

## SELECT COMMITTEE ON TOBACCO HARM REDUCTION

Professor Emily Banks  
Responses to Questions on Notice from  
Hearing on Friday, 13 November 2020

**QoN 016-01, Senator Hughes.** Do you think including a low nicotine content device in your study skews the result towards vaping devices having a low rate of success to helping people quit?

### Response

GRADE (Grading of Recommendations, Assessment, Development and Evaluations) is a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making recommendations based on that evidence.<sup>1</sup> It is considered current best practice and is used widely, including by organisations such as the National Health and Medical Research Council of Australia.<sup>2</sup> It relates the quality of evidence to the level of certainty (or uncertainty) of recommendations and conclusions. The quality of the evidence relates to the risk of bias, indirectness, inconsistency and imprecision of the evidence and potential for publication bias.<sup>2</sup> Evidence that is of low quality overall generally leads to lower levels of certainty in conclusions and recommendations.<sup>3</sup>

The review of evidence on the efficacy of e-cigarettes for smoking cessation identified 3,973 studies and, from these, identified nine randomised controlled trials (RCTs) for inclusion.<sup>4</sup> The risk of bias and GRADE assessments for the review are included in its supplementary material, which is online and has been made available to the inquiry.<sup>4,5</sup> As noted in the review, the RCTs included varied widely including in terms of setting, quality, size, interventions, dose of nicotine, potential competing interests, length and completeness of follow up and additional interventions, such as behavioural support.<sup>4</sup> The overall quality of the evidence on e-cigarettes for smoking cessation was rated as low. Major contributing factors to this rating were the small overall numbers of outcome events – i.e. smokers quitting successfully – and the fact that six of the nine included studies were rated as having a high risk of bias.<sup>4</sup> These ratings were conducted prior to the knowledge of the outcomes of the review and the lead author of the review was not involved in this assessment.

The overall rating of the evidence as being of low quality is a key contributor to the main conclusion of the review: that the current evidence is insufficient to conclude that e-cigarettes are efficacious as an aid to smoking cessation.<sup>4</sup>

There are multiple issues with the studies included in the review and multiple reasons to consider their influence on the overall results. In order to avoid “cherry picking” of specific studies for exclusion, particularly when the results of the review are known, it is useful to consider the impact of exclusion of any single study or group of studies, including considering potential sources of bias – noting that they are “post hoc”.

Exclusion of any individual study in the review, including Lee et al 2019,<sup>6</sup> would not change the overall quality rating but would reduce the numbers of events, increasing imprecision – which was already rated as being of serious concern. Hence, the exclusion of this or any other study would not lead to a change in the overall GRADE assessment of “low”. As already noted in the review, consideration of potential competing interests and length of follow up also did not change the conclusions of the review, but further diminished the body of evidence.<sup>4</sup>

Three of the identified RCTs compared nicotine-delivering e-cigarettes (ENDS) to no intervention or usual care and three compared ENDS to e-cigarettes that did not deliver nicotine.<sup>4</sup> Lee et al 2019 was not among these trials, so these inconclusive results are unchanged if it is excluded. Three RCTs compared ENDS with approved nicotine replacement therapy, of which the Lee et al trial was one. The promising nature of these findings, especially those driven by the single high quality study of Hajek et al<sup>7</sup> – the only trial of the nine (or eight) to demonstrate a significant benefit – also remains whether not Lee et al is included.

This means that the overall conclusion of the review – that the current evidence is insufficient to conclude that e-cigarettes are efficacious as an aid to smoking cessation – would not change with the exclusion of Lee et al, 2019. Nor would the promising nature of the evidence, especially with respect to use of e-cigarettes in a therapeutic context.

The evidence on e-cigarettes is evolving rapidly and it is likely the evidence base will improve substantially in the near future. Additional high quality evidence, particularly that which informs support for smokers to quit, is eagerly awaited.

## References

1. GRADE Working Group. GRADE Handbook. Available from <https://gdt.gradepro.org/app/handbook/handbook.html>. H. Schünemann, J Brożek, G Guyatt and Z Oxman. 2013.
2. National Health and Medical Research Council. Assessing certainty of evidence. Available from: [https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence#toc\\_288](https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence#toc_288) (accessed 27 November 2020).
3. Balshem H, Helfand M, Schünemann H, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology* 2011; **64**(4): 401-6.
4. Banks E, Yazidjoglou A, Brown S, et al. Systematic review and meta-analysis of evidence on the efficacy of e-cigarette use for sustained smoking and nicotine cessation. *medRxiv* 2020110220224212 2020 <https://doi.org/10.1101/2020.11.02.20224212>.
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7. Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy. *N Engl J Med* 2019; **380**(7): 629-37.