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Original Investigation

Nicotine Levels in Electronic Cigarettes

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Abstract

Introduction: The electronic cigarette (EC) is a plastic device that imitates conventional cigarettes and was developed to deliver nicotine in a toxin-free vapor. Nicotine in a solution is heated and vaporized when a person puffs through the device and is inhaled as a vapor into the mouth. The EC is a new product on the market and little is known about its safety and nicotine delivery efficacy. The aim of the study was to analyze nicotine levels in vapor generated from various EC brands and models. The study was designed to assess efficacy and consistency of various ECs in converting nicotine to vapor and to analyze dynamics of nicotine vaporization.

Methods: Sixteen ECs were selected based on their popularity in the Polish, U.K. and U.S. markets. Vapors were generated using an automatic smoking machine modified to simulate puffing conditions of real EC users. Nicotine was absorbed in a set of washing bottles with methanol and analyzed with gas chromatography.

Results: The total level of nicotine in vapor generated by 20 series of 15 puffs varied from 0.5 to 15.4 mg. Most of the analyzed ECs effectively delivered nicotine during the first 150–180 puffs. On an average, 50%–60% of nicotine from a cartridge was vaporized.

Conclusions: ECs generate vapor that contains nicotine, but EC brands and models differ in their efficacy and consistency of nicotine vaporization. In ECs, which vaporize nicotine effectively, the amount inhaled from 15 puffs is lower compared with smoking a conventional cigarette.

Introduction

The electronic nicotine delivery system, commonly called electronic cigarette or e-cigarette (EC), is a plastic device that was designed to imitate a regular cigarette and to deliver a nicotine-containing aerosol when puffed by the user. ECs have gained popularity around the world. They are mostly promoted via the Internet but recently also by the entertainment industry. They are available through online stores or retail outlets such as small kiosks in shopping malls. ECs were developed in 2004 in China, who remains the main manufacturer of these devices. ECs have not been manufactured by any tobacco or pharmaceutical companies and as a consumer product were not tested and approved by regulatory agencies (e.g., U.S. Food and Drug Agency (FDA), U.K. Medicines and Healthcare Products Regulatory Agency [MHRA]) before their introduction to the global market (Trtchounian & Talbot, 2010).

Each EC contains a: (a) cartridge(s) (CA) that contains nicotine solution in propylene glycol or glycerin, (b) heating element to vaporize the nicotine solution, (c) microprocessor with a sensor that activates the heating element when the EC is puffed, (d) rechargeable battery, and sometimes (e) LED diode that imitates the glow of a burning cigarette cone. The principle of the EC is to deliver nicotine in a form of aerosol that does not contain any tobacco specific toxins. It is puffed in a similar way to a regular cigarette. When a sensor detects airflow, it activates a heating element that is in a contact with the cartridge containing nicotine solution. As a result of increased temperature and airflow, nicotine is vaporized and an aerosol with droplets of solution is generated and inhaled by the EC user (Cahn & Siegel, 2010; Etter, Bullen, Flouris, Laugesen, & Eissenberg, 2011; Henningfield & Zaatari, 2010; Pauly, Li, & Barry, 2007; Wollscheid & Kremzner, 2009).

The most common solvents for nicotine are propylene glycol and glycerin, as when heated they form an aerosol that closely imitates cigarette smoke. The other components of the solution include water, ethanol, and various additives but these can differ in presence and proportion between EC brands. Cartridges are available in various flavors such as tobacco, menthol, strawberry, apple, chocolate, vanilla, and many others. They are usually labeled according to their nicotine content as "extra strong/very high," "strong/high," "regular/medium," "light/low," "ultra light/very low," or "zero/no nicotine" if they are nicotine free. The nicotine content is determined by the manufacturers and often varies between brands and within a brand's models. Some types of EC cartridges, commonly called "cartomizers" or "atomized cartridges", contain a built-in heating element and others can be refillable by the user with ready-to-use nicotine refill solutions (RS), commonly called "liquids," "e-liquids," or "juices." The latter are more popular among

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some users since their use is more cost-effective than nonrefillable cartridges. These solutions are also available in a similar range of flavors and concentrations of nicotine.

There is some inconsistency in existing data regarding the efficacy of ECs as nicotine delivery devices. The U.S. FDA evaluated two brands of EC for nicotine content. Nicotine was detected in both products for all cartridges labeled as containing low, medium, and high levels of nicotine. The sparging apparatus was used to quantify the amount of nicotine released during use of these devices. Levels found were consistent with the labeling (low, medium, and high); however, the cartridge labeled "no nicotine" still delivered some nicotine (Westenberger, 2009). Another study also found nicotine in cartridges labeled as containing no nicotine (Hadwiger et al., 2010).

Although nicotine seems to be present in ECs, it might not be delivered effectively to the blood stream. Three human studies found no or negligible increases in nicotine blood levels after acute use of EC in naïve users, but it has been also shown that using some brands of EC alleviates nicotine craving (Bullen et al. 2010; Eissenberg, 2010; Vansickel, Cobb, Weaver, & Eissenberg, 2010). One study found substantial amounts of cotinine, a metabolite of nicotine, in the saliva of EC users suggesting that experience with the device is likely to influence blood nicotine levels (Etter & Bullen, 2011).

There are at least three important factors that determine the efficacy of nicotine delivery from EC to the body. The first is the nicotine content of a cartridge. Puffing an EC with high nicotine levels should lead to inhalation of higher doses of the drug. Second is the efficacy of the vaporization process that determines how much nicotine is actually transferred from a cartridge into the aerosol. Finally, bioavailability of nicotine from the EC aerosol is a key factor, since it limits the amount of inhaled nicotine that is absorbed into the blood stream and reaches the nicotinic receptors in the brain. This study was designed to explore the first two of the above factors by measuring nicotine levels in cartridges and refill solutions and evaluating the nicotine vaporization efficacy of various models of EC brands.

Materials and Methods

EC, Cartridges, and Nicotine Refill Solutions

We decided to study the most popular brands of ECs available in domestic, European, and U.S. markets. Since the Internet seems to be the main distribution channel for these products, we browsed google.com and google.pl web search engines, price comparison websites, online marketplaces, and Internet discussion forums for EC users and identified 30 popular brands of ECs. We ranked them based on numbers of records in web search engines and chose the 15 brands with the highest number of records. Only one model was chosen per brand, except for the brand Janty, for which we decided to test two popular models (eGo and Dura). The characteristics of ECs evaluated in the study are provided in Table 1, and all products are presented in Supplementary Figure 1.

All products were purchased from commercial sources. Eleven ECs were purchased from Polish online shops, four from U.K.-based services, and one from a U.S. online shop. All brand names were removed from the products, and each product was randomly assigned a code to blind lab technicians to the brand tested.

Cartridges and refill solutions were purchased from the same sources to ensure they were compatible with tested ECs. In order to achieve variability of the products, we decided to test 20 cartridges and 15 nicotine refill solutions. Since they came with various strengths and aromas, there were additional cartridges and refill solution that were not part of the 16 chosen ECs. Characteristics of cartridges and nicotine refill solutions evaluated in the study are provided in Table 2, and all cartridges are presented in Supplementary Figure 2.

We paired each tested EC with cartridges of the same brand name and from the same batch and series, that is, the cartridges were from the same packaging box of the same brand and model and have the same nicotine content and flavor according to their manufacturer. Total of six cartridges were used for test, three unused cartridges were used to measure nicotine content and three original cartridges were used for EC testing.

Nicotine Aerosol Generation From EC

Aerosol from ECs was generated using smoking machine "Palaczbot" (Technical University of Lodz, Poland) designed for the purpose of this study. This is a one-port linear piston-like smoking machine with adjustable puffing regimes in a very wide range, controlled by computer software. Test conditions were determined to reflect real-life puffing patterns of EC users. We recruited 10 volunteers (aged 35 ± 20 years, 8 males) who used various brands and models of EC for at least one month and measured their puffing topography with modified and calibrated CressMicro monitors (Borgwaldt Ltd., Germany). The average puffing topography was as follows ($M \pm SD$): puff duration of 1.8 ± 0.9 s, intervals between puffs of 10 ± 13 s, puff volume 70 ± 68 ml, and number of puffs taken in one puffing session was 15 ± 6. All testing procedures in this work were carried out using the same averaged puffing conditions. A total of 300 puffs were taken from each EC in 20 series of 15 puffs with intervals between series of 5 min each. Each EC was tested three times on 3 following days after batteries were recharged during nights.

Nicotine Analysis in EC Aerosol

Nicotine from EC aerosol was absorbed using liquid extraction to organic solvent technique. EC was connected with short Teflon pipes with a set of two 200-ml gas washing bottles with coarse spargers. Each washing bottle contained 50 ml of methanol with quinoline as an internal standard (10 μg/ml). Both washing bottles were immersed in acetone–dry ice bath in order to avoid any losses of volatile solvent. A picture of set for vapor generation from EC and nicotine absorption is presented in Supplementary Figure 3.

Samples of 0.25 ml were collected from each washing bottle every 15 puffs, with a total of 150 puffs, and every 30 puffs with a total of 300 puffs. A total of 30 samples were collected during each testing procedure for each EC.

Nicotine was analyzed using gas chromatography method with Thermionic Specific Detector (GC-TSD, Varian Inc.). We modified the standard NIOSH 2551 method for determination of nicotine in air (National Institute for Occupational Safety and Health, 1998). CP-Sil 8CB, 25 m × 0.25 mm × 0.39 mm (1.2 μm; Varian

Table 1. Nicotine Amounts in Original Cartridges and Estimated Levels Delivered to Vapor With 150 and 300 Puffs by Analyzed Electronic Cigarettes

								Nicotine levels released to vapor from cartridge		
								Estimated based on its analysis in vapor (mg)		Estimated based on its analysis in used cartridges (mg)[a]
EC code	Brand name	Model	Retailer	Country	Source of product	Cartridge (Table 2)	Nicotine amounts in original unused cartridges (mg, %)	With 150 puffs (%)	With 300 puffs (%)	With 300 puffs (%)
EC 01	Joye	510	Inspired s.c.	Poland	Online	CA 11	4.2 ± 0.0 (100)	1.7 ± 0.6 (40)	1.8 ± 0.1 (43)	1.8 ± 0.2 (43)
EC 02	Janty	eGo	Janty	Poland	Online	CA 04	4.7 ± 0.3 (100)	2.6 ± 0.3 (55)	2.8 ± 0.2 (60)	3.2 ± 0.1 (75)
EC 03	Janty	Dura	Janty	Poland	Online	CA 04	4.7 ± 0.3 (100)	2.4 ± 0.7 (51)	2.8 ± 0.8 (60)	2.7 ± 0.2 (57)
EC 04	DSE	901	Farsee	Poland	Online	CA 15	9.4 ± 0.8 (100)	2.2 ± 0.6 (23)	2.5 ± 0.4 (27)	3.3 ± 0.7 (35)
EC 05	Trendy	808	Damhess	Poland	Online	CA 08	1.6 ± 0.2 (100)	0.3 ± 0.2 (19)	0.5 ± 0.1 (31)	1.1 ± 0.1 (68)
EC 06	Nicore	M401	Atina Poland	Poland	Online	CA 10	4.9 ± 0.3 (100)	1.9 ± 0.3 (39)	2.3 ± 0.5 (47)	3.0 ± 0.9 (61)
EC 07	Mild	201	Mild	Poland	Online	CA 07	19 ± 0.5 (100)	8.4 ± 1.1 (44)	8.8 ± 1.6 (46)	14 ± 0.8 (77)
EC 08	Colinss	Age	Colinss	Poland	Kiosk	CA 06	11 ± 1.5 (100)	4.7 ± 1.0 (43)	7.2 ± 1.0 (65)	6.3 ± 0.6 (57)
EC 09	Premium	PR111	Premium	Poland	Online	CA 09	12 ± 0.7 (100)	5.1 ± 1.1 (43)	7.4 ± 0.6 (61)	8.2 ± 0.9 (68)
EC 10	Ecis	510	Arcotech	Poland	Online	CA 12	4.9 ± 0.3 (100)	2.6 ± 0.4 (53)	3.1 ± 0.7 (63)	4.0 ± 0.2 (81)
EC 11	Dekang	Pen	Ecigars Polska	Poland	Kiosk	CA 01	18 ± 0.8 (100)	8.7 ± 1.0 (48)	15.4 ± 2.1 (85)	14 ± 0.8 (74)
EC 12	Intellicig	Evolution	Intellicig	United Kingdom	Online	CA 16	8.0 ± 0.9 (100)	1.6 ± 0.2 (20)	2.3 ± 0.1 (29)	2.4 ± 0.2 (30)
EC 13	SkyCig	SkyCig	SkyCig	United Kingdom	Online	CA 17	12 ± 0.1 (100)	2.3 ± 0.8 (19)	2.5 ± 0.4 (21)	2.5 ± 0.4 (21)
EC 14	Liberro	Black	LiberroLtd	United Kingdom	Online	CA 18	19 ± 0.5 (100)	6.1 ± 0.9 (32)	11.2 ± 1.1 (59)	10 ± 1.3 (55)
EC 15	Njoy	NPro	NJoy	United States	Online	CA 19	16 ± 0.3 (100)	5.0 ± 1.7 (31)	7.5 ± 2.4 (47)	8.9 ± 2.4 (56)
EC 16	Gamucci	110228	GamucciLtd	United Kingdom	Online	CA 20	15 ± 0.2 (100)	8.1 ± −0.1 (54)	10.7 ± 0.5 (71)	12 ± 0.4 (78)

Note. All results are $M \pm SE$ ($n = 3$). Values in brackets are percentages of nicotine levels measured in original unused cartridges.

[a]Levels of nicotine released with 300 puffs were calculated as differences between mean amount of nicotine in original cartridges of the same type and brand and nicotine amounts in used cartridges removed from EC after 300 puffs.

Table 2. Results of Nicotine Analysis in Original Cartridges and Refill Solutions

Product code	Brand name	Model/flavor	Retailer	Country	Source of product	Labeled nicotine concentration (mg)	Determined nicotine concentration (mg)[a]	Relative difference in concentration (%)	*p* Value[b]
Cartridges									
CA 01	SGC	Regular	Ecigars Polska	Poland	Online	18	18 ± 0.8	0	.6159
CA 02	n/a	Tabaco	n/a	Poland	Kiosk	16	14 ± 1.2	−12	.0362
CA 03	Colinss	Tabaco	Colinss	Poland	Online	18	13 ± 1.0	−28	.0008
CA 04	Janty	Marlboro	Janty	Poland	Online	16	5 ± 0.3	−69	.0000
CA 05	n/a	Tobacco	n/a	Poland	Kiosk	0	0 ± 0.0	0	.0000
CA 06	Colinss	Camel	Colinss	Poland	Online	18	11 ± 1.5	−39	.0012
CA 07	Mild	Marlboro	Mild	Poland	Online	18	19 ± 0.5	6	.1047
CA 08	Trendy	Trendy	Damhess	Poland	Online	18	2 ± 0.2	−89	.0000
CA 09	Premium	Tabacco	Premium	Poland	Online	16	12 ± 0.7	−25	.0013
CA 10	Nicore	Marlboro	AtinaPoland	Poland	Online	18	5 ± 0.3	−72	.0000
CA 11	n/a	Marlboro	n/a	Poland	Kiosk	4	4 ± 0.0	0	.0000
CA 12	Ecis	Mentol	Arcotech	Poland	Online	11	5 ± 0.3	−55	.0000
CA 13	Mini	Regular	n/a	Poland	Kiosk	4	5 ± 0.2	25	.0010
CA 14	Mini	Regular	n/a	Poland	Kiosk	0	0.3 ± 0.0	0	.0000
CA 15	Mini	Regular	Farsee	Poland	Online	16	9 ± 0.8	−44	.0002
CA 16	Intellicig	Regular	Intellicig	UK	Online	8	8 ± 0.9	0	.6192
CA 17	SkyCig	Regular	SkyCig	UK	Online	12	12 ± 0.1	0	.0000
CA 18	Liberro	Classic	Liberro Ltd.	UK	Online	18	19 ± 0.5	6	.0605
CA 19	NPro	Regular	Njoy	USA	Online	18	16 ± 0.3	−11	.0009
CA 20	Gamucci	Regular	Gamucci	UK	Online	16	15 ± 0.2	−6	.0020
Refill solutions									
RS 01	Dekang	Fortune Strike	Ecigars Polska	Poland	Online	14	14 ± 0.7	0	.6199
RS 02	Red	USA Mix	Inspired s.c.	Poland	Online	24	19 ± 0.3	−21	.0000
RS 03	Colinss	Camel	Colinss	Poland	Online	18	16 ± 0.7	−11	.0056
RS 04	Ecis	High Marlbo	ECIS-shop.eu	Poland	Online	16	18 ± 1.3	11	.0725
RS 05	Extreme	Standard H	Dami PHPU	Poland	Kiosk	16	15 ± 0.5	−6	0362
RS 06	Virginia	n/a	Dami PHPU	Poland	Kiosk	18	16 ± 1.4	11	.8084
RS 07	n/a	Mint Medium	n/a	Poland	Kiosk	11	10 ± 0.8	−9	.2262
RS 08	n/a	MintVery High	n/a	Poland	Kiosk	24	21 ± 1.1	−13	.1216
RS 09	Ecigar.pl	Regular	Ecigars Polska	Poland	Online	24	25 ± 1.1	4	.1331
RS 10	Mild	Tabacco	Chic	Poland	Online	18	18 ± 1.4	0	.9291
RS 11	Janty	TXS-Z Texas	Janty	Poland	Online	0	0 ± 0.0	0	.0000
RS 12	Janty	TXS-H Texas	Janty	Poland	Online	16	16 ± 0.3	0	.5329
RS 13	Janty	Mint-H	Janty	Poland	Online	16	4 ± 0.1	−75	.0000
RS 14	Nicore	Liquid	Atina Poland	Poland	Online	18	23 ± 2.4	28	.0029
RS 15	EssentialOil	Virginia Tabacco	n/a	Poland	Online	12	14 ± 0.4	17	.0015

Note. [a]Mean ± *SE*.

[b]One-sample *t* test. n/a=not available (information not indicated directly on packages).

Inc.) capillary column with flow rate of helium of 2.4 ml/min were used. Temperature of injector and detector was 300 °C, column temperature increased from 60 to 200 °C (20 °C/min) and hold for 5 min. Injection volume was 1 µl, and quinoline was used as an internal standard. Calibration curve was generated to cover the range of nicotine concentration from 0.5 to 50 µg/ml, which corresponds to cumulative nicotine levels in EC aerosol from 0.2 to 20 mg. The method was validated as per the International Conference on Harmonization guideline Q2 (R1; ICH, 2005). Precision of the method was 18%, and quantitation limit was 0.05 µg/ml. Exemplary chromatogram of the analyzed sample is presented in Supplementary Figure 4.

Nicotine Analysis in Cartridges and Refill Solutions

Nicotine was analyzed in three cartridges of the same batch and series, taken from one box of each brand included in the study. Moreover, nicotine was also analyzed in used cartridges after 300 puffs were taken in the experiments described above. Knowing the amounts of nicotine in the original and used cartridges, it was possible to estimate how much nicotine was released to vapor. Measured amounts of nicotine in original/unused cartridges were also compared with values declared by manufacturers and retailers on their packages.

After gently removing a cartridge from its package, it was placed in a glass 200-ml flask and 50 ml of ethyl acetate was added along with 100-µl internal standard solution (quinoline 50 mg/ml in methanol). The flask was covered with parafilm and placed in an ultrasound bath. After 30 min, 1 ml of the extract was collected and analyzed with the chromatography method described above. Three cartridges of each model were tested. Calibration solutions of nicotine in propylene glycol with a concentration range of 0.01–40 mg/ml were prepared by weighting proper nicotine amounts and dissolving them in solvent. Calibration and control cartridges were prepared by spiking empty cartridges with 0.5 ml of calibration solution. The whole analytical procedure was then performed to calibrate and validate the method (ICH, 2005). Precision of the method was 15%, recovery of 98%, and quantitation limit was 0.1 mg/cartridge.

In order to analyze nicotine in refill solutions, samples of 100 µl of each examined solution were diluted with 10 ml methanol, and after adding internal standard (100 µl quinoline solution 50mg/ml in methanol), were vigorously shaken for 10 min and analyzed as described above. Three samples of each refill solution model were tested. To calibrate and validate the method, the same nicotine solutions as described above for the cartridges procedure were used. Precision of the method was 17%, recovery of 102%, and quantitation limit was 0.05 mg/ml.

Statistical Analysis

For each analyzed EC, a nicotine delivery profile was generated. The profiles represent the relationship between cumulative dose of nicotine released from a cartridge to aerosol and number of puffs. Each point represents *M* values from three test runs whereas bars correspond to the values of *SE*s. Differences in nicotine amounts released to aerosol among analyzed ECs were compared using nonparametric ANOVA with Tukey test for comparisons. Measured amounts of nicotine in original cartridges were compared with values declared on their packages using one-sample *t* test. For all tests Statistica 6.0 (Statsoft) software was used.

Results

Levels of Nicotine in EC Aerosol

Aerosol was visibly being produced during the full 300 puffs taken from each product tested. Results are presented as absolute values in mg of nicotine but also as percentages of nicotine levels measured in original unused cartridges. Absolute and relative levels of nicotine released with 150 and 300 puffs of the examined ECs are summarized in Table 1. Absolute and relative levels of nicotine released with 300 puffs were also calculated as differences between mean nicotine amount in original unused cartridges of the same brand and model and amounts that remained in the cartridge after 300 puffs. Delivery profiles of nicotine from cartridges to vapor for each analyzed ECs are presented in Figure 1.

Levels of nicotine in vapors released from analyzed ECs with 150 puffs varied from 0.3 ± 0.2 (EC 05) to 8.7 ± 1.0 mg (EC 11) and with 300 puffs from 0.5 ± 0.1 (EC 05) to 15.4 ± 2.1 (EC 11; Table 1).

Analyzed ECs varied in efficacy and consistency of nicotine vaporization ($p < .05$). For example, EC 11 and EC 16 vaporized nicotine with 300 puffs with a high efficacy of 85% and 71%, respectively (Table 1). EC 08, 09, 11, 14, and 16 delivered nicotine from cartridges to vapor consistently throughout 300 puffs (short bars on nicotine delivery profiles represent low standard error [*SE*] values; Figure 1). Contrarily, EC 05 was characterized by very low consistency and was very ineffective in nicotine vaporization, delivering to vapor only 31% of the nicotine present in the cartridge (Table 1).

Levels of Nicotine in Original Cartridges and Refill Solutions

Results of the tested cartridges and refill nicotine solutions for nicotine content are presented in Table 2. We found that nicotine amounts in 9 out of 20 of the analyzed cartridges differed by more than 20% from values declared by their manufacturers (CA 03, 04, 06, 08, 09, 10, 12, 13, and 15). The differences of the same magnitude were detected among 3 out of 15 nicotine refill solutions (RS 02, 13, and 14). For some brands, declared amounts of nicotine were the same as those analyzed by us, indicating the manufacturer's credibility.

Discussion

Electronic cigarettes are new products available on international markets. They differ not only by brand names, models, and designs but also by technical characteristics. There has not been any comprehensive testing of various brands and models to see how they differ between each other in nicotine delivery. In our study, we analyzed 16 various EC models, chosen based on their popularity, to see if the products effectively exposed their users to significant amounts of nicotine.

There have been some preliminary studies indicating that ECs may expose their users to nicotine. In most of the studies, nicotine was found in cartridge and refill solutions but there is no data so far if any nicotine is actually effectively vaporized (Coulson, 2009; Ellicott, 2009; Exponent, 2009; Kieckbush, 2009, 2010; Laugesen, 2008, 2010; Valance & Ellicot, 2008; Westenberger 2009). Three published studies with human subjects who used one of the products showed little or no delivery of nicotine to the blood stream, even when products that contained high nicotine levels were used (Bullen et al., 2010; Eissenberg, 2010; Vansickel, Cobb, Weaver, & Eissenberg, 2010). One potential factor affecting this might be poor nicotine delivery from cartridges to vapors, resulting in low nicotine levels inhaled by studied subjects.

Based on our preliminary observations, we decided to test products with conditions, which closely reflect how experienced "EC smokers" use their products. We tested each product using 20 series of 15 puffs. We found that 300 puffs of ECs that contained "high nicotine" cartridges delivered between 0.5 and 15.4 mg of nicotine, whereas EC with cartridges labeled as "low" or "medium" delivered between 0.5 and 3.1 mg of the drug. The efficacy of nicotine vaporization differed across ECs. Evaluated ECs vaporized 21% to 85% of relative amounts of nicotine present in the cartridges. The high variability in performance properties of ECs was recently reported by Trtchounian, Williams, and Talbot (2010). They found that EC brands produced aerosols, which varied in density from puff to puff. Our findings seem to

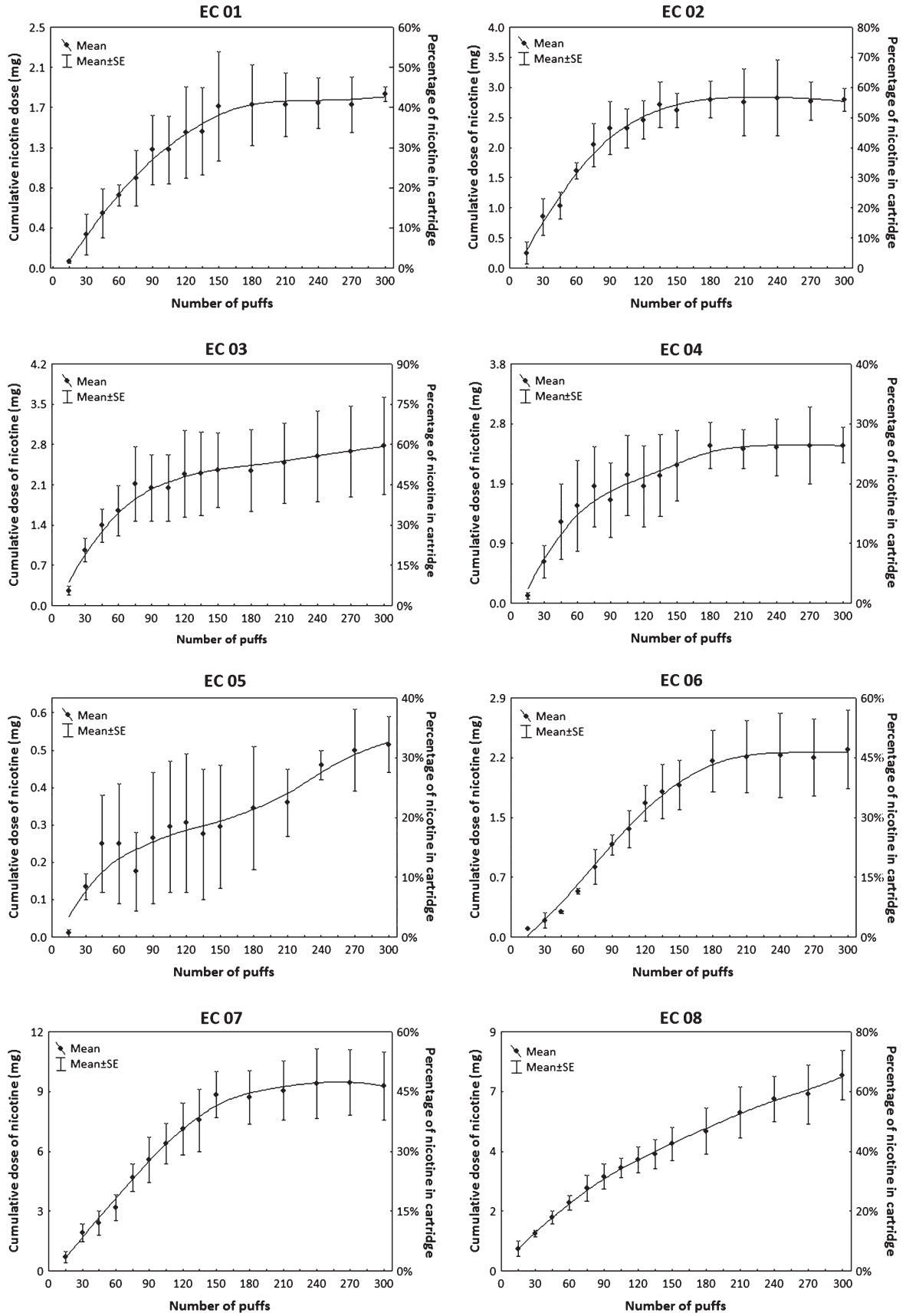

Figure 1. Nicotine delivery profiles for tested electronic cigarettes.

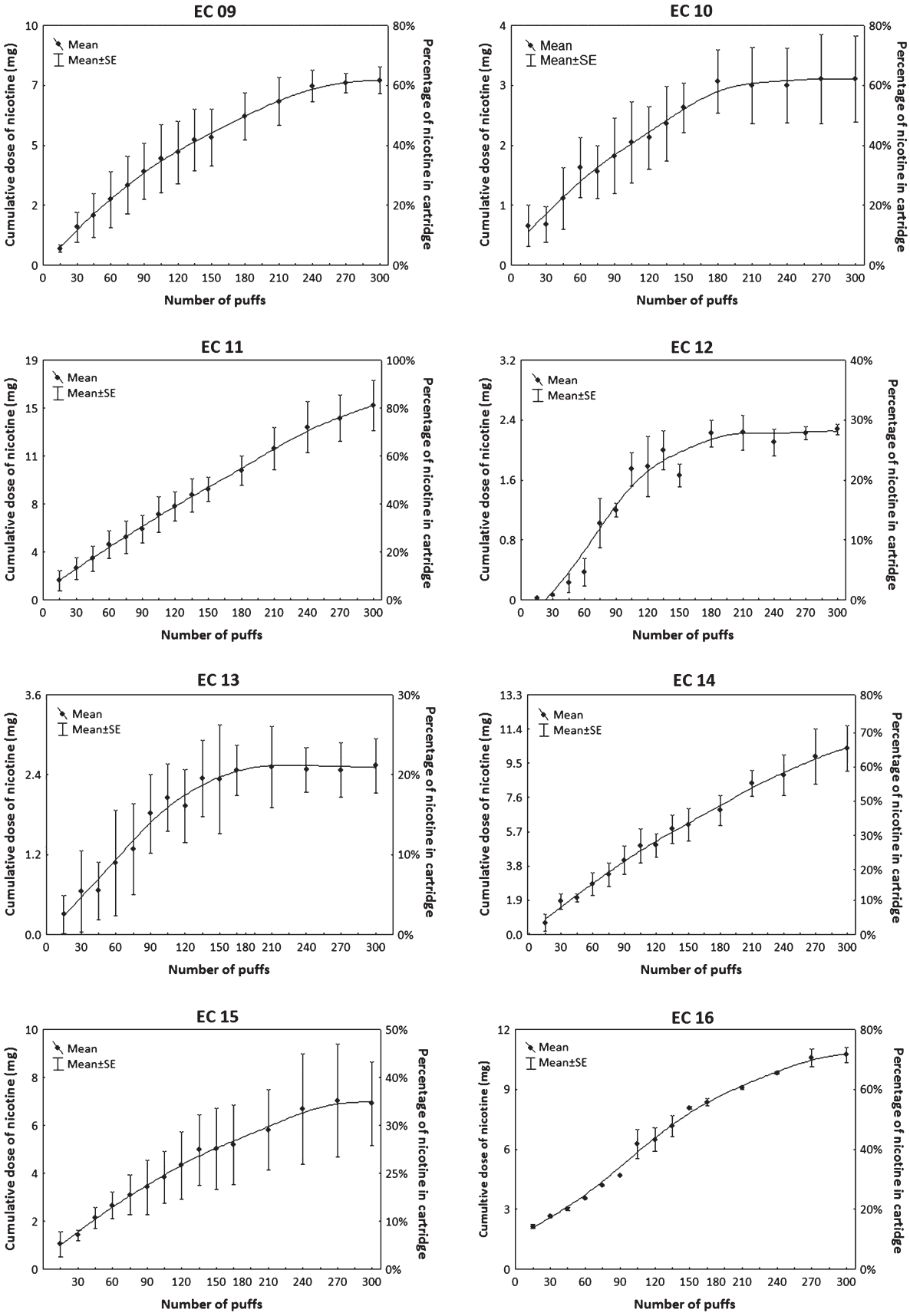

Figure 1. (Continued).

confirm their hypothesis about not uniform nicotine delivery from ECs.

Nicotine levels from a single puff of 70 ml may be estimated to be between 1.7 and 51.3 μg. Results of repeated testing of ECs with three different cartridges with the same label (menthol high) by the FDA gave varying results from 26.8 to 43.2 μg nicotine per 100 ml puff, which is close to the upper levels observed in the present study (Westenberger, 2009). Despite the fact that we tested products with lower puff volumes than in the FDA study (70 vs. 100 ml), we found high consistency between the results of one product tested in both studies (EC15; 5.0 vs. 5.3 mg nicotine per 150 puffs).

Assuming a series of 15 puffs is equivalent to smoking one cigarette; this allows us to make some dose comparisons. One series of 15 puffs might have delivered 0.025–0.77 mg nicotine, which is lower than a dose inhaled from one smoked tobacco cigarette (from 1.54 to 2.60 mg; Djordjevic, Stellman, & Zang, 2000).

By systematically analyzing how much of the nicotine was released from an EC with every 15 puffs, we were able to generate a nicotine delivery profile for each tested product. Analysis of the profiles indicates that only part of the nicotine present in a cartridge is vaporized and only some of the nicotine from cartridge is inhaled by EC users (on average 50%–60%). Thus, making conclusions on how much nicotine is inhaled by EC users based on the content in cartridges might lead to overestimation of the effective dose. Improvement of the vaporization efficacy would make more or even all the nicotine present in a cartridge available for EC users.

Moreover, nicotine delivery profiles provided interesting data on efficacy of the vaporization process, indicating that most of the nicotine is delivered during the first 150–180 puffs. Based on this finding, potential users of the products should be instructed to replace nicotine cartridge every 150 puffs in order to achieve effective and steady nicotine exposure.

Our results also suggest that some products are inconsistent in delivering nicotine. These products might deliver different levels of nicotine to their users each time they are used even if containing cartridges of the same nicotine content. This finding is consistent with the results found in a study by Williams and Talbot (2011). The authors reported that the ECs they tested lasted for a variable number of puffs, and some variation was found in models within a brand, when different cartridges were used.

We also found significant differences between labeled and true levels of nicotine in cartridges and refill solutions. Traces of nicotine were also detected in one of two cartridges labeled as containing no nicotine. These findings indicate that information about nicotine levels provided on product packages may be misleading to customers. In order to sell the best quality products to customers, manufacturers of ECs should develop and implement quality standards for their products and follow good manufacture policy. The authority to independent agencies should be given to control quality of the products available on market.

We presented a preliminary evaluation of 16 ECs, 20 cartridges, and 15 refill solutions and our study was not intended to provide an accurate characterization of any particular brand. There are many potential limitations in the generality and reliability of our findings because of a relatively small number of samples from each product. Further research is needed to investigate if the variability in nicotine delivery is primarily due to brand variability or a combination of brand variability and fluctuation within brands.

Our study reflects the early stage of objective research on ECs and raises new questions. First, how high might nicotine levels be if users were instructed to puff them as hard as possible? Puff duration for individuals using ECs in YouTube videos was longer than we used in the study to simulate EC use with smoking machine (4.3 vs. 1.8 s; Hua, Yip, & Talbot, 2011). Longer puff duration may help EC users compensate for the poor delivery of nicotine from ECs. Second, what is the prime site of nicotine absorption from EC? Does nicotine from EC reach blood stream via buccal mucosa only? or is there any lung absorption? Substantial amounts of cotinine, a metabolite of nicotine, found in the saliva of EC users suggest that experience with the device is likely to influence blood nicotine levels (Etter & Bullen, 2011). Finally, can ECs produce the arterial plasma spikes reflecting substantial lung delivery as have been shown with tobacco cigarettes?

Supplementary Material

Supplementary Figures 1–4 can be found online at http://www.ntr.oxfordjournals.org

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Declaration of Interests

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