Fluoride and Children's I.Q. Decrements

Risk Assessment for Reference Dose and Health-Based Safe Drinking Water Level

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Summary of a paper submitted to a peer-reviewed journal for publication

Some Definitions:

- RfC Reference Concentration. The concentration in water of a contaminant that can be ingested for life with virtually no adverse effect.
- RfD Reference Dose. The dose, e.g. milligrams per day, that can be ingested for life with virtually no adverse effect

More Definitions

- LOAEL Lowest Observed Adverse Effect Level. The lowest dose that results in an observed adverse effect.
- NOAEL No Observed Adverse Effect Level. The dose below which no adverse effect is observed.

More Definitions

- BMD Benchmark Dose. The dose of a toxicant that causes a "benchmark" response (BMR) level of adverse effect. We use a BMR of loss of 1 IQ point.
- BMCL Lower 95% Confidence Limit on the concentration of a toxicant that causes the BMR.

Still More Definitions

- UF Uncertainty Factor. A factor of 1 - 10 used to account for uncertainties in estimating an RfD. E.g., to convert a LOAEL to a NOAEL, or account for intra-human genetic diversity.
- MF Modifing Factor. A factor of 1 - 10 to account for, e.g. severity of an adverse effect.

Excerpt from Am. Dental Assoc. Letter to Congress sent Sept. 4, 2014

Some skeptics are working diligently to spread misinformation about fluoride to communities and public officials, with the goal of ending community water fluoridation. These false statements and fear-mongering are dangerous because they could jeopardize fluoridation efforts, setting back the progress we have made to prevent tooth decay, especially among children. Before fluoridation, the typical schoolchild developed three to four new cavities each year. In some communities, people considered the loss all of one's teeth before old age as normal. Today, many people simply do not have that type of decay burden—thanks in large part to the role fluoridation plays in preventing decay.

What the following risk assessment, using standard EPA methodology, shows is a refutation of the libelous ADA letter. We stand ready, indeed we are eager, to confront these and other libels from ADA and its supporters before a Joint Congressional Committee hearing, where all parties must give sworn testimony subject to penalties for perjury.

Primary Drinking Water Standards

- Under the Safe Drinking Water Act (SDWA 2002) the enforceable primary standard, Maximum Contaminant Level (MCL) is set as close as technically and economically feasible to the non-enforceable, health based standard, Maximum Contaminant Level Goal (MCLG).
- The MCLG must protect the entire population against any known or anticipated adverse effect on health, with an adequate margin of safety. Thus the MCLG cannot allow any more than the RfD to be ingested.

IQ Loss Risk Assessment

- Our assessment is based primarily on the work of Choi et al. (2012) – a meta-analysis showing 26 of 27 studies of fluoride exposure on children's IQ showed loss of IQ at higher vs lower exposures……
- along with the work of Xiang et al. (2003a, 2003b, 2013), which was included as part of the Choi et al. 2012 publication.

Basis for our Assessment

- We assumed that there is probably a fluoride exposure Level below which the Adverse Effect of IQ decrease is Not Observed, called NOAEL.
- We used two sets of fluoride exposures that caused loss of IQ, viz., 3 ppm from the Choi et al. study, called LOAEL. And the data set from Xiang et al. 2003a.

Findings

- Safe* levels of fluoride in drinking water (MCLG):

- From Choi et al. data: 0.018[a] ppm
- From Xiang et al. data 0.013[b]ppm
- Current EPA standard 4 ppm
- Likely new EPA standard ~ 2 ppm

- a Using LOAEL/NOAEL = uncertainty factors
- b Benchmark Dose Method
- * Levels before accounting for other fluoride exposure
- ppm = milligrams/Liter, mg/L

Table 1. Selected IQ studies in which the "high" fluoride area has 3 mg/L or less fluoride (Choi et al. 2012)

Study	I.Q. Change	Statistically significant	High fluoride concentration ~ mg/L
Lin et al. 1991	-9.6	Yes	0.88
Xu et al. 1994	-14.0	Yes	1.8
Yang et al. 1994	-7.5	No	2.97
Yao et al. 1997	-6.5	Yes	2
Hong et al. 2001	-6.6	Yes	2.90
Wang SH et al. 2001	-7.5	No	2.97
Seraj et al. 2006	-13.4	Yes	2.5
Poureslami et al. 2011	-6.2	Yes	2.38
Average	-8.4	Yes	2.3

Work of Xiang et al. 2003a,b, 2013

- Children in villages of Wamiao (hi F^-) and Xinhuai (lo F^-) were studied

- IQs, arsenic and fluoride in drinking water, blood-lead levels, and urinary iodine were measured. No statistically significant differences in As, Pb, I levels between groups.

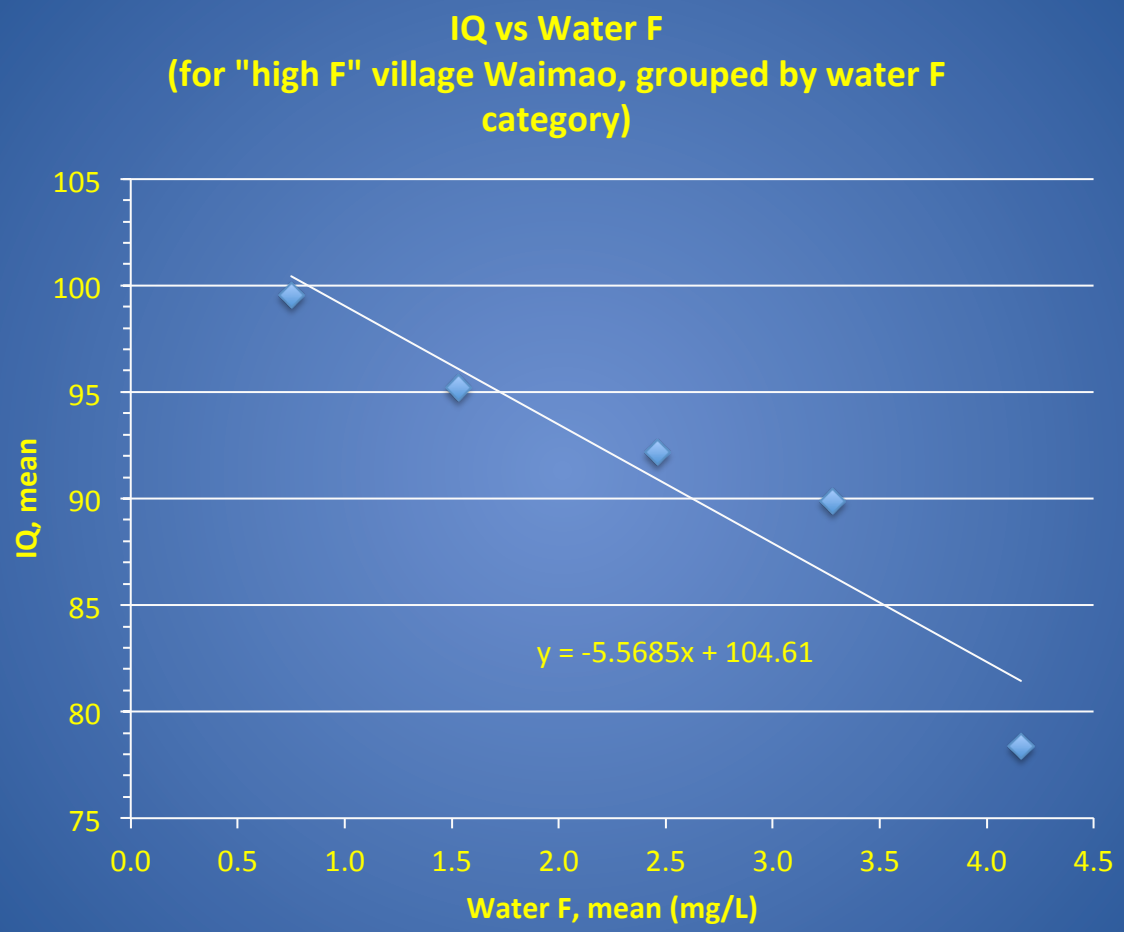
Table 2 Fluoride Levels and IQs at Six Locations (Xiang et al. 2003a)

Group	No. Samples	Fluoride Level	No. Children	IQ
		Mean ±S.D.		Mean ±S.D.
A	9	0.75±0.14	9	99.56±14.13
B	42	1.53±0.27	42	95.21±12.22*
C	111	2.46±0.30	111	92.19±12.98**
D	52	3.28±0.25	52	89.88±11.98**
E	8	4.16±0.14	8	78.38±12.68**
F	290	0.36±0.22	290	100.41±13.21**

*p<0.05; **p<0.01 compared with Group F. Groups A – E are from wells in Wamaio; Group F is from a well in Xinhuai

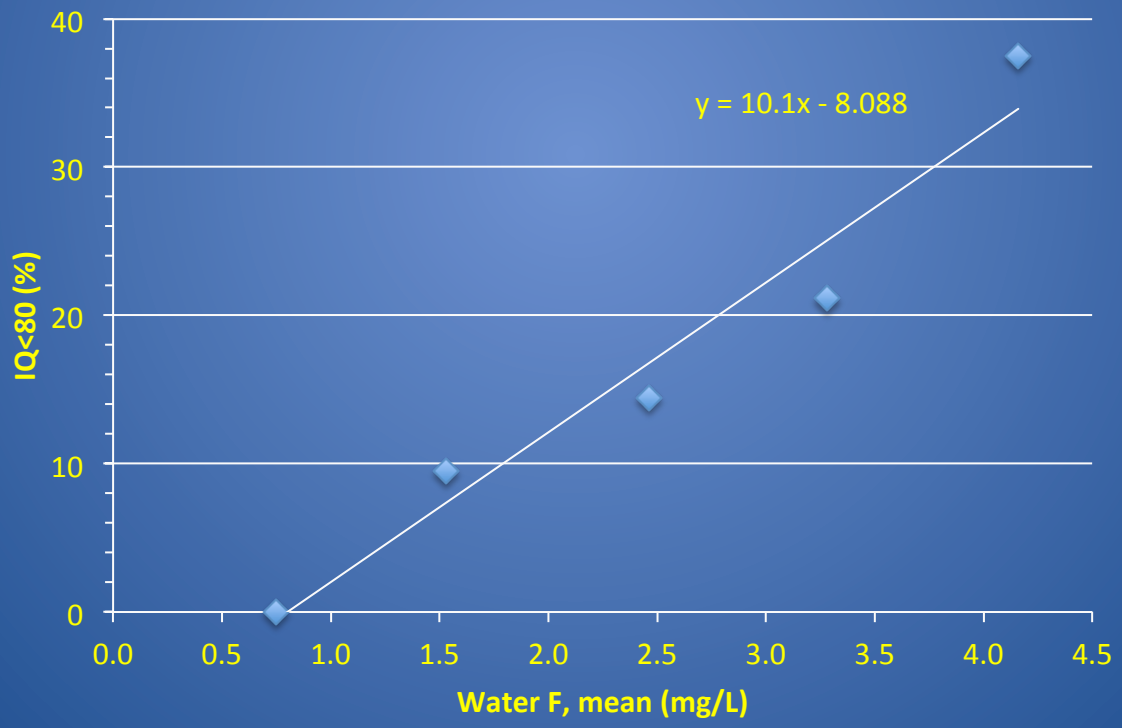
Graphical presentation of these data follow on the next two slides

Impact Significant for Individual Children

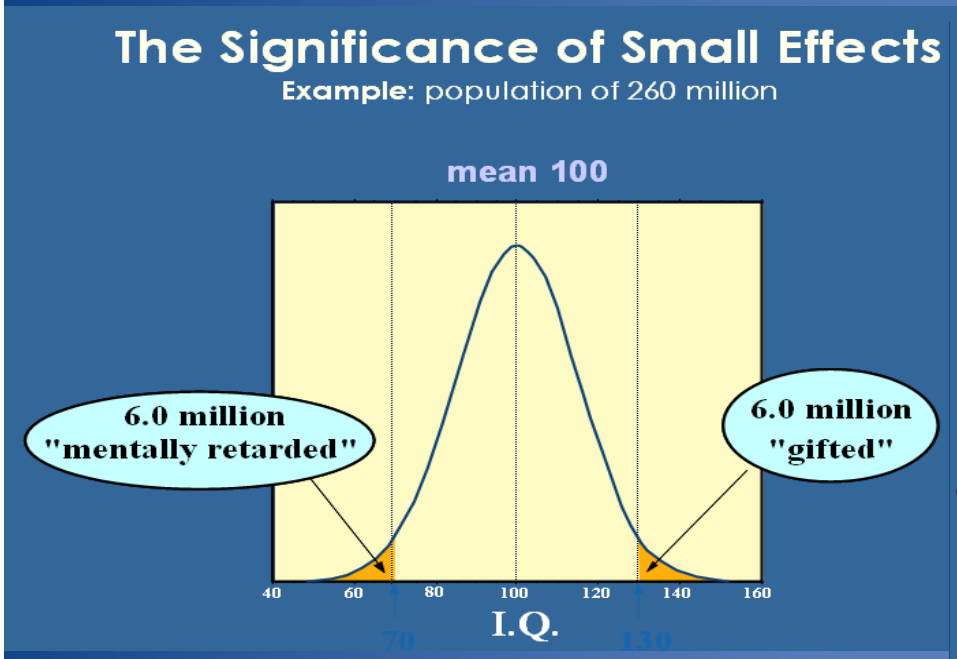


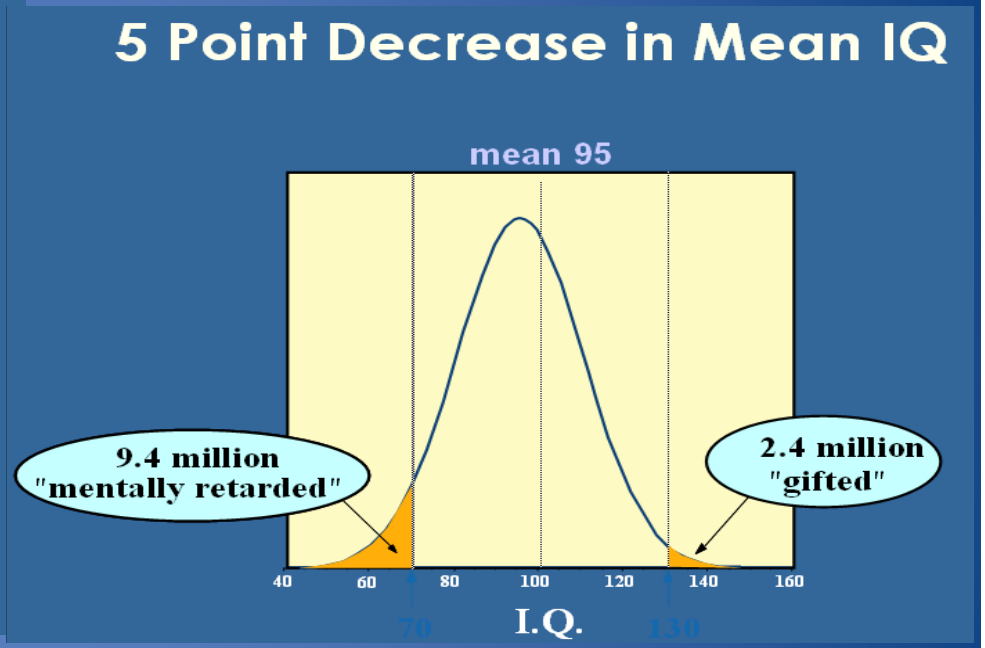
Impact Significant at the National Level

Figure 2
Percent IQ<80 vs Water F
(for "high F" village Waimao, grouped by water F category)

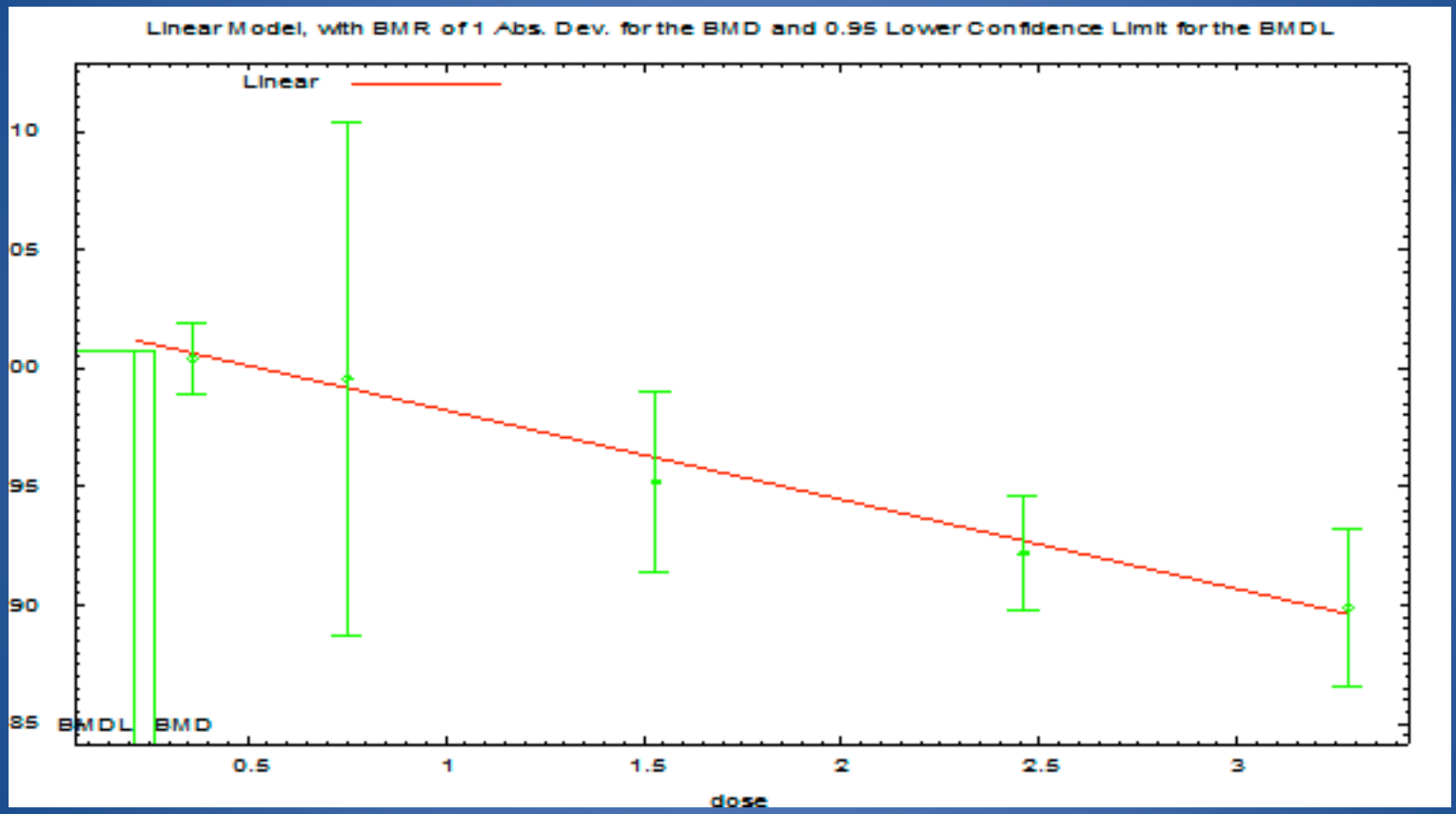


Impact of 5 Point Loss of IQ Throughout a Population of 260,000,000





Benchmark Dose Modeling of Xiang 2003a Data – EPA BMD Software



Lower Confidence Level on Benchmark Concentration (BMCL)for Loss of 1 IQ Point: ***0.22 mg/L***

RfC/RfD Calculation from BMD Modeling

- 0.22 mg/L x 0.60 L/day (H_2O intake*) = 0.13 mg/day
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- RfD = BMDL** ÷ [(UF)x(MF)]
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- RfD = 0.13 mg/day ÷ [10 x 1] = 0.013 mg/day
-
- We use U_H human variability factor of 10, and MF of 1 to account for severity of effect (EPA 1998)

*For Choi et al. children: 1.5 x mean H_2O intake of U.S. Children (EPA 2010)

** From the 95% Lower Confidence Limit, BMCL, of 0.22 mg/L

MCLG Calculation

MCLG = 0.013 mg/day ÷ 1.04 L/day* = 0.013 mg/L

* 95th percentile U.S. children water intake (Table 5-3 EPA 2010)

- Human breast milk fluoride level ca. 0.004 mg/L (Ekstrand 1981)

LOAEL/NOAEL Calculations Summary

- We calculated a daily dose that caused the IQ loss, then applied standard uncertainty factors (EPA 2002) to reach a dose that should not cause that effect. ***3.0 mg/L x 0.60 L/day = 1.8 mg/day***
- ***1.8 mg/day÷ 10 (U_L) x 10 (U_H) = 0.018*** mg/day
- That is the reference dose, RfD
- We used the 95 percentile of U.S. childrens H_2O intake (Table 5-3 EPA 2010) to reach a Maximum Contaminant Level Goal.
- ***0.018 mg/day ÷ 1.04 L/day = 0.017 mg/L***

U_L converts LOAEL to NOAEL; U_H accounts for intra-human variability

Summary of Results From LOAEL/NOAEL + Uncertainty Factors and BMD Methods

Table 3. Drinking Water Fluoride Levels, LOAELs, RfDcs, MCLGs

Water Fluoride Level~mg/L	3.0	BMD Analysis
LOAEL~mg/day	0.18	0.13[a]
Uncertainty Factors, U_L, U_H	10 x 10	10
RfD~mg/day	0.018	0.013
MCLG~mg/L	0.017	0.013

a. Based on benchmark concentration lower 95% confidence level 0.22 mg/L for benchmark response of 1 IQ point loss

U_L to convert LOAEL to NOAEL U_H Intra-human variability

The MCLG (SDWA 2002) shown above has not taken into account other fluoride exposures, and these exposures exceed the RfD's shown in Table 3 on which the MCLGs are based. See next slide.

Non-H_20 Fluoride Exposure Data from Table 2-9 (NRC 2006); Body Mass Data from EPA 2011

Table 5 Comparison of Daily Doses and RfD by Age

Age	Body Mass	Non-H_2O Exp.	Daily Dose	% of Highest RfD
	kg	mg/kg/day	mg/day	RfD 0.018 mg/day
Nursing infant	4.8	0.0078	0.037	210
Non nursing	4.8	0.0151	0.072	400
1 year	10	0.389	0.39	2200
3 years	15	0.339	0.43	2400
5 years	17.4	0.339	0.59	3300

These data show that children receive from *NON-WATER* sources more fluoride than even our highest MCLG/RfD

Conclusion

There is no safe level of fluoride in drinking water, and the MCLG should be set at zero.

Recommendations

- Since current fluoride exposures exceed the RfD values, steps to reduce fluoride exposures should be taken.
- Addition of fluoride to drinking water should cease.
- Fluoride supplement tablets should be banned.
- Fluoridated tooth paste use by children should be by prescription for children at special risk.

REFERENCES

Choi, A.L., et al., 2012. Developmental fluoride neurotoxicity: A systematic review and meta-analysis. *Environmental Health Perspectives* 2012;120(10):1362-1368.

Ekstrand, J. 1981. No evidence of transfer of fluoride from plasma to breast milk. *British Med. Journal* 1981; 283:761-762.

EPA 2002. A review of the reference dose and reference concentration process. EPA/630/P-02/002F. December 2002. Available at: www.epa.gov/raf/publications/pdfs/rfd-final.pdf Accessed May 1, 2014

EPA 2011. Exposure Factors Handbook. Available at: http://www.epa.gov/ncea/efh/pdfs/efh-chapter08.pdf Accessed August 25, 2014

Hong F. 2001. A study of fluorine effects on children's intelligence development under different environments. Chin Prim Health Care. 2001;15:56–57. Available at: http://www.fluoridealert.org/chinese/. (accessed 22 April 2014).

Lin, F.F. et al. 1991. The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang. (In Chinese) *Endem. Dis. Bull.* 6(2): 62-67.

EPA 2010 Fluoride: Dose-response analysis for non-cancer effects. Health and Ecological Effects Division, Office of Water. December 2010. Availabe at: www.http://water.epa.gov/action/advisories/drinking/upload/Fluoride_dose_response.pdf Accessed September 2, 2014

Added: EPA 1998. TRAC 5/28-29/98 TOPIC: FQPA SAFETY FACTOR (10X). Staff Paper # 2. Available at: www.epa.gov/oppfead1/trac/10xiss.htm. (accessed April 29, 2014).
:

NRC 2006. Fluoride in drinking water: A scientific review of EPA standards. Committee on Fluoride in Drinking Water, National Research Council. Pdf available from National Academies Press at: http://www.nap.edu/catalog/11571.html.

Poureslami, H.R. et al. 2011. High fluoride exposure in drinking water: effect on children's IQ. One new report. *Int. J. Pediatr. Dent.* 2011;21(suppl 1):47.

SDWA 2002. Safe Drinking Water Act (As amended through P.L.107-377, December 2002). Title XIV of the Public Heath Service Act (The Safe Drinking Water Act). Title XIV. Section 1412(b)(4) Goals and Standards. Available at: http://www.epw.senate.gov/sdwa.pdf

Seraj, B. et al. 2006. Effect of high fluoride concentration in drinking water on children's intelligence. (abstract in English) *J. Dental Med.* 2006:19(2):80-86. Available at: http://journals.tums.ac.ir/upload_files/pdf/_/2530.pdf

Wang, S.H. et al. 2001. Effects of high iodine and high fluorine on children's intelligence and thyroid function. (In Chinese) *Chin. J. Endemiol.* 2001:20(4):288-290.

Xiang, Q. et al. 2003(a). Effect of fluoride in drinking water on children's intelligence. *Fluoride* V2003;36(2); 84-94.

Xiang, Q. et al. 2003(b). Blood lead of children in Wamiao-Xinhuai intelligence study. *Fluoride* 2003;36(3):198-199.

Xiang, Q. et al. 2013. Level of fluoride and arsenic in household shallow well water in Wamiao and Xinhuai Villages in Jaingsu Province, China. *Fluoride* 2013;48(4):192-197.

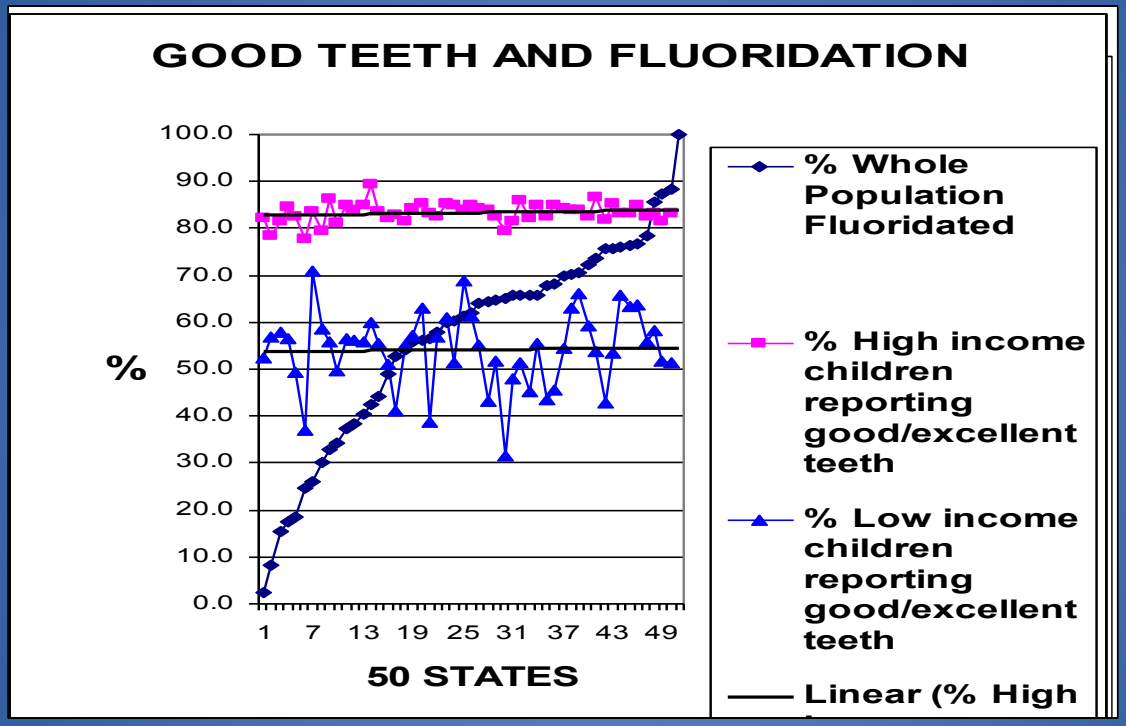
Yao, L.M. et al. 1997. Comparison of children's health and intelligence between the fluorosis areas with and without altering water sources. (in Chinese). *Lit. Inf. Prev. Med.* 1997;3(1):42–43.

Xu, Y.L. et al. 1994. Effect of fluoride on children's intelligence. (In Chinese). *Endem. Dis. Bull.* 1994;2:83-84.

Yang, Y. et al. 1994. Effects of high iodine and high fluorine on children's intelligence and the metabolism of iodine and fluorine. (In Chinese) *Chin. J. Pathol.* 1994;15(5):296-298.

Yao, L.M. et al. 1997. Comparison of children's health and intelligence between fluorosis areas with and without altering water sources. (In Chinese) Lit. *Inf. Prev. Med.* 1997; 3(1):42-43.

RANKING 50 STATES
FLUORIDATION DOES NOT IMPROVE TEETH



For the Rich

Or the Poor

- Higher Income = Better Teeth
- No significant common cause

http://mchb.hrsa.gov/oralhealth/portrait/1cct.htm **National Survey of Children's Health.**
U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Bureau.
The National Survey of Children's Health 2003. Rockville, Maryland: U.S. Department of Health and Human Services, 2005
http://www.cdc.gov/oralhealth/waterfluoridation/fact_sheets/states_stats2002.htm http://pubs.usgs.gov/circ/2004/circ1268/htdocs/tab