

## E-Cigarettes: A Disruptive Technology That Revolutionizes Our Field?

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Electronic cigarettes (EC) or electronic nicotine delivery systems (ENDS) were invented by the Chinese pharmacist Lik Hon and were initially developed by the Chinese company Ruyan. Early models looked very much like cigarettes, and therefore EC was a relatively appropriate name. However, they are now available in numerous shapes and sizes with different components (“mods”) that can be assembled by users (“vapers”); therefore ENDS may be a more accurate name for these devices. They were first marketed in Europe and the United States in 2006. Sales of ENDS were initially modest, possibly because the technology was unreliable and the nicotine delivery was very limited.<sup>1</sup> ENDS were first met by curiosity and an open mind by most researchers and tobacco policy advocates. After some years with modest growth on the market but with radical technological development and a big growth in tobacco company interest, sales of ENDS increased dramatically around 2010 and have now surpassed sales of nicotine replacement therapy (NRT) despite its 35 years on the market. Some financial analysts project that ENDS will overtake the sales of traditional cigarettes within 10 years.<sup>2</sup> Among adults in the United States, awareness of ENDS increased from 41% in 2010 to 80% in 2013. Ever use increased from 10% to 37% among smokers and from 3% to 10% among former smokers.<sup>3</sup>

With the steep increase in market penetration and an absence of interest in ENDS from the pharmaceutical industry, the tobacco industry has decisively moved into the ENDS business. Today almost all of the big international tobacco companies have their own ENDS products. That may explain the change in attitude among tobacco policy advocates from an initial open mind to a much more negative outlook. Few clinicians and researchers want to be engaged in research that can benefit the tobacco industry. Many anti-tobacco policy makers believe that ENDS will not benefit public health at the population level, even if they may provide a harm reduction mechanism for certain cigarette smokers who are unwilling or unable to quit. The discussion around ENDS has become very polarized with two very different letters of advice being sent to Margaret Chan, the Director General of WHO by different groups of researchers, with very different perspectives on the value and potential dangers of ENDS.

ENDS present new regulatory challenges to governments. They have been banned in several countries such as Australia, New Zealand, Canada, and Sweden. Regulatory agencies in other countries are struggling with how to regulate them. In the United States, the Center for Tobacco Products at the FDA has started a process to regulate ENDS by deeming the FDA’s jurisdiction over them, but the process

of implementing specific regulations is likely to be slow and politically fraught. In the EU, ENDS are permitted and have been given two roads in its Tobacco Products Directive of 2014.<sup>4</sup> They can be regulated as either a medicine like NRT, or as a general consumer product. In the medicine route, they can be advertised with efficacy claims and there are no limitations on nicotine content in the cartridges. The consumer goods route will not allow efficacy claims, advertising and unlimited nicotine content.

The polarized views are to an extent a consequence of the limited research that has been conducted on the short-term and long-term health effects of ENDS. ENDS are a relatively new product in the marketplace and their design is still evolving. Thus, there has not been sufficient time for the long-term health effects of ENDS to be determined with any certainty. Studies are just beginning to address questions such as whether ENDS help cigarette smokers quit and whether ENDS recruit young people into nicotine dependence. Many opinions have been formed in the absence of sound evidence. For this reason, *N&TR* has decided to devote a whole issue to research on ENDS to help further understand them and their role in the tobacco/nicotine landscape. This special issue includes a wide variety of papers from chemical composition of ENDS liquids to performance to user characteristics. The papers provide many new insights. In particular concerns have been voiced about unnecessary toxicants in ENDS often resulting from heated flavorings. Many sweet-flavored ENDS contain diacetyl and propionyl, chemicals that are approved for food use, but can have adverse effects on the respiratory system. The concentrations obtained were however 10–100 times lower than seen in cigarettes.<sup>5</sup> Nicotine poisoning also might result from ingestion or skin contact with ENDS liquids. A poison centre in Texas reported an increase in the number of reports for ENDS, mostly due to ingestion (78%). The most frequent effects were vomiting (20%), nausea (10%), and headache (4%). Most of the exposures occurred in young children.<sup>6</sup> The extent to which nicotine and other substances can be absorbed by non-vapers remains to be studied.<sup>7</sup> The accuracy of labeling is not always very good but improving. One study reported that the nicotine content of two-thirds of samples assessed were more than 10% outside stated levels.<sup>8</sup>

Efforts to quantify the health effects of ENDS are complicated by the difficulty of measuring the doses of nicotine and other chemicals inhaled by the user. Nicotine yield in vapor can vary as much as 50 times due to puff topography, liquid strength and composition, and design features of ENDS, such as capacity to raise temperature.<sup>9</sup> Newer ENDS can be controlled either by a button or by an air-flow sensor. The airflow rates required to produce aerosol and the aerosol adsorbances were lower for button-activated models than for airflow-activated models. Pressure drop was also lower across button activated products which causes users to drag harder on air-flow activated systems.<sup>10</sup> Among experienced users using their preferred product it was found that 10 puffs at 16 ng/ml could give an increase in plasma nicotine concentrations similar to tobacco cigarettes.<sup>11</sup> Some pulmonary absorption of nicotine seems to take

place since peak nicotine levels were achieved within 5 min of starting ENDS use. The study also found that the amount of nicotine obtained by users increases over time as users become more experienced.<sup>12</sup> There are many ways to determine the nicotine delivery of ENDS. In order to arrive at a standard by which different products can be compared, it has been suggested that the total dose and its rate should be measured, for example, as the nicotine per puff or per second by a given ENDS design under a given use condition.<sup>13</sup> Using the nicotine flux as a parameter for characterizing ENDS was questioned in a letter to the editor. It was questioned on the grounds that it could drive down the nicotine delivery and make ENDS less effective while it would provide no benefit in terms of safety.<sup>14</sup>

ENDS, when compared with smokeless tobacco, are being quickly embraced by cigarette smokers, either as a replacement for cigarettes or in addition to cigarettes.<sup>15</sup> It is not yet clear whether nicotine dependence will decrease, increase, or remain constant among cigarette smokers who switch to ENDS. ENDS users report being less dependent than they retrospectively reported having been on cigarettes prior to switching. However longer use, button operated systems and higher nicotine containing cartridges were associated with higher dependence.<sup>16</sup> American adult smokers reported that ENDS had greater appeal than smokeless tobacco. When asking vapers about expectancies, ENDS were more positively rated than cigarettes on health risks, reduction of craving and withdrawal symptoms, sense of taste and negative social impression, but had less positive expectancies for weight control, stimulation and reduction of stress and negative effect. ENDS were rated as superior to NRT for taste, satisfaction, health risks, negative physical feelings, cost and reduction of craving, negative effect and stress.<sup>17</sup> In a two-year longitudinal study of metropolitan US adult smokers, intensive ENDS users were six times as likely as non-users or triers to report quitting smoking cigarettes<sup>18</sup> and longer duration of use has been found to be associated with fewer cigarettes smoked.<sup>19</sup> Among hospitalized smokers ENDS use was more common among heavier, younger, and higher educated smokers.<sup>20</sup> Between 2011 and 2013, the number of never-smoking youth who had tried ENDS increased three-fold, and intention to smoke cigarettes has been reported to be greater among those who had tried ENDS compared with those who had not tried ENDS.<sup>21</sup> Another study found that 8% of non-smoking young adults had tried ENDS and 14% of this group of reported that they were current users.<sup>22</sup>

A National Institutes of Health-sponsored workshop identified research priorities that included standards to measure the contents and emissions of ENDS, biomarkers of exposure, physiological effects on tissues and organs, and potential as both a cessation aid and a gateway product to cigarette smoking.<sup>23</sup> With this issue the guest editors hope that *N&TR* has contributed to a better informed discussion of ENDS.

## Declaration of Interests

None declared.

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