Review of: "Nicotine pouches- a research and regulatory policy agenda to maximise public health benefits and minimise harms"

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Potential competing interests: I undertake clinical trials of smoking cessation medications and interventions. In this role I have received grants from Pfizer, and non-financial support from manufacturers of smoking cessation medications for products to be tested in these trials. I have also undertaken two trials of e-cigarettes for smoking cessation (with e-cigarettes purchased from a NZ e-cigarette online retailer [NZVAPOR, https://www.nzvapor.com/], e-liquid for one trial purchased from Nicopharm, Australia [https://www.nicopharm.com.au/] and nicotine patches supplied by the New Zealand Government via their contract with Novartis [Sydney, Australia]). Neither NZVAPOR nor Nicopharm have links with the tobacco industry. I have also undertaken trials looking at the effect of reduced nicotine cigarettes on smoking cessation. These trials involved the use of cigarettes purchased from tobacco companies. More than 10 years ago I provided consultancy to the manufacturers of smoking cessation medications, received honoraria for speaking at a research meeting and received benefits in kind and travel support from a manufacturer of smoking cessation medications. None of the above parties had any role in the design, conduct, analysis or interpretation of the trials I led or was involved in, or writing of the resulting publications.

This article reviews the available literature on reduced harm nicotine pouches, plus research gaps and potential regulatory approaches for these products. The paper is well written, and comprehensive. I have provided some minor comments below for the authors to consider:

- Second paragraph: I suggest some more context is provided around the statement “this is largely true also for Swedish snus.” i.e. assume the reader may not know what Swedish snus is. I know this detail is provided further on in the article, but some detail is required when the product is first mentioned.

- Please provide some discussion about how nicotine pouches may also address some of the behavioral aspects of oral tobacco use. A comment is made towards the end of the article about the large number of people in LMICs who use oral tobacco – but I think this link needs to be much earlier in the article.

- A number of sentences are missing a subject, eg. “This should….” And “This suggests…” and “ This will be…” are examples

- Define “MHRA” and “FDA”.

- A definition of ‘spitless tobacco’ is required.

- Don’t use the abbreviation “e-cigs” – state it in full

- The statement “In the US, for the 24 weeks ending on May 30, 2020, nicotine pouches grew by 498%” is missing “….sales of…”

- State the earliest date used in the PubMed search.

- Table 3: Present the order of papers in the table by date of publication. Please also add the study design and sample size for the original research studies. Also a quick summary of what the studies found would be useful (this is currently only done for 2 of the studies).

- Table 3: The Niconovum oral pouch was also used in this trial: Walker N, Howe C, Bullen C, Grigg M, Glover M, McRobbie H, Laugesen M, Jaing J, Chen M-H, Whittaker R, Rodgers A. Does improved access and greater choice of nicotine replacement therapy affect smoking cessation success? Findings from a randomised controlled trial. Addiction, 2011: 106 (6): 1176-1185.

- Regarding the statement “…lack of availability of adequate clinical studies to unequivocally prove e-cigarettes’ role in cessation…” Can this statement please be updated to reflect the wording of the Cochrane living review of e-cigarettes for smoking cessation (plus reference the review).

- Regarding the statement “Oral nicotine pouches come in an array of flavors…” I would also point out that other NRT oral products also come in a variety of flavors.