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ReCent

E Cigarettes - The Big Picture

South African Edition

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different

E-Cigarette use is on the up, with large tobacco companies now major players in this market. Should we be worried?

E-Cigarettes – The Big Picture

Ever since the US Surgeon General, Luther L. Terry, released “Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service”, in 1964, tobacco has ultimately become enemy number one when it comes to issues such as preventable cancer, respiratory, and cardiovascular-related morbidity and mortality.

Given mankind’s persistent endeavour to innovate and advance, it should come as no surprise that E-Cigarettes (ECs) were invented, and have become increasingly popular, not just amongst smokers, but also to a lesser extent (although worryingly), non-smokers.

On the face of it, the premise is simple: tobacco is bad and we shouldn’t consume tobacco products; ECs do not contain tobacco but rather the nicotine that smokers crave and so if one can get their nicotine dose without smoking, all will be right in the world.

Unfortunately, as life insurers, we cannot take that premise at face value, not with the complexity of social norms and behaviours associated with tobacco use and of course, the ever growing body of evidence that ECs, while possibly safer than cigarettes, are not actually safe.

While discussing the potential health effects of ECs, this article will also evaluate the past with regards to cigarette smoking and, very importantly, the behavioural aspect of smoking as well as how the trend of EC use seems to be quite similar to that of cigarettes.



Tobacco has ultimately become enemy number one when it comes to issues such as preventable cancer, respiratory, and cardiovascular-related morbidity and mortality.

Life insurance companies started charging smokers higher premiums for their life insurance policies in the 1970s, quite a few years after the 1964 report came out about the dangers of smoking. The accepted norm today is that users of ECs are charged smoker rates which, given the complexity of health, behavioural and social complexities around ECs, is the right thing to do.

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A brief history of smoking, and mistakes from the past

To revise the harmful effects of cigarette smoking would be a redundant exercise, however, what is worth revising is the tortuous path that led to the denormalisation of smoking, lest we head down the same path with ECs. Smoking became entrenched in the US population around 1940 and the use of cigarettes peaked at around 4,500 cigarettes per adult per year around 1964, a key year in the history of the denormalisation of smoking.

Despite epidemiologic data about the harmful effects of smoking being published in the 20th century, it was only in 1957 that the US Surgeon General first acknowledged a causal relationship between smoking and lung cancer. Denial of the dangers of smoking was largely driven by the tobacco industry through various mechanisms such as misinformation, advertising and bold attempts to discredit scientific literature.

On June 7, 1962, recently appointed Surgeon General Luther L. Terry announced that he would convene a committee of experts to conduct a comprehensive review of the scientific literature on the smoking question. On January 11, 1964 - choosing a Saturday to minimize the effect on the stock market and to maximize coverage in the Sunday papers - Terry announced the findings of an increase in mortality, an increase in diseases like bronchitis and a link with cardiovascular disease. As Terry remembered, the event two decades later, the report “hit the country like a bombshell. It was front page news and a lead story on every radio and television station in the United States and many abroad.”¹

The medical fraternity remained divided though, and after the release of the report of the Surgeon General, the American Medical Association (AMA) published a seven page brochure for the general public titled “Smoking: Facts You Should Know”, which described a range of “suspected health hazards”.²

- 1 Rockville, M.D., 2014. The Health Consequences of Smoking-50 Years of Progress. A Report of the Surgeon General, US Department of health and human services. Office of the Surg. Gen., Atlanta US, p.944.
- 2 American Medical Association, 1964. Smoking: Facts You Should Know. Chicago: American Medical Association.



Smoking became entrenched in the US population around 1940 and the use of cigarettes peaked at around 4,500 cigarettes per adult per year around 1964.

The tobacco industry used this division to propagate its message that it was not clear that cigarettes were harmful.

The first Surgeon General's warning on a cigarette packet in 1967 read: "Caution: Cigarette Smoking May Be Hazardous to Your Health", which contrasted with the 1964 report, however, subsequent analyses have shown how the tobacco industry used its connections within government to negotiate a weak warning label.³

Around this time it was agreed that advertising of tobacco products could include information on the tar and nicotine content of cigarettes, which would later be used by companies to provide misinformation about the relative health benefits of smoking lighter cigarettes.⁴ The tobacco industry's marketing efforts promoted doubt around smoking's effects on health, something which changed during the 1970s with an increased emphasis on ads that featured claims about tar and nicotine content, implying reduced exposures to cancer-causing agents.



Key words such as "light," "smooth," and "mild," were used to convey health-related messages. In the 1980s, these health messages became more subtle, relying on imagery of active, healthy models.⁵

3 Brandt, A., 2009. The cigarette century: the rise, fall, and deadly persistence of the product that defined America. Basic books.

4 Rockville, M.D., 2014. The Health Consequences of Smoking-50 Years of Progress. A Report of the Surgeon General, US Department of health and human services. Office of the Surg. Gen., Atlanta US, p.944.

In 1979, the Surgeon General's report, "Smoking and Health", was released under Joseph Califano, the Secretary of the Department of Health, Education, and Welfare, marking the 15-year anniversary of the 1964 report. His foreword to the volume read "But why, the reader may nevertheless ask, should government involve itself in an effort to broadcast these facts and to discourage cigarette smoking? ... Why, indeed? For one reason, because the consequences are not simply personal and private. Those consequences, economic and medical, affect not only the smoker, but every taxpayer".⁴

Smoking was a social ill that cost everyone, rather than being an individual choice of one's own health. Until now smoking was still normal, but with the recognition of the economic and health effects to communities affected by smoking, both directly and through second-hand smoke, smoking would eventually become denormalised. The tobacco industry didn't acknowledge the growing body of evidence and sought to sow doubt by discrediting the health findings on the effects of secondhand smoke. In addition their efforts to hide the fact that nicotine was addictive were very successful and it was only in 1988 that nicotine was officially acknowledged by the Surgeon General as an addictive substance. This was another blow to the tobacco industry, because cigarettes were not only a socially damaging product but also addictive and therefore those who smoked, and who couldn't stop, were not entirely to blame for their actions.

Since the 1964 Surgeon General's Report, the tobacco industry's extensive campaign to counteract anti-smoking efforts through marketing, public relations, political influence, and creation of doubt about the scientific evidence is clear to see.

Apart from the recognition of individual dangers to health caused by smoking, several factors were crucial in denormalising smoking:⁴

1. The emergence of a non-smokers' rights movement and evidence linking exposure to second-hand smoke to disease;
2. An understanding of regular cigarette smoking as an addictive behaviour and one that begins in adolescence;
3. A focus on the tobacco industry itself as a key influence on smoking behaviour and the importance of countering its actions.

Ultimately it was the realisation of smoking as a socio-economic burden and the actions that followed, that ultimately denormalised smoking. What we also know is that the psycho-socio-behavioural aspects of smoking are complex and go beyond just nicotine addiction. Given that ECs were conceived from cigarettes, the same type of psychology around their use would seem intuitive.

Thus any review of ECs without addressing this aspect would fall short in its attempt to highlight the potential problem ECs present.

“Smoking is a complex behaviour which has reflected deep social, cultural, and economic forces, as well as a powerful biological process of addiction.”⁵

Psycho-socio-behavioural aspects of smoking and nicotine addiction

Nicotine exerts its effects on multiple brain systems which affect behaviour, thinking and feeling, thus separation of biological from psychological factors in understanding and addressing addiction is fruitless. Rather, it is the interaction of social, individual, and biological aspects that promote and perpetuate smoking and tobacco use (which includes ECs).

This psychological aspect of smoking behaviour is evident when one considers that not all users of the nicotine patch are successful at quitting despite the patch delivering the nicotine that is missing when smoking stops; in addition to this, the desire to smoke still exists in people using the patch.

Smoking also has psychological triggers such as boredom, anxiety or stress, where smoking quantity varies against what would be expected.

The expected outcome of a purely biological addiction would be steady smoking at regular intervals as nicotine levels drop

⁵ Brandt, A., 2009. The cigarette century: the rise, fall, and deadly persistence of the product that defined America. Basic books.

in the smoker after their last cigarette. Following from this, certain triggers have been associated with increased tobacco use such as driving, or drinking alcohol, again indicating a psycho-behavioural component.⁶

The exceptionally high smoking resumption rates even at six months, one year and two years after stopping smoking in themselves tell a story of a deeply entrenched psycho-socio-behavioural habit that is not purely explained by a biological model.⁷

It is a behavioral disorder typified by persistent desires and unsuccessful efforts to quit, thus resulting in continued smoking.

Researchers believe that some of the pleasurable experiences associated with smoking are not solely attributable to nicotine. For instance, research suggests that the sensorimotor aspects of smoking (for example, the taste, the smell, the handling of the cigarette) can become reinforcing in and of themselves, largely as a result of their association with smoking.⁷

Given the primary role of ECs in the delivery of nicotine, it seems apparent that the acceptance of ECs as a social norm has the clear potential to partially, or even completely, renormalise smoking culture.

While regulation of smoking is stringent and well developed and we will never again see a co-worker smoking a cigarette at the desk opposite us, the bio-psycho-behavioural characteristics of tobacco addiction are quite clearly at risk of being mirrored with the use of ECs.

Notwithstanding what should be a clear societal norm, i.e. that nicotine addiction and EC smoking behaviour is not acceptable, prevalence and usage of ECs is on the rise and being driven by the same companies that drove tobacco use in the last century.

⁶ <http://www.quit-smoking-advisor.com/06-Psychology-of-Smoking/cigarette-addiction.html>

⁷ <http://www.encyclopedia.com/history/encyclopedias-almanacs-transcripts-and-maps/psychology-and-smoking-behavior>

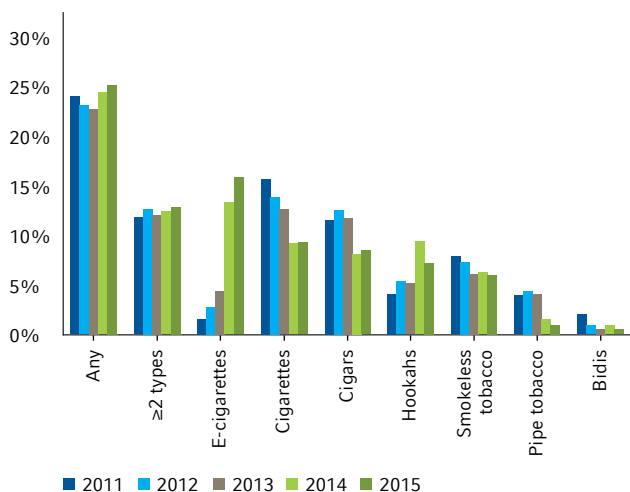
Prevalence and usage of E-Cigarettes

Since ECs have become mainstream, the demographic of users has shifted from generally being smokers wishing to quit, to ex-smokers and now an increasing proportion of ‘never smokers’.

Quite worrying, but not surprising, given the aggressive marketing of ECs, is the fact that newer EC users tend to be younger. Studies are now showing that first time EC use can occur in children as young as 12 years old.⁸

When one looks at adolescent use of tobacco products which include ECs, EC use is rising. As found by Singh et al and represented in the graphic, is that cigarette use seems to be decreasing among adolescents in the USA, however, there is a significant increase in the use of ECs.⁹

Estimated percentage of high school students who currently use any tobacco products, ≥2 tobacco products, and select tobacco products - National Tobacco Survey 2011 - 2015



- 8 Pisinger, C., 2014. Why public health people are more worried than excited over e-cigarettes. *BMC medicine*, 12(1), p.226.
- 9 Singh T, Arrazola RA, Corey CG, et al. Tobacco use among middle and high school students - United States, 2011-2015. *MMWR Morb Mortal Wkly Rep* 2016; 65:361.

Of special concern is the fact that young never-smokers are experimenting with ECs. Thus the use of ECs might undermine decades of efforts to denormalise smoking^{9, 10}.

In addition, the prevalence of smoking in one study increased with increasing rates of EC use, from 24% to 38% during a period of only three years, indicating a renormalisation of smoking.¹¹

Given these statistics and usage patterns, we need to ask ourselves: what is driving the increased use of ECs?

Regulation, marketing, and brand ownership

Regulation of ECs varies significantly in different parts of the world, ranging from complete bans on sales (i.e. making them illegal) to absolutely no regulation at all.

Part of the problem with regulation centres around whether they are classed as a tobacco product or a medicinal product, used for smoking cessation. Even the United States was delayed in regulating ECs - ultimately only in August 2016 did the FDA extend its regulatory power to include ECs.¹² It is this fragmented regulation of ECs that has allowed marketing of ECs to flourish and attract young customers as well as older ones to their products.

The marketing of ECs has largely mimicked that of the tobacco industry of old, with advertising techniques such as television adverts, sports and cultural sponsorship, celebrity endorsement, point of sale displays and some newer tactics such as the use of social media, online advertising and bespoke product design and innovation.

- 10 Choi, K., Fabian, L., Mottey, N., Corbett, A. and Forster, J., 2012. Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: findings from a focus group study. *American journal of public health*, 102(11), pp.2088-2093.
- 11 Goniewicz, M.L., Gawron, M., Nadolska, J., Balwicki, L. and Sobczak, A., 2014. Rise in electronic cigarette use among adolescents in Poland. *Journal of Adolescent Health*, 55(5), pp.713-715.
- 12 <http://www.fda.gov/tobaccoproducts/labeling/rulesregulationsguidance/ucm394909.htm>



Research on ECs has focused on cells of the respiratory tract.

One example of such marketing is that of Skycig; in October 2013, just when Skycig was taken over by Lorillard (a large American tobacco company whose CEO in 1994 testified before congress that nicotine was not addictive), the company signed a deal with English football club Wolverhampton Wanderers.

Under this first club-specific sponsorship deal, fans of the football club would be allowed to buy and use ECs within certain areas of Wolves' home stadium.¹³

Tobacco companies took a while to invest significantly into the EC market. However, with the industry worth around \$3 billion globally, from 2012 to date tobacco company investment in EC companies, both in the UK, US and other markets, has been significant, with multimillion dollar investments - some exceeding \$100 million per deal. Of course what followed these investments was significant marketing spend. Tobacco companies already have established distribution points and the resources to cover the costs of marketing and the demands that will likely come with future regulation.¹⁴

Given the patterns of use and understanding who stands to gain from the use of ECs, the questions to ask about ECs are: Are they 100% safe and do they offer a health benefit? The answer to both is, of course, no.

¹³ <http://www.tobaccotactics.org/index.php?title=E-cigarettes>

Health risks of E-Cigarettes

As insurers, the obvious risk relates to health effects of ECs but it also offers the industry an opportunity to continue the anti-tobacco advocacy started in the 1970s when differential smoker/non-smoker rates were first charged.

At this point in time, research is fragmented¹⁴ and there is not a body of epidemiological literature and longitudinal studies like there is for traditional cigarettes. Thus, as the following paragraphs will demonstrate, the long term health effects of ECs are not entirely clear. However there is sufficient evidence to say that ECs are not harmless; this is an adequate departure point, along with the bio-psycho-behavioural aspects discussed, for the insurance industry to assess ECs in the same way as tobacco.

What is extremely promising is the fact that advancements in research technology (such as genomics, transcriptomics, mass spectrometry, and others) mean we won't have to wait 50 years to see what ECs do to our bodies - which is great news. Because of these newer techniques, the evidence is mounting, and in addition to that, the nature of evidence is giving us insights which the watch-and-wait method of the past century could never show us.

¹⁴ Pisinger, C. and Døssing, M., 2014. A systematic review of health effects of electronic cigarettes. *Preventive medicine*, 69, pp.248-260.

Research on ECs has focused on cells of the respiratory tract. While not new research, studies have shown that nicotine promotes cancer cell proliferation by inhibiting apoptosis¹⁵ and promoting the blood supply of cancer cells and their movement to different sites in the body, which is bad news for long time smokers who may already have early stages of cancer and have switched to ECs.

Nicotine has also been implicated in a dose-dependent loss of lung endothelial barrier function, associated with oxidative stress and inflammation.¹⁶ In addition, it is known to affect neurodevelopment in children and adolescents.¹⁷ Recent studies have found that ECs alter the profile of innate defense proteins in airway secretions, inducing similar and unique changes relative to cigarette smoking,¹⁸ and that gene-expression changes induced by ECs were similar to those seen with traditional cigarette smoke, although to a lesser degree. Importantly though, the results were found not only in cell cultures but also in cells tested in human test subjects.^{19, 20} In addition, transcriptome changes (changes in the proteins produced from DNA code) in human bronchial epithelial cells (HBEC) were detected in one study, the significance of which

is unclear.²¹ When assessing metabolites in HBECs, they have been found to undergo changes which are comparable and overlapping to that seen in cigarette smoking.²² The table below summarizes the effects of ECs on respiratory cells.²³

Current knowledge of the effects of EC and EC liquids on pulmonary cell types

Cell Type	Effects		
Epithelium	↑ Cytotoxicity	↓ Cell viability	↑ Infection
Fibroblasts	↑ Cytotoxicity	↓ Cell viability	Altered morphology
Inflammatory Cells	↑ Macrophages	↑ Cytokine secretion	↑ Infection
Endothelium	↓ Cell Viability	↓ Electrical resistance	

One survey study of over 45,000 students (with a mean age of 14.6 years) in Hong Kong found that EC use was associated with respiratory symptoms (cough or phlegm), regardless of cigarette smoking status.²⁴

Similarly, a survey of 11th- and 12th-grade students in California found an association between self-reported chronic bronchitic symptoms (chronic cough, phlegm, or bronchitis in the past year) and current or past EC use; this remained, after adjustment for confounders such as cigarette smoking or second-hand smoke exposure. In addition to this, risk increased with frequency of current use of ECs.²⁵

15 This is programmed cell death; a mechanism used by our bodies to get rid of old or damaged cells.

16 Schweitzer, K.S., Chen, S.X., Law, S., Van Demark, M., Poirier, C., Justice, M.J., Hubbard, W.C., Kim, E.S., Lai, X., Wang, M. and Kranz, W.D., 2015. Endothelial disruptive proinflammatory effects of nicotine and e-cigarette vapor exposures. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 309(2), pp.L175-L187.

17 Schraufnagel, D.E., 2015. Electronic cigarettes: vulnerability of youth. *Pediatric allergy, immunology, and pulmonology*, 28(1), pp.2-6.

18 Reidel, B., Radicioni, G., Clapp, P.W., Ford, A.A., Abdelwahab, S., Rebuli, M.E., Haridass, P., Alexis, N.E., Jaspers, I. and Kesimer, M., 2018. E-cigarette use causes a unique innate immune response in the lung, involving increased neutrophilic activation and altered mucin secretion. *American journal of respiratory and critical care medicine*, 197(4), pp.492-501.

19 Moses, E., Wang, T., Corbett, S., Jackson, G.R., Drizik, E., Perdomo, C., Perdomo, C., Kleerup, E., Brooks, D., O'Connor, G. and Dubinett, S., 2017. Molecular impact of electronic cigarette aerosol exposure in human bronchial epithelium. *Toxicological Sciences*, 155(1), pp.248-257.

20 Park, S.J., Walser, T.C., Perdomo, C., Wang, T., Pagano, P.C., Licican, E.L., Krysan, K., Larsen, J.E., Minna, J.D., Lenburg, M.E. and Spira, A., 2014. Abstract B16: The effect of e-cigarette exposure on airway epithelial cell gene expression and transformation. *Clinical Cancer Research*, 20(2 Supplement), pp.B16-B16.

21 Shen, Y., Wolkowicz, M.J., Kotova, T., Fan, L. and Timko, M.P., 2016. Transcriptome sequencing reveals e-cigarette vapor and mainstream-smoke from tobacco cigarettes activate different gene expression profiles in human bronchial epithelial cells. *Scientific reports*, 6.

22 Aug, A., Altraja, S., Kilk, K., Porosk, R., Soomets, U. and Altraja, A., 2015. E-cigarette affects the metabolome of primary normal human bronchial epithelial cells. *PloS one*, 10(11), p.e0142053.

23 Rowell, T.R. and Tarran, R., 2015. Will chronic e-cigarette use cause lung disease?. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 309(12), pp.L1398-L1409.

24 Wang, M.P., Ho, S.Y., Leung, L.T. and Lam, T.H., 2016. Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA pediatrics*, 170(1), pp.89-91.

25 McConnell, R., Barrington-Trimis, J.L., Wang, K., Urman, R., Hong, H., Unger, J., Samet, J., Leventhal, A. and Berhane, K., 2016. Electronic-cigarette Use and Respiratory Symptoms in Adolescents. *American Journal of Respiratory And Critical Care Medicine*, (ja).

Flavoured ECs without nicotine have also been found to induce an inflammatory response in human monocytes²⁶ which in the context of airway inflammation could impact on health.

Among other changes, unrelated to the lungs, a recent study found that EC vapour without nicotine was associated with fatty liver in animal models.²⁶ In addition, bladder carcinogens have been reported in EC users in a study with a non-smoking and non-EC using control group.²⁷

Little is known about the overall safety or the carcinogenic effects of EC vapour but a growing body of evidence is developing which, at the very least, indicates that ECs are not harmless. Perhaps, quite tellingly, there is no research indicating a health benefit to ECs, unless that benefit is a relative one, i.e. they may cause less harm than smoking traditional cigarettes. Ultimately, we should continue to work toward a tobacco and EC free world.

“...no problem can be solved from the same level of consciousness that created it...” ~ Albert Einstein

Summary

It seems clear that the topic of ECs bears a strikingly similar trend to that witnessed in the 20th century with regards to cigarettes and tobacco. That is, the individual health risks have become the highlight of debate, with arguments and counter arguments for and against their use.

Research methodology is being questioned and, in conjunction with regulation disparities, the marketing and promotion of ECs has been allowed to flourish with not only smokers (the original target market) but the youth being encouraged

to take up the use of ECs. This is allowing the continued complex behaviour of smoking to continue among smokers. However what is more concerning is that it is allowing the re- and new establishment of this complex behaviour in ex-smokers, and new EC smokers.

The smoking issue was tackled piece by piece until eventually societal health concerns and adoption of literature won the battle to de-normalise smoking. By adopting the same approach now, the renormalisation of smoking is possible.

The issue of EC use needs to be addressed holistically from a regulatory, marketing, behavioural, and health point of view lest we end up with a new generation of nicotine-addicted youth and young adults.

From an insurance point of view, the trend in ECs is worrying, and as risk management experts, addressing only the health aspects of ECs would be short sighted. Certainly, when looking at ECs holistically, the least we should do is rate EC users as smokers.

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26 Muthumalage, T., Prinz, M., Ansah, K.O., Gerloff, J., Sundar, I.K. and Rahman, I., 2018. Inflammatory and Oxidative Responses Induced by Exposure to Commonly Used e-Cigarette Flavoring Chemicals and Flavored e-Liquids without Nicotine. *Frontiers in physiology*, 8, p.1130.

27 <https://www.endocrine.org/news-room/2018/e-cigarettes-may-lead-to-accumulation-of-fat-in-the-liver>

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