



## Review

## A systematic review of health effects of electronic cigarettes

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## ABSTRACT

**Objective:** To provide a systematic review of the existing literature on health consequences of vaping of electronic cigarettes (ECs).

**Methods:** Search in: PubMed, EMBASE and CINAHL. Inclusion criteria: Original publications describing a health-related topic, published before 14 August 2014. PRISMA recommendations were followed. We identified 1101 studies; 271 relevant after screening; 94 eligible.

**Results:** We included 76 studies investigating content of fluid/vapor of ECs, reports on adverse events and human and animal experimental studies. Serious methodological problems were identified. In 34% of the articles the authors had a conflict of interest. Studies found fine/ultrafine particles, harmful metals, carcinogenic tobacco-specific nitrosamines, volatile organic compounds, carcinogenic carbonyls (some in high but most in low/trace concentrations), cytotoxicity and changed gene expression. Of special concern are compounds not found in conventional cigarettes, e.g. propylene glycol. Experimental studies found increased airway resistance after short-term exposure. Reports on short-term adverse events were often flawed by selection bias.

**Conclusions:** 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 ECs. However, they can hardly be considered harmless.

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## Introduction

The electronic cigarette (EC), also called e-cigarette, e-cig, electronic vaping device, personal vaporizer or electronic nicotine delivery system (ENDS) has been on the market for a decade. ECs are marketed as safe products providing a sensation of traditional smoking without the harmful effects, delivering pure nicotine and releasing harmless water vapor that vanishes in seconds (Anon, 2014; Smoke, 2014). Puffing activates the battery-operated heating element in the atomizer and the liquid. The liquid consists of various combinations of propylene glycol, glycerin, nicotine, tobacco extracts, flavorants and/or adulterants which vaporize to an aerosol/vapor. The newer generations of ECs seem to be very efficient nicotine delivery systems (Etter and Bullen, 2011a; Wall et al., 1988). Almost all regular users use ECs with nicotine Etter and Bullen, 2011b.

In the beginning, ECs were primarily produced by small manufacturers in China and sold on the Internet without drawing major attention. In the last few years, major tobacco companies such as Lorillard, British American Tobacco, Altria, Reynolds and Imperial Tobacco have launched their own EC brands and are buying up existing ones. Marketing and sale has exploded and EC-shops and -lounges pop-up everywhere. For the first time in more than 40 years tobacco companies are back on TV with cigarette ads CNN Money, 2014. Industrial economists project that the ECs will surpass conventional cigarettes (CC) in about three decades, and the global EC market is expected to hit \$10 billion by 2017 (Lopes, 2013; Stocks, 2013).

The epidemic spread of this new product raises great concern in some health and public health professionals sglanz, 2014 and great enthusiasm in others, who support the idea of “harm reduction” and see the EC as a long-awaited alternative to the conventional cigarette. Tobacco is the most deadly product on the market, and it is estimated that it will cause 1 billion deaths in the 21st century Eriksen et al., 2012.

Discussions concerning this new product are characterized by strong feelings and beliefs, as well as strong economic interests, making it very difficult to obtain unbiased information. There are many important issues concerning the EC, the most important being their long-term health effects.

The aim of this article is to give a systematic and critical review of the existing literature on the health consequences of vaping of ECs and discuss the implications of our findings for public health. Furthermore, as a first, we want to investigate how many of the published articles have a conflict of interest.

## Objectives

We examined the published data to:

- Identify original publications on ECs which describe a health-related topic.

- Examine critically the design of the studies, the funding and other conflicts of interest and their influence on conclusions drawn.
- Assess the existing evidence on the safety of ECs.

## Methods

We have followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines whenever meaningful.

### Eligibility criteria

Original articles or abstracts on ECs of any topic relevant to health. Published before 14 Aug 2014 – in any language.

### Exclusion criteria

Recommendations, expert statements, reviews, technical reports and other non-original papers. Papers on smoking cessation, abuse liability, nicotine levels, withdrawal symptoms, poisonings, prevalence, attitudes and beliefs.

### Search

A search was carried out in PubMed, EMBASE and CINAHL (Appendix 1, detailed search).

Keywords: “electronic cigarette” or “e-cigarette” or “electrically heated cigarette” or “ENDS and cigarette” or “electronic nicotine delivery system” or “electronic nicotine delivery device” or “e-liquid”. No limits.

### Study selection

We identified 2147 papers (Fig. 1).

## Identification

Screening of title left 1101 articles on ECs. After reading the abstract, papers were rejected which did not report a health-related topic. Agreement of authors was necessary to exclude a paper. Papers on symptoms were included even if the main focus of the article was, for example, smoking cessation, leaving  $n = 271$ . Out of these, 177 were duplicates, described the same study population or did not report original data, leaving 94 papers. Full documents were obtained for the final inclusion. Additionally, we thoroughly looked through the reference lists of the articles for missed papers and investigated reports for overlooked papers (Anon, 2012, 2013a,b; Burstyn, 2013; Schaller et al., 2013). Eight studies were identified (Anon, 2009; Gennimata et al., 2014; Heavner et al., 2010; Laugesen et al., 2008; Lauterbach and Laugesen, 2012; Lauterbach et al., 2012; Trehy et al., 2011; U.S.Food and Drug Administration, 2009): one was a laboratory analysis (U.S.Food and Drug Administration, 2009)

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