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Comment regarding categorization of Third-hand smoke exposure in "Third-hand Exposure at Homes: Assessment Using Salivary Cotinine"

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We read with interest "Third-hand Exposure at Homes: Assessment Using Salivary Cotinine" by Lidon-Monayo et al. (Lidon-Moyano et al., 2020), which highlights the importance of recognizing thirdhand smoke (THS) as a ubiquitous but largely unrecognized source of indoor environmental pollution and a grave public health hazard (Jacob et al., 2017). In this study, the authors categorized 736 nonsmoking adults into one of three tobacco smoke exposure (TSE) groups (1) Not Exposed to SHS or THS (i.e., Unexposed group): live with nonsmokers and have no home SHS: (2) Only THS Exposed (i.e., THSe-only group);- live with smokers but have no home SHS; and (3) SHS and THS Exposed (i.e., SHSe/THSe group): live with smokers and have home SHS and THS. We find the categorizations of participants in the unexposed group and the THSe-only group problematic. With respect to the unexposed group, given decades of high smoking prevalence and unrestricted indoor smoking in Spain and other industrialized countries, there are good reasons to expect significant remaining reservoirs of THS pollutants in private homes and work environments that are now homes and workplaces of nonsmokers, respectively. Data reported in Figure 2 (Lidon--Moyano et al., 2020) suggest that 50% of participants in the unexposed group may unknowingly be exposed to SHS or THS. With respect to the THSe-only group, it is important to remember that nonsmokers who live with smokers can still be exposed to SHS if they are occasionally exposed to active smoking, if there are inconsistent smoking bans, if they live in multiunit housing (MUH) where other residents smoke, or if smoking occurs in close proximity to their homes (Gatzke-Kopp et al., 2019; Matt et al., 2020a). For example, if participants in the THSe-only group lived with smokers who immediately came inside their home after smoking or lived in homes where smoking occurred on a balcony or at a window, then these participants could have been exposed to SHS through off-gassing or seepage of SHS (Jacob et al., 2017; Sheu et al., 2020). Further, 54.2% of THSe-only participants were exposed to SHS in other locations, and these participants may have been better placed in the SHSe/THSe group. Additionally, 51.5% of participants in the unexposed group were exposed to SHS in other settings; thus, this group was also exposed to SHS and THS. Nonsmokers in both of these two groups could subsequently be exposed to THS pollutants via inhalation, ingestion, and dermal absorption from pollutants present in smokers' homes (Jacob et al., 2017). The presence of THS pollution is evident in research conducted in nonsmoking environments where smoking has previously occurred, such as in homes of former smokers (Matt et al., 2016), in casinos and hotels that are now smoke-free (Matt et al., 2014, 2018), and in homes where thorough cleaning methods have unsuccessfully eliminated THS (Matt et al., 2020b). In these and other studies, nicotine on surfaces, in dust, and in the air serves as an environmental marker of THS pollution, and nicotine present on nonsmokers' hands may serve as a biomarker of THSe (Mahabee-Gittens et al., 2018, 2019; Matt et al.,

Homes: Assessment Using Salivary Cotinine"

2014, 2016, 2018, 2020b).

The authors used cotinine to assess THSe, but since cotinine is a nicotine metabolite biomarker of recent TSE which measures both SHSe and THSe (Jacob et al., 2017), cotinine alone cannot accurately measure THSe. While there is currently no gold standard biomarker for exclusive THSe, new research suggests nicotine that accumulates on the hands of nonsmokers who live with smokers or who live in homes with THS pollution may be a useful marker of THSe as it reflects a source of nicotine exposure linked to THS pollution on surfaces and in house dust (Mahabee-Gittens et al., 2018, 2019). Given the mixed SHS and THS exposures in both the unexposed and THSe-only groups, which the authors correctly state as a potential limitation, the cotinine results and statistical analyses to examine differences in the groups are difficult to interpret and may not provide a true assessment of differences in THS compared to mixed exposure. Thus, future studies designed to evaluate adults who are exclusively exposed to THS should use rigorous self-report and biochemical validation to enroll nonsmokers with: a) self-report of no known source of SHSe which includes strict private home or MUH smoking bans; b) biomarker validation of nonsmoking status via cotinine or exhaled carbon monoxide testing; c) evidence of THS pollution in their homes as measured with dust nicotine or tobacco specific nitrosamines (e.g., NNK) above a specified cut-off level; and d) hand nicotine levels above a specified cut-off level. Unfortunately, it is unknown if, in regions where indoor and outdoor smoking was and/or still is normative behavior and THS pollution reservoirs are long-standing, it is possible to find populations that are completely protected from THSe and SHSe. Nevertheless, research is needed to identify biomarkers specific to THSe and ascertain the differences in biomarker levels and clinical effects associated with THSe compared to no TSE and mixed SHS and THS among groups that are categorized using the strictest available classifications. This is particularly important as the debate about a tobacco endgame envisions a possible future in which tobacco smoking vanishes but long-term reservoirs of potent tobacco smoke toxicants persist in indoor environments.

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Declaration of competing interest

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E.M. Mahabee-Gittens et al.

interests or personal relationships that could have appeared to influence the work reported in this paper.

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