

Title: E-cigarettes and oral health: a balanced viewpoint.

Dear Editor,

The topic of e-cigarettes and oral health is of utmost importance and we were pleased to see this addressed by a recent review that was published in *Oral Diseases* (Javed *et al.*, 2017). However, we would like to raise several concerns with this review.

The authors incorrectly cite Holliday *et al* (2016) as the authors of a study reporting 'that e-cigarette-exposed cells presented reduced viability and clonogenic survival, along with increased rates of apoptosis and necrosis in vitro'. The correct citation for this study is Yu *et al* (2016). Holliday *et al* (2016) is actually a highly critical commentary of the Yu *et al* (2016) study, published in the journal *Evidence-Based Dentistry*. The format of this journal includes the abstract of the original study followed by a commentary. The PubMed records for this journal are somewhat confusing as they include the abstract of the original study with only a minor reference indicating it is a commentary. It can appear from the PubMed record that we are the authors of the original study. However, we would have expected the authors of a review paper such as this to have read beyond the PubMed entry and hence avoided this error. We request a corrigendum be issued. Interestingly the Yu *et al* (2016) study is not included in this review calling into question the search methodology employed by Javed *et al* (2017).

The introduction section of the Javed *et al* (2017) review includes several negative comments regarding e-cigarettes. It omits several key reviews and evidence synthesis, which if included, would have given the reader a better understanding of the differing viewpoints on the topic (McNeil *et al.*, 2015; Hartmann-Boyce *et al.*, 2016; Royal College of Physicians, 2016; O' Leary *et al.*, 2017). The review makes little attempt to compare the relative risks of e-cigarette aerosol to those of combustible tobacco smoke. This is a highly relevant comparison given that over 99% of regular e-cigarette users are smokers or ex-smokers (Delnevo *et al.*, 2016; West *et al.*, 2017). Many of the primary studies reported in this review have been criticised for lacking this relevant control group and this should have been worthy of discussion in a review paper.

The Javed *et al* review confuses 'whole tobacco smoke' and 'nicotine'. For example, when discussing implant failures they state 'tobacco smoking including nicotine is associated with an increased risk of implant failure'. They then extrapolate that 'nicotine derived from e-cig' may have similar effects. None of the three cited studies had nicotine as a variable or even suggested that nicotine was the causative agent, meaning this statement is unfounded. A previous review of tobacco and periodontitis suggested that 'nicotine may be unfairly blamed' for the negative effects observed in smokers (Palmer *et al.*, 2005).

There is no mention of any quality assessment of the included studies or discussion of study limitations. In the oral health section, the authors cite their own previous study (Sundar *et al.*, 2016) which has been criticised regarding its design, primarily a lack of appropriate controls (Cancer Research UK and UK E-cigarette Research Forum, 2016). In the Javed *et al* (2017) review, for example, the authors state 'nicotine exposed cells presented with significantly increased comet tail length and γ -H2AX foci....'. It is not possible to derive this from the data presented in their study as their samples varied both flavour and nicotine concentration meaning the relative importance of each cannot be established.

To conclude, the review by Javed *et al* represents an opinion piece rather than systematic balance literature review. We have concerns regarding the rigour of the search methodology, quality assessment of the included studies and hence the conclusions.

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Conflicts of interest- None.

References

Cancer Research UK and UK E-cigarette Research Forum (2016) *Electronic Cigarette Research Briefing- November 2016*.

http://www.cancerresearchuk.org/sites/default/files/ukecrf_research_update_201611.pdf

Delnevo, C.D., Giovenco, D.P., Steinberg, M.B., Villanti, A.C., Pearson, J.L., Niaura, R.S. and Abrams, D.B. (2016) 'Patterns of Electronic Cigarette Use Among Adults in the United States', *Nicotine Tob Res*, 18(5), pp. 715-9.

Hartmann-Boyce, J., McRobbie, H., Bullen, C., Begh, R., Stead, L.F. and Hajek, P. (2016) 'Electronic cigarettes for smoking cessation', *Cochrane Database Syst Rev*, 9, p. Cd010216.

Holliday, R., Kist, R. and Bauld, L. (2016) 'E-cigarette vapour is not inert and exposure can lead to cell damage', *Evid Based Dent*, 17(1), pp. 2-3.

Javed, F., Kellesarian, S.V., Sundar, I.K., Romanos, G.E. and Rahman, I. (2017) 'Recent Updates on Electronic Cigarette Aerosol and Inhaled Nicotine Effects on Periodontal and Pulmonary Tissues', *Oral Dis*.

McNeil, A., Brose, L., Calder, R. and Hitchman, S. (2015) *E-cigarettes: an evidence update. A report commissioned by Public Health England*. Public Health England.

O' Leary, R., MacDonald, M., Stockwell, T. and Reist, D. (2017) *Clearing the Air: A systematic review on the harms and benefits of e-cigarettes and vapor devices*. Victoria, BC. Centre for Addictions and Research of BC.

Palmer, R.M., Wilson, R.F., Hasan, A.S. and Scott, D.A. (2005) 'Mechanisms of action of environmental factors--tobacco smoking', *J Clin Periodontol*, 32 Suppl 6, pp. 180-95.

Royal College of Physicians (2016) *Nicotine without smoke. Tobacco harm reduction. A report by the Tobacco Advisory Group of the Royal College of Physicians*.

Sundar, I.K., Javed, F., Romanos, G.E. and Rahman, I. (2016) 'E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts', *Oncotarget*, 7(47), pp. 77196-77204.

West, R., Beard, E. and Brown, J. (2017) 'Trends in electronic cigarette use in England (STS140122)', *Smoking Toolkit Study*.

Yu, V., Rahimy, M., Korrapati, A., Xuan, Y., Zou, A.E., Krishnan, A.R., Tsui, T., Aguilera, J.A., Advani, S., Crotty Alexander, L.E., Brumund, K.T., Wang-Rodriguez, J. and Ongkeko, W.M. (2016) 'Electronic cigarettes induce DNA strand breaks and cell death independently of nicotine in cell lines', *Oral Oncol*, 52, pp. 58-65.