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Public Health Panorama
Division of Information, Evidence, Research and Innovation (DIR)
WHO Regional Office for Europe
UN City
Marmorvej 51
DK-2100, Copenhagen Ø
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Dear Editor,

On behalf of the undersigned organizations, we are writing to express our concerns with the paper titled "AEROTOXIC SYNDROME: A NEW OCCUPATIONAL DISEASE?" published in the June 2017 issue of *Public Health Panorama*. The paper by Michaelis et al asks whether "aerotoxic syndrome" is a new occupational disease and claims to have identified a clear cause and effect relationship linking symptoms, diagnoses, and findings to the occupational environment. From our review of this paper, we see no evidence identifying such a relationship and given the controversial nature of the subject matter, wish to convey our concerns about the methodology of the study.

The paper reports two studies: in the first, pilots of BAe146 series aircraft were approached via a pilot union, with a response rate of 14% and an unstated mixture of written questionnaire and telephone interview responses by one of the authors, the content of which are not included in the publication. In the absence of any information from the 86% of non-respondents, and any detail on the questions asked to the respondents, it is not possible to evaluate or exclude selection bias or interviewer bias. Therefore, any conclusions from the first study must be extremely guarded.

In the second study, 15 potential cabin air quality incidents were analyzed. The studies were gathered from a variety of sources, and are said to have been selected because of being consistent with hyperventilation and hypoxia, but no detail is provided as to how this selection process was conducted or what characterized the studies which were excluded. It is therefore once again not possible to evaluate the potential for bias in the analysis. In almost all of the 15 selected cases, symptoms were reported, in many cases by multiple individuals, and a variety of medical findings were reported. The listed complaints were in many cases chronic. These findings are interesting but in the absence of any quantitative analysis constitute only a case series and do not elucidate the genesis of the symptoms.

The two separate studies were then combined to create a comparison between the reported symptoms in the two data sets. No quantitative analysis is applied but there appears to be overlap in symptomatology between

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the two groups, with listed symptoms for certain chemicals present in oil and de-icing fluids, and with symptoms of hypoxia/hyperventilation.

From the data presented it can be said that there is a group of people who suffer ongoing and significant symptoms which they attribute to cabin air events, but little more can be concluded. The authors go on to discuss toxicology of potential on-board contaminants, and propose a pathway by which chronic low-level exposure to organophosphates combined with intermittent high-dose exposure might cause neurotoxic effects, but the data from this study do not establish evidence for this proposal.

In the descriptions of both studies the authors refer to participants having died, in the same sentence as describing ill-health; this has the effect of implying that death was related to cabin air exposure, but nothing is presented to indicate whether this is claimed.

Our most serious concern with the paper is the claim, quoting only the lead author's PhD thesis, that the Bradford-Hill criteria for causation have been met. Having reviewed both this paper and the quoted thesis, we disagree with this claim and assert that few of the criteria for causation have been satisfied.

Over the past two decades several major studies of cabin air have been carried out internationally and none have identified levels of toxic substances approaching clinical significance. While encouraging thorough scientific research in all areas of aerospace medicine, our review of the available literature leads us to suggest that significant symptoms being suffered by a group of individuals, here labelled as aerotoxic syndrome, are not explained by toxins in cabin air, and that other causes must be sought. This paper, because of potential bias and lack of replicability, has not altered our assessment.

Sincerely,



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