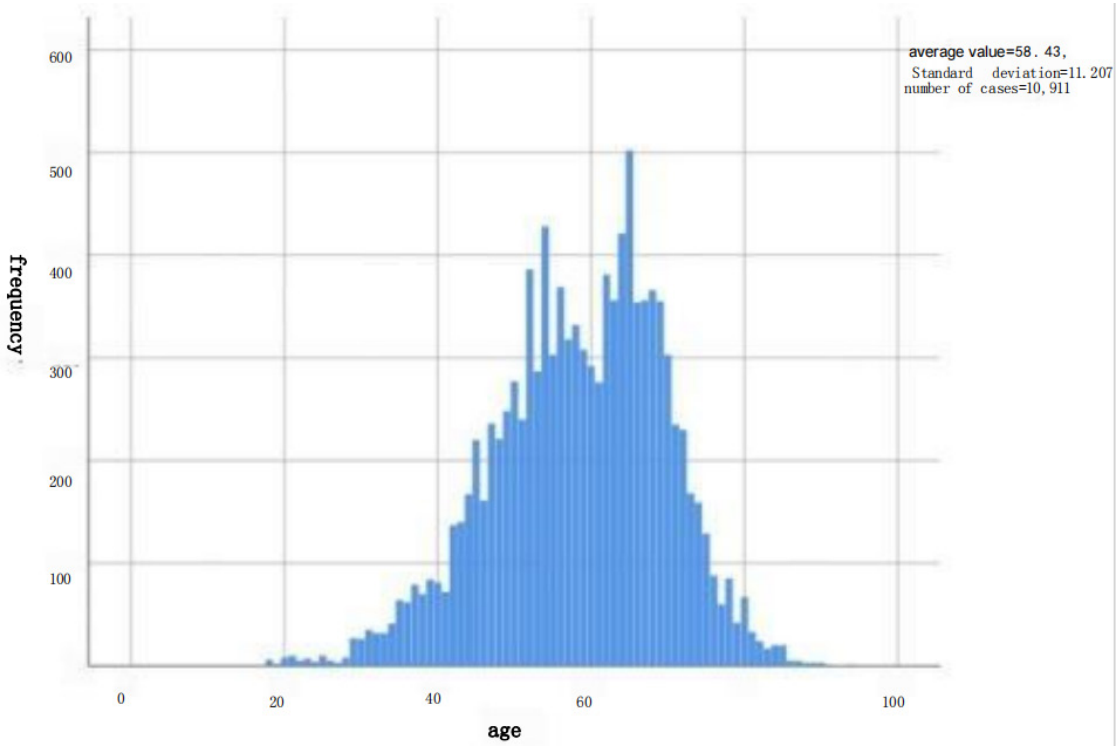

Figure 1. Age Distribution of the Health Examination Population in Fuyu County

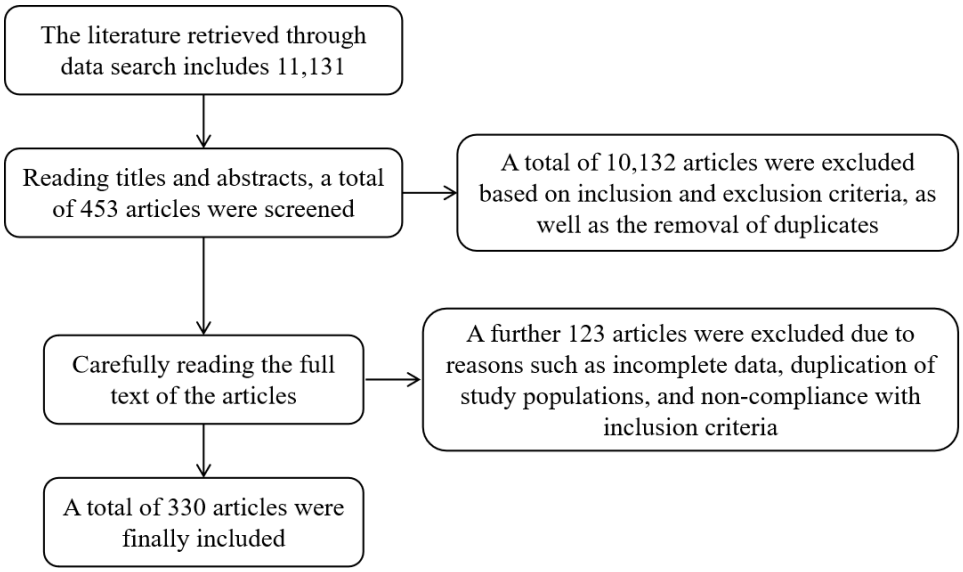

Figure 2. Flowchart of the Literature Retrieval and Selection Process

Table 1. Prevalence of Thyroid Nodules in Different Populations in Fuyu County

		Total Cases	Diseased Cases	Prevalence (%)
Gender	Male	3521	1385	39.3
	Female	7390	3937	53.3
Age	18-39 years	620	177	28.5
	40-59 years	4931	2207	44.8
	⩾ 60 years	5360	2938	54.8
Blood Pressure	Normal	4545	2150	47.3
	High	6366	3172	49.8

Table 2. Logistic Regression Analysis of Risk Factors for Thyroid Nodules in Fuyu County

Variable	Coefficient	Standard Error	Waldχ^2	*P*	*OR*
Gender	0.677	0.043	246.950	0.000	1.969
Age	0.537	0.034	244.622	0.000	1.712
Blood Pressure	0.055	0.041	1.803	0.179	1.057
Constant	-6.594	0.356	342.403	0.000	0.001

Table 3. Subgroup Analysis of Thyroid Nodule Prevalence Nationwide

Subgroup Analysis		Number of Studies	Total Cases	Diseased Cases	Prevalence (%)	95% *CI* (%)	I^2 (%)	*P*
Gender	Male	239	977961	254094	30.1	28.2-32.1	99.8	0.000
	Female	247	836264	309571	40.1	27.8-42.4	99.8	0.000
Age	< 18 years	44	70323	3504	11.8	10.1-13.5	97.4	0.000
	18-39 years	103	207006	51875	24.1	22.2-26.0	99.1	0.000
	40-59 years	142	590244	173805	40.0	36.5-43.4	99.9	0.000
	⩾ 60 years	144	228000	109851	54.3	51.0-57.6	99.7	0.000
Blood Pressure	Normal	10	20724	6296	36.2	27.4-44.9	99.4	0.000
	High	10	9737	3379	47.5	31.5-63.5	99.7	0.000
Region	Northeast China	21	26123	105980	34.8	23.3-46.2	99.9	0.000
	Heilongjiang	12	38154	16227	37.6	29.0-46.1	99.7	0.000
	Jilin	4	6289	1450	23.0	10.3-35.6	99.4	0.000
	Liaoning	5	61537	8446	37.6	10.9-64.3	100.0	0.000
	Jiangsu	23	62757	18783	31.6	27.1-36.0	99.4	0.000
	Shanghai	19	92709	46982	53.8	48.1-59.4	99.5	0.000
	Anhui	8	66447	25248	23.8	9.7-37.9	99.9	0.000
	Guangdong	22	360654	52748	35.2	24.6-45.8	99.9	0.000
	Hebei	43	353732	112716	31.6	25.8-37.3	100.0	0.000
	Zhejiang	40	132745	43318	28.9	24.1-33.7	99.8	0.000
	Shandong	14	49651	11114	37.7	24.2-51.2	99.9	0.000
	Xinjiang	15	44147	11178	31.7	25.8-37.6	99.6	0.000
	Gansu	7	9250	2202	27.9	21.2-34.6	98.3	0.000
	Sichuan	13	44520	14179	36.2	26.5-45.9	99.8	0.000
	Beijing	29	407090	152553	38.7	35.0-42.4	99.8	0.000
	Tianjin	7	11459	4541	37.4	29.8-44.9	98.4	0.000
	Shanxi	6	73577	25124	29.6	16.4-42.8	99.8	0.000
	Inner Mongolia	3	9064	4439	48.5	30.6-66.4	99.7	0.000
	Chongqing	5	26789	9199	42.1	34.3-49.9	99.0	0.000
	Hainan	2	1722	1274	74.0	71.9-76.1	0.0	0.675
	Ningxia	5	41974	10225	30.9	23.2-38.5	99.6	0.000
	Guangxi	3	1987	459	23.1	21.2-25.0	0.0	0.974
	Shaanxi	7	48520	13112	30.7	26.3-35.2	98.6	0.000
	Henan	7	34332	15053	41.6	30.2-52.9	99.6	0.000
	Hubei	2	14358	3582	43.0	27.6-58.4	99.8	0.000
	Guizhou	6	15857	2168	12.3	0.3-24.3	99.8	0.000
	Fujian	6	51770	13701	23.9	5.4-42.3	100.0	0.000
	Yunan	3	32250	12260	38.5	31.9-45.2	98.4	0.000
	Qinghai	3	12583	3690	36.9	24.1-49.7	99.3	0.000
	Jiangxi	2	1381	726	52.5	49.5-55.4	6.0	0.302

Continuation Table:

Subgroup Analysis		Number of Studies	Total Cases	Diseased Cases	Prevalence (%)	95% *CI* (%)	I^2 (%)	*P*
	Hunan	4	7580	1448	24.9	15.6-34.2	99.1	0.000

Table 4. Meta-analysis of Thyroid Nodule Prevalence in Different Gender Groups in the Three Northeastern Provinces

Subgroup Analysis		Number of Studies	Total Cases	Diseased Cases	Prevalence (%)	95% *CI* (%)	I^2 (%)	*P*
Northeast China	Male	15	20117	6958	33.2	27.1-39.4	98.9	0.000
	Female	16	35802	16920	44.5	38.2-50.9	99.3	0.000
Heilongjiang	Male	9	9741	3208	34.7	26.3-43.1	98.8	0.000
	Female	10	25965	12422	45.5	36.9-54.0	99.5	0.000
Jilin	Male	3	2010	385	21.0	13.4-28.7	93.4	0.000
	Female	3	3086	981	32.7	22.1-43.2	97.2	0.000
Liaoning	Male	3	8366	3365	41.0	34.4-47.5	94.6	0.000
	Female	3	6751	3517	53.2	49.3-57.0	84.3	0.002