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## Letter to the Editor re: Medical Consequences After a Fume Event in Commercial Airline Crews

### Dear Editor:

For the past 25 years, aerotoxic syndrome has been acknowledged as a term to describe the constellation of symptoms that airline crews have documented consequent to breathing engine oil fumes.<sup>1</sup> The authors of "Medical Consequences After a Fume Event in Commercial Airline Crews" conducted a retrospective, nested, matched case-control within a cohort study to determine if effects could be attributed to such exposure.<sup>2</sup>

It is puzzling, therefore, that the authors did not limit their definition of "cases" to crews who had reported exposure to oil fumes; instead, they included exposure to "any type of smoke and/or odor from the air conditioning system." On aircraft, this would also include fan failures, hydraulic and deicing fluids, jet fuel, and exhaust. The authors' case definition eliminates the ability to assess the specificity of effects from exposure to oil fumes. Also, although beyond the authors' control, the distinction between cases and controls is likely blurred by the fact that airline crews are not trained to recognize and report the effects of exposure to oil fumes. And, in our experience, the quality and consistency of medical workups and care that crews receive after reporting exposure to oil fumes is uneven, at best.<sup>1</sup>

While the authors applied what could have been a statistically powerful epidemiological study design, they did not make even simple exposure assessments to permit dose-response and related evaluations. They did not refine or discriminate between the levels of exposure within the case group, even though event details that would serve as surrogate measures of exposure were, presumably, available. Finally, it is well-known that a minority of aircrew are susceptible to the triggering influence of chemicals contained in fume events, manifesting in clinical symptoms. So, despite the seemingly large sample size, the design of the study swamps any signal from the relatively small number of constitutively susceptible crew. Given this design, the statistical power of the study to discriminate is far too weak to detect a signal.

These limitations, unfortunately, render the entire study of little-to-no meaning. In brief, the study design, as executed, diluted effects, rendering the hypothesis biased toward the null.

If it were possible for the authors to construct a replicable method of refining exposure and limit the case group to "fume events" (ideally accomplished with a biomarker specific to engine oil fumes), then their findings might well be worthy of consideration and add to the body of knowledge on the topic of aerotoxic syndrome.

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2. Klerlein M, Dubiez L. Medical consequences after a fume event in commercial airline crews. *Aerosp Med Hum Perform.* 2025; 96(1):12–17.

### In Response:

The letter addressed to you by Judith T.L. Anderson et al. in response to our article highlights the fact that our work did not include elements related to the characterization of the technical origin of the studied fume events. This point is entirely valid and reflects the difficulty of this characterization in the absence of precise measurement of the pollutants present during fume events. The ongoing AviSan<sup>1</sup> study will allow us to address this point more accurately and specifically verify the hypothesis of the presence of organophosphorus compounds in the cabin air at the time of the fume events. Furthermore, the authors of this

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letter emphasize that it is well known that the onset of clinical signs affects only a small minority of crewmembers after a fume event exposure. The aim of our study was precisely to confirm this point on a very large scale, and we are pleased to see that we are in agreement with the authors of the letter on this matter.

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