Reviewer's report

**Title:** Exposure to environmental tobacco smoke based on urinary cotinine levels among Israeli nonsmoking adults: a cross-sectional study of the first Israeli biomonitoring study

**Version:** 1 **Date:** 7 October 2013

**Reviewer:** Gideon St.Helen

Reviewer's report:

General comment:

The manuscript by Levine and colleagues describes data from the first Israeli Biomonitoring Study and focuses on measurements of urine cotinine among self-reported nonsmokers to characterize their exposure to secondhand smoke. The Israeli Biomonitoring Study is a cross-sectional study and seeks to measure exposure to environmental pollutants in a representative sample of the Israeli population, secondhand smoke being one of these environmental pollutants. The authors found “widespread and high” secondhand smoke exposure based on high proportions of >LOD urine cotinine. Comparisons with smokers are also presented in the study with results as to be expected. The data are presented in the context of a national smoke-free legislation which is about to go into effect. Therefore this study will serve as an important benchmark from which the effectiveness of the smoke-free air law will be assessed periodically. Given that the data are from a larger study which was not specifically designed for the objectives of the manuscript under review, the manuscript has some limitations that are not readily address but may not be fatal. Of note, the authors present the study as a nationally representative sample of the population. Although the study protocol was designed to sample in a nationally representative manner, this was not achieved (as noted in the limitations). Further, the sample size is relatively small and was non-randomized. In addition, it is not clear to what extent subjects did not misclassify their smoking status. While 5 “nonsmokers” with urine cotinine >150 ng/mL were omitted, several other subjects had urine cotinine that exceeded 50 ng/mL, the well accepted discriminator of smokers and non-smokers, and self-identified smokers had urine cotinine levels that were characteristic of nonsmokers. It would have been helpful if there was information on time since last cigarette among “smokers” or time since last exposure to SHS among “non-smokers”. This would have allowed for better discussion of higher than usual cotinine among “nonsmokers” or lower than usual cotinine among “smokers”. Further, it wasn’t clear whether unhealthy individuals, pregnant women, or drug users were included or excluded in the study, all factors that affect biomarker levels. Despite these limitations and minor comments below, the manuscript is of importance in the field of tobacco control. Biomonitoring is an important element in assessing the effectiveness of smoke-free air laws and this study presents data that form the foundation of future assessments.
Specific comments (All minor essential revisions)

Abstract
1. The abstract is clear, well-written, and summarizes the results of the study very well.
2. The results justify the conclusions made

Background:
3. The term secondhand smoke (SHS) is more commonly used vs. ETS.
4. First paragraph: omit the reference to thirdhand smoke. SHS and THS should not be conflated.
5. 4th paragraph, sentence starting with “Cotinine, the main metabolite”: replace “main metabolite” with “primary proximate metabolite”
6. 4th paragraph, sentence starting with “the cotinine level provide”…With a half-life of 16-18 hrs, cotinine is eliminated from the body given no further exposure to tobacco smoke in 3-4 days. So it should be mentioned that cotinine as a biomarker presents information on ongoing or recent SHS exposure instead of “over time”.
7. 5th paragraph, last line: replace “actual ETS” with “systemic exposure to ETS”
8. 6th paragraph: The Israeli smoke-free legislation is mentioned in the background but no further information is given to the reader about what this new law entails. Is it outdoors, indoors, workplaces, public places? Give more context to this new legislation and whether there currently exists any other laws in Israel relating to tobacco smoke.

Methods
1. Study design is well presented
2. Relatively small sample size but this cannot be corrected now
3. One weakness is the inclusion criteria. The researchers did not make health status, drug use, and pregnancy inclusion/exclusion criteria. These are known to affect drug pharmacokinetics and therefore concentration of urine cotinine levels measured. Are the results for healthy individuals?
4. There’s a weakness with the questionnaire item on smoking status. “Do you currently smoke”? What does “currently” mean? Current smoking is often identified by the question, “have you smoked in the past 30 days?” This is a better question than what was asked in this manuscript.
5. Stat analysis: analyses done are appropriate.
6. “using the lognormal distribution” does this mean that biomarker concentrations were logtransformed before stat analyses? May be better to state the latter.
7. I don’t see the need to include fruits and vegetables in this analysis. It has been established that any potential nicotine from these is negligible to say the
least. Spearman correlations are not appropriate here if you want to assess whether eating fruits and vegetables affect cotinine levels. It should be included as a covariate in regression models. I am not certain whether this was done in the multivariate analyses. If yes, make it clearer.

8. A cutpoint of >150 ng/mL urine cotinine is a very high cutpoint to discriminate smokers from nonsmokers. This is based on an older study. Why wasn’t 50 ng/mL (ug/L) used instead as a discriminator?

Results

9. 3rd paragraph: striking difference is followed by borderline statistical significance. This is contradictory.

10. Not always clear which cut-point is being referred to at times (<1 or <4 ug/L). Be clearer.

Discussion

1. 2nd paragraph: The statement “findings validate self-reported smoking status”: this is not altogether supported given the 5 self-identified nonsmokers omitted due to really high cotinine as well as several nonsmokers with >50 ng/mL and “smokers” with really low cotinine levels. Why is the urine cotinine of smokers <LOD? Is there any data on time from last cigarette? The authors should address these discrepancies in self-report and cotinine levels.

2. The authors state “This observation gives further evidence to harmful effects of this common habit” in reference to water pipes. The data presented does not allow the authors to make this conclusion. Measurement of cotinine does not necessarily indicate harmful effects.

Conclusion

1. Despite the limitations of the study in terms of sample size, representativeness, discrepancies with self-reported smoking status, the data presented support the conclusions made.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing interests to declare.