Written evidence submitted by the
Cochrane Tobacco Addiction Review Group (ECG0041)

About our organisation
Cochrane is a global non-profit that produces systematic reviews of healthcare interventions, free from commercial sponsorship and other conflicts of interest. Cochrane’s work is recognized as representing an international gold standard for high quality, trusted information. The Cochrane Tobacco Addiction Review Group was established in 1996 and is based at the Nuffield Department of Primary Care Health Sciences, University of Oxford, UK. The group prepares and maintains systematic reviews of interventions relevant to tobacco control and its work has informed national and international guidelines, including those from NICE and the WHO.

Our relevance to this enquiry
We have systematically reviewed the evidence on electronic cigarettes as a smoking cessation aid, with our review first published in 2014 and updated in 2016. The review is free to access within the UK and can be found here:
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010216.pub3/full. (1) To conduct this review, we searched numerous databases for scientific literature, reviewing all available evidence on electronic cigarettes for smoking cessation, which includes assessing the strengths and weaknesses of the available evidence. We have since updated these searches (March 2017) in preparation for another article on this topic, which places us in a unique position in terms of our knowledge of the evidence to date.

We note that the Committee has asked for written submissions addressing health; our expertise relates to two of the three specific points raised by the Committee, namely the impact on human health of e-cigarettes — themselves and relative to ‘conventional’ smoking — and any gaps in the science knowledge-base in this area, and the benefits and risks of e-cigarettes as a ‘stop smoking’ tool and any gaps in the knowledge-base on this. We address these briefly below but full detail can be found in our review (link above). We are also happy to answer any questions or provide any further information that may be of use to the Committee.

The impact on human health of e-cigarettes
Our expertise here relates to the impact on human health compared to conventional cigarettes.

What the evidence shows so far
Cigarettes are uniquely deadly and though evidence does not suggest electronic cigarettes are risk free, evidence does suggest they are significantly less harmful than conventional cigarettes. None of the studies included in our review (which ranged from short- to mid-term, up to two years) detected serious adverse events considered possibly related to electronic cigarette use. The most commonly reported adverse effects were irritation of the mouth and throat. Due to a lack of long-term studies, the long-term safety of ECs is unknown. However, in some studies, reductions in biomarkers (e.g. measurements of toxins in people’s blood and breath) were observed in smokers who switched to vaping consistent with reductions seen in smoking cessation. (1) As electronic cigarettes are relatively new, there are not many studies in people with pre-existing conditions. However, results from individual studies in people with COPD, asthma, and hypertension have generally shown improvements in symptoms and have not detected serious adverse effects.(2-4)

In public discourse on electronic cigarettes, safety concerns often cite the fact that they contain nicotine. This in itself should not be a cause for concern. Cravings for cigarettes are less intense when nicotine is substituted for smoking, thus nicotine can facilitate quitting smoking, as is the case with nicotine replacement therapy. While cigarette addiction, if not overcome, kills half of its
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victims, addiction to nicotine replacement therapy or e-cigarettes is far less hazardous. (5) Moreover, only a minority of people who transfer to nicotine replacement therapy are persistent users. (6) While there is less evidence on persistent use of e-cigarettes after quitting, one cohort study estimated that over half of people who quit smoking with the aid of e-cigarettes were no longer using e-cigarettes six months later. (7)

In summary, our findings from independently reviewing the best available evidence on the topic suggest that for existing smokers of conventional cigarettes, switching to electronic cigarettes is likely to lead to significant improvements in health. These findings are based in studies of people who smoked conventional cigarettes, but findings are consonant with findings from the Royal College of Physicians which were based on comparisons of the composition of carcinogens and toxicants in tobacco smoke and vapour from electronic cigarettes. (8)

Gaps in the knowledge base
As electronic cigarettes have been used for only a few years, there is little evidence on their safety when used as a long-term or permanent replacement for smoking. As almost all regular use of electronic cigarettes occurs in former or current smokers, interpreting future epidemiological data will be difficult. In the meantime, findings from short- to medium-term studies, studies of biomarkers, and studies of toxicants all suggest electronic cigarettes are significantly less harmful than conventional cigarettes.

Benefits and risks of e-cigarettes as a ‘stop smoking’ tool
What the evidence shows so far
There is evidence from the combined results of two trials that electronic cigarettes with nicotine, compared with electronic cigarettes without nicotine, help smokers to stop smoking long-term (this is equivalent to placebo-controlled trials, which is standard when assessing the effectiveness of pharmacotherapy). (9, 10) In people who received electronic cigarettes without nicotine, approximately 4% had quit at six months, compared to 9% in people who received electronic cigarettes with nicotine. (1) This corresponds to findings from placebo-controlled trials of nicotine replacement therapy. (5) In studies conducted only in people provided with electronic cigarettes with nicotine (i.e. no comparison arm), quit rates ranged from 12.5% to over 50% at six months or longer. (1) There is evidence from one trial that electronic cigarettes may lead to six-month quit rates similar to those achieved with nicotine replacement therapy, but the confidence interval is wide. (9)

In summary, findings from the best available evidence suggest electronic cigarettes with nicotine may help people stop smoking. Of note, a separate systematic review found the opposite, but we would caution against using these findings as a basis for decision-making, as the methodological rigour of the assessment has been questioned. (11, 12)

Gaps in the knowledge-base
The main weakness of the above evidence is that the two trials which contribute to our overall result regarding smoking cessation used electronic cigarettes which are no longer available due to poor nicotine delivery, meaning the observed effect of electronic cigarettes with nicotine compared to those without nicotine may be smaller than if tested using devices which are currently available. Particular gaps in the evidence identified by the Cochrane review are summarised below:

- Although the gold standard in examining the efficacy of medicines, including those used to help people stop smoking, is to compare active treatment with placebo, testing electronic cigarettes containing nicotine against electronic cigarettes without nicotine presents a
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conservative paradigm, as electronic cigarettes provide nicotine replacement as well as behavioural and sensory replacement for cigarettes. More randomized controlled trials are needed comparing electronic cigarettes with ‘usual care’ or minimal treatment, and with alternative pharmacological and behavioural treatments.

- Data are also needed on the proportion of smokers who successfully quit smoking with the help of electronic cigarettes and who continue to use electronic cigarettes long-term.
- Given the variety of products on the market and the product evolution, data are needed from studies which test electronic cigarettes with good nicotine delivery.
- Data are also needed from studies that provide electronic cigarettes in a way that would be used in real-world settings (e.g. taking into account individual preferences for strengths, flavours and devices).

Declarations of interest

The Cochrane Tobacco Addiction Group is funded entirely by the National Institute of Health Research (NIHR), the research arm of the NHS. We have no conflicts of interest to declare.

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References

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