E-cigarettes: controversies within the controversy

10 years have passed since e-cigarettes were first marketed in the UK. Since then, e-cigarettes have engendered substantial controversy in the realms of public health and respiratory medicine.

The modern e-cigarette—the prototype Ruyan device, invented by Hon Lik in China in 2003—was designed to resemble a traditional cigarette and to deliver nicotine to the user via an inhalable aerosol. Since then, technological development of e-cigarettes has been exponential. By 2014, the USA alone had more than 460 e-cigarette brands, with a myriad of accessories and more than 7000 flavours of e-liquid available. Action on Smoking and Health (ASH) currently estimate that 2·8 million people in the UK use e-cigarettes.

The e-cigarette market has developed from a handful of minor manufacturers to larger companies and mergers of companies, all developing their own products and brands. Investment in e-cigarettes from so-called big tobacco companies in the UK, especially since 2013, has aroused controversy. The Royal College of Physicians (RCP) report on e-cigarettes published in April, 2016, stressed concerns regarding the increasing involvement of big tobacco—a view shared by Robert West, Professor of Health Psychology at University College London (London, UK)—claimed that both non-daily and daily use of new-generation devices which are allegedly increasingly effective at substituting smoking. The first lawsuit by a manufacturer was filed against the FDA only days later. The RCP report points out regarding big tobacco interest in e-cigarettes, they “will remain a fraction of the market in tobacco products, with cigarettes remaining the dominant product category.”

In May, 2016, The US Food and Drugs Agency (FDA) published its e-cigarettes regulations, regarding “the manufacture, import, packaging, labeling, advertising, promotion, sale, and distribution” of e-cigarettes. The e-cigarette industry and its advocates responded with claims that the regulation proposed would be unaffordable for the vast majority of businesses—except, controversially, big tobacco companies—and would hinder development and sale of new-generation devices which are allegedly increasingly effective at substituting smoking. The first lawsuit by a manufacturer was filed against the FDA only days later.

The conflicting views on the efficacy of e-cigarettes to promote smoking cessation are at the centre of controversies surrounding their proposed harm reduction properties. In 2014, David Nutt—Professor of Neuropsychopharmacology at Imperial College London (London, UK)—claimed that e-cigarettes had a potential effect on health care comparable to the success of antibiotics. Months earlier, smoking cessation experts had predicted that tobacco use could be eliminated in the UK within 5–10 years if e-cigarettes were allowed to flourish. However, despite the clear increase in marketing, development, and use of e-cigarettes in the UK, the number of users represents only a minority of adult smokers. Robert West—one of the predictors of tobacco use elimination—has since pointed out that if e-cigarettes were the “game changer” many believed them to be, causing all smokers to switch from tobacco to e-cigarettes, “we might have expected to see a bigger effect than we have seen so far, which has actually been relatively small.” This discrepancy is probably due—at least in part—to the inferior speed of nicotine delivery and absorption from e-cigarettes compared with conventional cigarettes, as previously identified by Forfalsinos and colleagues.
Ultimately, as with any other proposed treatment relevant to respiratory medicine, we look towards systematic reviews to provide us with the best existing estimate of the efficacy of e-cigarettes in smoking cessation. The 2016 Cochrane review of e-cigarettes for smoking cessation identified only two randomised controlled trials (RCTs), just one of which included a comparison to nicotine replacement therapy. Meta-analysis of the data from these RCTs indicated that nicotine-containing e-cigarettes increased smoking cessation compared with nicotine-free e-cigarettes. The overall quality of evidence was graded as low due to a small number of underpowered trials and hence imprecision of the effect estimates. This review should be considered as insufficient evidence to guide clinical practice, particularly in light of the absence of trials comparing e-cigarettes to nicotine replacement therapy with health professional support. Linda Bauld of the University of Stirling (Stirling, UK) argues in her commentary that more RCTs are needed, although a small number are ongoing.

However, disagreement even exists around the appropriateness of RCTs to ascertain data on efficacy. Carl Phillips, former Scientific Advisor for the Consumer Advocates for Smoke Free Alternatives (CASSA), maintains that RCTs are a “bad study method” for e-cigarettes. This view, of course, contradicts commonly held views that such trials represent the gold-standard method for assessment of the efficacy of an intervention.

Others have conducted meta-analyses in which RCTs and observational studies have been pooled together to derive a single estimate of the effect of e-cigarettes on smoking cessation. In a study published in The Lancet Respiratory Medicine, Kalkhoran and Glantz reported reduced rates of smoking cessation with e-cigarettes in a meta-analysis of studies which varied methodologically. Their suggestion that e-cigarettes suppress the chances of successful smoking cessation opposed the Cochrane review findings, fuelling further controversy and dividing opinions on the efficacy of e-cigarettes in smoking cessation.

In an important, simultaneously published overview of the RCP report, four of its key members commented on the safety of e-cigarettes, stating that “e-cigarettes are unlikely to be harmless, and that long term use is likely to be associated with long term sequelae, including an increased risk of chronic obstructive pulmonary disease, lung cancer, possibly cardiovascular disease, and some other long term conditions associated with smoking.” In a 2015 review, Rowell and Tarran (University of North Carolina, Chapel Hill, NC, USA) discuss the potential for e-cigarettes to cause respiratory disease. Nicotine itself has been associated with risk of lung cancer; the thermal decomposition of the solvents used in e-cigarettes can produce carbonyls such as formaldehyde and acetaldehyde. Acrolein, another carbonyl, is strongly associated with the pathogenesis of COPD. Moreover, one of the flavouring additives used—diacetyl—which adds a buttery flavour—is potentially associated with risk of bronchiolitis obliterans. Indeed, the updated NCSCT guideline advises avoidance of e-liquids containing diacetyl, which has been found in many brands.

The RCP report, however, maintains that e-cigarettes remain significantly less harmful than the conventional cigarette, and cite the figure—as did Public Health England in 2015—that the “hazard to health arising from long-term use of e-cigarettes is unlikely to exceed 5% of the harm from smoking tobacco”. Opposing opinion comes from Robert Combes of Cavendish Consulting (UK) and Michael Balls of the University of Nottingham (Nottingham, UK). In their commentary they argue that to postulate that e-cigarettes are a “low risk” product is, “in the light of current knowledge, a reckless and irresponsible suggestion.” They continue with the argument that the assertion of the RCP and Public Health England “ignores the possibilities that users might be repeatedly exposed to hitherto undetected contaminants and by-products, as well as to carcinogenic chemicals, or their precursors”. With the uncertainty surrounding both the effectiveness of e-cigarettes on smoking cessation and their safety, how are we in the health-care community placed to effectively discuss e-cigarettes with our patients and colleagues? The data are not currently available for users to make a fully informed choice on this issue.

What is certainly true is that the controversies surrounding e-cigarettes are complex, multiple, and are not dissipating rapidly.

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For Linda Bauld’s comment see Nicotine Tob Res 2016; 18: 1925
For Kalkhoran and Glantz’s meta-analysis see Lancet Respir Med 2016; 4: 116–28
For the overview of the RCP report see BMJ 2016; 353: 1745
For Rowell and Tarran’s review see Am J Physiol Lung Cell Mol Physiol 2015; 309: 1398–409
For Combes and Balls’ commentary, see Altern Lab Anim 2015; 43: 417–25

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