No Evidence Supports the Claim That Water Fluoridation Causes Hypothyroidism
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SUMMARY

Subjects
These analyses used data from medical practices in England, specifically from the 2012 Public Health England National General Practice Profiles, so the practices were the "subjects" in the study.

Only general practices that could be mapped to a water supply zone, had profile scores for a measure of impoverishment, had mean age and gender distribution data available, and included at least 900 patients were included. This resulted in 7935 practices being included in the study out of a total of 8020 in all of England.

Key Study/Risk Factor
The key risk factor was mean water fluoride concentrations for each practice as determined from matching practices to specific water supply zones (with known water fluoride levels). The study also categorized water fluoride concentrations as #0.3 mg/L, 0.3 mg/L to 0.7 mg/L, or >0.7 mg/L. Another set of analyses compared two groups of practices – one in an area with water fluoride levels >0.3 mg/L in the West Midlands and another in the Greater Manchester area with water fluoride levels of #0.3 mg/L.

Main Outcome Measure
The main outcome measure was based on the proportion of practices' populations with hypothyroidism (i.e., prevalence of hypothyroidism in each general practice) adjusted for age, gender, and poverty status.

These proportions were subsequently divided into tertiles, and ultimately into two groups – a high proportion group with between 3.58% and 8.48% of patients affected with hypothyroidism and a low-to-medium group with 0.18% to 3.57% of patients affected. This dichotomous outcome of "high" or "low-to-medium" hypothyroid prevalence was the main outcome measure.

Main Results
In binary logistic regression modeling, the study found that practice membership in the high hypothyroid group was associated with higher water fluoride concentrations. Specifically, the study reported that the odds of a practice being in the high hypothyroidism group was 1.37 (95% confidence interval [CI] 1.12, 1.68) when the practice was in an area with water fluoride levels of 0.3 mg/L to 0.7 mg/L and was 1.62 (95% CI 1.38, 1.90) when the practice was in an area with water fluoride levels greater than 0.7 mg/L, relative to areas with water fluoride levels less than 0.3 mg/L. It was also reported that the odds ratio for being in the high hypothyroid group was 1.95 (95% CI 1.39, 2.70) for the higher fluoride area (>0.3 mg/L) of the West Highlands relative to Greater Manchester (#0.3 mg/L).

Conclusions
The authors concluded that fluoride exposure should be considered as a contributing factor to hypothyroidism and that the study results raised concerns about the validity of community water fluoridation as a safe public health measure.
COMMENTARY AND ANALYSES

There are several concerns about the study design, methods, clarity of data presentation, and analysis that preclude the authors from reaching the strong conclu- sions made in this article. Beginning with the background section, the authors contest T he Public Health England Report on water fluo- ridation for the missing information on the association between hypothyroidism and water fluoridation in spite of “previous studies which have suggested that there may be a link between fluoride consumption and hypo- thyroidism.” The reference given is a review from EPA (Environmental Protection Agency, US) standards1 that actually did not suggest “a link” but pointed out the lack of evidence of such association needing further investigation. The EPA report stresses the need for good and well-designed studies including “collecting data on general dietary status and dietary factors that could influence the response, such as calcium, iodine, selenium and aluminum intakes.”

The first misconception in this study is its classification as only a cross-sectional while in fact it is an ecological study. Ecological studies, although useful, are well known for the possibility of ecological fallacy, since they assume group characteristics apply to all individuals. In this case, the study assumes that people living in an area with water fluoridation all have higher exposure to fluoride than those in the nonfluoridated area. While the mean fluoride exposure in a fluoridated area is likely to be higher than the mean exposure in a nonfluoridated one, studies have shown very high variation in individual fluoride exposures regardless of water fluoride concentration.2 Moreover, ecological studies ignore migration and dynamics of the population within the country even among those over age 40 years.3 Being an ecological study with information from one point in time, causation cannot in any way be implied from the study; however, the authors clearly seem to imply causation in the Discussion and Conclusion sections.

Another important issue is the imprecision of both outcome and exposure measurements. Outcome information is obtained from QOF (Quality and Outcome Framework), which is a voluntary program of information for rewarding good practices of general practices in England. 4 Therefore, the outcome variable being the pro- portion of patients in English general practices with hypothyroidism, certain practice characteristics (e.g., age of provider, provider training) may have accounted for much of the observed difference. Again, given that studies have long shown differences in procedures per- formed by different practices,5 the lack of data on practices is a significant shortcoming. Moreover, there could have been many other factors that better explain the risk of hypothyroidism, but such data apparently weren’t available for this study. Fluoridation in the UK is based on decisions by health departments, which may be associated with other risk factors for hypothyroidism.

Lack of control of some confounders is also an important contributing factor for the weakness of this study. While some confounders such as sex, age, and measure of poverty were taken into consideration, a number of things weren’t considered, most notably iodine exposure. Moreover, the EPA’s report recommends the inclusion of selenium, calcium, and aluminum intake that may influence thyroid-stimulating (TSH) hormones.1,6 Also, the effect of residual confounders cannot be forgotten since there is a reasonable variation in ecological variables used as confounders.
Another important concern is how the authors handled and presented the statistical analysis. No reason- able descriptive table helps us understand the data, and Table 1 presents only general means and standard deviations. Given evidence that water fluoridation and other variables do not have normal distributions, standard de- viations are essentially meaningless. Moreover, since the outcome and the exposure are continuous variables, the best option for analysis would be to keep them as continuous in a regression (linear or not linear) unless there is clear evidence of model assumption violations. Regardless of the authors’ decision to use logistic regression with categorization of both exposure and outcome, a scatter plot would be essential to show us the pattern of this association (linear, non-linear, or presence of threshold).

After the first meaningless descriptive table, the authors jump to final odds ratios with no bivariate analysis to allow us to have a clear picture of data distribution.

Thus, we cannot rule out that the cut-points chosen by the authors were selected with the sole intent to find those cut-points that would result in significant associations (while ignoring other cut-points that may have yielded very different results). Also, the decision for categorization based on the effect of fluoride on dental caries prevention does not make sense, since it has nothing to do with any possible biological effect on hypothyroidism (TSH levels or thyroid function).

Moreover, when the authors selected the West Highlands and Greater Manchester areas to compare, and why did they select the water fluoride concentrations of #0.3 mg/L vs. >0.3 mg/L for this comparison, instead of the three categories they had used for the earlier comparisons? What would the results have been had they compared the West Highlands area to another low water fluoride area or several of the nonfluoridated ones? The lack of more complete findings raises concerns that authors chose to report on this particular comparison because it matched the message they wanted to convey – i.e., that fluoride is harmful.

In summary, this study is an ecologic one that has several significant flaws, making it almost meaningless with regard to assessing any possible association between water fluoridation and hypothyroidism. As such, this study provides no evidence of a causal relationship between water fluoride concentration and hypothyroidism.

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