Fluoride Developmental Neurotoxicity: Dose-Response Analyses of Recent High Quality Studies

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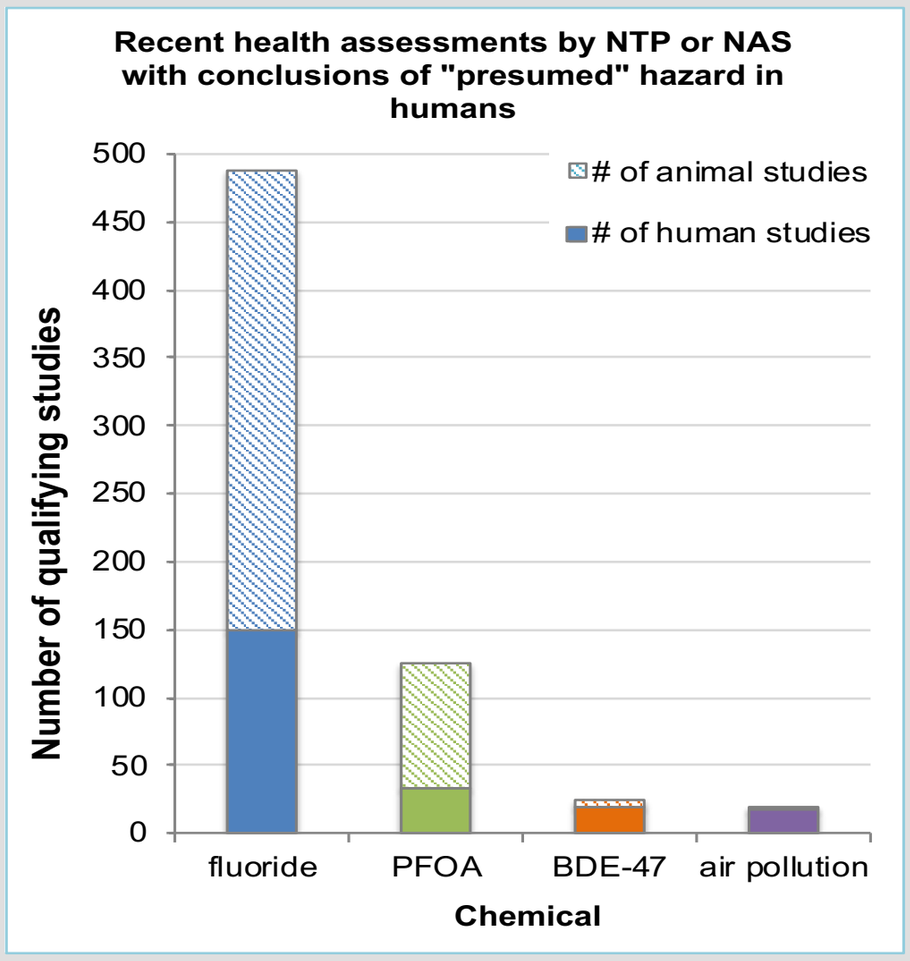

American Environmental Health Studies Project

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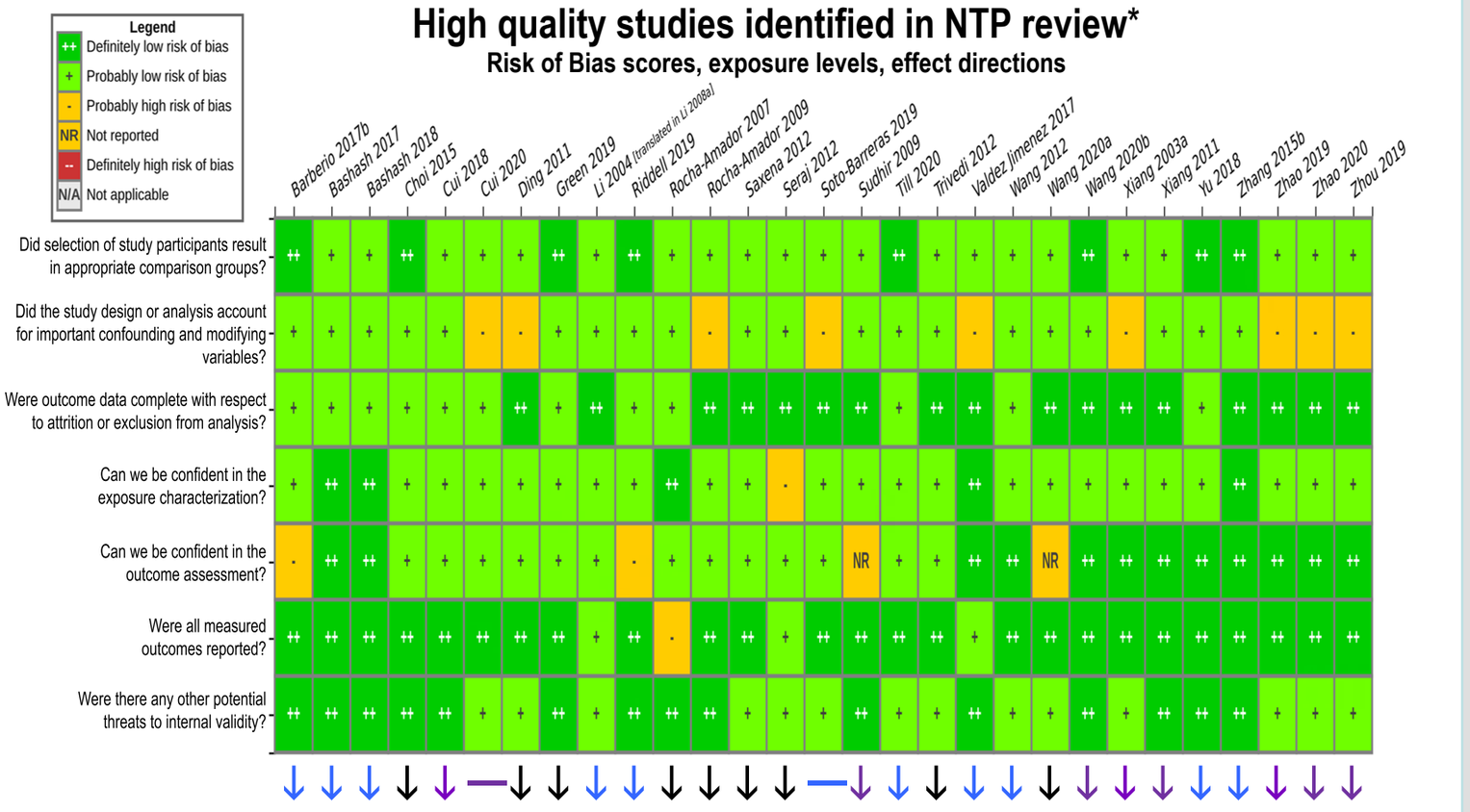


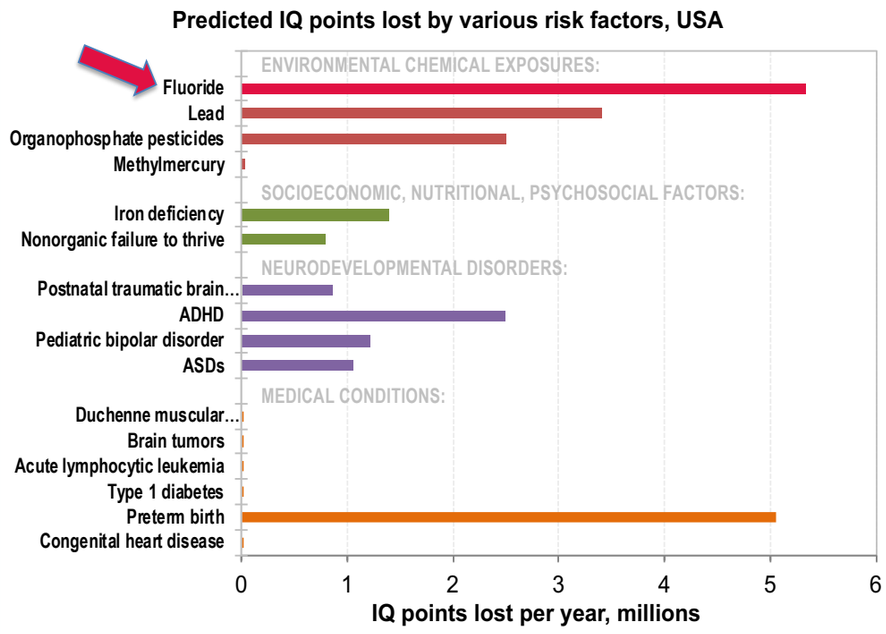
29 high quality studies

27 found statistically significant adverse effects (↓) and 2 found no effect (–)

↓ = exposures below 0.7 mg/L water F or equivalent (10 studies)

↓ = exposures below 1.5 mg/L water F or equivalent (8 studies)

↓ = exposures above 1.5 mg/L water F or equivalent (9 studies)



Dose-response analysis summaries

Study	Effect Magnitude β	BMDL
Xiang 2003	**–5.7** IQ / 1 mg/L water F	0.27 mg/d
Xiang 2003	**+10%** IQ<80 / 1 mg/L water F	
Zhang 2015b	**–9.7** IQ / 1 mg/L urine F	0.16 mg/L
Cui 2018	**–12.3** IQ / 1 mg/L urine F	0.00 mg/L
Bashash 2017	**–6.3** IQ / 1 mg/L urine F	0.10 mg/L
Bashash 2018	**+5.7** pts / 1 mg/L urine F	
Green 2019	**–4.5** IQ / 1 mg/L urine F	0.12 mg/L
Till 2020	**–8.8** IQ / 1 mg/L water F	0.06 mg/L
average	**–7.9 IQ / 1 mg/L**	**0.09 mg/L**

Notes

1.) Exposures measured as urine F concentrations are considered equivalent to drinking water F concentrations.

2.) Community water fluoridation concentration is typically 0.7 – 1.0 mg/L.

3.) For studies with multiple subpopulations, outcomes or exposure measures, the most sensitive significant association was chosen, consistent with standard risk assessment practice.

4.) Benchmark Dose analyses (BMD) used response (BMR) of –1 IQ point as adverse effect.

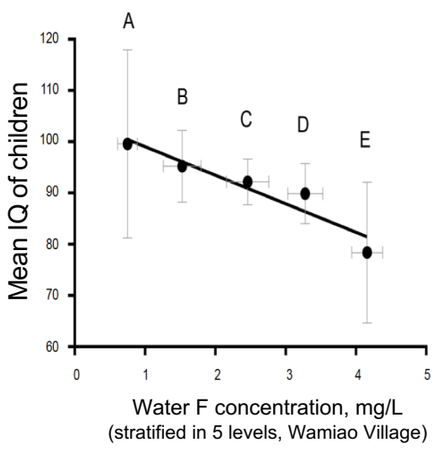
5.) No intra-species Uncertainty Factor (UF) applied to BMDLs.

6.) BMDLs for Xiang 2003 from Hirzy 2016; for Bashash 2017, Green 2019 from Grandjean 2019; for Zhang 2015b, Cui 2018, Till 2020 by Neurath using PROAST BMD software or linear dose-response method of Grandjean 2019.

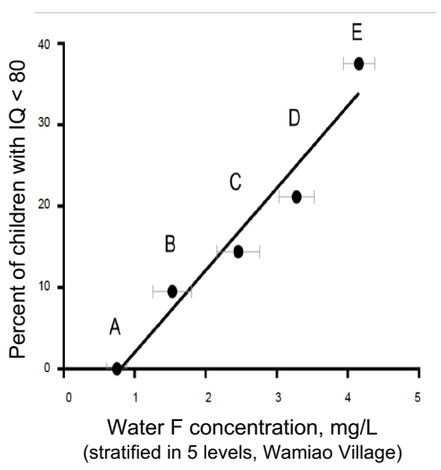
Examples of studies suitable for dose-response analyses

Dose-response curves and BMD analyses based on data or figures in each paper

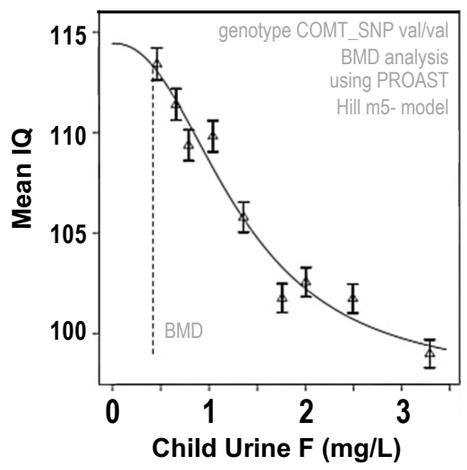
Xiang 2003



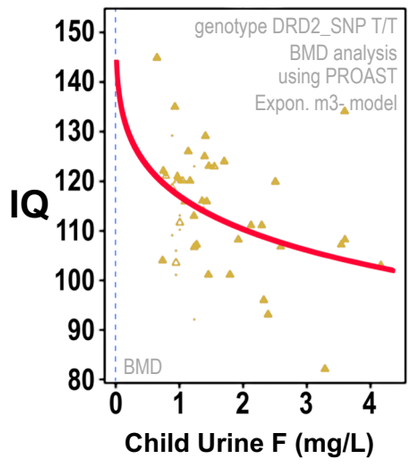
Xiang 2003



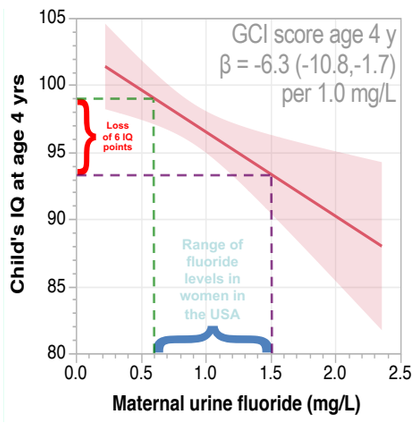
Zhang 2015b



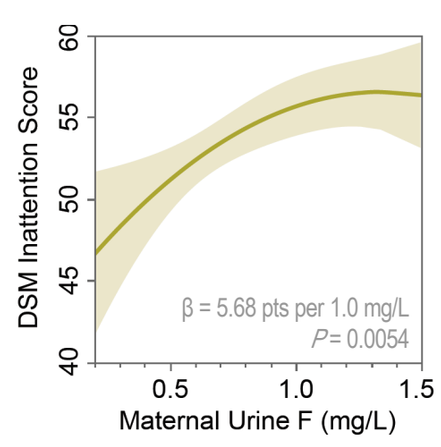
Cui 2018



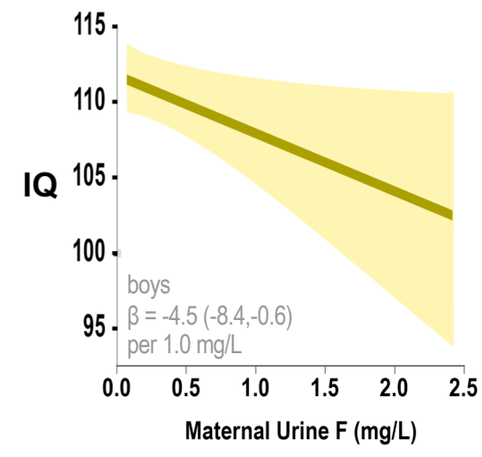
Bashash 2017



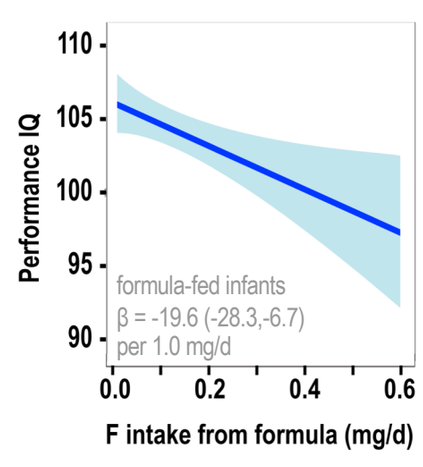
Bashash 2018



Green 2019



Till 2020



References

*Adapted from NTP draft monograph data:
https://hawcproject.org/assessment/405/
https://hawcproject.org/summary/visual/524/

Hirzy 2016
https://www.fluorideresearch.org/494Pt1/files/FJ2016_v49_n4Pt1_p379-400_pq.pdf

Grandjean 2019
https://doi.org/10.1186/s12940-019-0551-x

PROAST BMD software:
https://proastweb.rivm.nl/

additional information:
http://fluoridealert.org/studies/neurath-powerpoint-developmental-neurotoxicity/