Fluoridation and hypothyroidism – a commentary on Peckham *et al.*

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IN BRIEF

- Highlights that correlation is not causation.
- Suggests that public health policy must be based on the highest quality scientific evidence.
- Recommends that governments and health professionals can remain assured that the safety of water fluoridation is not in question.

OPINION

In many countries around the world community water fluoridation is a key element in the campaign for better dental public health. Its safety and effectiveness have been confirmed through decades of research, and the practice has been strongly endorsed by reputable health authorities. A strong evidence base is critical for the implementation of fluoridation and other public health measures. Health professionals must ensure that the highest quality evidence is promoted, and weak evidence identified and discredited.

In February 2015, the *Journal of Epidemiology and Community Health* published the Peckham *et al.* paper 'Are fluoride levels in drinking water associated with hypothyroidism in England? A large observational study of GP practice data and fluoride levels in drinking water'.[1] The authors' conclusion, that the study '...raises questions about the safety of community fluoridation and consideration should be given to reducing all sources of fluoride in the environment', has attracted substantial media attention around the world.

Peckham *et al.* studied reported levels of hypothyroidism from English GP medical practices and compared levels of hypothyroidism with levels of fluoride in each region's drinking water. They conducted a second analysis comparing the prevalence of hypothyroidism in the fluoridated West Midlands and non-fluoridated Greater Manchester.

The authors began by stating: 'Community water fluoridation has been an accepted public dental health intervention since its introduction in the USA in the 1950s.' This statement needs no reference since it is common knowledge, although fluoridation was actually introduced in Grand Rapids, Michigan in 1945, but Peckham gains an inappropriate self-citation by referencing it with a previous paper in *Scientific World Journal* by himself and Awofeso opposing water fluoridation.[2] *Scientific World Journal* has a well-publicised history of colluding with other journals to self-cite authors' papers to increase journal impact factors.[3] The referenced Peckham and Awofeso paper is unusual in that many unattributed paragraphs, including factual errors, are almost identical to paragraphs from a previous Awofeso paper.[4] This paper in turn has unattributed paragraphs almost identical to paragraphs on webpages belonging to the National Institute of Dental and Craniofacial Research[5] and a popular chemistry website.[6]

Peckham *et al.*'s hypothyroidism paper claims to have '...used a cross-sectional study design...', but the study can be more correctly described as an ecological study. A cross-sectional study usually attempts to correlate exposure and outcome variables recorded from sampled individuals, whereas an ecological study derives data for either the exposure or outcome variable or both from population data, for example, censuses, government data or previous studies, rather than individual subjects. Attributing a causal association between exposure and outcome variables in ecological studies is difficult, as they are particularly susceptible to bias and confounding. The ecological fallacy, by which inferences about individuals can be incorrectly made based on findings from population data, is well known.

Peckham *et al.* then state: 'The effects of fluoride on the thyroid have long been observed', with the strong implication that these effects involve suppression of thyroid activity. They reference a 1961 Feltman and Kosel paper on prenatal and postnatal ingestion of fluorides[7] to support this statement. But Feltman and Kosel's only mention of the thyroid is a single sentence that other researchers '...report that fluoride is a thyroid inhibitor'. Their only references for this statement are a personal communication with US Public Health Service researcher Floyd De Eds, and a 1954 paper that studied delayed tooth eruption in rats following removal of the pituitary gland. The evidence supporting Peckham *et al.*'s statement is extremely weak.

Peckham *et al.* added, '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', referencing a 1958 Galletti and Joyet paper[8] to support this statement. However, Galletti and Joyet only investigated the effect of fluorides on patients with hyperthyroidism, and did not find that fluoride was linked to goitre. Galletti and Joyet noted that two authors in the 1920s and 30s '...had postulated that goitrous states could be attributed to fluorine intake', but 'other investigators, however, could not reproduce these definite changes in the thyroid, and thus the thyreostatic activity of fluorine is still questioned'. Regarding the reduction in thyroid activity in patients with hyperthyroidism treated with fluoride, Galletti and Joyet concluded '...such an action appears only occasionally among persons subjected to massive doses of this substance', a situation clearly not comparable to community water fluoridation.

In 2006, the British Thyroid Association endorsed a statement quoting a number of major international reviews, and concluding 'none has found any credible evidence of an association between water fluoridation and any disorder of the thyroid'.[9] Elsewhere in the paper, Peckham *et al.* reference the European Union's 2011 SCHER report into health and

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environmental risks of fluoride[10] in implying the dangers of water fluoridation, but ignore SCHER's conclusion 'Human studies do not suggest adverse thyroid effects at realistic human exposures to fluoride.'

Peckham *et al.*[1] accept that iodine intake is a key determinant of thyroid status, but then confidently state that '...it is unlikely that there are significant differences between people residing in fluoridated and non-fluoridated areas'. This, despite earlier in their paper referencing another UK study[11] which found greatly differing urinary iodine levels in groups of schoolgirls from major UK cities, with 17% of participants showing moderate to severe deficiency.

Peckham *et al.* also reference the 2006 National Research Council (NRC) report[12] to support their contention that water fluoridation is associated with thyroid dysfunction, but the NRC made no such finding. The NRC noted a range of study results, few relevant to water fluoridation, and recommended further research. Following the 2006 NRC report, the US-based Centres for Disease Control (CDC) reiterated their support for fluoridation, stating that: 'CDC considers comprehensive reviews by the NRC and other systematic scientific studies in its recommendation that community water fluoridation is a safe, effective, and inexpensive method to reduce tooth decay among populations with access to community water systems. Water fluoridation should be continued in communities currently fluoridating and extended to those without fluoridation.'[13]

Peckham *et al.* show little understanding of confounding factors, and have made only a token attempt at considering their impact. The authors mention the ecological fallacy, but then ignore its implications in strongly implying a causal link between water fluoridation and hypothyroidism.

An ecological study can only provide strong evidence for a causal link between two variables if it accounts for the effects of all confounders. However, not all variables are potential confounders. Confounding factors are only those variables statistically associated with both exposure and outcome variables; that is, differently represented in the subgroups of each, and not on a causal pathway between the two. Through statistical associations with both exposure and outcome variables, confounders can exaggerate, reduce or completely negate any true association between the two.

In the Peckham *et al.* study, potential confounders of age, gender, and Index of Multiple Deprivation scores (a proxy for socioeconomic status) were considered. Age is certainly associated with the outcome variable, hypothyroidism. People with hypothyroidism are much more likely to be older, since hypothyroidism is more commonly a condition of middle-aged and elderly people. But is age associated with fluoridation status? Specifically, is the mean age of people in fluoridated cities different to that of people in non-fluoridated cities? If people in fluoridated cities are significantly older than in non-fluoridated cities, age as a confounder could easily result in an overestimation of any true causal effect of fluoridation on hypothyroidism seen in those cities. Conversely, if people in fluoridated cities are significantly younger than in non-fluoridated cities, age as a confounder could significantly underestimate any true causal effect of fluoridation on hypothyroidism. Peckham *et al.* report some variability (49.0 ± 10.1%) (mean ± SD) of patients aged >40 across all practices, but they fail to specify where these variations exist, or if they represent true population differences or merely differences in patients attending medical practices. Many patients with hypothyroidism remain undiagnosed for years,[14] and the profile of patients attending medical practices may be very different to the profile of the general population. It is uncertain from the data whether age should have been considered as a potential confounder, but Peckham *et al.* provide no evidence to suggest that large UK cities have greatly differing age profiles that could confound any association between fluoridation status and hypothyroidism.

Similarly, gender can only be a confounding variable if it is differentially represented in subgroups for both the exposure and outcome variables. Gender is certainly associated with hypothyroidism; women are much more likely to be diagnosed.[15] But is gender associated with the fluoridation status of UK cities? Peckham *et al.*'s own data suggest almost no gender variation across UK cities; (49.9 ± 2.4%) (mean ± SD) of people are female. In this case, gender is unlikely to be a confounding variable, and need not have been considered by the authors. Tables 2 and 3 in the paper show differences between unadjusted and adjusted odds ratios for the associations between fluoride levels and the prevalence of hypothyroidism, but fail to explain which variables contributed to those differences. But should any other variables have been considered as potential confounders?

The possible confounding factor that immediately comes to mind is iodine intake, previously and inexplicably discounted by Peckham *et al.* Iodine intake could potentially be associated with fluoridation status. Vanderpump *et al.* have already shown that schoolgirls in fluoridated Birmingham appear to be more likely to show moderate-to-severe iodine deficiency than schoolgirls in many non-fluoridated UK cities,[11] and the levels of moderate-to-severe iodine deficiency vary considerably across the UK even when comparing only non-fluoridated cities. And iodine intake is associated with the outcome variable, hypothyroidism. Iodine intake could certainly confound any statistical association between fluoridation status and hypothyroidism. So why wasn't this considered by the authors? Authors also failed to consider the impacts of smoking, medications and other factors known to contribute to hypothyroidism.

Confounders in epidemiological studies are not randomly or conveniently selected from a grab bag of variables; experts in the field must select potential confounders after a thorough literature assessment of their possible impact on both exposure and outcome variables. Peckham *et al.* do not appear to be experts in epidemiology or thyroid diseases. Peckham is an economist and health policy expert, Lowery a psychologist, and Spencer's expertise is in environmental science. One can only speculate why authors did not collaborate or consult with an endocrinologist or ENT specialist, but Peckham's known opposition to water fluoridation may be relevant here.

Peckham *et al.*'s paper concludes, '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'. Three references are given to support this statement; however, two of the references provided make no such alarmist recommendation. The only one of the three that does so is Peckham's own 2014 paper.[2]

Peckham *et al.* fail to understand the limitations of a poorly conducted ecological trial, and the paper contains serious biases and flaws. Literature reviews have been highly selective and critical analysis of that literature has been poor. The authors show a disturbing tendency to focus on a small number of poor quality studies that reinforce their own views, while ignoring contradictory evidence from much stronger studies and reviews. Peckham *et al.* should have heeded the adage 'correlation is not causation' before coming to a conclusion at odds with a large body of reputable evidence from around the world. In my opinion, the paper's conclusions can and should be dismissed.

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