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## ANALYSIS



## Evidence about electronic cigarettes: a foundation built on rock or sand?

Public Health England recently endorsed the use of e-cigarettes as an aid to quitting smoking. **Martin McKee** and **Simon Capewell** question the evidence on safety and efficacy underpinning the recommendations

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Those responsible for safeguarding the health of the public must often tackle complex and controversial issues. Public Health England (PHE) has been courageous in entering the debate on the role of electronic cigarettes in tobacco control. In a new report it concludes that e-cigarettes are much safer than conventional cigarettes,<sup>1</sup> and one of its authors is quoted as describing them as a potential “game changer” in tobacco control.<sup>2</sup> Media coverage suggests that the debate is now over, with a BBC correspondent describing the evidence as “unequivocal.”<sup>3</sup> However, although British organisations such as the Royal College of Physicians of London<sup>3</sup> and ASH UK,<sup>4</sup> have endorsed some of the report’s conclusions, albeit with caveats, many others have come to the opposite opinion. These include the British Medical Association, the UK Faculty of Public Health, the US Centers for Disease Control and Prevention, the American Lung Association, the World Health Organization,<sup>5</sup> the European Commission,<sup>6</sup> and other leading international health bodies.<sup>7</sup> The available evidence about e-cigarettes suggests that the debate is far from over and questions remain about their benefits and harms.

### Defining the role of e-cigarettes

Fundamental divisions seem to exist between those engaged in this debate. Supporters of e-cigarettes focus narrowly on existing smokers, comparing the devices’ effects with those of smoking conventional cigarettes. As well as being an aid to quitting, e-cigarettes are seen as having a role for people who do not want to quit, offering a safer substitute for some of the cigarettes they would otherwise smoke.

Meanwhile, those on the other side of the debate express concern about uptake of e-cigarettes among people, especially children and adolescents, who would not otherwise smoke and about their long term health effects. They argue that although e-cigarettes do not contain some of the most harmful substances found in conventional cigarettes, such as tar, they do contain

other substances such as formaldehyde (a carcinogen) and diverse flavourings. Thus, it is equally important to include non-smoking as a comparator. They also draw attention to important epidemiological evidence that contrary to what is widely believed, reduced smoking (as opposed to quitting) may not reduce overall risk of death.<sup>8</sup> The expression “dual use,” which acknowledges that two thirds of e-cigarette users also smoke, rarely occurs in the PHE report. Although some dual use is inevitable during the quitting process, if this persists long term health concerns remain. A recent cohort study by McNeill and colleagues showed that dual use among daily “vapers” apparently remained above 80% after 12 months follow-up, which is worrying.<sup>9</sup>

### Quality of the evidence

A fundamental principle of public health is that policies should be based on evidence of effectiveness. So does the available evidence show clearly that e-cigarettes are as effective as established quitting aids? Unfortunately not. The recent Cochrane review is widely cited,<sup>10</sup> but it included only two randomised controlled trials, both with important limitations, and concluded that the evidence was of “low or very low quality by GRADE standards.” The PHE report authors concede the weakness of the evidence, noting how a single observational study with substantial limitations offers “some of the best evidence to date on the effectiveness of e-cigarettes for use in quit attempts.”

Where there is uncertainty about risks, the precautionary principle should apply. Thus, in the absence of scientific consensus that the substance is not harmful to the public, the burden of proof that it is not harmful falls on those taking an action. The quality of the evidence cited by PHE therefore becomes crucial. The headline message from the PHE report, widely quoted in the media, is that “best estimates show

e-cigarettes are 95% less harmful to your health than normal cigarettes,” seemingly leaving little room for uncertainty about long term risks. Yet a recent systematic review,<sup>11</sup> which the PHE report surprisingly fails to cite, came to a different conclusion. It found serious methodological problems in many of the 76 studies it reviewed, and one third of the studies (34%) were published by authors with conflicts of interest. The systematic review also expressed concern about the effects of various substances in e-cigarettes, some but not all of which are also found in conventional cigarettes. It concluded that “due to many methodological problems, severe conflicts of interest, the relatively few and often small studies, the inconsistencies and contradictions in results, and the lack of long-term follow-up no firm conclusions can be drawn on the safety of e-cigarettes. However, they can hardly be considered harmless.”

We might also expect that the prominently featured “95% less harmful” figure was based on a detailed review of evidence, supplemented by modelling. In fact, it comes from a single meeting of 12 people convened to develop a multicriteria decision analysis (MCDA) model to synthesise their opinions on the harms associated with different nicotine containing products; the results of the meeting were summarised in a research paper.<sup>12</sup> The authors state: “The sponsor of the study had no role in any stage of the MCDA process or in the writing of this article, and was not present at the workshop.” However, given the importance of complete transparency in an area as controversial as this, it is legitimate to ask about the sponsors. One is a company called EuroSwiss Health.<sup>13</sup> An internet search reveals little about its activities other than that it funded the meeting, but it is one of several companies registered at the same address in a village outside Geneva with the same chief executive. He is reported to have previously received funding from British American Tobacco (BAT)<sup>14</sup> for writing a book on nicotine as a means of harm reduction,<sup>15</sup> although the book states that “the statements, findings, conclusions and recommendations contained in the book were developed independently of BAT.” He also endorsed BAT’s public health credentials in its 2013 sustainability report.<sup>16</sup>

The paper also acknowledges support from Lega Italiana Anti Fumo (Italian Anti-Smoking League), whose chief scientific adviser was one of the 12 people attending the meeting. He declares funding from an e-cigarette manufacturer but not the funding he is reported elsewhere to have received previously from tobacco company Philip Morris International.<sup>17</sup> The rationale for selecting the members of the panel is not provided, but they include several known e-cigarette champions, some of whom also declare industry funding in the paper.<sup>12</sup> Some others present at the meeting are not known for their expertise in tobacco control. The meeting was also attended by the tobacco lead at PHE. Furthermore, their paper tellingly concedes that “A limitation of this study is the lack of hard evidence for the harms of most products on most of the criteria.” However, none of these links or limitations are discussed in the PHE report.

## Uncertainty around harms

The PHE report asserts that the available evidence suggests that e-cigarettes are not currently re-normalising smoking among children and young people in the UK. However, this remains a major concern for health professionals and parents. In England, experimentation with e-cigarettes among young people is worrying high, with over one fifth of 11-15 year olds having ever used e-cigarettes<sup>18</sup>; 73% of the young people surveyed who had tried e-cigarettes were non-smokers. Uptake of e-cigarettes among young non-smokers is a particular concern, given that

nicotine use in young people may disrupt brain development with long term, irreversible consequences for brain function.<sup>19</sup> The authors categorically dismiss the possibility that e-cigarettes may be a gateway to smoking, arguing that even the concept of a children’s gateway should be rejected. This view seems premature, particularly given recently emerging evidence<sup>20</sup> such as an American study, published after the PHE report, which concluded that “those who had ever used e-cigarettes at baseline compared with nonusers were more likely to report initiation of combustible tobacco use over the next year.”<sup>21</sup> Furthermore, none of the research so far can be considered conclusive, and longer term studies are needed.

Evidence on the risk of e-cigarette aerosol to bystanders in enclosed public spaces is sparse. However, the PHE report seems to equate lack of evidence with evidence of lack of effect. It claims that there is “no identified risk to bystanders,” a view that may be premature.

The report has many other omissions, such as concerns about product safety, including forged safety certificates reported by a BBC *Fake Britain* documentary in December 2014, and the lack of evidence of risks from long term dual use with conventional cigarettes.<sup>22</sup> Yet perhaps its most striking feature is its consistent adoption of the most optimistic position on the limited evidence available. To take one example, the report offers reassurance that e-cigarettes when “used as intended pose no risk of nicotine poisoning to users.” This is true, but it is equally true of all poisons. The report rightly calls for nicotine to be in child-proof containers given the attraction of colourful packaging. However, it quotes a report of over 2400 poisoning cases in the United States up to February 2014<sup>23</sup> as saying “none resulted in any serious harm,” although the US report included reference to a death attributed to suicide. Nor does it cite the report’s conclusion that “the public should be aware that e-cigarettes have the potential to cause acute adverse health effects and represent an emerging public health concern.”

The PHE authors also fail to consider the practical consequences of their recommendations. If e-cigarettes are so safe, presumably there will be no restriction on using them in cars. This will make the forthcoming ban on smoking in cars with children virtually unenforceable because it will be extremely difficult to determine what is causing a cloud of smoke or vapour in a moving car.

Finally, the PHE summary states, “The accuracy of nicotine content labelling currently raises no major concerns.” Surely, England’s leading public health agency cannot be indifferent to a situation where consumer product information is known to be wildly inaccurate?<sup>6 24</sup>

## Where next for policy on e-cigarettes?

In 2016, the European Union Tobacco Products Directive<sup>25</sup> will come into force despite some of the most intensive tobacco industry lobbying ever seen.<sup>26</sup> Most of the lobbying effort concerned packaging of conventional cigarettes. However, there was also a powerful attack on the directive’s substantial restrictions on e-cigarettes. These restrictions will hopefully limit the negative effect of this flawed PHE report. Meanwhile, directors of public health and the wider community desperately need advice on e-cigarettes that is evidence based and free from any suspicion of influence by vested interests.

Happily, a consensus may be emerging. The English chief medical officer (CMO) recently said that, if e-cigarettes have a role in smoking cessation that should be as “licensed medicines. This would provide assurance on the safety, quality, and efficacy to consumers who want to use these products as quitting aids.”<sup>27</sup> That would, of course, require data to show that they were both

safe and effective because, as the CMO also notes, “there continues to be a lack of evidence on the long-term use of e-cigarettes.” We agree with this view.

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### Key messages

Public Health England's endorsement of the safety and efficacy of e-cigarettes is based on uncertain evidence

The quality of evidence that e-cigarettes help smokers to quit is weak

Recent evidence questions the conclusion that e-cigarettes are not a gateway to smoking

Until better evidence is available public health strategies should follow the precautionary principle