Reviewer’s report

Title: Fluoride exposure and sleep patterns among older adolescents in the United States: A cross sectional study of NHANES 2015-2016

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Reviewer: Christine Till

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This study examines the association between exposure to fluoride and sleep patterns among American adolescents (n=419 with water fluoride data). Participants were recruited between 2015-16 as part of the NHANES. The study measured plasma fluoride and tap water fluoride concentration at the same visit as the questionnaire evaluating sleep patterns. Results show a 1.97 times higher odds of reporting symptoms suggesting of sleep-apnea. Higher water fluoride concentration was also associated with a later wake time and bedtime. Plasma fluoride did not associate with any of the outcomes. This is an interesting study that addresses a topic where very little human data exist. I am supportive of this article and offer the following comments and suggestions:

1. Using the same NHANES population, Jain et al (2017) show that plasma fluoride levels were significantly higher among those who smoke compared with those who did not smoke. The authors may wish to consider exposure to smoke (first or second hand) as a covariate because smoking may impact the measurement of fluoride in plasma.

2. The authors comment in the limitations section that the sleep outcomes questionnaire is subject to recall biases. Has the measure of sleep disturbance been validated? If not, the authors should note this in the methods.

3. The mean water fluoride level of 0.39 mg/L for a country with three quarters of the population receiving fluoridated water seems very low. Why may this be? Was there oversampling from non-fluoridated regions?

4. The paper makes reference to disruption of pineal gland function as a possible mechanism for altered sleep patterns. Support for this idea comes from an unpublished dissertation (Luke 1997) showing reduced synthesis of melatonin in gerbils with high exposure to fluoride. This thesis also reported some sex effects (e.g. female gerbils with high fluoride exposure showed accelerated pubertal development whereas male gerbils with high fluoride exposure had a lighter testicular weight than males with low fluoride). Did the authors consider sex as a potential effect modifier?

5. I appreciate how the authors note that a diagnosis of ADHD can precede sleep disturbances. Hence, a potential mechanism for disrupted sleep could relate to having a disorder like ADHD (which has also been linked to fluoride exposure). On the other hand, sleep disturbances can also
impair an individual's functioning and resemble ADHD. Thus, a diagnosis of ADHD could also arise secondary to sleep disturbances. (this is more of a comment that sleep disturbance can have a significant effect on behavioral function and therefore represents an important outcome).

6. Limitations: The study sample ranged in age from 16-19 years. This is an age range where sleep may be disrupted for many other reasons (e.g. video games, studying, job, social influences, etc.). Future studies examining the role of fluoride on sleep patterns should also expand the age range to determine whether the effects are consistent in younger and older individuals and to test the association with cumulative exposure to fluoride over a longer lifetime.

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No financial competing interests. I have collaborated with the first author (Dr. Ashley Malin), but was not involved in any way with the current study.

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