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Ambient $PM_{2.5}$ and thyroid health: A cross-sectional study of 24,333 participants in Zhejiang, China

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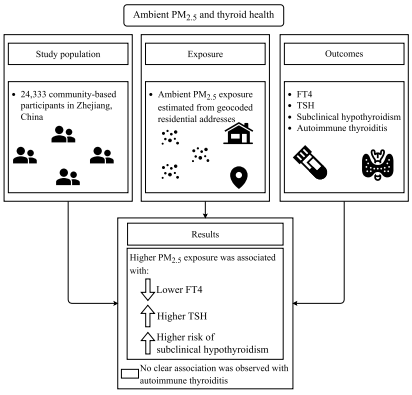
HIGHLIGHTS

- We assessed ambient $PM_{2.5}$ and thyroid health in 24,333 community-based participants.
- Higher $PM_{2.5}$ exposure was associated with lower FT4 and higher TSH.
- Higher $PM_{2.5}$ exposure was associated with higher odds of subclinical hypothyroidism.

GRAPHICAL ABSTRACT



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ABSTRACT

Evidence on the association between ambient fine particulate matter ($PM_{2.5}$) exposure and thyroid dysfunction remains inconsistent, with limited evidence from community-based populations encompassing both minors and adults while accounting for iodine nutrition. We aimed to evaluate the associations of ambient $PM_{2.5}$ exposure with complementary dimensions of thyroid health in a community-based population in Zhejiang Province, China. We conducted a cross-sectional study of 24,333 participants between 2022 and 2025. $PM_{2.5}$ exposure was estimated using participants' geocoded residential addresses. Linear and generalised linear mixed-effects models were used to estimate the associations of $PM_{2.5}$ with free thyroxine (FT4), thyroid-stimulating hormone (TSH), subclinical hypothyroidism, and autoimmune thyroiditis. Stratified analyses were conducted by age, sex, and body mass index (BMI). Our results showed that each 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with lower FT4 [-3.57% (95% confidence interval (CI): −4.39%, −2.75%)], higher TSH [12.15% (95% CI: 7.92%, 16.56%)], and higher odds of subclinical hypothyroidism [odds ratio (OR) 1.27 (95% CI: 1.06, 1.51)]. Exposure to $PM_{2.5}$ was not clearly associated with autoimmune thyroiditis. The association with lower FT4 was more pronounced among participants aged < 18 years and those with BMI < 18.5 kg/m^2, whereas the associations with higher TSH

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and higher odds of subclinical hypothyroidism were more pronounced among participants aged ≥ 50 years and those with BMI ≥ 24.0 kg/m^2. Overall, our findings suggest that higher ambient $PM_{2.5}$ exposure was associated with lower thyroid function.

1. Introduction

Thyroid dysfunction is a prevalent endocrine disorder with far-reaching implications for growth, metabolism, cardiovascular function, and neurodevelopment. TSH and FT4 provide complementary information on thyroid function: TSH reflects pituitary feedback to circulating thyroid hormones, and FT4 reflects circulating thyroid hormone availability [15,35]. Their joint interpretation permits the identification of thyroid dysfunction. Some of these abnormalities may occur without overt clinical manifestations and may be detectable only through laboratory biomarkers. Such subclinical disturbances may herald progression to overt disease and confer cardiovascular and metabolic risks [2,6]. Autoimmune thyroiditis reflects immune-mediated thyroid abnormality and provides an additional dimension for assessing thyroid health beyond circulating hormone levels [35,4]. Together, these measures characterise complementary dimensions of thyroid health, including circulating hormone availability, pituitary feedback, laboratory-defined thyroid dysfunction, and thyroid autoimmunity. In China, a nationally representative survey estimated that 12.93% of adults have subclinical hypothyroidism and 14.19% are positive for thyroid autoantibodies, underscoring the substantial disease burden [24].

Ambient fine particulate matter ($PM_{2.5}$) is one of the leading environmental risk factors worldwide and is subject to stringent air quality guidelines due to its well-documented adverse health effects [41]. Despite successful clean-air interventions substantially reducing $PM_{2.5}$ concentrations in China in recent years, population exposure remains sufficiently high to pose a continuing public health threat [10,44]. Toxicological studies provide plausible biological mechanisms linking $PM_{2.5}$ to thyroid disruption, including systemic oxidative stress, inflammatory responses, disruption of hypothalamic–pituitary–thyroid (HPT) axis regulation, and structural or functional injury to thyroid follicles [8,25,33].

Previous epidemiological studies have examined the associations of ambient air pollution with thyroid function biomarkers and thyroid disorders, but the evidence remains inconsistent [29]. Much of the existing evidence has come from pregnant women, newborns, or specific clinical populations, whose thyroid physiology and susceptibility differ markedly from those of the general population [11,12,16,17,31,32,45–47]. Population-based studies in adults from Korea, Spain, and China have suggested that air pollution may be associated with altered thyroid function or thyroid disorders, but the magnitude of associations has varied considerably across populations, exposure windows, and pollutants [19,37,42]. Iodine nutrition is a key determinant of thyroid function and the spectrum of thyroid disorders [48]. However, iodine status was not assessed or adjusted for in some previous studies [18,19,32]. Only a few studies have focused on community-based populations that include both minors and adults [20]. Studies simultaneously evaluating continuous thyroid function biomarkers, thyroid dysfunction, and thyroid autoimmunity in community-based populations spanning children, adolescents, and adults, while accounting for iodine nutrition, remain limited.

To address these gaps, we leveraged baseline data from a community-based population in Zhejiang Province, China, to evaluate the associations of ambient $PM_{2.5}$ exposure with complementary dimensions of thyroid health: thyroid function biomarkers (FT4 and TSH), laboratory-defined thyroid dysfunction (subclinical hypothyroidism), and thyroid autoimmunity (autoimmune thyroiditis). Our analyses accounted for multiple indicators of iodine nutrition. We additionally examined exposure–response relationships and assessed whether these associations differed by age, sex, and body mass index (BMI).

2. Methods

2.1. Study population and design

This cross-sectional analysis used baseline data from the Zhejiang Environmental Health Cohort (ZEHC), an ongoing prospective study designed to investigate the health effects of environmental exposures in Zhejiang Province, China. Participants were recruited between July 2022 and January 2025 from six sites selected to reflect geographic and socioeconomic diversity across the province: Changxing, Kecheng, Dongyang, Tiantai, Luqiao, and Jingning (Figure S1). Recruitment followed a stratified multistage random sampling design, as described in previous ZEHC studies [21,22].

Of 27,595 enrolled participants, we sequentially excluded: 154 found ineligible after post-collection verification; 980 lacking valid residential address data; 439 for whom the required exposure data were unavailable; 201 lacking thyroid marker data; and 1488 with missing model covariates or family identifiers. The final analytic sample comprised 24,333 participants. The participant inclusion and exclusion process is shown in Figure S2.

The study was approved by the Ethics Committee of Zhejiang Provincial Center for Disease Control and Prevention. Written informed consent was obtained from all adult participants and from the legal guardians of minor participants.

2.2. Air pollution exposure assessment

Daily ambient $PM_{2.5}$ concentrations from 2019 to 2024 at a 1 km × 1 km spatial resolution were obtained from the ChinaHighAirPollutants (CHAP) dataset, generated using spatiotemporal artificial intelligence models that integrate multiple data sources, including ground-based monitoring, satellite remote sensing, atmospheric reanalysis, and model simulations [38]. CHAP model performance has been validated, with 10-fold cross-validation R^2 values of 0.86–0.93 across pollutants [38–40,43]. We additionally extracted daily concentrations of particulate matter with an aerodynamic diameter ≤ 10 μm (PM_{10}) [39], ozone (O_3) [43], nitrogen dioxide (NO_2) [40], sulfur dioxide (SO_2), and carbon monoxide (CO) for the same period from the corresponding CHAP products. $PM_{10-2.5}$ was calculated by subtracting $PM_{2.5}$ from PM_{10}.

Residential addresses were geocoded to World Geodetic System 1984 coordinates and linked to daily gridded pollutant concentrations. The primary exposure metric was the average $PM_{2.5}$ concentration over the three years preceding the date of blood collection. Secondary exposure windows included 30-day and 1-year pre-sampling averages. Because the CHAP data used in this study were available through 2024, participants sampled in 2025 could not be assigned a complete 3-year $PM_{2.5}$ exposure window and were excluded.

2.3. Thyroid outcome assessment

Fasting venous blood samples were collected on the day of the medical examination at local health clinics. Serum was separated by centrifugation within 2 h, transported under cold-chain conditions to the central laboratory in Hangzhou, and analysed on a Cobas® e601 electrochemiluminescence immunoassay platform (Roche Diagnostics GmbH, Mannheim, Germany) for thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), thyroglobulin

antibody (TgAb), and thyroid peroxidase antibody (TPOAb). Values below the detection limit were substituted with half the limit; those above the upper limit were replaced with the upper-limit value.

The primary thyroid outcomes were FT4, TSH, subclinical hypothyroidism, and autoimmune thyroiditis. FT4 and TSH were analysed as continuous indicators of thyroid function. Subclinical hypothyroidism was defined as TSH > 4.20 μIU/mL with FT4 within the reference range of 12.0–22.0 pmol/L. Autoimmune thyroiditis was defined as TPOAb positivity (≥34 IU/mL) and/or TgAb positivity (≥115 IU/mL), consistent with previous thyroid epidemiological studies [23,24,42]. The secondary thyroid outcomes were FT3, TgAb positivity, and TPOAb positivity. FT3 was analysed as a continuous outcome, whereas TgAb positivity and TPOAb positivity were analysed as binary outcomes.

We additionally assessed other thyroid diseases to describe their distribution in this community-based population. Overt hypothyroidism was defined as TSH > 4.20 μIU/mL with FT4 < 12.0 pmol/L. Subclinical hyperthyroidism was defined as TSH < 0.27 μIU/mL with FT4 and FT3 within their reference ranges of 12.0–22.0 pmol/L and 3.1–6.8 pmol/L, respectively. Overt hyperthyroidism was defined as TSH < 0.27 μIU/mL with FT4 > 22.0 pmol/L and/or FT3 > 6.8 pmol/L [24,42].

2.4. Covariates

Covariate information was obtained from standardised questionnaires, physical examinations, sampling records, and laboratory measurements. Demographic and anthropometric factors included age (years, continuous), sex (male versus female), and BMI (kg/m^2, continuous). BMI was calculated as weight (kg) divided by height (m^2). Other covariates included sampling season (Spring [March–May], Summer [June–August], Autumn [September–November], or Winter [December–February]) and sampling year (2022, 2023, or 2024). Lifestyle and socioeconomic covariates included smoking status (Never, Former, or Current), drinking status (Never, Former, or Current), education (Primary school or below, Middle/High school, or College or above), annual household income (<60,000 CNY, 60,000–99,999 CNY, ≥100,000 CNY, or Unknown/Refused), and occupation (Student, White-collar worker, Manual worker, or Others/Not in labour force).

Urinary iodine concentration was measured by inductively coupled plasma mass spectrometry (ICP-MS; ICAPR02041, Thermo Fisher Scientific GmbH, Bremen, Germany). Iodine-related covariates included urinary iodine status (<100, 100–299, or ≥300 μg/L), salt type (Non-iodised salt, Both iodised and non-iodised salt, Iodised salt, or Unknown/Missing), and the consumption frequencies of seaweed, dried shrimp, and sea fish (Rarely/never, 1–3 days/month, 1–3 days/week, 4–6 days/week, or Daily).

2.5. Statistical analysis

Descriptive statistics were used to summarise participant characteristics across quartiles of $PM_{2.5}$ exposure. Continuous variables were presented as medians (interquartile ranges, IQRs), and categorical variables were presented as frequencies (percentages). Differences across $PM_{2.5}$ quartiles were assessed using the Kruskal–Wallis test for continuous variables and the χ^2 test or Fisher's exact test, as appropriate, for categorical variables.

Because FT3, FT4, and TSH were right-skewed, all these outcomes were natural log-transformed before modelling. We used linear mixed-effects models to estimate the associations of $PM_{2.5}$ exposure with FT3, FT4, and TSH and generalised linear mixed-effects models with a logit link to estimate the associations with subclinical hypothyroidism, autoimmune thyroiditis, TgAb positivity, and TPOAb positivity. Because overt hypothyroidism, subclinical hyperthyroidism, and overt hyperthyroidism were rare in this community-based sample, they were not included in the regression analyses to avoid sparse-data problems and unstable estimates in logistic models [13]. All models included a random intercept for family to account for within-household clustering. Two adjustment strategies were implemented: a minimally adjusted model (age, sex, BMI), and a fully adjusted model additionally including sampling season, sampling year, smoking status, drinking status, education, annual household income, occupation, urinary iodine status, salt type, seaweed consumption frequency, dried shrimp consumption frequency, and sea fish consumption frequency.

$PM_{2.5}$ exposure was modelled continuously (per 10 $\mu g/m^3$ increment) and as quartiles (relative to the lowest quartile). For the log-transformed FT3, FT4, and TSH outcomes, model coefficients were converted to percentage changes with 95% confidence intervals (CIs), calculated as $[\exp(10\beta)-1]\times 100\%$ for continuous $PM_{2.5}$ and $[\exp(\beta)-1]\times 100\%$ for $PM_{2.5}$ quartiles. For subclinical hypothyroidism, autoimmune thyroiditis, TgAb positivity, and TPOAb positivity, model coefficients were exponentiated and presented as odds ratios (ORs) with 95% CIs, calculated as $\exp(10\beta)$ for continuous $PM_{2.5}$ and $\exp(\beta)$ for $PM_{2.5}$ quartiles. To assess linear trends across quartiles, the median $PM_{2.5}$ concentration within each quartile was entered as a continuous variable in the corresponding models, and P for trend was obtained from the test of the coefficient for this continuous term.

To examine exposure–response relationships for the primary outcomes, $PM_{2.5}$ was modelled using natural splines with one internal knot at the 50th percentile and boundary knots at the 10th and 90th percentiles in the fully adjusted models. Likelihood ratio tests assessed the overall association (spline model versus null model) and deviation from linearity (spline model versus linear model).

To assess potential effect modification of the associations with the primary outcomes by age, sex, and BMI, interaction terms between $PM_{2.5}$ and each modifier were added separately to the fully adjusted models. The P for interaction was obtained from likelihood ratio tests comparing models with and without the interaction term and was adjusted for multiple testing using the Benjamini–Hochberg false discovery rate procedure (FDR). Stratified analyses were further performed by age group (<18, 18–49, and ≥50 years), sex (male and female), and BMI group (<18.5, 18.5–23.9, and ≥24 kg/m^2). For sex, effect modification was assessed using a categorical interaction term; for age and BMI, effect modification was assessed using continuous age and continuous BMI, respectively. In subgroup-specific models, the stratification variable and covariates with no within-subgroup variation were omitted.

2.6. Sensitivity analysis

Several sensitivity analyses were conducted to assess the robustness of the findings. First, we repeated the analyses using alternative $PM_{2.5}$ exposure windows, including 30-day and 1-year average concentrations. Second, we conducted three participant-related sensitivity analyses: we excluded participants with self-reported current or previous thyroid disease (Yes versus No); in analyses restricted to adults, we additionally adjusted for self-reported family history of thyroid disease (Yes versus No), which was collected only among adults; and in analyses restricted to adult women, we additionally adjusted for self-reported menopausal status (Premenopausal, Perimenopausal, Postmenopausal, or Unknown/Missing), which was collected only among adult women. Third, to assess the sensitivity of the associations to co-pollutant adjustment, Pearson correlation coefficients were calculated among the concentrations of $PM_{2.5}$, $PM_{10-2.5}$, NO_2, SO_2, O_3, and CO, and separate two-pollutant models were fitted by additionally including $PM_{10-2.5}$, NO_2, SO_2, O_3, or CO, one at a time, in the fully adjusted model. Finally, we added a random intercept for study site to evaluate the potential influence of clustering by study site.

All analyses were performed using R software (version 4.5.2). All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant.

3. Results

3.1. Descriptive statistics

The summary characteristics of the participants are presented in Table 1. A total of 24,333 participants were included in the final analysis, with a median age of 49.00 years (IQR 24.00, 59.00) and a median BMI of 22.97 kg/m^2 (IQR 20.17, 25.65). More than half of the participants were female (59.4%), and most participants reported never smoking (86.5%) and never drinking (84.3%). The spatial distribution of participants across the six study sites is shown in Figure S1.

The median $PM_{2.5}$ concentration was 24.43 μg/m^3 (IQR 22.09, 27.20). For the primary thyroid outcomes, the median concentrations of FT4 and TSH were 16.87 pmol/L (IQR 15.30, 18.59) and 2.19 μIU/mL (IQR 1.51, 3.14), respectively. Overall, 2677 participants (11.0%) had subclinical hypothyroidism and 2952 participants (12.1%) had autoimmune thyroiditis. For the secondary thyroid outcomes, the median FT3 concentration was 5.21 pmol/L (IQR 4.71, 6.01), while 1960 participants (8.1%) had TgAb positivity and 2081 participants (8.6%) had TPOAb positivity. Overt hyperthyroidism, subclinical hyperthyroidism, and overt hypothyroidism were uncommon, with prevalence of 0.4%, 0.4%, and 0.5%, respectively. Across quartiles of $PM_{2.5}$ exposure, FT4, TSH, FT3, subclinical hypothyroidism, autoimmune thyroiditis, TgAb positivity, TPOAb positivity, and participant characteristics differed significantly (all $P < 0.001$; Table 1).

3.2. Associations of $PM_{2.5}$ exposure with thyroid outcomes

Higher $PM_{2.5}$ exposure was associated with lower FT4, higher TSH, and higher odds of subclinical hypothyroidism in the fully adjusted models (Table 2). Compared with participants in the lowest $PM_{2.5}$ quartile, those in the highest quartile had a 1.87% lower FT4 concentration (95% CI: −2.59%, −1.13%), a 12.04% higher TSH concentration (95% CI: 8.29%, 15.92%), and higher odds of subclinical hypothyroidism (OR 1.31, 95% CI: 1.12, 1.53). Each 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 3.57% decrease in FT4 (95% CI: −4.39%, −2.75%), a 12.15% increase in TSH (95% CI: 7.92%, 16.56%), and higher odds of subclinical hypothyroidism (OR 1.27, 95% CI: 1.06, 1.51). The corresponding OR for autoimmune thyroiditis was 0.97 (95% CI: 0.82, 1.15) per 10 μg/m^3 increase in $PM_{2.5}$ and 0.98 (95% CI: 0.84, 1.14) for the highest quartile compared with the lowest quartile. P for trend was < 0.001 for FT4, TSH, and subclinical hypothyroidism, and 0.488 for autoimmune thyroiditis. In the fully adjusted continuous models, $PM_{2.5}$ was not significantly associated with FT3 (% change per 10 μg/m^3: −0.79, 95% CI: −1.59, 0.01), TgAb positivity (OR 0.90, 95% CI: 0.73, 1.10), or TPOAb positivity (OR 0.96, 95% CI: 0.79, 1.17; Table S1).

To examine exposure–response relationships, we fitted $PM_{2.5}$ using natural splines in the fully adjusted models (Fig. 1). The exposure–response curves showed a trend towards lower FT4, higher TSH, and higher odds of subclinical hypothyroidism with increasing $PM_{2.5}$ concentrations. The curve for autoimmune thyroiditis showed a non-linear pattern.

3.3. Subgroup analyses

We conducted subgroup analyses to evaluate potential effect modification of the associations between $PM_{2.5}$ exposure and thyroid outcomes (Fig. 2 and Table S2). After adjustment for multiple testing, differences in estimates were mainly observed across age and BMI groups, rather than by sex. The association between higher $PM_{2.5}$ exposure and lower FT4 was more pronounced among participants aged < 18 years and among those with BMI < 18.5 kg/m^2. By contrast, the associations of higher $PM_{2.5}$ exposure with higher TSH and higher odds of subclinical hypothyroidism were more pronounced among participants aged ≥ 50 years and among those with BMI ≥ 24.0 kg/m^2. No evidence of effect modification by sex was observed for any outcome, and no distinct subgroup pattern was observed for autoimmune thyroiditis.

3.4. Sensitivity analyses

We conducted several sensitivity analyses to examine the robustness of the associations between $PM_{2.5}$ exposure and thyroid outcomes (Table 3 and Tables S4–S5). The associations of higher $PM_{2.5}$ exposure with lower FT4 and higher TSH were observed when the 30-day and 1-year exposure windows were used. The association with higher odds of subclinical hypothyroidism was observed for the 1-year but not the 30-day exposure window. The associations with lower FT4 and higher TSH were also observed after excluding participants with self-reported current or previous thyroid disease, in analyses restricted to adults with additional adjustment for family history of thyroid disease, and in analyses restricted to adult women with additional adjustment for menopausal status. The ORs for subclinical hypothyroidism remained above 1 in these participant-related analyses, although the association was not significant in the analysis restricted to adult women.

$PM_{2.5}$ was highly correlated with $PM_{10–2.5}$, NO_2, and CO, with Pearson correlation coefficients ranging from 0.88 to 0.94, and was less strongly correlated with O_3 and SO_2 (Table S4). In the two-pollutant models, the associations with lower FT4 and higher TSH remained after adjustment for $PM_{10–2.5}$, NO_2, SO_2, or O_3, although the magnitudes of the estimates varied. After adjustment for CO, the FT4 estimate was attenuated and the TSH estimate changed direction, with neither association remaining statistically significant. The estimates for subclinical hypothyroidism also varied considerably across the two-pollutant models, ranging from an OR of 4.03 after adjustment for $PM_{10–2.5}$ to an OR of 0.63 after adjustment for CO.

When a random intercept for study site was added, the associations remained in the same direction for FT4, TSH, and subclinical hypothyroidism, but the estimates for TSH and subclinical hypothyroidism increased in magnitude to 31.42% and an OR of 3.28, respectively. No clear association between $PM_{2.5}$ exposure and autoimmune thyroiditis was observed across the sensitivity analyses.

4. Discussion

In this large cross-sectional analysis of 24,333 participants from Zhejiang Province, China, exposure to higher ambient $PM_{2.5}$ was associated with lower circulating FT4, higher TSH, and higher odds of subclinical hypothyroidism. In contrast, higher ambient $PM_{2.5}$ exposure was not clearly associated with autoimmune thyroiditis. Subgroup analyses further suggested that the association with lower FT4 was more pronounced among participants aged < 18 years and those with BMI < 18.5 kg/m^2, whereas the associations with higher TSH and higher odds of subclinical hypothyroidism were more evident among participants aged ≥ 50 years and those with BMI ≥ 24.0 kg/m^2. There was little evidence that these associations differed by sex. Sensitivity analyses generally supported the associations with lower FT4 and higher TSH, while the positive association with subclinical hypothyroidism was observed in several, but not all, sensitivity analyses.

Our findings are generally consistent with previous epidemiological evidence suggesting that $PM_{2.5}$ exposure may be associated with thyroid function and hypothyroid-related outcomes, although the evidence remains heterogeneous. In the Spanish Di@bet.es study, a nationwide population-based survey of adults, annual $PM_{2.5}$ exposure estimated using air-quality models and monitoring data was associated with lower serum FT4 concentrations and higher odds of elevated TSH, which is consistent with our findings of lower FT4 and higher TSH [37]. In a national cross-sectional study of 73,900 Chinese adults, residential $PM_{2.5}$ exposure estimated using 1 km × 1 km exposure data was associated with higher odds of laboratory-defined subclinical hypothyroidism, supporting our finding of higher odds of subclinical hypothyroidism among participants with higher $PM_{2.5}$ exposure [42]. Prospective

Table 1
Characteristics of study participants by quartiles of $PM_{2.5}$ exposure.

Characteristic	Overall	Q1 (<22.09 μg/m³)	Q2 (22.09–24.43 μg/m³)	Q3 (24.43–27.20 μg/m³)	Q4 (≥27.20 μg/m³)	*P* value[a]
N	24333	6085	6104	6064	6080	
Exposure						
$PM_{2.5}$, μg/m³	24.43 (22.09, 27.20)	21.32 (20.11, 21.56)	22.50 (22.34, 24.06)	26.51 (24.72, 26.91)	29.76 (28.98, 30.10)	
Outcomes						
FT4, pmol/L	16.87 (15.30, 18.59)	16.50 (14.97, 18.14)	17.50 (15.75, 19.34)	16.55 (15.07, 18.23)	17.01 (15.54, 18.52)	< 0.001
TSH, μIU/mL	2.19 (1.51, 3.14)	2.06 (1.46, 2.99)	2.10 (1.45, 3.06)	2.22 (1.53, 3.18)	2.36 (1.64, 3.35)	< 0.001
Subclinical hypothyroidism, *n* (%)	2677 (11.0%)	573 (9.4%)	570 (9.3%)	725 (12.0%)	809 (13.3%)	< 0.001
Autoimmune thyroiditis, *n* (%)	2952 (12.1%)	685 (11.3%)	773 (12.7%)	832 (13.7%)	662 (10.9%)	< 0.001
FT3, pmol/L	5.21 (4.71, 6.01)	5.12 (4.61, 5.99)	5.56 (4.89, 6.44)	5.09 (4.69, 5.64)	5.17 (4.70, 5.88)	< 0.001
TgAb positivity, *n* (%)	1960 (8.1%)	438 (7.2%)	498 (8.2%)	592 (9.8%)	432 (7.1%)	< 0.001
TPOAb positivity, *n* (%)	2081 (8.6%)	498 (8.2%)	559 (9.2%)	579 (9.5%)	445 (7.3%)	< 0.001
Overt hyperthyroidism, *n* (%)	102 (0.4%)	24 (0.4%)	21 (0.3%)	29 (0.5%)	28 (0.5%)	0.643
Subclinical hyperthyroidism, *n* (%)	105 (0.4%)	29 (0.5%)	23 (0.4%)	28 (0.5%)	25 (0.4%)	0.825
Overt hypothyroidism, *n* (%)	127 (0.5%)	32 (0.5%)	33 (0.5%)	43 (0.7%)	19 (0.3%)	0.026
Demographic and anthropometric characteristics						
Sex, *n* (%)						< 0.001
Female	14449 (59.4%)	3503 (57.6%)	3634 (59.5%)	3803 (62.7%)	3509 (57.7%)	
Male	9884 (40.6%)	2582 (42.4%)	2470 (40.5%)	2261 (37.3%)	2571 (42.3%)	
Age, years	49.00 (24.00, 59.00)	50.00 (25.00, 60.00)	50.00 (15.00, 60.00)	51.00 (32.00, 59.00)	42.00 (18.00, 57.00)	< 0.001
BMI, kg/m²	22.97 (20.17, 25.65)	23.15 (20.08, 25.95)	22.76 (19.83, 25.39)	23.25 (20.83, 25.75)	22.66 (19.72, 25.50)	< 0.001
Sampling characteristics						
Sampling season, *n* (%)						< 0.001
Spring	6060 (24.9%)	1405 (23.1%)	3259 (53.4%)	641 (10.6%)	755 (12.4%)	
Summer	8065 (33.1%)	3431 (56.4%)	1008 (16.5%)	775 (12.8%)	2851 (46.9%)	
Autumn	6103 (25.1%)	996 (16.4%)	1179 (19.3%)	2093 (34.5%)	1835 (30.2%)	
Winter	4105 (16.9%)	253 (4.2%)	658 (10.8%)	2555 (42.1%)	639 (10.5%)	
Sampling year, *n* (%)						< 0.001
2022	9212 (37.9%)	755 (12.4%)	1341 (22.0%)	2424 (40.0%)	4692 (77.2%)	
2023	7721 (31.7%)	3091 (50.8%)	3528 (57.8%)	1085 (17.9%)	17 (0.3%)	
2024	7400 (30.4%)	2239 (36.8%)	1235 (20.2%)	2555 (42.1%)	1371 (22.5%)	
Behavioural characteristics						
Smoking status, *n* (%)						< 0.001
Never	21038 (86.5%)	5292 (87.0%)	5490 (89.9%)	5210 (85.9%)	5046 (83.0%)	
Former	505 (2.1%)	83 (1.4%)	97 (1.6%)	167 (2.8%)	158 (2.6%)	
Current	2790 (11.5%)	710 (11.7%)	517 (8.5%)	687 (11.3%)	876 (14.4%)	
Drinking status, *n* (%)						< 0.001
Never	20523 (84.3%)	5130 (84.3%)	5305 (86.9%)	5083 (83.8%)	5005 (82.3%)	
Former	201 (0.8%)	41 (0.7%)	36 (0.6%)	74 (1.2%)	50 (0.8%)	
Current	3609 (14.8%)	914 (15.0%)	763 (12.5%)	907 (15.0%)	1025 (16.9%)	
Socioeconomic characteristics						
Education, *n* (%)						< 0.001
Primary school or below	10284 (42.3%)	3703 (60.9%)	2499 (40.9%)	1694 (27.9%)	2388 (39.3%)	
Middle/High school	10881 (44.7%)	1778 (29.2%)	2840 (46.5%)	3429 (56.5%)	2834 (46.6%)	
College or above	3168 (13.0%)	604 (9.9%)	765 (12.5%)	941 (15.5%)	858 (14.1%)	
Annual household income, *n* (%)						< 0.001
< 60,000 CNY	4742 (19.5%)	1660 (27.3%)	1315 (21.5%)	1031 (17.0%)	736 (12.1%)	
60,000–99,999 CNY	3369 (13.8%)	816 (13.4%)	1017 (16.7%)	826 (13.6%)	710 (11.7%)	
≥ 100,000 CNY	7566 (31.1%)	1101 (18.1%)	1819 (29.8%)	1988 (32.8%)	2658 (43.7%)	
Unknown/Refused	8656 (35.6%)	2508 (41.2%)	1953 (32.0%)	2219 (36.6%)	1976 (32.5%)	
Occupation, *n* (%)						< 0.001
Student	5414 (22.2%)	1347 (22.1%)	1577 (25.8%)	988 (16.3%)	1502 (24.7%)	
White-collar worker	4424 (18.2%)	1045 (17.2%)	1042 (17.1%)	1329 (21.9%)	1008 (16.6%)	
Manual worker	3884 (16.0%)	1362 (22.4%)	968 (15.9%)	470 (7.8%)	1084 (17.8%)	
Others/Not in labour force	10611 (43.6%)	2331 (38.3%)	2517 (41.2%)	3277 (54.0%)	2486 (40.9%)	
Iodine nutrition						
Urinary iodine status (μg/L), *n* (%)						< 0.001
< 100	6066 (24.9%)	1792 (29.4%)	1905 (31.2%)	1379 (22.7%)	990 (16.3%)	
100–299	13775 (56.6%)	3444 (56.6%)	3278 (53.7%)	3473 (57.3%)	3580 (58.9%)	
≥ 300	4492 (18.5%)	849 (14.0%)	921 (15.1%)	1212 (20.0%)	1510 (24.8%)	
Salt type, *n* (%)						< 0.001
Non-iodised salt	3265 (13.4%)	800 (13.1%)	1021 (16.7%)	836 (13.8%)	608 (10.0%)	
Both iodised and non-iodised salt	8718 (35.8%)	2551 (41.9%)	3050 (50.0%)	1939 (32.0%)	1178 (19.4%)	
Iodised salt	10962 (45.0%)	2386 (39.2%)	1842 (30.2%)	3050 (50.3%)	3684 (60.6%)	
Unknown/Missing	1388 (5.7%)	348 (5.7%)	191 (3.1%)	239 (3.9%)	610 (10.0%)	
Seaweed consumption frequency, *n* (%)						< 0.001
Rarely/never	11363 (46.7%)	2900 (47.7%)	2979 (48.8%)	2972 (49.0%)	2512 (41.3%)	
1–3 days/month	7430 (30.5%)	1811 (29.8%)	1646 (27.0%)	1908 (31.5%)	2065 (34.0%)	
1–3 days/week	4573 (18.8%)	1109 (18.2%)	1153 (18.9%)	1037 (17.1%)	1274 (21.0%)	

(*continued on next page*)

Table 1 (*continued*)

Characteristic	Overall	Q1 (<22.09 μg/m^3)	Q2 (22.09–24.43 μg/m^3)	Q3 (24.43–27.20 μg/m^3)	Q4 (≥27.20 μg/m^3)	*P* value[a]
4–6 days/week	690 (2.8%)	177 (2.9%)	219 (3.6%)	112 (1.8%)	182 (3.0%)	
Daily	277 (1.1%)	88 (1.4%)	107 (1.8%)	35 (0.6%)	47 (0.8%)	
Dried shrimp consumption frequency, *n* (%)						< 0.001
Rarely/never	14498 (59.6%)	3022 (49.7%)	3461 (56.7%)	4089 (67.4%)	3926 (64.6%)	
1–3 days/month	6036 (24.8%)	1808 (29.7%)	1459 (23.9%)	1330 (21.9%)	1439 (23.7%)	
1–3 days/week	3078 (12.6%)	1004 (16.5%)	899 (14.7%)	582 (9.6%)	593 (9.8%)	
4–6 days/week	463 (1.9%)	147 (2.4%)	176 (2.9%)	45 (0.7%)	95 (1.6%)	
Daily	258 (1.1%)	104 (1.7%)	109 (1.8%)	18 (0.3%)	27 (0.4%)	
Sea fish consumption frequency, *n* (%)						< 0.001
Rarely/never	10594 (43.5%)	2402 (39.5%)	2254 (36.9%)	3149 (51.9%)	2789 (45.9%)	
1–3 days/month	7935 (32.6%)	1834 (30.1%)	2014 (33.0%)	1935 (31.9%)	2152 (35.4%)	
1–3 days/week	4832 (19.9%)	1444 (23.7%)	1447 (23.7%)	916 (15.1%)	1025 (16.9%)	
4–6 days/week	688 (2.8%)	266 (4.4%)	267 (4.4%)	54 (0.9%)	101 (1.7%)	
Daily	284 (1.2%)	139 (2.3%)	122 (2.0%)	10 (0.2%)	13 (0.2%)	

Abbreviations: BMI, body mass index; FT3, free triiodothyronine; FT4, free thyroxine; $PM_{2.5}$, fine particulate matter; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone.

Notes: Continuous variables are presented as median (interquartile range), and categorical variables are presented as *n* (%).

a. *P* values for continuous variables were derived from Kruskal-Wallis rank sum tests, and *P* values for categorical variables were derived from chi-squared tests or Fisher's exact tests, as appropriate.

evidence from UK Biobank further suggested that air pollution exposure was associated with an increased risk of incident thyroid dysfunction, particularly hypothyroidism, although that study considered multiple pollutants and clinically ascertained outcomes rather than $PM_{2.5}$ exposure and laboratory thyroid measurements alone [26]. However, not all studies have reported consistent thyroid-related associations. In Korean adults, annual exposure to PM_{10}, NO_2, SO_2, and CO showed pollutant-specific associations with thyroid function biomarkers, with NO_2 and CO associated with higher TSH and lower FT4, whereas PM_{10} was not clearly associated with TSH or FT4 in the total population [19]. In another Korean study, short-term exposure to multiple pollutants was associated with lower FT4 for $PM_{2.5}$ and O_3 and with higher TSH for NO_2 and CO, but the association between $PM_{2.5}$ and TSH was not evident [20]. The heterogeneity across different studies may reflect differences in exposure windows, pollutant type and composition, iodine nutrition, population characteristics, and outcome definitions. Our study extends this evidence to a large community-based population including both minors and adults.

We found that higher $PM_{2.5}$ exposure was not significantly associated with autoimmune thyroiditis in our study. In a comparable national cross-sectional study of 73,900 Chinese adults, residential $PM_{2.5}$ exposure estimated using 1 km × 1 km exposure data was associated with laboratory-defined autoimmune thyroiditis and TgAb positivity, but not with TPOAb positivity [42]. A Korean nationwide cohort of children and adolescents also reported that air pollution exposure was associated with incident autoimmune thyroid diseases defined using diagnostic records, although this diagnosis-based outcome is not directly comparable with our antibody-based definition of autoimmune thyroiditis [5]. Differences across studies may reflect variation in population structure, age, antibody assays, antibody thresholds, and outcome definitions, including TPOAb positivity, TgAb positivity, combined antibody positivity, autoimmune thyroiditis, and diagnosis-based autoimmune thyroid disease. For antibody-based outcomes, threshold selection may be particularly important because fixed cut-offs may not classify autoimmune thyroiditis consistently across populations [30].

In subgroup analyses, the associations of $PM_{2.5}$ exposure with FT4, TSH, and subclinical hypothyroidism varied by age and BMI after FDR adjustment, but no evidence of effect modification by sex was observed. The subgroup patterns differed across thyroid outcomes. The association between higher $PM_{2.5}$ exposure and lower FT4 appeared more evident among participants aged < 18 years or 18–49 years and among those with lower BMI. By contrast, the associations with higher TSH and higher odds of subclinical hypothyroidism appeared more evident among participants aged ≥ 50 years and among those with BMI ≥ 24.0 kg/m^2. Previous studies provide partial support for age- and BMI-related susceptibility. In Korean adults, the association of annual exposure to PM_{10}, NO_2, SO_2, and CO with serum TSH and FT4 was assessed, and air pollution-related changes in thyroid function were more pronounced among older adults and participants who were overweight or obese [19]. In another Korean study, the association of short-term exposure to multiple pollutants with thyroid function was assessed, and stronger associations were reported among participants with higher BMI [20]. For sex, the Spanish Di@bet.es study assessed annual $PM_{2.5}$ exposure and thyroid-related outcomes in a nationwide population-based survey of adults and did not observe clear heterogeneity by sex or menopausal status, which is consistent with our finding of no evidence of effect modification by sex [37]. Because directly comparable evidence on susceptible populations remains limited, these findings should be interpreted cautiously and confirmed in future studies with repeated thyroid measurements and adequate power for interaction analyses.

The associations with lower FT4 and higher TSH were generally observed across analyses using alternative exposure windows and participant-related restrictions or additional adjustment. The association with subclinical hypothyroidism was less consistent across model specifications, although most OR estimates were greater than 1. Because subclinical hypothyroidism was defined by dichotomising continuous TSH and FT4 measurements, some loss of information was unavoidable, which may have reduced statistical precision and increased sensitivity to model specification [1]. The TSH estimates varied more markedly in several models. The higher within-person biological variation of TSH relative to FT4 may have contributed to greater residual variability and lower precision in the TSH models [3]. Expressing the associations as percentage changes per 10 μg/m^3 may make the absolute differences between model-specific estimates appear more pronounced. In particular, the changes after adjustment for CO may reflect the high correlation between $PM_{2.5}$ and CO. When correlated pollutants act as surrogates for shared pollution sources, the interpretation of pollutant-specific coefficients in multipollutant models depends on the relationships among the pollutant measurements and the outcomes, and the collinearity may also complicate their interpretation [36]. The variation in the TSH estimate after adding a random intercept for study site may partly reflect limited within-site variation in $PM_{2.5}$ exposure. Overall, these analyses provided additional support for the directions of the FT4 and TSH associations, while indicating greater model sensitivity for TSH and subclinical hypothyroidism.

Several biological mechanisms may explain why higher $PM_{2.5}$ exposure was associated with lower FT4, higher TSH, and higher odds of

Table 2
Associations of $PM_{2.5}$ exposure with thyroid outcomes.

Outcomes / $PM_{2.5}$ exposure	Minimally adjusted model		Fully adjusted model	
	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
FT4, % change (95% CI)				
Q1 (<22.09 $\mu g/m^3$)	Reference		Reference	
Q2 (22.09–24.43 $\mu g/m^3$)	5.40 (4.80, 6.00)	< 0.001	2.33 (1.69, 2.97)	< 0.001
Q3 (24.43–27.20 $\mu g/m^3$)	1.20 (0.61, 1.79)	< 0.001	−1.08 (−1.80, −0.37)	0.003
Q4 (≥27.20 $\mu g/m^3$)	2.10 (1.50, 2.70)	< 0.001	−1.87 (−2.59, −1.13)	< 0.001
P for trend[a]		0.163		< 0.001
Per 10 $\mu g/m^3$ increase	0.34 (−0.30, 0.98)	0.296	−3.57 (−4.39, −2.75)	< 0.001
TSH, % change (95% CI)				
Q1 (<22.09 $\mu g/m^3$)	Reference		Reference	
Q2 (22.09–24.43 $\mu g/m^3$)	1.44 (−1.12, 4.06)	0.274	0.64 (−2.21, 3.57)	0.664
Q3 (24.43–27.20 $\mu g/m^3$)	7.97 (5.24, 10.78)	< 0.001	4.41 (1.00, 7.94)	0.011
Q4 (≥27.20 $\mu g/m^3$)	10.96 (8.13, 13.86)	< 0.001	12.04 (8.29, 15.92)	< 0.001
P for trend[a]		< 0.001		< 0.001
Per 10 $\mu g/m^3$ increase	12.37 (9.30, 15.52)	< 0.001	12.15 (7.92, 16.56)	< 0.001
Subclinical hypothyroidism, OR (95% CI)				
Q1 (<22.09 $\mu g/m^3$)	Reference		Reference	
Q2 (22.09–24.43 $\mu g/m^3$)	0.98 (0.87, 1.11)	0.754	0.95 (0.82, 1.09)	0.443
Q3 (24.43–27.20 $\mu g/m^3$)	1.30 (1.16, 1.47)	< 0.001	1.07 (0.92, 1.25)	0.383
Q4 (≥27.20 $\mu g/m^3$)	1.45 (1.29, 1.63)	< 0.001	1.31 (1.12, 1.53)	< 0.001
P for trend[a]		< 0.001		< 0.001
Per 10 $\mu g/m^3$ increase	1.54 (1.36, 1.74)	< 0.001	1.27 (1.06, 1.51)	0.008
Autoimmune thyroiditis, OR (95% CI)				
Q1 (<22.09 $\mu g/m^3$)	Reference		Reference	
Q2 (22.09–24.43 $\mu g/m^3$)	1.14 (1.02, 1.28)	0.020	1.09 (0.96, 1.24)	0.196
Q3 (24.43–27.20 $\mu g/m^3$)	1.16 (1.03, 1.29)	0.011	1.11 (0.96, 1.29)	0.165
Q4 (≥27.20 $\mu g/m^3$)	1.04 (0.93, 1.18)	0.464	0.98 (0.84, 1.14)	0.773
P for trend[a]		0.717		0.488
Per 10 $\mu g/m^3$ increase	1.06 (0.93, 1.19)	0.379	0.97 (0.82, 1.15)	0.714

Abbreviations: CI, confidence interval; FT4, free thyroxine; OR, odds ratio; $PM_{2.5}$, fine particulate matter; TSH, thyroid-stimulating hormone

Notes: For FT4 and TSH, linear mixed-effects models with a random intercept structure for family were fitted using log-transformed outcomes, and results are presented as percent change. For subclinical hypothyroidism and autoimmune thyroiditis, generalised linear mixed-effects models with a random intercept structure for family were fitted, and results are presented as odds ratios. The minimally adjusted model included sex, age, and body mass index. The fully adjusted model further included sampling season, sampling year, smoking status, drinking status, education, annual household income, occupation, urinary iodine status, salt type, seaweed consumption frequency, dried shrimp consumption frequency, and sea fish consumption frequency.

a. *P* for trend was calculated by entering the median $PM_{2.5}$ concentration of each quartile as a continuous variable in the corresponding model.

subclinical hypothyroidism. A recent review summarised that $PM_{2.5}$ may affect thyroid diseases through interrelated pathways involving oxidative stress, inflammatory responses, HPT-axis disruption, and structural or functional injury to thyroid follicles [33]. Experimental studies have shown that $PM_{2.5}$ exposure can increase reactive oxygen species generation and lipid peroxidation, as indicated by increased malondialdehyde, and reduce antioxidant enzyme activity in thyroid tissue [7,8]. Persistent oxidative injury may further promote ferroptosis and damage thyroid follicular cells, thereby reducing thyroid hormone synthetic capacity. Inflammatory responses may also contribute to thyroid dysfunction, as $PM_{2.5}$ exposure has been associated with increased inflammatory signalling in the circulation, thyroid tissue, and hypothalamus, which may aggravate follicular injury and interfere with HPT-axis regulation [27,28]. Under normal physiological conditions, hypothalamic thyrotropin-releasing hormone (TRH) stimulates pituitary TSH secretion, TSH promotes thyroidal production of thyroxine (T4) and triiodothyronine (T3), and circulating thyroid hormones suppress TRH and TSH secretion through negative feedback [15]. Therefore, $PM_{2.5}$-related oxidative and inflammatory injury may reduce thyroid hormone production, leading to lower circulating FT4 and compensatory TSH elevation. In addition, $PM_{2.5}$ and its components may alter key proteins involved in iodide uptake, thyroid hormone synthesis, and hormone transport, further disturbing thyroid hormone homeostasis [14,34,9].

This study has several limitations. First, the cross-sectional design limits causal inference. Thyroid biomarkers were measured only once at baseline, so we could not determine whether $PM_{2.5}$ exposure preceded the development of thyroid dysfunction. Moreover, the binary thyroid outcomes were defined on the basis of this single laboratory assessment and were not confirmed by physician-confirmed diagnoses. Second, exposure misclassification is possible. We assigned $PM_{2.5}$ exposure using geocoded residential addresses and a high-resolution gridded dataset, but residential exposure estimates could not fully capture individual time–activity patterns, indoor air pollution, occupational exposure, or residential mobility during the exposure window. Third, the exposure assessment was based on total $PM_{2.5}$ mass concentration and did not distinguish specific chemical components or emission sources. $PM_{2.5}$ was also highly correlated with several co-pollutants, which limited our ability to distinguish pollutant-specific associations despite the use of separate two-pollutant models. Fourth, information bias or residual confounding cannot be excluded. Although we adjusted for major demographic, lifestyle, socioeconomic, temporal, and iodine-related factors, several questionnaire-based covariates were self-reported and may have been affected by recall or reporting bias. Medication use that may affect thyroid function and pregnancy status were not included in the models because relevant data were unavailable, which may have resulted in residual confounding. Fifth, participants were recruited from six study sites, and long-term $PM_{2.5}$ exposure showed limited variation within some sites. Although a study-site random intercept was included in a sensitivity analysis, residual spatial confounding and sensitivity to the modelling of study-site clustering cannot be excluded. Finally, although participants were recruited from six sites selected to capture geographic and socioeconomic diversity in Zhejiang Province, the findings may not be generalisable to populations with different pollution profiles, iodine nutrition, healthcare access, or demographic structures.

5. Conclusion

In conclusion, higher ambient $PM_{2.5}$ exposure was associated with lower FT4, higher TSH, and higher odds of subclinical hypothyroidism in this large cross-sectional study, but not with autoimmune thyroiditis. Taken together, higher ambient $PM_{2.5}$ exposure was associated with lower thyroid function. Further prospective studies with repeated thyroid measurements, improved assessment of personal exposure and thyroid-related factors, and evaluation of pollutant components and mixtures are needed to confirm these findings and clarify susceptible

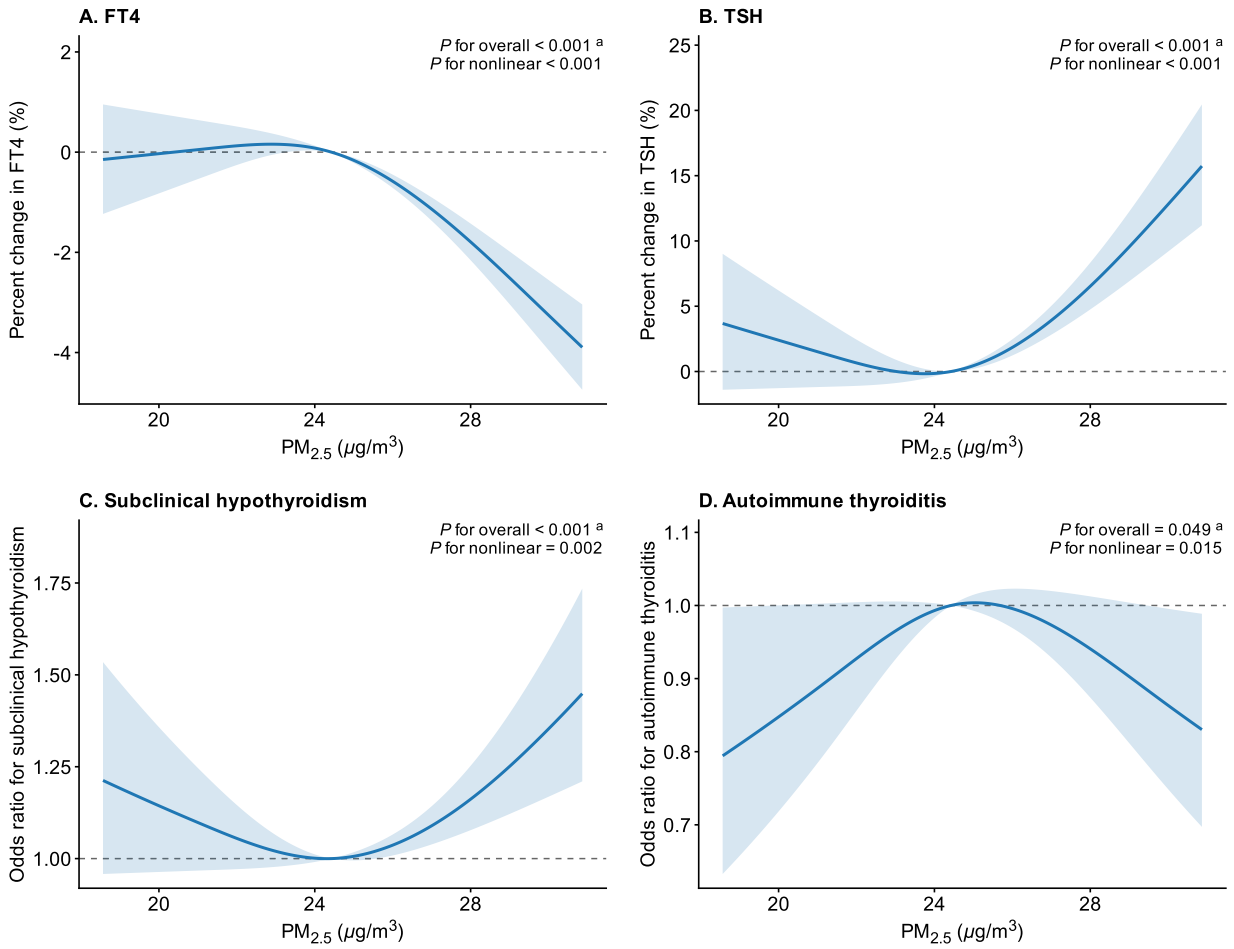

Fig. 1. Exposure-response associations of $PM_{2.5}$ exposure with thyroid outcomes. Abbreviations: FT4, free thyroxine; $PM_{2.5}$, fine particulate matter; TSH, thyroid-stimulating hormone. *Notes:* Panel A shows the exposure–response association between $PM_{2.5}$ exposure and FT4; Panel B shows the association with TSH; Panel C shows the association with subclinical hypothyroidism; and Panel D shows the association with autoimmune thyroiditis. For FT4 and TSH, linear mixed-effects models with a random intercept structure for family were fitted using log-transformed outcomes, and the results are presented as percent change relative to the median $PM_{2.5}$ concentration. For subclinical hypothyroidism and autoimmune thyroiditis, generalised linear mixed-effects models with a random intercept structure for family were fitted, and the results are presented as odds ratios relative to the median $PM_{2.5}$ concentration. $PM_{2.5}$ was modelled using natural splines with one internal knot at the 50th percentile and boundary knots at the 10th and 90th percentiles. Models were fully adjusted for sex, age, body mass index, sampling season, sampling year, smoking status, drinking status, education, annual household income, occupation, urinary iodine status, salt type, seaweed consumption frequency, dried shrimp consumption frequency, and sea fish consumption frequency. a. *P* for overall was obtained from likelihood ratio tests by comparing the spline model with the model without $PM_{2.5}$, and *P* for nonlinear was obtained by comparing the spline model with the corresponding linear model.

populations and biological mechanisms.

Abbreviations

BMI, body mass index; CHAP, ChinaHighAirPollutants; CI, confidence interval; CO, carbon monoxide; FDR, false discovery rate; FT3, free triiodothyronine; FT4, free thyroxine; HPT, hypothalamic–pituitary–thyroid; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; $PM_{2.5}$, fine particulate matter; PM_{10}, particulate matter with an aerodynamic diameter ≤ 10 μm; $PM_{10-2.5}$, coarse particulate matter calculated as PM_{10} minus $PM_{2.5}$; SO_2, sulphur dioxide; T3, triiodothyronine; T4, thyroxine; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone; ZEHC, Zhejiang Environmental Health Cohort.

Environmental Implication

Evidence regarding the association between ambient $PM_{2.5}$ exposure and thyroid dysfunction remains inconsistent, with limited data from community-based populations including both minors and adults. We found that higher residential $PM_{2.5}$ exposure was associated with lower free thyroxine, higher thyroid-stimulating hormone, and higher odds of subclinical hypothyroidism. These findings provide population-based evidence that ambient $PM_{2.5}$ exposure may be associated with lower thyroid function under real-world exposure conditions, highlighting the need to consider thyroid-related outcomes in air pollution health risk assessment and public health protection strategies.

CRediT authorship contribution statement

Lizhi Wu: Writing – review & editing, Validation, Supervision, Resources, Project administration, Investigation, Conceptualization. **Shengzhi Sun:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Conceptualization. **Pengcheng Tu:** Writing – review & editing, Resources, Investigation. **Zhijian Chen:** Writing – review & editing, Resources, Investigation. **Mingluan Xing:** Writing – review & editing, Validation, Resources, Investigation. **Xueqing Li:** Writing – review & editing, Resources, Investigation. **Zhengmao Zhuang:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Wangnan Cao:** Writing – review & editing, Resources, Methodology, Conceptualization.

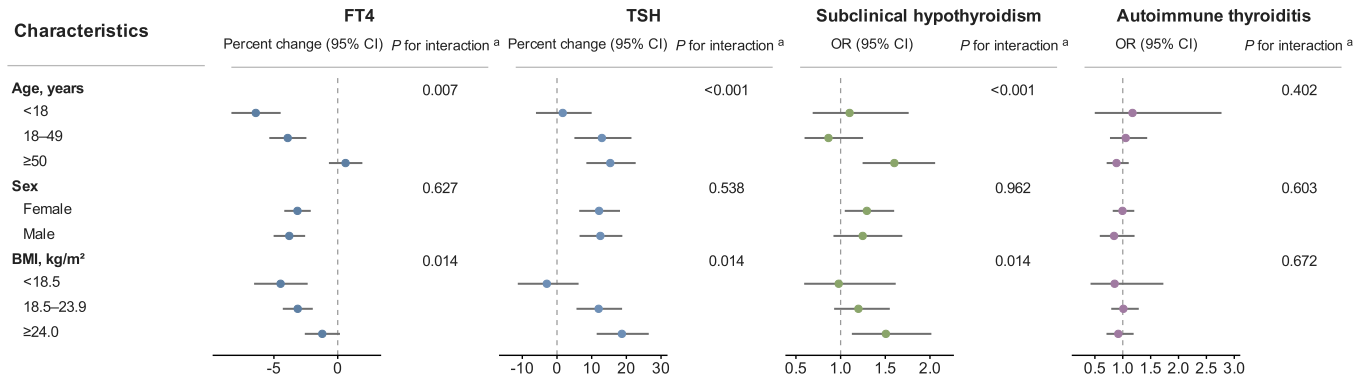

Fig. 2. Subgroup analyses of the associations of $PM_{2.5}$ exposure with thyroid outcomes. Abbreviations: BMI, body mass index; CI, confidence interval; FDR, false discovery rate; FT4, free thyroxine; OR, odds ratio; $PM_{2.5}$, fine particulate matter; TSH, thyroid-stimulating hormone. *Notes*: Estimates are reported per 10 $\mu g/m^3$ increase in $PM_{2.5}$. For FT4 and TSH, linear mixed-effects models with a random intercept structure for family were fitted using log-transformed outcomes. For subclinical hypothyroidism and autoimmune thyroiditis, generalised linear mixed-effects models with a random intercept structure for family were fitted. Models were adjusted for sex, age, body mass index, sampling season, sampling year, smoking status, drinking status, education, annual household income, occupation, urinary iodine status, salt type, seaweed consumption frequency, dried shrimp consumption frequency, and sea fish consumption frequency. Covariates with no within-subgroup variation were omitted from the corresponding subgroup model. a. *P* for interaction was obtained from likelihood ratio tests comparing models with and without interaction terms and was adjusted for multiple testing using the Benjamini–Hochberg FDR procedure.

Table 3
Sensitivity analyses for the associations of $PM_{2.5}$ exposure with thyroid outcomes.

Analysis	FT4, % change		TSH, % change		Subclinical hypothyroidism, OR		Autoimmune thyroiditis, OR	
	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
Main fully adjusted model	−3.57 (−4.39, −2.75)	< 0.001	12.15 (7.92, 16.56)	< 0.001	1.27 (1.06, 1.51)	0.008	0.97 (0.82, 1.15)	0.714
Exclude participants with thyroid disease history	−4.02 (−4.86, −3.19)	< 0.001	14.97 (10.69, 19.41)	< 0.001	1.23 (1.02, 1.49)	0.028	0.90 (0.74, 1.08)	0.258
Additional adjustment for family history in adult population	−1.41 (−2.38, −0.44)	0.005	15.76 (10.53, 21.23)	< 0.001	1.37 (1.12, 1.69)	0.003	0.93 (0.78, 1.11)	0.433
Additional adjustment for menopausal status in adult women	−1.70 (−2.89, −0.50)	0.006	13.63 (6.89, 20.80)	< 0.001	1.25 (0.98, 1.58)	0.070	0.96 (0.79, 1.18)	0.719
Additional adjustment for co-pollutants								
$PM_{10-2.5}$	−8.35 (−10.30, −6.36)	< 0.001	46.56 (32.84, 61.69)	< 0.001	4.03 (2.54, 6.39)	< 0.001	0.97 (0.61, 1.56)	0.902
NO_2	−7.90 (−9.32, −6.46)	< 0.001	22.84 (14.48, 31.81)	< 0.001	1.68 (1.22, 2.32)	0.002	0.89 (0.64, 1.22)	0.461
SO_2	−3.02 (−3.92, −2.12)	< 0.001	8.42 (3.94, 13.10)	< 0.001	1.05 (0.87, 1.27)	0.606	0.92 (0.77, 1.11)	0.379
O_3	−6.17 (−7.20, −5.12)	< 0.001	19.70 (13.75, 25.97)	< 0.001	1.80 (1.42, 2.28)	< 0.001	1.17 (0.92, 1.49)	0.204
CO	−0.94 (−2.74, 0.90)	0.314	−6.07 (−13.58, 2.11)	0.142	0.63 (0.43, 0.93)	0.019	1.02 (0.70, 1.49)	0.907
Including study site as a random intercept	−3.14 (−6.06, −0.13)	0.041	31.42 (13.96, 51.55)	< 0.001	3.28 (1.74, 6.19)	< 0.001	0.97 (0.82, 1.15)	0.714

Abbreviations: CI, confidence interval; CO, carbon monoxide; FT4, free thyroxine; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; $PM_{2.5}$, fine particulate matter; PM_{10}, particulate matter with an aerodynamic diameter ≤ 10 μm; $PM_{10-2.5}$, coarse particulate matter calculated as PM_{10} minus $PM_{2.5}$; SO_2, sulphur dioxide; TSH, thyroid-stimulating hormone.

Notes: $PM_{10-2.5}$ was calculated by subtracting $PM_{2.5}$ from PM_{10}. Estimates are reported per 10 $\mu g/m^3$ increase in $PM_{2.5}$. For FT4 and TSH, linear mixed-effects models with a random intercept structure for family were fitted using log-transformed outcomes. For subclinical hypothyroidism and autoimmune thyroiditis, generalised linear mixed-effects models with a random intercept structure for family were fitted. Models were fully adjusted for sex, age, body mass index, sampling season, sampling year, smoking status, drinking status, education, annual household income, occupation, urinary iodine status, salt type, seaweed consumption frequency, dried shrimp consumption frequency, and sea fish consumption frequency.

Ethics approval

The study was approved by the Ethical Review Committee of Zhejiang Provincial Center for Disease Control and Prevention.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2026.143231.

Data Availability

Data will be made available on request.

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