

From: [Kumar, Jayanth@CDPH](mailto:Kumar.Jayanth@CDPH)
To: [Liu, Honghu, Ph.D.](#); [Moss, Mark Eric](#)
Subject: Meta-analysis
Date: Thursday, March 24, 2022 6:18:00 AM
Attachments: [Table 1.SMD Analysis.PED.docx](#)
[Fig.Combined Meta.docx](#)
[Standardized Scores LOESS \(42 data points\).pdf](#)
[FluorideMeta-analysis.3.19.22.docx](#)

Honghu and Mark,

Attached, please find a draft manuscript with tables and figures for your review and comment. I highlighted the statistical part for your special attention. The lines in red could be deleted to make room for other additions. The maximum word limit is 4000.

I think the reviewers will have many questions about Supplementary Figure B 3. Absolute IQ (restricted cubic spline) -- see StdIQ_N25.png because it appears to contradict other findings. I tried to limit the analysis to data <1.5 mg/L. I used the Flexplot in Jamovi to create a Loess regression for graphical presentation. This is consistent with our main question to limit the studies to F exposure <1.5. What do you think?

Because of the poor quality of the studies, the NAS committee commented on the NTP dose-response analysis.

“Much of the evidence presented in the report comes from studies that involve relatively high fluoride concentrations. Little or no conclusive information can be garnered from the revised monograph about the effects of fluoride at low exposure concentrations (less than 1.5 mg/mL). ***NTP therefore should make it clear that the monograph cannot be used to draw any conclusions regarding low fluoride exposure concentrations, including those typically associated with drinking-water fluoridation.*** Drawing conclusions about the effects of low fluoride exposures (less than 1.5 mg/mL) would require a full dose–response assessment, which would include at a minimum more detailed analyses of dose–response patterns, models, and model fit; full evaluations of the evidence for supporting or refuting threshold effects; assessment of the differences in exposure metrics and intake rates; more detailed analyses of statistical power and uncertainty; evaluation of differences in susceptibility; and detailed quantitative analyses of effects of bias and confounding of small effect sizes. Those analyses fall outside the scope of the NTP monograph, which focuses on hazard identification and not dose–response assessment. ***Given the substantial concern regarding health implications of various fluoride exposures, comments or inferences that are not based on rigorous analyses should be avoided.***”

Looking forward to your review and comments.

Jay