Are fluoride levels in drinking water associated with hypothyroidism prevalence in England? A large observational study of GP practice data and fluoride levels in drinking water

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ABSTRACT

Background While previous research has suggested that there is an association between fluoride ingestion and the incidence of hypothyroidism, few population level studies have been undertaken. In England, approximately 10% of the population live in areas with community fluoridation schemes and hypothyroidism prevalence can be assessed from general practice data. This observational study examines the association between levels of fluoride in water supplies with practice level hypothyroidism prevalence.

Methods We used a cross-sectional study design using secondary data to develop binary logistic regression models of predictive factors for hypothyroidism prevalence at practice level using 2012 data on fluoride levels in drinking water, 2012/2013 Quality and Outcomes Framework (QOF) diagnosed hypothyroidism prevalence data, 2013 General Practitioner registered patient numbers and 2012 practice level Index of Multiple Deprivation scores.

Findings We found that higher levels of fluoride in drinking water provide a useful contribution for predicting prevalence of hypothyroidism. We found that practices located in the West Midlands (a wholly fluoridated area) are nearly twice as likely to report high hypothyroidism prevalence in comparison to Greater Manchester (non-fluoridated area).

Interpretation In many areas of the world, hypothyroidism is a major health concern and in addition to other factors—such as iodine deficiency—fluoride exposure should be considered as a contributing factor. The findings of the study raise particular concerns about the validity of community fluoridation as a safe public health measure.

BACKGROUND

Community water fluoridation has been an accepted public dental health intervention since its introduction in the USA in the 1950s.[1] In England, some 10% of the population receives fluoridated water at a target level of 1 ppm (1 mg/L). A recent Public Health England report evaluated a range of secondary health data concluding that water fluoridation is a safe public health measure.[2] However, data on hypothyroidism were not analysed in this report despite previous studies which have suggested that there may be a link between fluoride consumption and hypothyroidism.[3] Hypothyroidism and undetected subclinical hypothyroidism are associated with a number of health problems.[3–6] While thyroid dysfunction is a common endocrine disorder, there are few population studies that examine the association of this disease with fluoride intake.[3]

In the UK, management of hypothyroidism is undertaken by primary care physicians (general practitioners, GPs) and patients' thyroid function (levels of thyroid-stimulating hormone and thyroxine) is tested annually as one element of the GP pay-for-performance system, the Quality and Outcomes Framework (QOF).[7] These data provide a measure of practice prevalence of hypothyroidism which can be geographically mapped against areas with and without fluoride added to the drinking water. This paper examines whether fluoride levels provide a useful contribution to a predictive model of practice level hypothyroidism, and whether there is any difference in hypothyroidism prevalence between practices serving areas where water is fluoridated in comparison to areas not fluoridated.

Approximately, six million people (10%) in England live in areas where drinking water contains natural fluoride or which has been artificially fluoridated at a target concentration of 1 ppm (1 mg/L).[2] Using prevalence data from the UK QOF, an analysis was undertaken to determine whether prevalence was affected by practice populations being situated in fluoridated areas at >0.7 mg/L and areas with lower levels of fluoride. While there are other sources of fluoride in people's diet (eg, tea[8]), drinking water is the most significant source of ingested fluorides in the UK.[9]

The effects of fluoride on the thyroid have long been observed.[10] In the 1950s, fluoride was used pharmacologically to reduce the activity of the thyroid in people with hyperthyroidism. Doctors selected fluoride as a thyroid suppressant based on study findings linking fluoride to goitre, and, as predicted, fluoride therapy did reduce thyroid activity in the treated patients.[11] Typically a dose of between 2 and 5 mg fluoride per day was found to be effective and this is within the range commonly consumed by individuals living in fluoridated areas.[12–14] Two reviews have examined the impact of fluoride on thyroid function concluding that fluoride is an endocrine disruptor with the potential to disrupt the function of tissues that require iodine.[3 15] In particular, it was suggested that the chief endocrine effect is decreased thyroid function at fluoride exposure levels as low as 0.01 mg/kg/day where iodine intake is inadequate.[1] The evidence relating to the relationship between fluoride intake and thyroid deficiency is mixed as studies either used observed goitre as the measure of impact or limited

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thyroid function measurements, or failed to take into account other factors, particularly inadequate iodine intake.[3 15–17] However, studies suggest that the impact of fluoride on the thyroid gland is independent of iodine and that fluoride may in fact enhance the detrimental effect of inadequate iodine intake.[3]

In most countries, estimates of the prevalence of hypothyroidism depend on small-scale epidemiological studies. Between 4% and 5% of the US population may be affected by deranged thyroid function, making it among the most prevalent of endocrine diseases.[3] In the UK, accurate measurement of the prevalence of hypothyroidism is possible as data on thyroid function for patients diagnosed with hypothyroidism have been collected by primary care physicians (GPs) since April 2004 as part of the national QOF system.[7] In 2007/2008, the prevalence in the UK was 2.8% and this increased to 3.2% by 2012/2013. Prevalence data provide 'raw prevalence' (unadjusted for other factors such as age) and QOF registers may differ from other sources of prevalence data because of coding or definitional issues.[18] However, QOF registers provide a reliable, universal recording of hypothyroidism status (99.7% in 2011/2012) of sufficient quality to enable comparison of prevalence rates between practices.

The QOF prevalence data do not account for other factors that might influence individual practice prevalence. Age and sex are key factors affecting hypothyroidism, prevalence being more common in older women and 10 times more common in women than in men.[19] As discussed above, iodine intake is an important factor in thyroid disorders. In the UK, while iodine intake levels have been considered adequate since the middle of the 20th century,[20] concern has been expressed about iodine deficiency in pregnant women and teenage girls.[21 22]

Objectives

The aim of this study is to examine whether there are differences in prevalence of hypothyroidism between populations in fluoridated and non-fluoridated areas. The objective therefore was to:

- Identify the mean and maximum fluoride levels in drinking water for practice populations in England;
- Assess, at a population level, whether variations in prevalence of hypothyroidism are associated with the fluoride levels in drinking water.

METHODS

Study design

We used a cross-sectional study design using secondary data to develop two binary logistic regression models of predictive factors for 'high' hypothyroidism prevalence at practice level using 2012 data on fluoride levels in drinking water, 2012/2013 QOF hypothyroidism prevalence data, 2013 GP registered patient numbers and 2012 Index of Multiple Deprivation (IMD) scores for GP practices. In the first model, we included all UK data; in the second, we analysed data from two comparable *built-up* areas (as defined by the Office for National Statistics in 2011),[23] one known to be fluoridated by the drinking water provider (West Midlands) and another known not to be fluoridated by the drinking water provider (Greater Manchester). Area was included as a covariate in this second model.

Setting

The setting was England, which had a population of 56.1 million people in 2011 with a median age of 39.[22]

Participants

Inclusion criteria were informed by the criteria used by Public Health England to select practices for inclusion in the National General Practice Profiles.[24] Practices in England with a code in QOF 2012/2013 were included if they had a list size >900 which was <20% different to the number of patients registered on the GP Payments System as of April 2013 and if a practice level IMD score was available. Additionally, GP practices were included if they could be mapped to a water supply zone (WSZ) using Ordnance Survey CodePoint and if fluoride levels in drinking water were available for that WSZ.

Variables

Independent variables considered for inclusion in the model were: the average (mean) concentration of fluoride in drinking water (mg/L), maximum concentration of fluoride in drinking water (mg/L), practice level IMD scores, the proportion (%) of the practice population aged 40 and over and the proportion (%) of the practice population that was female. The latter two variables were chosen because evidence shows that hypothyroidism prevalence is greater in women and increases with age.[17 19] Forty and over was chosen as the age cut-off as a large population study in Tayside, UK, found that the biggest jump in hypothyroidism incidence for women was between the third and fourth decade.[25] The dependent variable was practice level hypothyroidism prevalence.

Data sources/measurement

Hypothyroidism prevalence and practice list size for the period April 2012–March 2013 were obtained for all GP practices in England from the QOF data set. Practice level IMD scores were acquired from the Public Health England National General Practice Profiles for 2012. General practice registered populations by quinary age band and gender for April 2013 were obtained from the GP Payments System data set Health and Social Care Information Centre (HSCIC) and converted to proportions of practice patients by female gender and those aged 40 and over. Mean and maximum fluoride concentrations were provided by the Drinking Water Inspectorate (DWI) based on the WSZ in which the practice postcode was located. It is a statutory duty for water companies to monitor water quality and provide corresponding data to the DWI. They monitor fluoride concentration using samples taken from randomly chosen consumers' taps and/or water supply points (treatment works, service reservoirs and blending points). Annual sampling frequency is between 1 and 8 for WSZ samples and between 1 and 48 for supply point monitoring; frequency is determined by local factors including WSZ population and average daily output of water.[26]

Bias

Potential sources of bias include: information bias, that is, differential water sampling frequency between fluoridated and non-fluoridated areas; and response and detection bias, whereby patients are more inclined to request a hypothyroidism test and GPs give greater consideration to queried hypothyroidism in fluoridated areas, are possible but unlikely. The 2014 GP Patient Survey shows that proportions of patients (by Clinical Commissioning Group) that saw or spoke to their GP (for any reason) within the last year ranges between 80% and 89%.[27] This further reduces the likelihood that detection/response bias may influence the data.

Statistical methods

Data were analysed using IBM SPSS Statistics for Windows, V.22.0 (IBM Corp, Armonk, New York, USA). Practices were divided into two groups: those with low-to-medium hypothyroidism prevalence (lower two tertiles, 0.18: 3.57%), and high hypothyroidism prevalence (upper tertile, 3.58: 8.48%). The binary logistic regression models were developed to predict the likelihood of a practice being categorised as having recorded high levels of hypothyroidism. Variables considered for inclusion were: the proportion of female patients and proportion of patients aged ≥40 registered with the practice, IMD score and WSZ fluoride levels. Proportions were entered in the original unit interval form, and IMD score was transformed into three groups (lower, middle and upper tertiles). All water contains some fluoride, but fluoride levels of <0.3 mg/L are considered to confer no benefit to dental health.[26] International consensus (USA, Canada, Ireland) for supplementing fluoride suggests a range of 0.7 and 1.2 mg/L should be targeted. Consequently, fluoride level was converted into one of three groups: low (≤0.3 mg/L), medium (>0.3, ≤0.7 mg/L) and high (>0.7 mg/L). Two alternative measures of fluoride were considered: mean fluoride concentrations and maximum fluoride concentrations (see figure 1). A second model was built which included only practices in two *built-up* areas,[23] the West Midlands and Greater Manchester (see figure 1). These two areas were selected because they are demographically comparable but one is fluoridated by the water provider and the other is not.

Nagelkerke pseudo R^2 was used to estimate the models' contribution to the observed variance, and the Hosmer and Lemeshow test was used to evaluate classification.

RESULTS

Study sample

Of the 8020 practices in England, data for 7935 practices (98.9%) met the criteria for inclusion. Of the 85 that were not included: 40 practices had list sizes <900, population data by age were missing for 7 practices, fluoride levels were not available for 13 practices, 14 practices had a difference between the QOF list size and population data from GP Payments System of

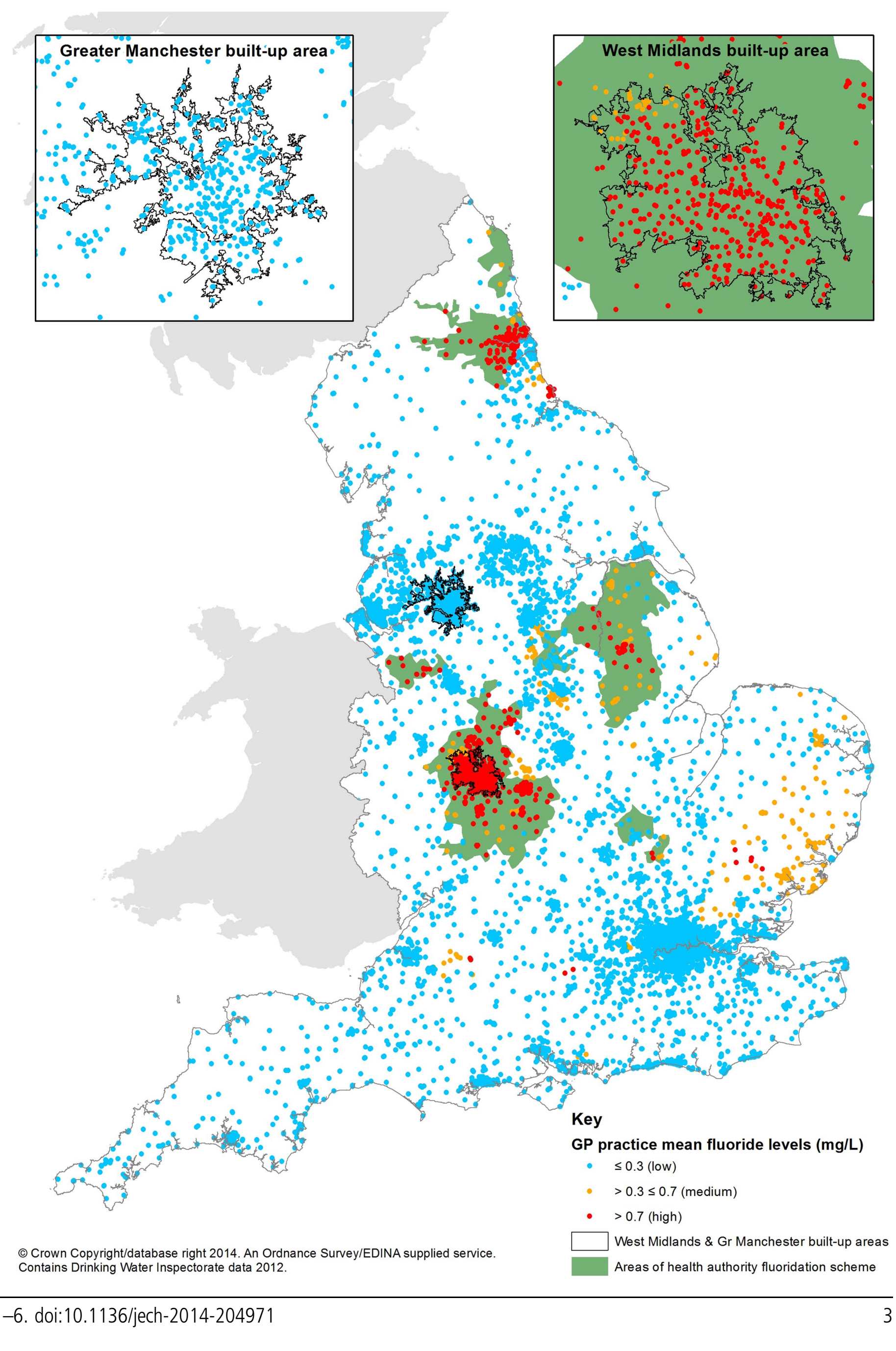

Figure 1 General practitioner (GP) practice mean fluoride levels and fluoridated areas in England in 2012.

Table 1 Summary of variables considered for the predictive models

	All practices Mean±SD
N (number of practices)	7935
List size (number of patients)	7022±4281
Hypothyroidism prevalence (%)	3.18±1.05
Mean fluoride (mg/L)	0.22±0.27
Maximum fluoride (mg/L)	0.28±0.32
Patients aged >40 (%)	49.0±10.1
Females (%)	49·9±2·4
Index of multiple deprivation score	23.84±12.23

>20% and IMD scores were unavailable for 11 practices (table 1).[24]

Model development

The first iteration of the model (which included mean fluoride levels) accounted for 37% of the observed variance and the second (which included maximum fluoride levels) was nominally better accounting for 37.5% of the variance (model χ^2=2501.74 (6); p=0.000; N=7935). The final model correctly predicts 75.6% of cases, which represents a useful improvement from 66.5% prediction rate without the covariates. Misclassification is anticipated to be unlikely (χ^2=6.815 (8); p=0.557). All covariates were significant predictors of practice level hypothyroidism prevalence (table 2). After adjusting for the effects of the other covariates, the model predicts that the odds of a practice recording high levels of hypothyroidism is 1.4 times higher in areas with maximum fluoride of >0.3 and ≤0.7 mg/L and 1.6 times higher in areas with maximum fluoride in excess of 0.7 mg/L, than it is for practices in areas with maximum fluoride ≤0.3 mg/L. For every additional 1% of women or 1% of people aged 40 and over registered, the odds of a practice recording a high level of hypothyroidism increases by multiples of 1.2, and the odds of a practice reporting high levels of hypothyroidism is 1.7 times higher where the IMD is ‘medium’ or ‘high’.

IMD levels from Public Health England practice profiles[24] Fluoride levels from DWI.[26]

The second model was restricted to data from the West Midlands and Greater Manchester. Maximum fluoride levels were >0.3 mg/L for all practices in the West Midlands and ≤0.3 mg/L in Greater Manchester. The model accounted for 33.7% of the observed variance. The model improved prediction rates from 71.4% to 76.4%. Misclassification is anticipated to be unlikely (χ^2=2.438 (8); p=0.965). Proportion of over 40s and women registered with the practice were significant predictors of practice level hypothyroidism, and had a predictive capacity similar to the model developed with the national level data set. The utility of IMD categories as predictors was reduced in this model. After adjusting for the other covariates, the built-up area that a practice is located in is a significant predictor of practice level hypothyroidism. Prevalence than practices in the West Midlands have nearly twice the odds of recording a high level of hypothyroidism prevalence as practices in Greater Manchester (table 3; model χ^2=253.788 (5); p=0.000; N=946).

IMD levels from Public Health England practice profiles.[24]

Table 2 Unadjusted and adjusted ORs of upper tertile hypothyroidism prevalence according to fluoride levels in drinking water

	OR	Fluoride level OR 95% CI
Unadjusted		
Maximum fluoride >0.7 mg/L	1.452	1.268 to 1.662
Maximum fluoride >0.3, ≤0.7 mg/L	1.711	1.439 to 2.034
Maximum fluoride ≤0.3 mg/L		
Adjusted*		
Maximum fluoride >0.7 mg/L	1.621	1.379 to 1.904
Maximum fluoride >0.3, ≤0.7 mg/L	1.371	1.120 to 1.679
Maximum fluoride ≤0.3 mg/L		

*Adjusted for proportion of women registered with the practice, proportion of patients over 40 years old registered with the practice, Index of Multiple Deprivation. C-index=0.82.

Table 3 Unadjusted and adjusted ORs of upper tertile hypothyroidism prevalence according to water fluoridation by provider

	OR	Fluoride level OR 95% CI
Unadjusted		
West Midlands (yes)	1.536	1.156 to 2.041
Greater Manchester (no) 1		
Adjusted*		
West Midlands (yes)	1.935	1.388 to 2.699
Greater Manchester (no) 1		

*Adjusted for proportion of women registered with the practice, proportion of patients over 40 years old registered with the practice, Index of Multiple Deprivation categories (16.16–28.4; 28.41–68.36). C-index=0.81.

DISCUSSION

We hypothesised that higher levels of fluoride in drinking water would provide a useful contribution for predicting prevalence of hypothyroidism in a model that included other known predictors of elevated hypothyroidism risk (ie, female gender and older age). Our hypothesis was confirmed. In addition, we found a significantly higher prevalence of hypothyroidism in areas with high fluoride levels (>07 mg/L) compared with those with fluoride levels of 0.7 mg/L and below.

The study assumed that fluoride levels at sampling points are representative of fluoride concentration for the whole WSZ and the samples take into account variance over the year. Ecological bias exists in the study in that it assumes that aggregated statistics, that is, GP practice hypothyroidism registers, are representative of the individuals living in the area. CodePoint location coordinates may not give a precise location of practices as they are created by taking an average of the coordinates of all the individual addresses in the postcode, then snapping to the nearest of those addresses. The coordinates of that address are taken as representative of the whole postcode. Patients registered with a practice may also be distributed over a wide area, covering a number of WSZs and, therefore, the fluoride level for the practice postcode may not be accurate for practice patients. Many GP practices have branch surgeries in different geographical locations but the data sets do not distinguish between branch and main practices so all data are attributed to the main practice and thus the WSZ of the main practice.

The analysis does not take into account sources of fluoride ingestion other than that in drinking water. Fluoride is found in many dental products and food and drink.[3 8 9 13 14]

Nevertheless, it is believed that drinking water is still the primary source of fluoride in England, particularly in areas with fluoride concentration of 1 mg/L and over.[9] In addition to iodine intake discussed earlier, perchlorate levels also affect thyroid function but recent analysis suggests levels of perchlorate in England are very low.[28] However, the analysis does not take into account differences in consumption of tap water between males and females and different age groups. The National Tap Water Consumption Survey estimated that consumption of tap water was greater in women and increased with age, with those aged 40 or over consuming the most tap water.[29] These estimates of tap water consumption did not vary greatly between the 40–54 and 55+ age groups, ranging from 1.4 L/day for the former to 1.3/1.4 L/day for the latter; therefore, it is unlikely that these differences are significant nor do we anticipate substantial variations in consumption between different practice populations. While iodine intake is a key determinant of thyroid status, the major source of iodine in the UK is from the diet and it is unlikely that there are significant differences between people residing in fluoridated and non-fluoridated areas.[30]

Interpretation

The clear association found in our analyses between fluoride levels in drinking water and variations in hypothyroidism prevalence appears to confirm findings in earlier studies that ingestion of fluoride affects thyroid function.[1] The fact that the difference is significant suggests that there is substantial cause for public health concern. In England, approximately six million people receive water containing 1 mg/L of fluoride. Based on our modelling, we predict that after controlling for other factors, practice populations are significantly more likely to have higher levels of hypothyroidism in fluoridated areas than in non-fluoridated areas. This study only included data on diagnosed hypothyroidism, and it is possible that in fluoridated areas there would be a proportion of the population who will suffer from subclinical hypothyroidism. While diagnosed hypothyroidism can be well controlled by taking thyroid supplements, there are a number of health problems associated with undetected subclinical hypothyroidism and undiagnosed hypothyroidism where symptoms associated with hypothyroidism are observed but not attributed to thyroid dysfunction.[5 6 21 22] In many areas of the world, hypothyroidism is a major health concern and in addition to other factors—such as iodine deficiency—fluoride exposure should be considered as a contributing factor. This study suggests that in fluoridated areas, testing for hypothyroidism should be routinely considered where any symptom attributable to lowered thyroid function is observed.

Generalisability

The finding of this cross-sectional study has important implications for public health policy in the UK and in other countries where fluoride is added to drinking water or in other forms such as fluoridated milk and salt. While in England current policy is to artificially fluoridate water at 1 mg/L, in Canada and Southern Ireland the concentration is normally 0.7 mg/L with an upper limit of 1.2 ppm. In 2011, in the USA, the Department of Health and Human Sciences proposed setting a target concentration of 0.7 mg/L but this has not yet been formally recommended and currently concentrations vary between 0.7 and 1.3 mg/L. Our study, utilising >0.7 mg/L as the threshold for high levels of fluoride, suggests that the results are applicable to all countries where water is artificially fluoridated. A recent analysis by the European Union Scientific Committee on Health and Environmental Risk concluded that children aged 1–6 years old drinking 0.5 L of water per day and children aged 6–12 years old drinking more than 1.0 L/day with a concentration of fluoride of 0.8 mg/L and above would exceed the recommended maximum upper limits for fluoride ingestion.[13] This suggests that in England, given a target level of 1 mg/L, particularly in areas where mean fluoride levels are >1.0 mg/L, most children and potentially some adults will ingest excess fluoride.[13] To minimise the risk of increasing the prevalence of hypothyroidism, it is important, therefore, to limit fluoride ingestion from all sources. This would be particularly important in areas where iodine concentrations are low, given the potential action of fluoride as an iodine inhibitor.[3] From a public health perspective, this raises questions about the safety of community fluoridation and consideration should be given to reducing all sources of fluoride in the environment.[1 13 14]

What is already known on this subject

- Community water fluoridation is an established public dental health intervention in some countries.
- There have been a number of studies that suggest that the ingestion of fluoride is associated with hypothyroidism.
- There have been no population studies that have examined this.
- A recent analysis of health data on the impact of fluoridation in England did not examine hypothyroidism prevalence despite the availability of data within the national Quality and Outcomes Framework data set.

What this study adds

- This study is the first population level study of the association between fluoride levels in water and hypothyroidism.
- We found a positive association between fluoride levels and hypothyroidism. High hypothyroidism prevalence was found to be at least 30% more likely in practices located in areas with fluoride levels in excess of 0.3 mg/L.
- This population study supports earlier hypotheses that fluoride is associated with hypothyroidism. In the UK, water is fluoridated at 1 ppm (1 mg/L), and in areas where water is fluoridated, the model predicts that after controlling for other factors, practice populations are significantly more likely to have higher levels of hypothyroidism than those in non-fluoridated areas. Consideration needs to be given to reducing fluoride exposure, and public dental health interventions should stop interventions reliant on ingested fluoride and switch to topical fluoride-based and non-fluoride-based interventions.

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Contributors SP was responsible for the study concept and design. SS was responsible for the acquisition of the data. DL and SS were responsible for the analysis and interpretation of data. SP, SS and DL drafted the manuscript. All authors took part in critical revision of the manuscript. DL provided the statistical expertise.

Competing interests SP was involved in a campaign in Southampton (UK) to prevent the fluoridation of drinking water supplies.

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