Electronic cigarettes: incorporating human factors engineering into risk assessments

Ling Yang, Susan F Rudy, James M Cheng, Elizabeth L Durmowicz

ABSTRACT
Objective A systematic review was conducted to evaluate the impact of human factors (HF) on the risks associated with electronic cigarettes (e-cigarettes) and to identify research gaps. HF is the evaluation of human interactions with products and includes the analysis of user, environment and product complexity. Consideration of HF may mitigate known and potential hazards from the use and misuse of a consumer product, including e-cigarettes.

Methods Five databases were searched through January 2014 and publications relevant to HF were incorporated. Voluntary adverse event (AE) reports submitted to the US Food and Drug Administration (FDA) and the package labelling of 12 e-cigarette products were analysed.

Results No studies specifically addressing the impact of HF on e-cigarette use risks were identified. Most e-cigarette users are smokers, but data on the user population are inconsistent. No articles focused specifically on e-cigarette use environments, storage conditions, product operational requirements, product complexities, user errors or misuse.

Twelve published studies analysed e-cigarette labelling and concluded that labelling was inadequate or misleading. FDA labelling analysis revealed similar concerns described in the literature. AE reports related to design concerns are increasing and fatalities related to accidental exposure and misuse have occurred; however, no publications evaluating the relationship between AEs and HF were identified.

Conclusions The HF impacting e-cigarette use and related hazards are inadequately characterised. Through analyses of user–product–environment interfaces, product complexities and AEs associated with typical and atypical use are needed to better incorporate HF engineering principles to inform and potentially reduce or mitigate the emerging hazards associated with e-cigarette products.

INTRODUCTION
‘Human factors’ (HF) analysis refers to the evaluation of how human users interact with products and takes the user characteristics, environment of use and product complexity into consideration.1 HF are analysed in order to inform the implementation of design principles that focus on user–environment–product interactions and thus minimise the hazards and risks associated with a product use. Human factors engineering (HFE) principles are intended to make products easier or harder (as appropriate) to use and to reduce or mitigate any potential hazards of product use, particularly hazards that are directly related to poor product design.2 Data from user profiles, product use studies and product malfunction or failure reports are analysed in order to improve the design of current and future products. HFE considers past and current product design, as well as the likely characteristics and behaviour of both intentional and unintentional product users, such as children who may have unattended access to the product.2 HFE has figured prominently in determining causative factors and remediation for consumer product failures, such as sudden unintended acceleration incidents in automobiles.3

Electronic cigarettes (e-cigarettes) are battery-powered devices that aerosolise a chemical mixture (‘e-liquid’) that typically contains nicotine, propylene glycol, flavourings and other constituents. The intent of this paper is not to compare the risks of e-cigarettes versus traditional cigarettes but rather to review use-related risks of e-cigarettes and identify strategies to reduce hazards associated with these products. Published and voluntary reports to the US Food and Drug Administration (FDA) suggest that e-cigarette use may have risks unrecognised by the general public. Risk of exposure to e-liquids from leaks or spills, e-cigarette ignition and explosion, and exposure to contaminants in the e-liquid and aerosols are HF concerns. These risks can be exacerbated through poor product design, user behaviour or both. The interaction among HF considerations and their possible results is illustrated in figure 1.

Electronic cigarette use-related hazards should be identified, understood and addressed through the application of HFE to e-cigarette design processes in order to minimise consumer risks. To expand the understanding of these issues and identify gaps in knowledge, scientific literature, voluntary adverse events (AEs) reported to FDA, media reports and a sample of 12 e-cigarette product labelling were analysed.

METHODS
Literature search and resource review
A systematic literature search of five reference databases (Web of Knowledge, PubMed, SciFinder, Embase and EBSCOhost) was conducted through January 2014 using search terms ‘electronic nicotine device’ OR ‘electronic cigarette device’ OR ‘electronic nicotine delivery systems’ OR ‘electronic nicotine delivery system’ OR ‘electronic cigarettes’ OR ‘e-cigarette’ OR ‘e-cig’ OR ‘e-cigs’ to identify research and publications related to e-cigarettes. Titles and abstracts of the 435 articles identified were manually screened for HF and user hazards relevance. Included articles were (1) written in English; (2) accessible and non-confidential using
The validity and strength of each study were determined based on a qualitative assessment of study objectives, design, population sampling strategies, depth of analysis, risk of bias and interpretation of results. Application of these criteria yielded a total of 31 articles for analysis; all articles were published between 2009 and 2014. We also reviewed the Center for Tobacco Products (CTP) daily news (news clips from a clipping service) for relevant information.

CTP AEs database analysis
AEs associated with e-cigarette use voluntarily reported to FDA/CTP between 2008 and 31 December 2013 were reviewed for their nature, seriousness, possible HF contribution and implications for product labelling. AE definitions applied to e-cigarettes were adapted from concepts in the regulations and guidance for investigational drugs and non-prescription products.

Labelling analysis of e-cigarette products by FDA/CTP
The labelling of 12 e-cigarette products from nine manufacturers (table 1) was analysed using a tool developed by the FDA. The tool is an unweighted list of 65 elements in broad categories, including claims; package design; product and manufacturer identification on the external package and main component parts; content, conspicuousness, readability and legibility of health cautions; and instructions for use. We scored each labelling element as ‘present’ or ‘absent’, included qualitative notations, and reported findings using descriptive statistics. The sample included products evaluated in published labelling analyses (n=7), products identified as popular by one or more independent analysts in late 2012 (n=8) and products for which AE reports had been received by the FDA (n=7). The sample included rechargeable starter kits, cartridges and cartomizers, e-liquids for refilling cartridges and disposable e-cigarettes. FDA-approved labelling of a prescription and a non-prescription nicotine replacement product were used as references. All levels of package labelling were reviewed and the products were measured to evaluate whether there were any potential choking hazards and to examine whether the labelling properly addressed the risk.

RESULTS

Users and use environment
Per a recent comprehensive review of US e-cigarette users by Pepper and Brewer, adult e-cigarette use in the USA increased from 1% in 2009 to 6% in 2011 and current smokers are more likely to use e-cigarettes than former and never-smokers. Electronic cigarette use among US adolescent and young adults has also increased in recent years. Additional data characterising the user population are limited.

Electronic cigarette product design
No articles specifically analysing e-cigarette operational requirements or complexity were identified. One US study identified...
leaking cartridges and noted that it was difficult to avoid contact with e-liquid when assembling or disassembling cartridges. An Italian study identified design concerns: specifically, the product could not be used as recommended, the cartridges and batteries did not last long enough. Other published labelling and packaging analyses identified either global or specific concerns. Cheah et al. analysed product design features, contents and eight labelling elements of 19 e-cigarette brands (including three brands available in the USA) and concluded that product labelling and packaging had pervasive inadequacy and misleading information. Trchounian and Talbot analysed 25 elements of the starter kit instruction manuals for six products from five US manufacturers and concluded that importation information about product contents, use and warnings was absent. A UK analysis noted that the e-cigarette packages analysed failed to produce mist when puffed, the atomizer had to be substituted and chargers were immediately replaced. Users indicated that acceptability of e-cigarettes could be improved by increasing manufacturing standards, by providing a battery cap-

<table>
<thead>
<tr>
<th>Brand name/manufacturer/(flavour(s))</th>
<th>Type of product/identifiers/nicotine content</th>
<th>Purchase date</th>
<th>Data supporting inclusion (see code descriptions below)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NJOY® NPRO Smoking Everywhere™</td>
<td>Starter kit Model #03-NP-WHT-SK nicotine content unknown</td>
<td>11/21/2011</td>
<td>A, B, C, D, E, F</td>
</tr>
<tr>
<td>NJOY® electronic cigarette refill cartridges Sottera (Traditional flavour)</td>
<td>Cartridges 2-pack nicotine content unknown</td>
<td>10/31/2011</td>
<td>A, B, C, D, E, F</td>
</tr>
<tr>
<td>Volcano Atomized Cartridges (CooCoo Coconut)</td>
<td>Cartridges 5 atomized cartridges nicotine content 16 mg</td>
<td>10/31/2012</td>
<td>B</td>
</tr>
<tr>
<td>Greensmoke Variety Pack (5 FlavorMax™ Cartomizers)</td>
<td>Cartomizers nicotine content</td>
<td>10/31/2012</td>
<td>B</td>
</tr>
<tr>
<td>Johnson Creek Original Smoke Juice (Red Oak™ Solstice™) Johnson Creek</td>
<td>e-Liquid nicotine content 'Low nicotine':11 mg/mL</td>
<td>10/31/2012</td>
<td>D</td>
</tr>
<tr>
<td>NicQuid® (Midnight Express)</td>
<td>e-Liquid nicotine content 0 mg nicotine (0.0%)</td>
<td>3/21/2013</td>
<td>G</td>
</tr>
<tr>
<td>OneJoy Sottera V2 Regular Full</td>
<td>Disposable e-cigarette 'Equal to about 2 packs' nicotine content</td>
<td>10/31/2012</td>
<td>B, E</td>
</tr>
<tr>
<td>Blu® Lorillard</td>
<td>Disposable e-cigarette 'Equals over one Pack' nicotine content</td>
<td>10/31/2012</td>
<td>B, C</td>
</tr>
</tbody>
</table>

A. “Top 5” product among those named in adverse event reports to the FDA as of 12/31/2012.
B. “Top 20 selling brand.”
C. Top 5 in e-cigarette sales for unique brands sold in convenience and FDM Stores combined March 2011–March 2012.
D. Extends work of FDA/Division of Pharmaceutical Analysis (DPA), St Louis, Missouri, USA.
E. To confirm published labelling analyses.
F. ‘Most popular brand’ in the USA.
G. This product was included in order to ensure that the sample included at least two of each of the types of products being marketed.
Labelling analysis of e-cigarette products by FDA/CTP

Concerns regarding product and manufacturer labelling were identified in the majority of the samples analysed (eg, 8 of 12 products did not have lot or batch numbers). Most cartridges appeared to be interchangeable. Ingredient labelling was problematic for all products: five products did not provide ingredients, and of the seven product packages that listed ingredients, two did not provide consistent information across all levels of packaging. One e-liquid package listed peanut, a potentially fatal allergen, as an ingredient, but a warning was not provided.18 The 10 nicotine-containing products had ambiguities in content labelling such as qualitative descriptors or quantitative notations that were inexact. Eight products, including two that did not contain nicotine, warned of potential nicotine toxicity. Four warned of potential nicotine poisoning, but none warned of potential fatal injury.

Seven external package labels listed a health caution; however, warning and precautionary content occupied less than 30% of a back panel or 20–100% of one side panel, was printed in small font and may not be conspicuous to the readers.39 About 50% of the products had no warning and precautionary content. The face plate also did not have any warning. About 27% of the products did not have lot or batch numbers. Most cartridges appeared to be interchangeable. Ingredient labelling was problematic for all products: five products did not provide ingredients, and of the seven product packages that listed ingredients, two did not provide consistent information across all levels of packaging. One e-liquid package listed peanut, a potentially fatal allergen, as an ingredient, but a warning was not provided.18 The 10 nicotine-containing products had ambiguities in content labelling such as qualitative descriptors or quantitative notations that were inexact. Eight products, including two that did not contain nicotine, warned of potential nicotine toxicity. Four warned of potential nicotine poisoning, but none warned of potential fatal injury.

Five of the 12 products did not include instructions for use. Instructions for seven products did not provide step-by-step use instructions, were written above eighth grade level or both.39 42 None of the products had labelling stating that the product is intended as a smoking cessation aid; however, one product insert contained cessation lifestyle advice and five products’ labelling suggested that the product is less risky than traditional cigarettes.

All products contained at least one component that qualified as a choking hazard.40 43 Only one starter kit directly warned of this hazard on the external package, but in small font. Three cartridges and the two e-liquids appeared to have C-R packaging44 and meet the US consumer guidance.45 Eight products warned to ‘keep out of reach of children.’ Three products had neither C-R packaging nor the ‘keep out of reach of children’ warning.

AEs associated with e-cigarette use and possibly related to HFs

Literature review of AEs

Events related to e-cigarette product exposure reported to the American Association of Poison Control Centers (AAPCC) increased 42% from 2011 (n=256) to 2012 (n=438). More than 30% of cases involved children younger than 5 years (n=84 in 2011; n=172 in 2012) and intentional misuse increased 56% (n=12 in 2011 and n=27 in 2012). Approximately 15% of the exposures were allergic or idiosyncratic responses and 25% required medical treatment.46 47 Intentional misuse cases included a completed suicide by injecting e-liquid (serum nicotine level was 2000 ng/mL)38 and a suicide attempt with ingestion and dermal application of e-liquid.49 Limited information about state-level aggregate Poison Control Center data suggests that common routes of exposure in children are ingestion, inhalation and dermal contact.50–53 Outside the USA, e-liquid ingestion was reported in five suicide attempts in two adults from Denmark54 and an Israeli toddler’s death.55

There were 14 e-cigarette ignition events injuring eight individuals, including at least two non-users; 13 were explosions of rechargeable devices. Two explosions occurred during use, resulting in burns, oral disfigurement and unilateral blindness.57 One disposable e-cigarette exploded while being removed from the package, resulting in sensory impairments and property damage.58 Eleven explosions during device charging have caused burns (n=2),59 60 smoke inhalation injuries (n=2),50 62 and property damage (n=8).52 61–69 Six reports suggest possible user-product interactions: three describe products left unattended while charging62 63 66 68; two state that the products lacked warnings or charging instructions,60 66 and one suggests that a charger intended for use with a different e-cigarette product may have been used.67

Analysis of product complaints and AEs voluntarily reported to the FDA

FDA received its first e-cigarette AE report in August 2008. As of 31 December 2013, FDA/CTP had received 91 voluntary reports with product or health effect complaints related to e-cigarettes, and 26 (29%) reports may have HF contributions.

Six reports were exclusively about product quality, performance, labelling or advertising and did not involve AEs. Of the 20 reports containing AEs, 8 were serious including an infant death from choking on a flavour cartridge, 4 explosions causing burn injuries of three adults and one child,59 2 confirmed nicotine overdoses (one with cartridge overheating and one with intentional dual use of traditional cigarettes) and 1 possible nicotine overdose with psychotic symptoms reported after e-liquid ingestion.

Twelve non-serious AE reports included non-specific physical complaints pertaining to advertisement, labelling or website issues (n=4), leakage of e-liquid resulting in oral or hand irritation (n=3); oral burns due to overheating or explosion (n=2); noxious smell and taste causing respiratory, gastrointestinal and constitutional symptoms (n=1); persistent after taste associated with difficulty using the charger (n=1); and possible product adulteration with marijuana (n=1). Complaints related to advertising, labelling, brochures or websites included unsubstantiated claims, inappropriate advertising from a healthcare provider’s office, lack of product brochure; inappropriate labelling (“products labelled as nicotine-free and harm-free, despite FDA website information e-cigarettes may contain nicotine”), lack of health cautions in the retail setting and difficulty reaching ‘the company’.

DISCUSSION

Although data on the contributions of HF to e-cigarette use are limited, many of the use-related concerns may be addressed by HFE in the product design, manufacture and dispensing processes. Currently, e-cigarette manufacturing is unregulated in the USA. There is significant variability in parameters such as the airflow rate required to produce aerosol, pressure drop, and lengths of time cartridges last, and aerosol production between and within e-cigarette brands.70

Electronic cigarette users

Although user characteristics have been explored in several studies, and consistently identify most e-cigarette users as smokers of traditional cigarette products, the studies identified

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Section 1501 of the Federal Hazardous Substance Act (FHSA) (Pub L No. 86–613 [1960]) defines a test of object size using the small-parts test fixture (SPTF).43 The SPTF is a truncated cylinder with a diameter of 3.17 cm (1.25 in), simulating the pharynx. An object is considered a small part if it fits completely within the SPTF. The SPTF was developed, in part, on the basis of data regarding the dimensions of airway foreign bodies recovered by bronchoscopy by Chevalier Jackson in the early 1900s.
are cross-sectional, and the data are limited and inconsistent across studies. Risks to individual users may be greater in those with underlying medical conditions, including asthma and hypersensitivity, and in youth, young adults and pregnant women. Given the complexity of some e-cigarette products, users with decreased manual dexterity, visual/hearing disabilities or limited cognitive skills may be at higher risk of use hazards. It is also unclear whether dual use of e-cigarettes and other nicotine-containing products will result in higher risks of nicotine toxicity and use-related hazards. Longitudinal national data, such as data from the ongoing Population Assessment of Tobacco and Health Study, a collaborative project between NIH and FDA/CTP, may provide a better understanding of the e-cigarette user population.

**Electronic cigarette use environment**

Electronic cigarettes may be used in many settings, including homes, public spaces (eg, parks and restaurants) and mobile environments (eg, automobiles). Although some states and localities have legislation limiting public use of e-cigarettes, the numbers and types of environments in which e-cigarettes are being used appear to be greater than those currently allowed for traditional cigarettes. Conditions such as ambient temperature and user distractions may impact appropriate product use and the storage environment may affect product quality, potency and function. In particular, the environment in which reusable devices are recharged may have important risk consequences. Research is needed to adequately characterise the environments in which e-cigarettes are used and stored.

**Electronic cigarette design**

The design and quality of e-cigarettes are diverse and inadequately characterised. Some of the known and potential associated e-cigarette risks, such as injuries and damage related to explosions, would likely be mitigated by improved product design and quality standards. For example, lithium batteries used in e-cigarettes carry a risk of overheating, explosion and electrolyte leakage due to their ability to store large amounts of energy in a compact space. Adoption of standardised manufacturing techniques with improved quality control processes may reduce battery hazards by reducing design flaws and manufacturing defects. These changes may also improve the tolerances associated with the environmental and storage conditions experienced during normal consumer use. In addition to design and manufacturing flaws, improper use and handling of the battery by the consumer can contribute to a condition known as ‘thermal runaway’ during which the internal battery temperature can increase, causing a fire or explosion. The use of industry-proven design safety features (such as overcharging protection circuits, thermal power cut-offs and internal overpressure relief mechanisms) and instructions for use that include the proper care and handling of the battery may help prevent thermal runaway.

Some e-cigarettes can be modified for use in ways other than intended, which may result in malicious adulteration, delivery of aerosols with higher concentrations of nicotine and toxins, and aerosolisation of products other than e-liquids, such as marijuana oils and waxes. Battery stacking and ‘dripping’ are examples of how the user can increase nicotine delivery. Designs that prevent product modification and use in ways other than intended may help to prevent or reduce adverse health effects associated with adulteration.

**Labelling and user interface**

The literature, AE reports review and labelling analysis identified e-cigarette labelling inadequacies, including ambiguous, incomplete or misleading information, as well as information provided in fonts that are likely not conspicuous to the user. Given the complexity of e-cigarette products and potential risks, instructions to ensure appropriate use and adequate safety labelling may be needed for e-cigarettes. For example, all e-cigarettes in the CTP labelling analysis contain small parts that pose a choking risk to children and pets, and a fatal choking event has been reported. Products with C-R packaging design and with choking risk warnings may reduce or prevent choking hazards. In addition, ingestion of nicotine-containing e-liquids, especially those with high concentrations (eg, 87.2 mg nicotine/mL), can be toxic, and poisoning events have been reported.

Concerns have been raised that nicotine deposited on surfaces can be converted into carcinogens and then inhaled or ingested by both users and non-users. Although the magnitude of the risks of overdose and poisoning events remains undefined, adequate product labelling to warn of nicotine exposures and toxicity, and C-R packaging may help mitigate risks.

**Incorporating HF approaches into e-cigarettes risk assessment**

Additional information on e-cigarette users, use environment and the product–user interface is needed in order to apply HFE risk assessment strategies. Analytical HF approaches include function and task analysis, heuristic analysis and expert reviews. Empirical approaches (use studies) derive information from actual or simulated use of products. Usability testing prior to product marketing may reveal design problems and improve product labelling and directions for use. Postmarketing surveillance and evaluations are also critical for monitoring AEs and capturing unexpected user errors; this can inform consumer education and the development of additional safeguards with improved product design.

**Limitations**

To be included in this review, an article had to be relevant to HF, written in English and focus on the US market. Thus, it is possible that some articles may have been overlooked. AEs submitted to FDA are from voluntary reporters, may not include all cases and may lack accurate or complete information. For our labelling analysis, we were not the first to open some of the samples, which may have limited our ability to review all levels of packaging and may have affected the appearance of tamper-evident packaging features. Our assumptions about the level of packaging intended for the retail consumer for the NicQuid sample and the interpretation of ambiguous labelling content such as numbers and text descriptors were not confirmed with the manufacturers. We analysed 12 e-cigarette products that may or may not be representative of e-cigarette products at large. One-quarter of our sample was from a single manufacturer (NJJOY), although the decision for inclusion was consistent with the product’s market share and other published labelling analyses.

Electronic cigarettes are increasingly popular and rapidly evolving. It is possible that the fatal dose of nicotine is estimated to be 30–60 mg for adults and 10 mg for children.
CONCLUSIONS
The impact of HFE on the hazards associated with e-cigarettes is not adequately characterised. HF risk management strategies may help to address e-cigarette related hazards. Given the complexity of e-cigarette products and the high concentrations of nicotine available for use, improvements in current labelling may help prevent or mitigate risks associated with e-cigarette use. AEs reported for e-cigarettes (explosions, burn injuries, poisonings, choking deaths and nicotine overdoses) may be reduced by improved product labelling and instructions, improved product and packaging design and improved manufacturing quality controls.

Future research priorities include collecting data to adequately characterise e-cigarette users, the user environment, identifying potential hazards associated with typical and atypical use, evaluating product complexities, determining appropriate manufacturing standards and design safety features, and determining the effectiveness of risk mitigation strategies.

What this paper adds

- This is the first comprehensive review applying principles of human factors engineering to e-cigarette-associated hazards.
- Reports of adverse health effects and product malfunctions associated with e-cigarette use are increasing as the popularity of these products increases and human factors appear to contribute to a substantial number of the events, including some serious events.
- Research is needed to further characterise the human factors that may cause or contribute to e-cigarette-associated adverse health effects and product malfunctions and to identify appropriate and effective risk mitigation strategies.

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Contributors
All authors reviewed the final version of the paper and approved it for publication. LY conceptualised and developed the article topic, conducted the literature search on product use and user environment, assisted in analysing the FDA adverse events (AE) reports, and composed the majority of the article. SFR contributed to topic conceptualisation, conducted the literature search on AE and product labelling, packaging, co-conducted the literature search on AEs and product labelling, packaging, co-conducted the product labelling review, analysed the FDA AE reports, composed article sections pertaining to the labelling review and AEs, contributed to the discussion and summary article sections, and reviewed article drafts. JMC conducted the literature search on e-cigarette product design and composed the article section pertaining to product design. ELD reviewed study abstracts, co-conducted the product labelling review, assisted in reviewing the FDA AE reports, assisted in composing various article sections and reviewed article drafts.

Competing interests
None.

Provenance and peer review
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