Review of: "Population estimates of biomarkers of exposure to carbon monoxide, nicotine, and NNK in smokers and non-smokers"

Bart De Geest[1]

1 Slovak Medical University

Potential competing interests: The author(s) declared that no potential competing interests exist.

The important contribution of this paper is to establish population estimates for biomarkers of exposure to carbon monoxide (carboxyhemoglobin - COHb), nicotine (Nicotine Equivalents -NEQ), and nicotine-derived nitrosamine ketone (NNK; total urinary 4-[methylnitrosamino]-1-[3-pyridyl]-1-butanol [NNAL] - NNAL) based on pooled weighted average from published literature. Smokers and non-smokers are compared.

The authors state in the Discussion: 'The availability of a single population level estimate should allow for estimating changes in the levels of these biomarkers among those adult smokers switching to a PRRP.'
1. These biomarkers are used to quantify exposure to tobacco smoke. Which of these biomarkers is the best estimate of exposure to tobacco smoke? What is the gold standard in this respect? I suppose that a biomarker may indeed be superior to data obtained by anamnesis. Nevertheless, what is then the gold standard?
2. What is the variability of these biomarkers in patients? Are the levels of these biomarkers stable in a 24 hour-period? Is there diurnal variation? Is there variation with age?
3. Which of these biomarkers has the best performance in terms of calibration and discrimination to predict specific hard clinical endpoints in smokers? After all, a biomarker should also have the ability to predict incidence of disease.
4. What are the levels of these biomarkers in subjects exposed to secondhand smoke?

The authors state in the abstract: 'Assessment of potentially reduced risk tobacco products (PRRPs) can be facilitated with availability of a single baseline population estimate for biomarkers of exposure (BOEs) for selectconstituents in cigarette smoke.'
1. With regard to PRRPs, potential mechanisms of disease causation may be entirely distinct and therefore, these biomarkers may not capture risk at all. It is a distinct class of environmental exposures that may require a completely different set of biomarkers. Will changes in these biomarkers be predictive of altered risk?
2. Products like e-cigarettes manufactured according to certain quality and safety standards are considered to be less risky to health than smoking. This is more an assumption than a fact. Long-term effects are simply not known.
3. Whereas data on biomarkers in the population as calculated by the authors provide an important framework, the starting perspective of the paper 'Assessment of potentially reduced risk tobacco products (PRRPs)' does not seem to be the true field of application. These biomarkers will, in the absence of hard clinical data, not constitute a framework to assess the

safety of PRRPs. The risk is that misperceptions may arise in relation to the safety of these products.