The finding’s of the NTP’s 6-year fluoride neurotoxicity evaluation
What did the NTP find?
The NTP’s “moderate confidence” conclusion for developmental neurotoxicity in human studies supports a “presumed hazard” conclusion when applying NTP’s OHAT methodology.

“Moderate confidence” is the 2nd highest OHAT confidence conclusion.

“Presumed hazard” is the 2nd highest OHAT hazard conclusion and is applied when human studies give “moderate confidence” and there is a “relatively large and consistent body of evidence”
Did NTP find a “relatively large and consistent body of evidence”?

“Moderate confidence” is the 2nd highest OHAT confidence conclusion.

“Presumed hazard” is the 2nd highest OHAT hazard conclusion and is applied when human studies give “moderate confidence” and there is a “relatively large and consistent body of evidence”
Latest NTP 2022 monograph

• **52 of 55** human studies found reduction in IQ from fluoride

• **18 of 19** human studies rated low Risk of Bias by NTP found reduction in IQ from fluoride

“The pattern of results across the 55 studies was consistent; 52 (95%) reported an inverse association”

“Subgroup analyses by sex, age group, study location, outcome assessment type, and exposure assessment type further support the **consistent and robust pattern** of an inverse association between fluoride exposure and children’s IQ”
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"Subgroup analyses by sex, age group, study location, outcome assessment type, and exposure assessment type further support the consistent and robust pattern of an inverse association between fluoride exposure and children’s IQ”

When NTP was still making hazard assessments in 2020, how large and consistent was the body of evidence needed to support a “presumed hazard” conclusion?
Latest NTP 2022 monograph

- **52 of 55** human studies found reduction in IQ from fluoride
- **18 of 19** human studies rated low Risk of Bias by NTP found reduction in IQ from fluoride

“Subgroup analyses by sex, age group, study location, outcome assessment type, and exposure assessment type further support the **consistent and robust pattern** of an inverse association between fluoride exposure and children’s IQ”

The body of evidence has strengthened

Earlier NTP 2020 monograph

- **44 of 46** human studies found reduction in IQ from fluoride
- **8 of 9** human studies rated low Risk of Bias by NTP found reduction in IQ from fluoride

NTP 2020 monograph concluded fluoride posed a “**presumed hazard**” of developmental neurotoxicity
Dose-Response

Did NTP find a safe threshold?
Dose-Response

Did NTP find a safe threshold?

“there was no obvious threshold as illustrated by the figure ...”

[BSC WG report page 326]
Water Fluoride Exposure

*eFigure 17. Pooled Dose-Response Association Between Fluoride in Water and Standardized Mean Differences in Children's IQ*

- Left panel: circles indicate standardized weighted mean differences (SMDs) in individual studies; size of bubbles is proportional to precision (inverse of variance) of the standardized mean differences.
- Right panel: water fluoride levels were modeled with restricted cubic spline terms in a random-effects model (solid line). Dashed lines represent the 95% confidence intervals for the spline model. Please see *eTable 2* for characteristics of the studies included in the dose-response meta-analysis (studies with water fluoride exposure and at least two exposure levels).

Commented [l19]: See Doc03_Meta-analysis, 3.F., page 4

Commented [l18]: See Doc08_Meta-analysis, 8.R., page 10 and 11

July 2022

**Dose-Response Meta-Analysis**

*eFigure 17*
July 2022

Dose-Response Meta-Analysis

eFigure 17

No evidence of a threshold at 1.5 mg/L or 0.7 mg/L water F concentration.
Dose-Response Relationships

**Fluoride-IQ**
(NTP 2022)

**Lead-IQ**
(Lanphear et al 2005)
The comment implies that our conclusions are based solely on “studies [that] were conducted on populations with higher exposures from water than are routinely found in the United States.” This implication is not accurate.

... the confidence assessment also includes findings from studies with fluoride exposures that are similar to, or lower than, those associated with optimally fluoridated water supplies in the United States.

As demonstrated in Green et al. (2019), who used repeated individual urinary measurements, drinking water measures likely capture only a portion of a person’s total exposure to fluoride as personal preferences and habits may increase total exposures to unknown levels. Therefore, this document, as well as any associated communication, focuses on total fluoride exposures from all sources, not just drinking water.
Summary of NTP findings

- "moderate confidence" of developmental neurotoxicity
- Large and very consistent body of evidence supports "presumed hazard" conclusion
- No safe threshold observed
- "Moderate confidence" conclusion applies to water fluoride of 0.7 mg/L
No wonder the divisions of HHS that promote fluoridation have tried to alter, delay, and suppress the NTP evaluation!
From documents obtained through Freedom of Information Act (FOIA) the political pressure has come from fluoridation promoting divisions of HHS including NIDCR, CDC Oral Health, and the PHS Surgeon General’s office, together with dental lobby groups like the American Dental Association.

These government and dental agencies have been vigorously promoting fluoridation for over 70 years.

They are using the same science manipulation tactics the lead, tobacco, and chemical industries have used to defend their toxic products.
Request to BSC members:

Uphold the scientific integrity of the NTP and its dedicated staff

FREE the NTP report
Dose-Response

Did NTP find a safe threshold?
Dose-Response

Did NTP find a safe threshold?

NTP also did dose-response meta-analysis of studies with individual-level continuous exposure measures.

These included the highest quality longitudinal cohort studies.
Dose-Response

Did NTP find a safe threshold?

The BSC workgroup recommended NTP display results of these dose-response analyses graphically and we concur.

Nevertheless, the consistency of these studies finding adverse effects on IQ with various regression models at several ranges of exposures can be assessed from eTable 4.
Did NTP find a safe threshold?

NTP fit linear, quadratic, and spline models, and restricted included studies by several cut-off exposure levels.

Evidence for or against a safe threshold can be derived from comparing model results at the different cut-off exposure levels.
Latest NTP 2022 meta-analysis

- 44 of 56 dose-response meta-analysis regression models found lower IQ as F increases
- 23 of 24 linear dose-response meta-analysis regression models found lower IQ as F increases
- 9 of 14 dose-response meta-analysis regression models restricted to studies with <1.5 mg/L F found lower IQ as F increases
- 5 of 6 linear dose-response meta-analysis regression models restricted to studies with <1.5 mg/L F found lower IQ as F increases

### Table A. 2. Inorganic Fluoride Exposure-Model Selection

<table>
<thead>
<tr>
<th>Fluoride Exposure</th>
<th>Parameter</th>
<th>All data</th>
<th>F&lt;1.5 mg/L</th>
<th>F≥1.5 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water Fluoride - All Studies</td>
<td>Average dose</td>
<td>28.9</td>
<td>32.2</td>
<td>25.7</td>
</tr>
<tr>
<td>Linear Model</td>
<td>regression coefficient</td>
<td>0.12</td>
<td>0.10</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>SE</td>
<td>0.08</td>
<td>0.07</td>
<td>0.12</td>
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<tr>
<td>Water Fluoride - Low Risk children</td>
<td>Number of Children</td>
<td>113</td>
<td>143</td>
<td>25</td>
</tr>
<tr>
<td>Linear model</td>
<td>regression coefficient</td>
<td>0.14</td>
<td>0.14</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>SE</td>
<td>0.06</td>
<td>0.06</td>
<td>0.10</td>
</tr>
</tbody>
</table>

---

Pink highlighting on Beta coefficient indicates negative association between F and IQ.

[BSC WG report pages 697-699]
Pink highlighting on Beta coefficient indicates negative association between F and IQ.

Latest NTP 2022 meta-analysis

- **44 of 56** dose-response meta-analysis regression models found lower IQ as F increases

- **23 of 24** linear dose-response meta-analysis regression models found lower IQ as F increases

- **9 of 14** dose-response meta-analysis regression models restricted to studies with <1.5 mg/L F found lower IQ as F increases

- **5 of 6** linear dose-response meta-analysis regression models restricted to studies with <1.5 mg/L F found lower IQ as F increases

A majority of models have negative associations (IQ reduced as F increases), including a majority of models restricted to those studies with <1.5 mg/L
**Table 2. Dose-Response Meta-analysis Using Mean Effects—Model Selection**

<table>
<thead>
<tr>
<th>Exposure Analyte</th>
<th>Parameters</th>
<th>All data</th>
<th>&lt;1 mg/L</th>
<th>&lt;2 mg/L</th>
<th>&lt;5.0 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water Fluoride—All Studies</td>
<td>No Study/No Observations</td>
<td>20/39</td>
<td>21/27</td>
<td>5/4</td>
<td>57</td>
</tr>
<tr>
<td>Sodium (mg/L F)</td>
<td>p = 0.50</td>
<td>p = 0.01</td>
<td>p = 0.77</td>
<td>p = 0.80</td>
<td>p = 0.96</td>
</tr>
<tr>
<td>Linear Model</td>
<td>Beta (95% CI)</td>
<td>p = 0.28</td>
<td>p = 0.11</td>
<td>p = 0.17</td>
<td>p = 0.80</td>
</tr>
<tr>
<td></td>
<td>p = 0.01</td>
<td>p = 0.09</td>
<td>p = 0.01</td>
<td>p = 0.09</td>
<td>p = 0.09</td>
</tr>
<tr>
<td></td>
<td>AR = 15.18</td>
<td>AR = 16.13</td>
<td>AR = 15.16</td>
<td>AR = 15.16</td>
<td>AR = 15.16</td>
</tr>
<tr>
<td></td>
<td>p = 0.33</td>
<td>p = 0.24</td>
<td>p = 0.17</td>
<td>p = 0.17</td>
<td>p = 0.17</td>
</tr>
<tr>
<td>Quadratic Model</td>
<td>Beta (95% CI)</td>
<td>p = 0.34</td>
<td>p = 0.11</td>
<td>p = 0.04</td>
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</tr>
<tr>
<td></td>
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<td>AR = 15.16</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>p = 0.33</td>
<td>p = 0.24</td>
<td>p = 0.17</td>
<td>p = 0.17</td>
<td></td>
</tr>
<tr>
<td>Restricted Cohort—Linear Model</td>
<td>Beta (95% CI)</td>
<td>p = 0.23</td>
<td>p = 0.23</td>
<td>p = 0.80</td>
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<td>p = 0.02</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>AR = 15.18</td>
<td>AR = 16.13</td>
<td>AR = 15.16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Latest NTP 2022 meta-analysis**

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A majority of models have negative associations (IQ reduced as F increases), including a majority of models restricted to those studies with <1.5 mg/L F. Thus, no threshold is suggested.

Pink highlighting on Beta coefficient indicates negative association between F and IQ.

[BSC WG report pages 697-699]