

## LETTER

## Health effects of water fluoridation—how “effectively settled” is the science?

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The recent publication of a high-profile review<sup>1</sup> marks a milestone in the New Zealand (NZ) discourse regarding this controversial public health practice. Jointly sponsored by the Royal Society (RSNZ) and the Prime Minister’s Chief Science Advisor, the review strongly supports the Ministry of Health’s promotion of community water fluoridation (CWF) and concludes “there are no adverse effects of fluoride of any significance arising from fluoridation at the levels used in New Zealand.”

The developmental neurotoxicity of fluoride is well established, with plausible mechanisms, based on observational studies and preclinical toxicology,<sup>2–4</sup> but its relevance to CWF remains controversial due to uncertainties about exposure (dose × duration, across all sources), effect thresholds, and uncontrolled confounders. Significant IQ deficits in children exposed to high fluoride were reported by two meta-analyses;<sup>3,4</sup> the RSNZ review<sup>1</sup> considered only one of these and dismissed its relevance, apparently due in part to mistaking the average deficit to be around half an IQ point rather than half a standard deviation (seven IQ points).<sup>5</sup>

We consider below a recent NZ study that reported no IQ differences attributable to childhood exposure to CWF.<sup>6</sup> Although the RSNZ review cites this as indicating neurodevelopmental safety, several considerations suggest that the study failed to adequately assess possible IQ effects of fluoride exposure.

The IQ of the Dunedin birth cohort was analysed in relation to childhood residence in suburbs with or without CWF.<sup>6</sup> The authors control for socioeconomic status, but unmeasured confounders operating at suburb level are likely to influence IQ and were not considered in the analysis.<sup>7</sup> This is important, because residence determines CWF exposure and thus measurements are clustered within the same geographic groupings that determine the study’s ‘design’.<sup>8</sup>

Suburbs with CWF were mostly in central Dunedin while those without were peripheral; it is thus very likely that unmeasured factors co-vary with suburb. For example, most children without CWF exposure lived in Mosgiel, which borders a farming district and has rural characteristics. Rural children, as the authors note, typically have lower IQs than those from urban areas.

Controlling such confounders may be possible with hierarchical mixed-effects modelling, using random intercepts for the clustering factor—in this case, suburb.<sup>7</sup> Analyses could also include structured random effects to model spatial relationships within the data—for example, distance from the city centre. Hierarchical modelling may strengthen the study’s results, provided the geographical clusters are not inextricably confounded with fluoride exposure.<sup>8</sup>

Breastfeeding and fluoride supplementation also deserve further analysis. Given data suggesting the beneficial IQ effect of breastfeeding is more pronounced in CWF areas (Table 3),<sup>6</sup> a CWF × breastfeeding interaction, including all available duration data, should be reported. This is important because the breast actively excludes fluoride from milk,<sup>9</sup> particularly reducing exposure in CWF areas since infant formula is typically prepared with tap water.

Likewise, the authors do not report the distribution of fluoride tablet or toothpaste use according to CWF status; these additional fluoride sources, and available duration data, warrant inclusion in the multivariate model to better estimate exposure and enable more sensitive hypothesis testing.

More children were exposed to tablets (n=139) or toothpaste (n=874) than resided in non-CWF areas (n=99); comparing groups with overlapping total fluoride exposure thus compromises the study’s

statistical power to determine the single effect of CWF. Individualising exposure estimates is thus essential to test the possible impact of fluoride exposure on IQ. For example, a subset of children was exposed to CWF, fluoride tablets and toothpaste; their IQs would be of particular interest given intensified exposure.

Finally, the Dunedin study's analyses assumed that IQ is normally distributed. In fact this distribution has a negative skew, plausibly because infrequent combinations of environmental and genetic factors may disrupt brain development.<sup>10</sup> Neurotoxin exposure may thus have little effect on mean IQ, while markedly increasing the number of children with impairment (IQ<70, say).<sup>4</sup> The Dunedin dataset offers a unique opportunity to explore this possibility, taking into account all factors affecting fluoride exposure (CWF, tablets, toothpaste, breastfeeding) including duration of each. Individualised exposure and effect assessment, as suggested here, were recommended by the National Research Council (USA) in 2006.<sup>2</sup>

Available evidence regarding both benefits and harms of CWF is generally of low to moderate quality, making firm conclusions doubtful.<sup>11</sup> There are, for example, no prospective, randomised trials, and a Cochrane Review is not yet available. Public debate is typically polarised, reflecting disparate ethical and professional views of CWF; both sides are known to 'cherry pick' and distort evidence to suit their respective arguments.<sup>11</sup>

In describing the Dunedin study<sup>6</sup> as "extensive" and the risk of IQ effects from CWF as "imperceptibly small" the RSNZ review<sup>1</sup> appears to have overstated available evidence. Given the importance of the issue, and the numbers of children exposed, exhaustive and impartial evaluation of scientific evidence should be required to inform public policy.

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