Patterns of use and biomarkers of exposure among ‘dual’ tobacco cigarette and electronic cigarette users in Canada.

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted my by examiners.

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ABSTRACT

Background: Tobacco use remains the leading risk factor for preventable disease in Canada. Although tobacco smoke is the direct cause of smoking-induced diseases, nicotine addiction sustains the use of tobacco. Electronic cigarettes (e-cigarettes) are battery-powered devices that deliver nicotine in an aerosol form. Despite a restriction on the sale of nicotine-containing e-cigarettes in Canada, products with and without nicotine are accessible to Canadians. Although e-cigarettes are likely to be much less harmful than tobacco cigarettes, empirical evidence of potential reduced risk at the individual level is limited. To date, behavioural switching studies involving tobacco cigarettes and e-cigarettes are limited by restrictions placed on e-cigarette user and product characteristics, and few have examined biomarkers of exposure among concurrent (dual) users of these products. Furthermore, although dual users constitute the majority of e-cigarette users in Canada, little is known about their behaviour. The current study seeks to fill several critical evidence gaps regarding dual users' patterns of use and exposure to nicotine and tobacco smoke constituents in the Canadian context.

Objectives: The study examined: 1) Patterns of use and perceptions of tobacco cigarettes and e-cigarettes among dual users. In the context of product switching, the study examined: 2) Exposure to nicotine and compensatory behaviour; 3) Exposure to tobacco smoke constituents; 4) Symptoms of nicotine withdrawal for tobacco cigarettes and e-cigarettes, respectively; 5) Self-efficacy for abstaining from smoking tobacco cigarettes and using e-cigarettes, respectively; and 6) Perceived respiratory health.

Methods: An un-blinded within-subjects experiment was conducted with a sample of adult daily dual users (n=48) in Kitchener-Waterloo and Toronto, Ontario. Participants completed three consecutive seven-day periods in which the use of tobacco cigarettes and e-cigarettes was experimentally manipulated, resulting in four study conditions: dual use, exclusive use of tobacco cigarettes, exclusive use of e-cigarettes, and use of neither product. To control for order effects, the order in which participants experienced the study conditions was randomized. Participants' behaviours and exposure to nicotine and tobacco smoke constituents were assessed following each study condition. Patterns of use and product perceptions were examined at baseline using descriptive statistics. Repeated measures models were used to examine the

following outcomes: compensatory behaviour for nicotine, exposure to tobacco smoke constituents, symptoms of nicotine withdrawal, self-efficacy, and perceived respiratory health.

Results: Dual users were 36 years of age, mostly male (71%), and exhibited low to moderate nicotine dependence (FTCD: 4.7 (SD=1.9)). Study participants had smoked and vaped daily for 17.4 (SD=12.2) and 1.2 (SD=0.9) years, respectively, and all reported initiating use of tobacco cigarettes prior to e-cigarettes. Although dual users reported similar daily consumption of tobacco cigarettes and e-cigarettes (13.7 (SD=5.6) tobacco cigarettes per day vs. 10.9 (SD=11.4) bouts of e-cigarette use, p=0.09), a greater proportion reported smoking tobacco cigarettes within the first hour of waking (98% vs. 59% for e-cigarettes; p<0.001). Virtually all dual users reported using tank systems (92%) and e-cigarettes with nicotine (94%). The most commonly reported reasons for using e-cigarettes included: to smoke fewer tobacco cigarettes (79%), to help with cravings for tobacco cigarettes (71%), and because of the belief that e-cigarettes are less harmful than tobacco cigarettes (71%). Compared to tobacco cigarettes, dual users considered e-cigarettes as more socially acceptable (65%), less satisfying (67%), less pleasurable (64%), less harmful (87%), and less expensive (81%).

Findings from the product-switching experiment indicated that compared to dual use, levels of urinary cotinine were stable when participants exclusively smoked (p=0.524), but significantly decreased when they exclusively vaped (p=0.027), despite significant increases in e-cigarette consumption (p=0.001). Biomarkers of exposure, including exhaled carbon monoxide (CO), urinary 1-hydroxypyrene (1-HOP), and urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), were significantly lower when participants exclusively vaped, as compared to when they engaged in dual use (CO: -41%, p<0.001; 1-HOP: -31%, p=0.025; NNAL: -30%, p=0.017). A similar trend was observed among participants abstaining from both tobacco cigarettes and e-cigarettes, as compared to dual use (CO: -26%, p<0.001; 1-HOP: -14% (ns); NNAL: -35%, p=0.016). In addition, biomarkers of exposure showed an increasing trend among participants when they exclusively smoked as compared to dual use (CO: +21%, p=0.029; 1-HOP: +23%, p=0.048; NNAL: +8% (ns)). Study participants experienced significantly greater urges to smoke tobacco cigarettes when they were not permitted to do so (p=0.001). Although changes in participants' self-efficacy for abstaining from tobacco cigarettes depended on the order in which they experienced study conditions, the self-efficacy of all participants at the end of the product-

switching experiment did not differ significantly from their baseline values. In contrast, participants reported no significant changes in urges to use e-cigarettes ($p=0.460$) or in their self-efficacy to abstain from using e-cigarettes ($p=0.150$) across study conditions. Dual users reported significant improvements in various domains of respiratory health when they abstained from smoking tobacco cigarettes, including improvement in experiencing shortness of breath, cough, cough with phlegm, sounds emanating from the chest, and in perceived lung function ($p<0.001$ for all).

Conclusions: The findings suggest that dual use behaviour is similar to that in other jurisdictions, despite Canada's restrictive regulatory framework for these products. Tobacco cigarettes appear superior to e-cigarettes in their ability to deliver nicotine. Although abstaining from smoking tobacco cigarettes elicits cravings, it is also associated with significant improvements in perceived respiratory health. Consistent with other research, results from the current study demonstrate that abstaining from tobacco cigarettes is the most important factor in reducing exposure to tobacco smoke constituents. Therefore, dual use is likely to have public health benefit only to the extent that it leads to complete smoking cessation.

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I would like to thank all the members of the Hammond Lab for their friendship and support, and for making my time at the University of Waterloo memorable.

Finally, to my family and friends, and most of all, to Cassian – thank you for supporting me in this journey.

DEDICATION

In 1941, a young girl was forced to leave her beloved Ukrainian village behind and work in war-torn Germany. In the post-war years, she and her family would move several more times, across three continents, in search of a better life. That young girl was my grandmother, whose simple twist of fate made my life in Canada, and this work, possible. This thesis is dedicated to her.

TABLE OF CONTENTS

EXAMINING COMMITTEE MEMBERSHIP ii

AUTHOR'S DECLARATION iii

ABSTRACT iv

ACKNOWLEDGEMENTS vii

DEDICATION viii

TABLE OF CONTENTS ix

LIST OF FIGURES xiii

LIST OF TABLES xv

1 INTRODUCTION 1

1.1 Tobacco use in Canada 1
1.1.1 Product design and market 1
1.1.2 Health effects 2
1.1.3 Prevalence and patterns of use 4

1.2 E-cigarette use in Canada 4
1.2.1 Product design and market 4
1.2.2 Health effects 6
1.2.3 Prevalence and patterns of use 7

1.3 E-cigarettes and public health 7
1.3.1 Potential to reduce tobacco use 8
1.3.2 Potential negative effects 9

1.4 Dual use of cigarettes and e-cigarettes 10
1.4.1 Dual use in Canada 10
1.4.2 Patterns of dual use 10
1.4.3 Perceptions of and reasons for dual use 13
1.4.4 Exposure to nicotine and compensatory behaviour 13
1.4.5 Exposure to tobacco smoke constituents 15

1.4.6 Nicotine withdrawal 16
1.4.7 Self-efficacy 17
1.4.8 Perceived health and subjective effects 18

1.5 Policy context 18

1.6 Study rationale and research questions 19

2 METHODS 22

2.1 Study design 22

2.2 Study protocol 22
2.2.1 Recruitment 22
2.2.2 Eligibility 22
2.2.3 Study conditions and experimental groups 23
2.2.4 Study visits 25
2.2.5 Daily diaries 25
2.2.6 Remuneration 25
2.2.7 Ethics clearance 25

2.3 Study measures 26
2.3.1 Eligibility criteria and sociodemographic characteristics 26
2.3.2 Smoking behaviours 26
2.3.3 Vaping behaviours 27
2.3.4 Nicotine dependence 28
2.3.5 Nicotine withdrawal 29
2.3.6 Self-efficacy 29
2.3.7 Dual use behaviours 30
2.3.8 Perceptions of e-cigarettes 31
2.3.9 Perceived health and subjective effects 31
2.3.10 Biomarkers of exposure 34
2.3.11 Cognitive testing 35

2.4 Analysis 36
2.4.1 Sample characteristics 36
2.4.2 Baseline patterns and perceptions of dual use 36
2.4.3 Testing changes in continuous outcomes across study conditions 36
2.4.4 Testing changes in binary outcomes across experimental conditions 39
2.4.5 Power calculations 40

3 RESULTS 42

3.1 Sample characteristics 42
3.1.1 Sociodemographic characteristics 42
3.1.2 Nicotine dependence 43

3.2 Baseline patterns of use and perceptions among dual users 46
3.2.1 Patterns of product use 46
3.2.2 Types of products used 47
3.2.3 Places of product use 49
3.2.4 Reasons for e-cigarette use 50
3.2.5 Dual use characteristics 52
3.2.6 Perceptions of e-cigarettes 53

3.3 Randomization check 54

3.4 Patterns of product use across study conditions 54

3.5 Exposure to nicotine and compensatory behaviour 56
3.5.1 Patterns of use of tobacco cigarettes 56
3.5.2 Patterns of use of e-cigarettes 58
3.5.3 Urinary cotinine 60

3.6 Exposure to tobacco smoke constituents 62
3.6.1 Exhaled carbon monoxide 62
3.6.2 Urinary 1-hydroxypyrene 63
3.6.3 Urinary NNAL 64
3.6.4 Summary 66
3.6.5 Sensitivity analyses 67

3.7 Nicotine withdrawal 68
3.7.1 Urges to smoke tobacco cigarettes 69
3.7.2 Urges to use e-cigarettes 70

3.8 Self-efficacy 71
3.8.1 Self-efficacy for abstaining from tobacco cigarettes 72
3.8.2 Self-efficacy for abstaining from e-cigarettes 73

3.9 Perceived health and subjective effects 74
3.9.1 Perceived respiratory health 74
3.9.2 Perceived overall health 78
3.9.3 Perceived addiction 79
3.9.4 Perceived difficulty in abstaining from product use 80

4 DISCUSSION 82

4.1 Baseline characteristics and patterns of product use among dual users 82
4.1.1 Characteristics of dual users 82
4.1.2 Patterns of product use among dual users 82
4.1.3 Dual use behaviour 83
4.1.4 Compensatory behaviour and exposure to nicotine 84
4.1.5 Exposure to tobacco smoke constituents 85
4.1.6 Nicotine withdrawal and self-efficacy 88
4.1.7 Perceived health 89

4.2 Limitations and strengths 90

4.3 Future research 93

4.4 Policy implications 94

5 CONCLUSIONS 97

REFERENCES 98

APPENDICES 109
Appendix A: Recruitment materials 109
Appendix B: Informed consent 111
Appendix C: Study questionnaires 116
Appendix D: Participant recruitment statistics 163
Appendix E: Products used by dual users 164
Appendix F: Patterns of product use across study conditions 167
Appendix G: Key outcomes across study conditions 170
Appendix H: Interaction effects of key outcomes across study conditions 173
Appendix I: Sensitivity analyses 175
Appendix J: Additional findings: Nicotine withdrawal 188
Appendix K: Additional findings: Self-efficacy 192

LIST OF FIGURES

Figure 1: Variety of available e-cigarette products 5
Figure 2: Study design 24
Figure 3: Urinary cotinine[1] across study conditions (n=48) 60
Figure 4: Exhaled carbon monoxide across study conditions (n=48) 62
Figure 5: Urinary 1-hydroxypyrene[1] across study conditions (n=48) 63
Figure 6: Urinary NNAL[1] across study conditions (n=48) 64
Figure 7: Measures of nicotine withdrawal for tobacco cigarettes and e-cigarettes across study conditions (n=48) 68
Figure 8: Measures of self-efficacy for abstaining from tobacco cigarettes and e-cigarettes across study conditions (n=48) 71
Figure 9: Self-efficacy for abstaining from tobacco cigarettes across study conditions, by group (n=48) 73
Figure 10: Proportion of participants reporting better perceived lung function across study conditions (n=48) 75
Figure 11: Proportion of participants reporting better perceived respiratory health across study conditions (n=48) 76

Appendix figures

Figure A1: Sample recruitment flyer 109
Figure A2: Sample recruitment advertisement 110
Figure A3: Exhaled carbon monoxide across study conditions, by group (n=48) 173
Figure A4: Urinary cotinine[1] across study conditions (n=11) 176
Figure A5: Exhaled carbon monoxide across study conditions (n=11) 177
Figure A6: Urinary 1-hydroxypyrene[1] across study conditions (n=11) 178
Figure A7: Urinary NNAL[1] across study conditions (n=11) 179
Figure A8: Urinary NNAL[1] across study conditions, by group 181
Figure A9: Urinary cotinine[1] across study conditions (n=20) 183
Figure A10: Exhaled carbon monoxide across study conditions (n=20) 185
Figure A11: Urinary 1-hydroxypyrene[1] across study conditions (n=20) 186

Figure A12: Urinary NNAL[1] across study conditions (n=20) 187
Figure A13: Measures of nicotine withdrawal for tobacco cigarettes across study conditions (n=48) 188
Figure A14: Measures of nicotine withdrawal for e-cigarettes across study conditions (n=48) 190
Figure A15: Measures of self-efficacy for abstaining from tobacco cigarettes across study conditions (n=48) 192
Figure A16: Measures of self-efficacy for abstaining from e-cigarettes across study conditions (n=48) 194

LIST OF TABLES

Table 1: Study questionnaires and measures 33
Table 2: Sociodemographic characteristics of dual users, overall and by group 43
Table 3: Tobacco cigarette and e-cigarette dependence, as measured by the Fagerström Test for Cigarette Dependence (FTCD), among dual users (n=48) 44
Table 4: Tobacco cigarette and e-cigarette dependence, as measured by the Nicotine Dependence Syndrome Scale (NDSS), among dual users (n=48) 45
Table 5: Perceived addiction to tobacco cigarettes and e-cigarettes among dual users (n=48) 45
Table 6: Patterns of use of tobacco cigarettes and e-cigarettes among dual users (n=48) 47
Table 7: Self-reported e-cigarette product characteristics used by dual users (n=48) 48
Table 8: Self-reported product nicotine concentrations used, among those who reported using e-cigarettes with nicotine (n=45) 48
Table 9: Places of tobacco cigarette and e-cigarette use among dual users (n=48) 49
Table 10: Potential reasons for initiation and current use of e-cigarettes reported by dual users (n=48) 50
Table 11: The most important reason for initiation and current use of e-cigarettes reported by dual users (n=48) 51
Table 12: Dual use characteristics among dual users (n=48) 52
Table 13: Perceptions of e-cigarettes among dual users (n=48) 53
Table 14: Key outcomes among study participants at baseline, overall and by group 54
Table 15: Patterns of use of tobacco cigarettes and e-cigarettes across study conditions (n=48) 55
Table 16: Patterns of use of tobacco cigarettes across conditions of *Dual use* and *Exclusive use of tobacco cigarettes* (n=48) 56
Table 17: Patterns of use of e-cigarettes across conditions of *Dual use* and *Exclusive use of e-cigarettes* (n=48) 58
Table 18: Summary of biomarkers of exposure across study conditions (n=48) 66
Table 19: Changes in perceived health across study conditions (n=48) 78
Table 20: Perceived addiction to tobacco cigarettes and e-cigarettes across study conditions (n=48) 80
Table 21: Perceived difficulty in abstaining from smoking tobacco cigarettes or from using e-cigarettes, across study conditions (n=48) 81

Appendix tables

Table A1: Methods used for participant recruitment 163

Table A2: Tobacco cigarette brands smoked by dual users (n=48) 164

Table A3: E-cigarette device and e-liquid brands used by dual users (n=48) 165

Table A4: Daily patterns of use of tobacco cigarettes and e-cigarettes across study conditions (n=48) 167

Table A5: Key continuous outcomes across study conditions (n=48) 170

Table A6: Key binary outcomes across study conditions (n=48) 172

Table A7: Biomarkers of exposure across study conditions, among participants with exhaled carbon monoxide levels less than 5 ppm in the condition of *No product use* (n=11) 175

Table A8: Biomarkers of exposure across study conditions, among participants who did not report smoking tobacco cigarettes in the condition of *No product use* (n=20) 182

1 INTRODUCTION

1.1 Tobacco use in Canada

Tobacco use represents an immense public health challenge, given its role as one of the most important risk factors for non-communicable disease, including cardiovascular disease, respiratory diseases, and cancer (U.S. Department of Health and Human Services [USDHHS], 2014). The World Health Organization (WHO) (2013) attributes approximately six million deaths and half a trillion dollars of economic damage to the use of tobacco annually. Left unhindered, tobacco will kill as many as one billion people by the end of the century (WHO, 2013). In Canada, despite substantial declines in smoking prevalence over several decades, tobacco use remains the leading risk factor for preventable disease (Krueger, Turner, Krueger, & Ready, 2014). In addition, tobacco use places a significant burden on the economy. For instance, the annual costs associated with tobacco use amounted to approximately $21.3 billion in 2012 (Krueger et al., 2014).

1.1.1 Product design and market

Cigarettes are tobacco products that deliver various chemical compounds to the user via tobacco smoke, which is the product of combustion. Tobacco smoke is a complex aerosol mixture consisting of more than 7,000 chemical compounds, which forms as the vapors generated by combustion cool and condense upon delivery to the user (USDHHS, 2010; WHO International Agency for Research on Cancer [IARC], 2004). The main components (by weight) of tobacco smoke include nitrogen, oxygen, carbon dioxide, carbon monoxide, nitrogen oxides, and various sulfur-containing gaseous compounds. Carbon monoxide and carbon dioxide result from the combustion of tobacco and represent nearly 15% of the weight of the gas phase of tobacco smoke (USDHHS, 2010).

Nicotine is a key constituent of tobacco, with most commercial tobacco products carrying concentrations from six to 18 mg/g (0.6-1.8% by weight) (USDHHS, 2010). Nicotine in tobacco smoke exists in either a protonated or un-protonated (“free”) form, the levels of which depend upon various factors. Over the last century, the design of cigarettes has evolved to ensure that tobacco smoke has enough free nicotine for rapid transfer and delivery to the user, but not so much as to make smoking overly harsh (USDHHS, 2010).

Tobacco-specific nitrosamines (TSNAs) are a family of potent carcinogens, including NNK [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone], NNN [N'-nitrosonornicotine], NAB [N'-nitrosoanabasine], and NAT [N'-nitrosoanatabine]. As the name of this family of compounds suggests, TSNAs are specific to tobacco and tobacco smoke, due to their presence at high levels in these sources as compared with other consumer products (USDHHS, 2010). TSNAs are predominantly formed during the curing and processing of tobacco as well as through combustion (IARC, 2004); as a result, levels of TSNAs in tobacco and tobacco smoke can vary widely both between and within brands across markets (USDHHS, 2010).

Polycyclic aromatic hydrocarbons (PAHs) are chemical compounds formed by incomplete combustion of natural organic matter, such as wood, petroleum, and tobacco. Due to the fact that PAHs are found throughout the environment, exposure to these chemicals may have various and multiple sources (USDHHS, 2010). At least 500 PAHs have been found in tobacco smoke, of which 16 have been identified as causing or having the potential to cause cancer. Levels of PAHs in tobacco smoke have been shown to vary by the type of tobacco and the nitrate content of tobacco products (USDHHS, 2010).

1.1.2 Health effects

Tobacco smoke is the key medium through which a host of chemicals are delivered to smokers, resulting in various health effects. Smoking causes cancers of the lung, larynx, oral cavity, pharynx, esophagus, pancreas, bladder, kidney, cervix, and stomach, as well as acute myeloid leukemia; furthermore, there is evidence that suggests a causal relationship between smoking and colorectal and liver cancers (USDHHS, 2010). In addition to being a major cause of cardiovascular disease, cigarette smoking appears to have a multiplicative interaction effect with other major risk factors for coronary heart disease, including hyperlipidemia, hypertension, and diabetes mellitus (USDHHS, 2010). Tobacco smoke also causes various non-malignant respiratory diseases, including chronic obstructive pulmonary disease (COPD), emphysema, chronic bronchitis, and asthma, and further increases the risk of death from pneumonia (USDHHS, 2010).

Several classes of carcinogens, including TSNAs, PAHs, aromatic amines, aldehydes, volatile organic hydrocarbons, and metals, are present in tobacco smoke and have been implicated in various cancer-causing mechanisms. Extensive research has demonstrated the uptake of these

carcinogens by smokers, who have higher levels of carcinogen metabolites in their urine than do non-smokers (IARC, 2004; USDHHS, 2010). Many of the carcinogens noted above cause cancer via the production of DNA adducts, which, if left unrepaired, can cause various permanent mutations and damage to critical genes involved in the control of cellular growth (IARC, 2004). In particular, research has demonstrated the potency of NNK as a pulmonary carcinogen in both rat models and human smokers (IARC, 2004). The key constituents of tobacco smoke responsible for cardiovascular disease include oxidizing chemicals, nicotine, carbon monoxide, and particulate matter (USDHHS, 2010). Finally, various components of tobacco smoke, including acrolein, formaldehyde, nitrogen oxides, cadmium, and hydrogen cyanide, have the potential to injure the lungs, resulting in respiratory diseases (USDHHS, 2010).

Although tobacco smoke is the direct cause of smoking-induced diseases, nicotine addiction sustains the use of tobacco: among individuals who have ever tried smoking, approximately one-third become daily smokers; furthermore, among smokers who try to quit, less than five percent are successful at any one time (Benowitz, 2010; USDHHS, 2010). Nicotine is an addictive drug whose psychoactive impact depends upon the dose of nicotine delivered and the mode of its delivery to the human brain (USDHHS, 2014). The inhalation of tobacco smoke delivers nicotine rapidly into the bloodstream and to the brain, which promotes dependence and high levels of smoke exposure (IARC, 2004). This feature distinguishes tobacco cigarettes as highly appealing and addictive when compared to other tobacco and nicotine products (Zeller & Hatsukami, 2009).

Nicotine is a highly bioactive compound with a wide range of effects. Although relatively benign among adult populations, nicotine has been linked with diverse adverse health outcomes for the developing fetus and for adolescents, particularly with respect to brain development (USDHHS, 2014; England, Bunnell, Pechacek, Tong, & McAfee, 2015). In addition, nicotine poses risk of acute toxicity or poisoning from ingestion at high-enough doses (USDHHS, 2014).

Research evidence indicates that cigarette design features, such as tobacco blend, filter type and length, paper type and porosity, ventilation, and chemical additives, influence the yield of tobacco smoke constituents (USDHHS, 2010). Furthermore, smoking characteristics influence the delivery of these constituents to smokers. These include puff topography characteristics (puff number, duration, volume, flow rate, and inter-puff interval), cigarette length smoked, and

blockage of ventilation holes, and exhibit considerable variability across smokers (USDHHS, 2010). The size of constituent particles also plays an important role in their deposition and retention in the respiratory system, which influences risks for health (USDHHS, 2010). In sum, many factors may play a role in determining the exposure of smokers to toxic constituents found in tobacco smoke and the implications of such exposure for health.

1.1.3 Prevalence and patterns of use

According to the Canadian Tobacco, Alcohol and Drugs Survey (CTADS), as of 2015, 13.0% of the Canadian population aged 15 years and older were current smokers (Reid, Hammond, Rynard, Madill, & Burkhalter, 2017). Among current smokers, a majority reported smoking daily, with an average daily cigarette consumption of 13.8 cigarettes per day. Smoking prevalence varies by age, with the highest rates of prevalence among young adults aged 20-24 years (18.5%). Smoking prevalence also varies by sex, with higher prevalence among males (15.6%) than females (10.4%). In addition, male daily smokers consume nearly three cigarettes more per day than females (15.2 and 11.9, respectively) (Reid et al., 2017).

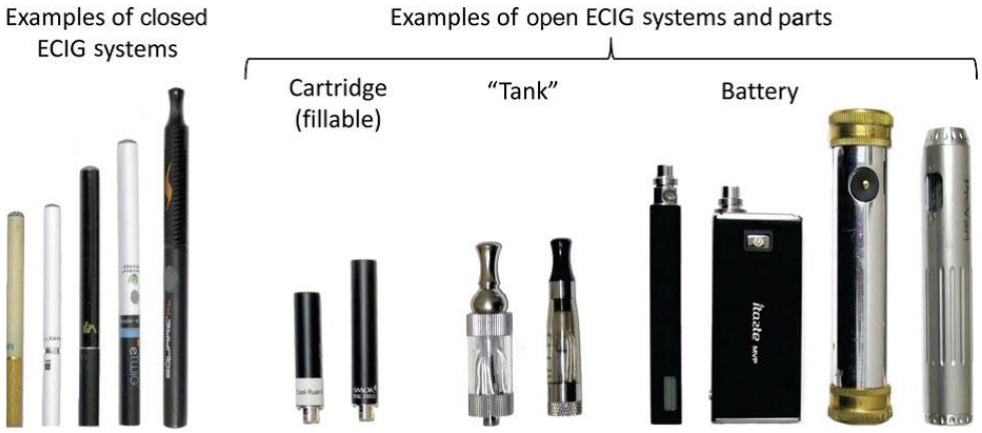
1.2 E-cigarette use in Canada

1.2.1 Product design and market

Hon Lik, a Chinese pharmacist, is credited with inventing the modern electronic cigarette (e-cigarette), a type of electronic nicotine delivery system. E-cigarettes use battery power to heat a solution, producing an aerosol that is inhaled by users (Besaratinia & Tommasi, 2014). E-cigarette solutions typically contain nicotine dissolved in propylene glycol and/or glycerin, and may contain various additives and flavours (Bertholon, Becquemin, Annesi-Maesano, & Dautzenberg, 2013). E-cigarettes have evolved to produce three distinct "generations" or classes of products: 1) disposable products; 2) products that use pre-filled cartridges that can be replaced by the user; and 3) products that are re-chargeable and have an open tank or reservoir that may be filled with liquid by the user (Grana, Benowitz, & Glantz, 2014). Disposable products and those that use pre-filled cartridges are "closed" systems (meaning they are not intended to be re-filled with liquid or for their component parts to be replaced by the user), and tend to be similar in appearance to tobacco cigarettes. In contrast, re-chargeable products (commonly referred to as "tank" systems), are typically bulkier, heavier, and visually distinct from tobacco cigarettes. These products are considered "open" systems, meaning they are intended to be re-filled with

liquid. Furthermore, these products allow users to modify product components, such as battery capacity and voltage, which subsequently influences users' vaping experiences (Breland, Soule, Lopez, Ramoa, El-Hellani, & Eissenberg, 2016; Grana, Benowitz & Glantz, 2014). Images of the variety of available e-cigarette products are shown in Figure 1.

Figure 1: Variety of available e-cigarette products



Notes:
Figure adapted from Breland et al, 2016.

Over the last decade, e-cigarettes have spread from China to the rest of the world, with rapid growth in the number of brands, models, and flavours available to consumers (Zhu, Sun, Bonnevie, Cummins, Gamst, Yin, & Lee, 2014). Although independent e-cigarette manufacturers were the only stakeholders in the global e-cigarette market in its early years, the tobacco industry has since entered by either acquiring independent companies or developing its own products (Kamerow, 2013). Consistent with other markets, e-cigarettes in Canada are available in both brick-and-mortar and online retail outlets, in a variety of types, flavours, and nicotine concentrations (Hammond, White, Czoli, Martin, Maggenis, & Shiplo, 2015). However, when compared to the United States (US), the Canadian market is distinct in its relative availability of nicotine-free products and in its dominant e-cigarette brands (Hammond et al., 2015), likely as a result of its current regulatory framework (discussed further below). In general, e-cigarettes are commonly marketed to smokers as potential cessation aids and/or as substitutes to use in situations that prohibit smoking (National Cancer Institute [NCI] & Centers for Disease Control and Prevention [CDC], 2014; Henningfield & Zaatari, 2010; Benowitz & Goniewicz, 2013).

1.2.2 Health effects

To date, available evidence regarding the health effects of e-cigarettes indicates that they are likely to be much less harmful than tobacco cigarettes, given that they do not contain tobacco, do not rely on combustion, and thus do not produce smoke (Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014). However, other constituents of e-cigarette liquids and aerosols may pose health risks to users.

First, nicotine – which may or may not be present in e-cigarettes – poses the same health risks as it does in tobacco cigarettes. Second, propylene glycol and/or vegetable glycerin are typical solvents used in e-liquids. Propylene glycol is an alcohol that is commonly used as: an additive in foods and cosmetics, a solvent in pharmaceuticals, an antifreeze, and as a key ingredient in theatrical mist or fog (Bertholon et al., 2013). Studies examining the health effects of theatrical staff exposed to such mist concluded that massive and prolonged exposure results in irritation of the airways (Bertholon et al., 2013). Vegetable glycerin is a non-toxic additive that is widely used in the food and chemical industry. However, it may pose a risk as used in e-cigarettes due to the fact that it can generate toxic acrolein at high temperatures (Bertholon et al., 2013). Next, flavouring agents are commonly added to e-cigarette liquids. Although most of these are commonly used in foods and indoor fragrances, data regarding the health effects related to their inhalation are not available (Bertholon et al., 2013; Breland et al., 2016). Finally, various contaminants, such as TSNAs, volatile organic compounds, polycyclic aromatic hydrocarbons, metals, carbonyls, glycols, and aldehydes have been identified in some samples of e-liquids, at variable amounts, although typically at levels far below those found in cigarettes (Bertholon et al., 2013; Breland et al., 2016; Fernandez, Ballbe, Sureda, Fu, Salto, & Martinez-Sanchez, 2015). Furthermore, the presence of several specific contaminants and irritants may be associated with specific flavours and/or as a result of excessive heating during product use (Behar, Davis, Wang, Bahl, Lin & Talbot, 2014; Farsalinos, Kistler, Gillman & Voudris, 2015; Farsalinos, Voudris & Poulas, 2015). In sum, although limited, available evidence indicates that e-cigarette aerosol exposure can result in short-term respiratory effects, such as irritation and cough, as well as nausea and vomiting; however, the long-term health effects of these products remain unknown (Grana, Benowitz & Glantz, 2014).

1.2.3 Prevalence and patterns of use

As of 2015, 13.2% of Canadian adults had ever tried an e-cigarette, while 3.2% reported using these products in the past 30 days, and 1.0% reported daily use (Reid, Hammond, Rynard, Madill, & Burkhalter, 2017). These findings represent significant increases in use of e-cigarettes from 2013 (Czoli, Reid, Rynard & Hammond, 2015). Prevalence of e-cigarette use varied by age, with the highest rates of ever use among youth aged 15-19 (25.7%) and young adults aged 20-24 (30.5%); these groups also had the highest prevalence of current use (6.3%). In addition, ever use of e-cigarettes was higher among males (16.1%) compared to females (10.5%) (Reid et al., 2017).

Prevalence of e-cigarette use was also found to vary greatly by smoking status, with greater rates of use among smokers compared to non-smokers. Rates of e-cigarette ever use were 51.0% among current smokers compared to 7.6% among non-smokers. Similarly, current use of e-cigarettes was 15.5% among current smokers and 1.4% among non-smokers. Although e-cigarette ever and current use did not differ by sex among smokers and non-smokers, differences in use rates were seen by age. With respect to ever use of e-cigarettes, use was highest among youth aged 15-19 (82.5% and 19.6%) and young adults aged 20-24 (80.0% and 19.4%), and declined with age, among both smokers and non-smokers, respectively. Prevalence of e-cigarette current use followed a similar pattern, with the highest rates of use among youth aged 15-19 (36.9% among smokers, and 3.0% among non-smokers) (Reid et al., 2017). Thus, data indicate that in the Canadian context, e-cigarette use is most common among young people and among smokers, and rates of use are increasing over time (Czoli, Reid, Rynard & Hammond, 2015; Reid et al., 2017).

1.3 E-cigarettes and public health

The presentation of e-cigarettes as modern, potentially acceptable alternatives to tobacco in today's market creates many new challenges for public health. Despite the fact that e-cigarettes appear to be risk-reducing for an individual's health (as compared to tobacco cigarettes), their use may not be harm-reducing for the overall population; this is because the public health impact of such products depends on users' behavior (Stratton, Shetty, Wallace, & Bondurant, 2001), which may differ in important respects across different subpopulations, with the potential to yield both positive and negative effects.

1.3.1 Potential to reduce tobacco use

E-cigarettes may present a potential public health benefit to the extent that they decrease smoking rates, thereby reducing smokers' exposure to harmful chemicals found in tobacco and tobacco smoke. The benefits of quitting smoking have been shown for smokers of all ages: the lifetime risk of premature death of smokers who quit completely and permanently early in life is very similar to that of non-smokers (Doll, Peto, Boreham & Sutherland, 2004; USDHHS, 2010). Although this evidence holds for two of the three main fatal conditions caused by smoking – cardiovascular disease and COPD – former smokers carry a persistent elevated risk for lung cancer, as compared to non-smokers of the same age (Doll et al., 2004; USDHHS, 2010). Nevertheless, in the face of an addictive habit that will claim the lives of one-half of all long-term smokers (Doll et al., 2004), and in light of the fact that less than two percent of smokers successfully quit smoking each year (Giovino, 2002), a potential decrease in the tobacco-related health burden could indeed be substantial.

The efficacy of e-cigarettes in smoking cessation is presently unclear. Many smokers report using e-cigarettes to quit smoking; indeed, quitting or cutting down smoking are the most commonly reported reasons for using e-cigarettes (Grana, Benowitz & Glantz, 2014; Carroll Chapman & Wu, 2014). To date, two randomized control trials have examined the use of e-cigarettes as a quit aid. One trial failed to find consistent differences across three e-cigarette conditions (Caponnetto, Campagna, Cibella, Morjaria, Caruso, Russo, & Polosa, 2013), while the other reported similar abstinence rates among participants assigned e-cigarettes as those assigned nicotine patches (Bullen, Howe, Laugesen, McRobbie, Parag, Williman, & Walker, 2013). However, it should be noted that these studies were limited by inadequate statistical power, and by their employment of early model e-cigarettes with uncertain or poor nicotine delivery profiles. A recent Cochrane review of these studies concluded that use of nicotine-containing e-cigarettes in these trials led to increased long-term cessation and a reduction in the number of cigarettes smoked, as compared to placebo e-cigarettes (McRobbie, Bullen, Hartmann-Boyce & Hajek, 2014; Hartmann-Boyce et al., 2016). Further research involving novel products is needed to evaluate the cessation potential of these devices (Lopez & Eissenberg, 2015).

1.3.2 Potential negative effects

E-cigarettes also have the potential to undermine public health in several ways. First, there is the possibility that smokers will take up these products, but use them in places or at times where or when smoking is prohibited. In essence, smokers may use these products as an aid to continue, rather than to quit, smoking. In the event that smokers do not achieve complete cessation (i.e., do not change their cigarette consumption or reduce their cigarette consumption, while taking up e-cigarettes), they are unlikely to experience any significant health benefits (Bjartveit & Tverdal, 2009; USDHHS, 2010).

A second concern is the potential of e-cigarettes to attract novel users and/or to reclaim former users. Of particular concern is the appeal of e-cigarettes to youth, who, according to the gateway hypothesis, may initiate nicotine use with e-cigarettes and, once addicted, progress to smoking cigarettes, exposing them to significant health risks (WHO, 2014). Advertising and promotion of e-cigarettes, as well as the vast availability of flavours of these products, have been cited with concern as potentially appealing to youth (Standing Committee on Health, 2015). Although not yet empirically examined, e-cigarettes may also pose a risk for relapse among former smokers, given the potential reduced harm profile they pose to individual users (Rass, Pacek, Johnson, & Johnson, 2015).

Third, e-cigarettes have the potential to weaken existing tobacco control policies. Public health professionals have expressed concern over the similarity of e-cigarettes to tobacco cigarettes, with respect to both product design and behavioural use (Standing Committee on Health, 2015). Due to this similarity, e-cigarettes may erode the social unacceptability of smoking that currently prevails (WHO, 2014). Given the successes of tobacco control policies in reducing smoking prevalence – by encouraging quit attempts by smokers and by preventing uptake by youth – the risk of renormalization may have a significant impact on public health (CDC, 2014; Holford et al, 2014).

Although some or all of these potential positive and negative effects may occur with respect to the ‘disruptive technology’ of e-cigarettes (Fagerström, Etter & Unger, 2015), the public health impact of these products will result from the net effect of these consequences on the smoking rate of the population (Benowitz & Goniewciz, 2013; Czoli et al., 2015; Zeller, 2012). The behavior of dual use, meaning the regular current use of both tobacco cigarettes and e-cigarettes,

is a particular issue that warrants public health attention because of its potential to yield both positive (i.e., smoking reduction/cessation) and negative (i.e., delay of cessation) impacts (Benowitz & Goniewicz, 2013; Rass et al., 2015).

1.4 Dual use of cigarettes and e-cigarettes

1.4.1 Dual use in Canada

Data from the 2015 CTADS describe prevalence of dual use in the Canadian context. Dual use appears to be common, given that the majority (63%) of current users of e-cigarettes also reported currently smoking tobacco cigarettes (Reid et al., 2017). The proportion of e-cigarette current users who were current smokers was lower among youth aged 15-19 (56%), as well as among adults aged 25-44 (56%), and greater among young adults aged 20-24 (68%), as well as among adults aged 45+ (70%) (Reid et al., 2017). Despite the high prevalence of dual use in Canada, evidence regarding dual use behaviours and dual users' exposure to specific chemical compounds is scarce. In addition to CTADS, several population surveys have been conducted examining e-cigarette use among Canadians (Czoli, Hammond, & White, 2014; Czoli, Hammond, Reid, Cole, & Leatherdale, 2015; Hamilton, Ferrence, Boak, Schwartz, Mann, O'Connor, & Adlaf, 2015; Shiplo, Czoli, & Hammond, 2015), although these studies did not examine behaviours among dual users as a distinct subpopulation. While findings from the International Tobacco Control Four-Country Survey from 2010-2011 reported rates of and reasons for use of e-cigarettes among former and current smokers, data are limited with respect to their outdated collection period, and by the fact that they are pooled across Canada, the US, the United Kingdom, and Australia (Adkison et al., 2013). Consequently, the current evidence base regarding dual use is drawn mainly from studies conducted in other contexts.

1.4.2 Patterns of dual use

Research evidence regarding the behaviour of dual use stems from six sources:

- An online survey of adult e-cigarette users (n=2807), of which 20% were currently smoking cigarettes (n=553), recruited via online e-cigarette forums between 2012 and 2014 (Etter, 2015);
- An online survey of adult dual users in the US (n=350), conducted in May 2014 (Rass et al., 2015);

- A national panel survey of current adult smokers in the US (n=2254), of which 24% were currently using e-cigarettes (n=582), conducted in April-May 2014 (Rutten et al., 2015);
- A case-control study of dual users (n=3530) matched for age and gender with formerly-smoking vapers (n=3530), recruited via online e-cigarette forums in April-July 2013 (Farsalinos, Romagna, & Voudris, 2015);
- A survey of 319 adult smokers and vapers in Munich, Germany, of which 30% were dual users, recruited using various methods in 2012 (Rüther et al., 2016);
- An online survey of young adults in the US, of which 31% were dual users, recruited online in August 2014 (Berg, 2016).

Rass and colleagues' (2015) survey data provide a detailed profile of dual users' patterns of use. In this study, dual use was defined as: use of e-cigarettes and tobacco cigarettes for at least three months each, use of e-cigarettes and tobacco cigarettes in the past week, and use of a nicotine-containing e-cigarette. Overall, dual users used tobacco cigarettes more than e-cigarettes, smoking tobacco cigarettes more times per day and more days per week, as compared to e-cigarettes. Furthermore, dual users appeared to be more dependent upon their tobacco cigarettes versus their e-cigarettes, as evidenced by: higher scores of nicotine dependence, less time to first use of the day, greater reluctance to give up the first use of the day, greater likelihood of daily use, and stronger cravings. With respect to the temporality of dual use behaviours, initiation of tobacco cigarette use after e-cigarette use was observed in only one of 350 study participants (Rass et al., 2015).

Etter (2015) reported a significant decrease in dual users' self-reported number of tobacco cigarettes smoked per day (CPD) since the initiation of e-cigarette use, from a mean of 23 to a mean of nine. Similarly, dual users from both US-based surveys reported changes in CPD since the initiation of e-cigarette use: in both studies (by Rass et al., 2015, and Rutten et al, 2015, respectively), slightly over half the sample reported reductions in CPD (50% and 54%); slightly less than half reported no change in CPD (45% and 41%); while very few dual users reported an increase in CPD (5% and 2%) (Rass et al., 2015; Rutten et al, 2015). Rass and colleagues (2015) provided some further detail on reduction of cigarette smoking among their sample of dual users: since initiation of e-cigarette use, the median CPD decreased significantly from 10 to seven, corresponding to a 30% reduction. Furthermore, among dual users in this sample, those who

used e-cigarettes daily had significantly greater reduction in CPD compared to non-daily users (Rass et al., 2015). Dual users in the case-control study by Farsalinos, Romagna, & Voudris, (2015) all reported a reduction in their consumption of tobacco cigarettes since taking up e-cigarettes: approximately two-thirds of dual users were smoking tobacco cigarettes daily (with a reduction in median CPD from 20 to four), while one-third were smoking tobacco cigarettes occasionally.

In an examination of dual users' past quit attempts and intentions to quit by Rass et al. (2015), 68% of dual users reported a past serious quit attempt for tobacco cigarettes, and 41% reported a serious quit attempt for tobacco cigarettes in the past year. Further, 68% reported having used nicotine replacement therapy (NRT), cessation medications, or other methods to assist in quitting tobacco cigarettes. Finally, a comparison of quit intentions for tobacco cigarettes and e-cigarettes showed that twice as many dual users were planning to quit using tobacco cigarettes (73%) versus e-cigarettes (36%) in the next year (Rass et al., 2015).

Rass et al. (2015) also found differences in the settings in which dual users used their products. Overall, dual users reported more commonly using e-cigarettes versus tobacco cigarettes indoors and in situations in which they were concerned about the health of others; in contrast, dual users reported a greater likelihood of using tobacco cigarettes versus e-cigarettes in hedonic situations or when feeling stressed or anxious (Rass et al., 2015).

Findings from Farsalinos, Romagna, & Voudris (2015) provide data regarding e-cigarette product characteristics used by dual users. Dual users commonly used second-generation (52%) or third-generation (41%) products, with very few using first-generation devices (6%). This finding appears to be supported by the survey of German dual users by Rüther and colleagues (2016), in which one-half (50.0%) of dual users reported using tank systems. Further, a majority of dual users used ready-to-use liquids (64%), as opposed to pre-filled cartomizers (3%) or do-it-yourself liquids (33%). Among a sample of German dual users, approximately one-half (51.2%) reported using only e-liquid with nicotine, while just 3.1% reported using only e-liquid without nicotine, and 37.4% reported using both types of e-liquid (Rüther et al., 2016). In addition, a study of young adult dual users in the US by Berg (2016) found that a large majority (94.3%) used e-liquids with nicotine. Dual users in the study by Farsalinos and colleagues (2015) also reported a reduction in nicotine levels of their e-liquids, from a median level of 17 mg/mL at

initiation of use to 12 mg/mL at the time of the survey. The most commonly used e-cigarette flavour reported by a sample of young adult dual users in the US was fruit (60.9%), followed by sweet flavours (e.g., vanilla, candy) (56.2%), menthol/mint (34.7%), and tobacco (27.4%) (Berg, 2016).

1.4.3 Perceptions of and reasons for dual use

Evidence regarding perceptions of products and behaviours among dual users is also limited. The perception of e-cigarettes as less harmful than tobacco cigarettes appears common, with a majority of participants supporting this belief: 87% in the study by Rass et al. (2015), and 90% in the study by Farsalinos, Romagna, & Voudris (2015). In addition, Rass et al. (2015) reported that a majority of dual users stated that e-cigarettes were less enjoyable (63%) and less addictive (57%) than tobacco cigarettes.

Several studies have examined dual users' reasons for using e-cigarettes. The most frequently reported reasons for e-cigarette use were to reduce or quit smoking, to reduce the health risks of smoking (either to the user or to others), or to deal with situations or places where smoking is prohibited (Berg, 2016; Etter, 2015; Patel et al., 2016; Rass et al., 2015; Rutten et al., 2015). Rass et al. (2015) further examined dual users' most important reason for e-cigarette use, for which the belief that e-cigarettes were less harmful to health than tobacco cigarettes (25%), and the wish to cut down smoking in preparation for a quit attempt (21%), were most frequently endorsed. Dual users in the case-control study by Farsalinos, Romagna, & Voudris (2015) similarly viewed using e-cigarettes to reduce or quit smoking and to reduce others' exposure to secondhand smoke as very important reasons for use, while economic considerations and avoiding smoking restrictions were acknowledged as less important reasons.

1.4.4 Exposure to nicotine and compensatory behaviour

Research in the tobacco domain has demonstrated that individuals smoke to achieve a particular dose of nicotine needed to sustain their addiction (Benowitz, 2001). This is evidenced by population-level data showing considerable variability in nicotine intake between smokers (following adjustment for daily cigarette consumption and consideration of cigarette brand smoked) (Jarvis, Boreham, Primatesta, Feyerabend & Bryant, 2001), yet remarkable stability with respect to levels of nicotine exposure among smokers over time (Hammond, Fong, Cummings & Hyland, 2005; Jarvis, Giovino, O'Connor, Kozlowski & Bernert, 2014). Self-

titration of nicotine is also evidenced in "switching" studies, wherein smokers adjust their smoking behaviour to maintain their desired dose across different tobacco products. For instance, smokers switching from 'regular yield' cigarettes to 'low yield' cigarettes may smoke more cigarettes per day, may take more and deeper puffs, may puff with a faster draw rate, and/or may block ventilation holes in the cigarette in order to acquire the nicotine they desire (Benowitz, 2001; Hammond et al., 2005). As a result of such compensatory behavioural changes, smokers of 'low yield' cigarettes are not likely to have a lower risk of disease, as compared to their 'regular yield' cigarette-smoking counterparts (Benowitz, 2001).

Currently, evidence regarding the delivery of nicotine via e-cigarettes is limited. In a review of eight studies of acute e-cigarette administration, Marsot & Simon (2015) reported that regular e-cigarette users showed measurable, yet highly variable, levels of plasma nicotine and cotinine (a key nicotine metabolite), although nicotine was delivered more slowly by e-cigarettes as compared to tobacco cigarettes. In addition, studies comparing levels of cotinine between e-cigarette users and tobacco cigarette smokers revealed that although cotinine levels among users of these different products can be similar, they are not always so (Adriaens, Van Gucht, Declerck, & Baeyens, 2014; Hecht et al., 2015; Göney, Çok, Tamer, Burgaz, & Şengezer, 2016; Wagener et al., 2016). Variability in these findings has been attributed to: user characteristics, including users' experience with particular devices, patterns of use (e.g., occasional versus regular use), and puff topography (e.g., more puffs, greater puff volume); as well as factors related to e-cigarette design, including the generation or class of product, and liquid nicotine content and concentration (Farsalinos, Spyrou, Stefopoulos, Tsimopoulou, Kourkoveli, Tsiapras, Kyrzopoulos, Poulas, & Voudris, 2015; Lopez & Eissenberg, 2015; Marsot & Simon, 2015; Wagener et al., 2016).

To date, published switching studies involving tobacco cigarettes and e-cigarettes have reported mixed results. In a within-subjects study by van Staden, Groenewald, Engelbrecht, Becker, & Hazelhurst (2013), the cotinine levels of 13 smokers decreased significantly over a 2-week period following adoption of a first-generation e-cigarette device. A similar study by McRobbie, Phillips, Goniewicz, Myers Smith, Knight-West, Przulj, & Hajek (2015) examined cotinine levels in a group of 33 smokers following use of a first-generation product for 1 month. Although cotinine levels among the full sample decreased significantly over the study period,

subgroup analyses comparing those participants who did not manage to stop smoking at follow-up (dual users) to those participants who were able to stop smoking at follow-up (abstainers) revealed important differences. Specifically, cotinine levels decreased among dual users, who had significantly higher baseline cotinine levels compared to abstainers, whereas cotinine levels remained stable among abstainers (McRobbie et al., 2015). Findings from two industry-sponsored studies similarly reported significant decreases in levels of cotinine and nicotine equivalents among smokers who switched to use of a Fontem Ventures first-generation device for 5 days (O'Connell, Graff, & D'Ruiz, 2016) and for 12 weeks (Cravo et al., 2016). In contrast, in a within-subjects study by Berg, Barr, Stratton, Escoffery, & Kegler (2014), 72 smokers using variable products over an 8-week period showed no marked changes in cotinine levels. Similarly, switching studies assessing dual use behaviour of smokers who adopted e-cigarettes have reported stable cotinine levels after 1 week of use (Meier, Wahlquist, Heckman, Cummings, Froeliger, & Carpenter, 2017) and after 8 months of use (Pacifici, Pichini, Graziano, Pellegrini, Massaro, & Beatrice, 2015). Finally, in a within-subjects study, 20 Polish smokers who adopted a pen-style M201 e-cigarette also showed stable levels of various nicotine metabolites (with the exception of nornicotine), following 2 weeks of use (Goniewicz et al., 2016). Taken together, these findings show that some smokers were able to successfully switch from tobacco cigarettes to e-cigarettes, compensating for nicotine via a new nicotine delivery product. In addition, it appears that baseline cotinine levels and the type of e-cigarette product used may partly determine whether this switch can be successfully completed.

1.4.5 Exposure to tobacco smoke constituents

Several studies examining the use of e-cigarettes in short, controlled sessions in the laboratory have shown that e-cigarettes do not deliver carbon monoxide to the user (Adriaens et al., 2014; Flouris et al., 2013; Vansickel, Cobb, Weaver, & Eissenberg, 2010; Wagener et al., 2016). Furthermore, it has been shown that exhaled carbon monoxide decreases over time, both among individuals who switch from use of tobacco cigarettes to use of e-cigarettes (Adriaens et al., 2014; Caponnetto et al., 2013; McRobbie et al., 2015; Pacifici et al., 2015; Polosa et al., 2014; van Staden et al., 2013; Goniewicz et al., 2016; Litt, Duffy, & Oncken, 2016), and among individuals who switch from use of tobacco cigarettes to dual use of tobacco cigarettes and e-cigarettes (McRobbie et al., 2015; Pacifici et al., 2015). Similar findings have been reported by industry-sponsored studies (Cravo et al., 2016; O'Connell et al., 2016).

Few studies have examined exposure to tobacco smoke constituents other than carbon monoxide. A study by Hecht and colleagues (2015) examined exposure to PAHs in exclusive e-cigarette users versus two samples of tobacco cigarette users. Comparisons showed that levels of a PAH biomarker, 1-hydroxypyrene (1-HOP), were significantly lower in e-cigarette users than in both samples of tobacco cigarette smokers, and furthermore, were similar to levels found in non-smokers (Hecht et al., 2015). To date, two studies examining smokers' switch to use of e-cigarettes have examined levels of 1-HOP. In an industry-sponsored study, O'Connell and colleagues (2016) reported significant decreases in levels of 1-HOP among clinically-confined subjects who switched to exclusive use of e-cigarettes, dual use, or who gave up tobacco and nicotine products entirely. Finally, Goniewicz and colleagues (2016) examined eight PAH biomarkers among smokers who used e-cigarettes for two weeks. The authors reported mixed findings, with some PAH biomarkers showing a significant decline, and others – including 1-HOP – showing no significant change. Goniewicz and colleagues (2016) note that these observed trends may have differed between participants who continued to smoke tobacco cigarettes and those who quit entirely, although their ability to formally examine such differences was limited by the small number of study participants.

Another key constituent of tobacco smoke that has been studied is NNAL [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol], a metabolite of the TSNA NNK [4-(metylnitrosamino)-1-(3-pyridyl)-1-butanone]. Comparative analyses have shown significantly lower levels of NNAL in samples of e-cigarette users as compared to samples of tobacco cigarette smokers (Hecht et al., 2015; Shahab et al., 2017), as well as compared to samples of dual users of tobacco cigarettes and e-cigarettes (Shahab et al., 2017). Similar findings were reported for comparisons between a group of exclusive tobacco cigarette smokers and two groups of e-cigarette users, with no difference in NNAL levels between the two groups of e-cigarette users (Wagener et al., 2016). In addition, both independent and industry-sponsored switching studies have shown that levels of NNAL declined significantly following abstinence from tobacco cigarettes (Cravo et al., 2016; Goniewicz et al., 2016; O'Connell et al., 2016).

1.4.6 Nicotine withdrawal

Studies examining use of e-cigarettes among smokers in short, controlled sessions in the laboratory have shown that e-cigarettes effectively reduce cravings for cigarettes (Adriaens et al.,

2014; Bullen, McRobbie, Thornley, Glover, Lin, & Laugesen, 2010; D'Ruiz, Graff, & Robinson, 2016; Vansickel et al., 2010; Walele, Sharma, Savioz, Martin, & Williams, 2016). Interestingly, these studies have used various e-cigarette products, including first- and second-generation devices, suggesting that these products' ability to reduce cravings may only partly depend on their ability to deliver nicotine.

In contrast, findings from real-world studies of the effects of e-cigarettes on nicotine withdrawal have been mixed. Switching studies involving smokers taking up first-generation (Meier et al., 2017) and second-generation (Wagener et al., 2014) e-cigarettes reported no significant changes in nicotine withdrawal symptoms following ad libitum use for one week. In contrast, in a switching study involving a sample of Polish smokers adopting an e-cigarette, Goniewicz and colleagues (2016) observed a statistically significant decline in nicotine withdrawal scores over a two-week period. Similarly, in an industry-sponsored parallel group study comparing smokers who switched to e-cigarettes with smokers who continued smoking their usual brand of tobacco cigarettes, subjects in both groups showed a steady decrease in cravings throughout the 12-week study, with no significant differences between the two groups (Cravo et al., 2016). Unfortunately, although the two randomized controlled trials of e-cigarettes (Bullen et al., 2013; Caponnetto et al., 2013), as well as the observational study of smokers adopting e-cigarettes by McRobbie and colleagues (2015), examined symptoms of nicotine withdrawal among participants, these results have not been published.

1.4.7 Self-efficacy

To date, evidence regarding the effects of e-cigarettes on smokers' self-efficacy to quit smoking is limited to two studies in which smokers switched to use of e-cigarettes for one week periods (Meier et al., 2017; Wagener et al., 2014). In the study by Meier and colleagues (2017), no significant change in smokers' confidence to quit smoking was reported. The authors speculate that this may be due to limited substitution of e-cigarettes for tobacco cigarettes, as evidenced by the lack of apparent change in smoking behaviours among their study participants following adoption of a first-generation e-cigarette, either with or without nicotine (Meier et al., 2017). In the study by Wagener and colleagues (2014), participants reported a significant increase in readiness to quit smoking, but not in confidence to quit smoking, during ad libitum use of e-cigarettes.

1.4.8 Perceived health and subjective effects

To date, the use of e-cigarettes has been associated with few adverse events. Following acute exposure, only mild adverse events have been reported, the most common of which included mouth and throat irritation, as well as cough (Bullen et al., 2010; O'Connell et al., 2016; Walele et al., 2016). In studies examining exposure over longer periods of time, and in observational studies reporting on regular use in real-life settings, reporting of adverse events has been similarly low, with no reports of serious adverse events related to e-cigarette use (Adriaens et al., 2014; Caponnetto et al., 2013; Cravo et al., 2016; McRobbie et al., 2015). Furthermore, studies of smokers switching to use of e-cigarettes have showed progressive decreases in the occurrence of negative effects commonly reported by smokers, including cough, dry mouth, chest tightness, shortness of breath, throat irritation, and headache (Caponnetto et al., 2013; Cibella et al., 2016; Polosa et al., 2014; van Staden et al., 2013; Goniewicz et al., 2016). Positive effects reported by users of e-cigarettes include: less cough and phlegm, improved breathing, improved taste and smell, increased appetite, and improved ability to exercise (Adriaens et al., 2014; Berg et al., 2014; van Staden et al., 2013).

1.5 Policy context

In Canada, e-cigarettes containing nicotine are regulated as drug delivery devices under the federal *Food and Drugs Act* (Health Canada, 2009a). E-cigarettes containing nicotine, with or without a health claim, require market authorization from Health Canada before they can be imported, marketed, or sold. To date, no such product has received market approval; therefore, e-cigarettes containing nicotine are prohibited in Canada. In contrast, e-cigarettes that do not contain nicotine and do not make health claims can be legally bought and sold. Health Canada has issued public advisories against the use of e-cigarettes, as these products "may pose health risks and have not been fully evaluated for safety, quality, and efficacy" (Health Canada, 2009b).

Despite restrictions on the sale of nicotine, evidence has shown that nicotine-containing e-cigarettes are accessible to Canadians. Although Health Canada has overseen seizures of such products at the border and has sent letters to retailers in violation of these regulations (Standing Committee on Health, 2015), the overall enforcement of these regulations appear weak. Research evidence shows that in addition to accessible online retail outlets, consumers may purchase nicotine-containing e-cigarettes in specialty 'vape' shops, which are operating openly in several

cities across the country (Hammond et al., 2015). Furthermore, population surveys have shown that Canadians of various ages use nicotine-containing e-cigarettes. For instance, among the 15% of Ontario high school students who reported ever using e-cigarettes in the 2013 Ontario Student Drug Use and Health Survey, approximately one-third (28%) had used e-cigarettes with nicotine (Hamilton et al., 2015). In addition, according to national CTADS data, nearly one-half (48%) of respondents who had used an e-cigarette reported that the last one they used contained nicotine (Reid et al., 2017).

In light of this situation and growing debate concerning these products (Miller, 2014), the Canadian House of Commons Standing Committee on Health held hearings on the subject. In March 2015, the Committee released a report highlighting recommendations for the regulation of e-cigarettes under a new, unique legislative framework that would include both e-cigarettes with and without nicotine, requiring various safety standards, prohibiting the use of e-cigarettes in public spaces, and restricting the promotion and accessibility of e-cigarettes to youth. In addition, the Committee recommended continued support for independent research regarding these products and their use among the Canadian population (Standing Committee on Health, 2015). Furthermore, several provinces, including British Columbia, Manitoba, Newfoundland and Labrador, New Brunswick, Nova Scotia, Ontario, Prince Edward Island, and Quebec, have developed policies for the sale, marketing and use of both nicotine- and non-nicotine-containing e-cigarettes (Province of British Columbia, 2015; Province of Manitoba, 2015; Province of Newfoundland and Labrador, 2016; Province of New Brunswick, 2015; Province of Nova Scotia, 2014; Province of Ontario, 2015; Province of Prince Edward Island, 2015; Province of Quebec, 2015). In addition, in response to the Standing Committee's report, federal legislation has been introduced in the Senate to amend the *Tobacco Act* and the *Non-smokers' Health Act* in order to regulate the manufacture, sale, labelling, promotion, and use of vaping products (Parliament of Canada, 2016).

1.6 Study rationale and research questions

The current study seeks to fill several critical evidence gaps regarding dual users' behaviours and exposure to nicotine and tobacco smoke constituents. Despite the fact that a majority of the e-cigarette-using population in Canada are dual users (Reid et al., 2017), scarcely anything is known about the way in which dual users use both tobacco cigarettes and e-cigarettes. The

current study will be the first to examine detailed patterns of use and perceptions of tobacco cigarettes and e-cigarettes among Canadian dual users, including frequency and consumption of product use, types of products used, product perceptions, reasons for product use, and settings in which products are used. Due to the fact that Canada has a distinct regulatory framework on e-cigarettes as well as a unique e-cigarette market, context-specific evidence regarding the behaviour of individuals who use such products is needed to inform policy.

The current study will also contribute to the evidence base regarding dual users' exposure to nicotine and tobacco smoke constituents, while addressing some of the limitations of published switching studies in the literature. First, many published studies have examined outdated devices suspected of poorly delivering nicotine (McRobbie et al., 2015; van Staden et al., 2013). Second, most study participants have been completely or partially naïve to e-cigarette use (Berg et al., 2014; McRobbie et al., 2015; Pacifici et al., 2015; Goniewicz et al., 2016), which may have implications for uptake and proper use of e-cigarettes, given the 'learning curve' that is at times needed to adjust to these devices (McQueen, Tower, & Sumner, 2011). Furthermore, in only one study were participants allowed to select their e-cigarette flavour and nicotine concentration (Pacifici et al., 2015), despite evidence supporting the selection of such product characteristics by e-cigarette users as highly important (Farsalinos, Romagna, Tsiapras, Kyrzopoulos, Spyrou & Voudris, 2013; Farsalinos et al., 2015b). Although placing restrictions on e-cigarette user and/or product characteristics may enhance the internal validity of study designs, such designs fail to capture realistic interactions between e-cigarette users and their devices, and as a result, are limited in their generalizability to user populations and products in today's market. Finally, published switching studies have been limited in their examination of a single product change, reflecting the potential risk of participants in two distinct states; of these, just two studies have explicitly examined the potential risks of dual users (McRobbie et al., 2015; Pacifici et al., 2015). Thus, a critical evidence gap involves examination of biomarkers of exposure across all conditions of use relating to tobacco cigarettes and e-cigarettes.

Finally, the current study will provide evidence to inform the debate regarding the public health impact of e-cigarettes. Given the critical role played by smoking topography in determining nicotine uptake and risk exposure, compensatory behaviour in the context of e-cigarette use carries important implications for public health. First, whether or not individuals exhibit

compensatory behaviour when using e-cigarettes may shed light on the potential of e-cigarettes to serve as an effective substitute for tobacco cigarettes. In other words, if individuals are able to compensate for nicotine by using e-cigarettes, these products may have the potential to replace tobacco cigarettes as a 'cleaner' source of nicotine. Second, the extent to which individuals using e-cigarettes exhibit compensatory behaviour will impact their exposure to constituents present in tobacco smoke. Thus, by examining dual users' product use behaviours and exposure to nicotine and tobacco smoke constituents, the current study will provide evidence to delineate some of the potential negative and positive effects e-cigarettes may have on public health.

The current study will examine the following specific research questions:

Research question 1: What patterns of use and perceptions of tobacco cigarettes and e-cigarettes are exhibited or held by dual users?

Research question 2: Is compensatory behaviour for nicotine exhibited among dual users when they switch from dual use to exclusive use of either tobacco cigarettes or e-cigarettes?

Research question 3: Is exposure to tobacco smoke constituents reduced among dual users when they switch from dual use to: exclusive use of tobacco cigarettes, exclusive use of e-cigarettes, or use of neither product?

Research question 4: Do cravings or self-efficacy change among dual users when they switch from dual use to: exclusive use of tobacco cigarettes, exclusive use of e-cigarettes, or use of neither product?

Research question 5: Does perceived health change among dual users when they switch from dual use to: exclusive use of tobacco cigarettes, exclusive use of e-cigarettes, or use of neither product?

2 METHODS

2.1 Study design

An un-blinded within-subjects experiment was conducted with a sample of adult (18+ years) dual users of tobacco cigarettes and e-cigarettes in Kitchener-Waterloo and Toronto, Ontario. Participants completed three consecutive seven-day periods in which the use of tobacco cigarettes and e-cigarettes was experimentally manipulated.

2.2 Study protocol

2.2.1 Recruitment

Study participants were recruited from September 2015 through March 2016 via advertisements using various media channels. Vape shops located in Kitchener-Waterloo, Guelph, Cambridge, and Toronto, were identified and contacted for assistance with recruitment. Shops that agreed to assist with recruitment were asked to do one or more of the following: post flyers in their stores; distribute flyers to their customers; post flyers online on their websites and/or blogs; and share flyers online via their email distribution list. Research staff also recruited potential participants by approaching vape shop customers as they exited the shops. Study advertisements were placed in local newspapers, including 'The Chronicle' and 'The Record' in Kitchener-Waterloo, as well as '24 Hours' and 'Metro' in Toronto. Online advertisements were also posted on Kijiji, Craig's List, Facebook, and Reddit. A sample recruitment flyer and advertisement are included in Appendix A.

2.2.2 Eligibility

A brief telephone screener was used to assess the eligibility of potential participants. In order to participate in the study, potential participants must have met the following criteria:

- Be 18 years of age or older
- Be able to read and understand English
- Have access to the internet on a daily basis
- Be a current cigarette daily smoker and smoke a minimum of five cigarettes per day
- Not have serious intentions to quit smoking in the next six months
- Be a current daily e-cigarette user

- Not have used other tobacco products, such as kreteks, bidis, cigars, pipe tobacco, smokeless tobacco or hookah/waterpipe in the past seven days
- Not have used any nicotine replacement therapy products, such as the patch, gum, inhaler or lozenges in the past seven days
- Not have used any medications, such as 'Zyban', 'Wellbutrin', or 'Champix' to help them quit smoking in the past seven days
- Not have participated in any group or individual counselling programs to help them quit smoking in the past seven days
- Not have ever experienced serious cardiac arrhythmias (tachycardia) or severe or worsening angina pectoris (chest pain)
- Not have had a heart attack or stroke within the last three months
- Not have had cancer within the last year
- Not have asthma, chronic obstructive pulmonary disease (COPD), a seizure disorder, or any life-threatening medical conditions with a prognosis of less than a year
- Not have a history of psychosis, schizophrenia, bipolar disorder, or suicidal thoughts, and
- Be available for four weekly visits over a three-week period.

Research staff provided eligible participants with an overview of the study protocol and answered any questions. Eligible participants who indicated they were interested in participating in the study were asked for their contact information and had their study visits scheduled in either Kitchener-Waterloo or Toronto.

2.2.3 Study conditions and experimental groups

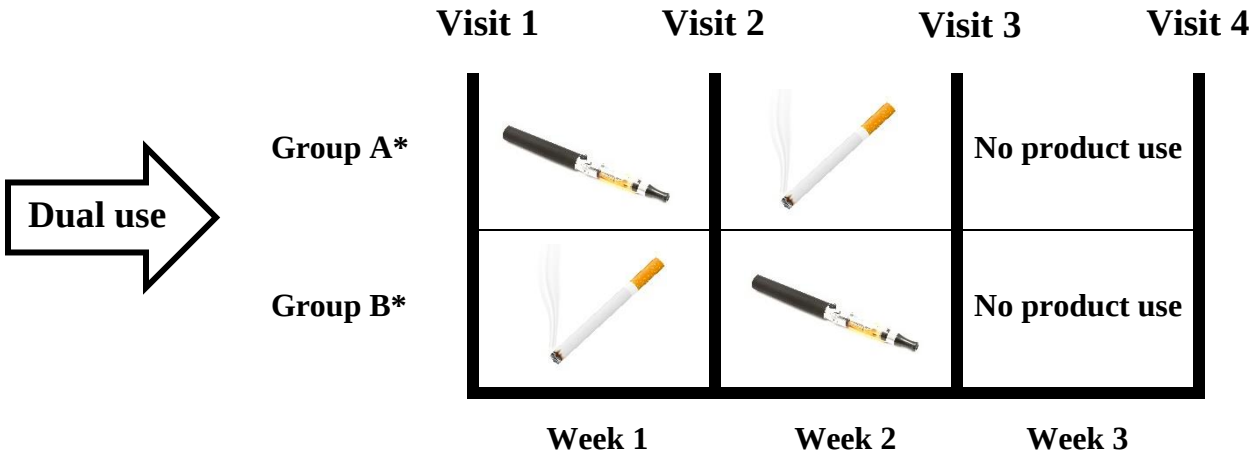
A depiction of the study design is presented in Figure 2. Participants completed three consecutive seven-day periods in which the use of tobacco cigarettes and e-cigarettes was experimentally manipulated:

- **Condition 1:** Baseline behaviour of dual use of tobacco cigarettes and e-cigarettes;
- **Condition 2:** Exclusive use of tobacco cigarettes;
- **Condition 3:** Exclusive use of e-cigarettes; and
- **Condition 4:** Use of neither tobacco cigarettes nor e-cigarettes.

To control for order effects, the order in which participants experienced the study conditions was randomized. Participants were randomly assigned to one of two condition orders, consisting of pre-defined sequences of product use:

- **Group A:** Participants were permitted to use e-cigarettes in Week 1, and tobacco cigarettes in Week 2; or
- **Group B:** Participants were permitted to use tobacco cigarettes in Week 1, and e-cigarettes in Week 2.

Figure 2: Study design



Notes:
* Study participants were randomized to one of two condition orders (Group A or Group B).

Seven-day study periods were used to ensure sufficient time for any changes in smoking and vaping behaviours to stabilize following a switch to a new behaviour (Hammond et al., 2005) and to account for the half-life and clearance rates of the most of the assessed biomarkers (described below). During each of the first two weeks of the study, participants were instructed to use the permitted product as desired, but to abstain from using the alternate product. During the final week of the study, all participants were asked to abstain from using both tobacco cigarettes and e-cigarettes. In order to assist participants in abstaining from both products in the final week of the study, they were provided with links to online smoking cessation resources developed by Health Canada and the Ontario Ministry of Health and Long-Term Care. For the

duration of the study, participants were also asked not to use alternative tobacco products (such as kreteks, bidis, cigars, pipe tobacco, smokeless tobacco or hookah/waterpipe), nicotine replacement therapy products (such as the patch, gum, inhaler or lozenges), smoking cessation medications (such as 'Zyban', 'Wellbutrin', or 'Champix'), or participate in individual or group counseling for smoking cessation. For the duration of the study, participants were not 'blinded' to the products they used, and were permitted to use any types of tobacco cigarettes and/or e-cigarettes they wished.

2.2.4 Study visits

Eligible participants were asked to attend four one-hour visits in Kitchener-Waterloo or Toronto: at baseline and after each of the three 7-day periods. At each study visit, participants were asked to complete a questionnaire regarding their smoking and vaping behaviours, and provide samples of exhaled breath and urine. Visit questionnaires were approximately 20 minutes in length and were completed using an iPad. Participants were asked to provide a 'spot' urine sample, which was frozen at -20°C immediately afterwards. Participants were also asked to provide two exhaled breath samples, which were measured using Bedfont Micro 4 Smokerlyzer and piCO+ Smokerlyzer machines (Bedfont Scientific Ltd.). Additional items and procedures at Visit 1 included: review of a study information sheet, and provision of informed consent. At Visits 1-3, participants were provided with instructions for the subsequent week, corresponding to their assigned group. Finally, at Visit 4, participants were provided with a study feedback letter, and thanked for participating in the study.

2.2.5 Daily diaries

Participants were asked to complete a 5-minute online daily diary about their consumption of tobacco cigarettes and e-cigarettes at the end of each day of the study. Links to the online daily diaries were emailed to each participant on the morning of each day by research staff.

2.2.6 Remuneration

In appreciation of their participation in the study, participants received a total of $295: $50 after Visit 1, $70 after Visit 2, $75 after Visit 3, and $100 after Visit 4.

2.2.7 Ethics clearance

This study was reviewed by and received clearance from the University of Waterloo Office of Research Ethics (ORE #20735). At Visit 1, research staff provided all potential participants with

an information letter about the study, reviewed all study activities, and answered any questions. Potential participants were then asked to provide written informed consent to acknowledge their agreement to participate in the study. Participant confidentiality was maintained by assigning each participant a unique identification number and keeping all collected data in a secure database. A copy of the study information letter and informed consent form are included in Appendix B.

2.3 Study measures

Sample copies of the study questionnaires are included in Appendix C. Measures drawn and/or adapted from the literature were used whenever possible. In some instances, the research team developed questionnaire items for several dimensions of vaping behaviour, due to the fact that there are few standardized behavioural assessments for this emerging behaviour.

2.3.1 Eligibility criteria and sociodemographic characteristics

Current daily smokers of tobacco cigarettes were defined as individuals who had smoked at least 100 tobacco cigarettes in their lifetime, had smoked a tobacco cigarette in the past 30 days, and reported smoking tobacco cigarettes every day. *Current daily users of e-cigarettes* were defined as individuals who had used an e-cigarette in the past 30 days, had used an e-cigarette at least once a day for each of the past seven days, and reported using e-cigarettes every day. Participants who qualified as current daily tobacco cigarette smokers and current daily e-cigarette users were termed **dual users** for the purposes of this study. Sociodemographic information included self-reported *age*, *gender*, *education*, and *ethnicity*.

2.3.2 Smoking behaviours

Participants' *smoking history* was evaluated by asking how long they had been smoking tobacco cigarettes daily. Validated measures of participants' *daily consumption of tobacco cigarettes* and *time to first tobacco cigarette* were collected on the basis of each day as well as for each study week. In addition, participants' *time since last tobacco cigarette* was collected for each day in the study. Data regarding participants' *usual brand of tobacco cigarettes* was also collected.

Participants were asked to indicate *where they smoked tobacco cigarettes* for each study week (at home, at school or work, at a restaurant or bar, in a vehicle, while walking on the street, in a park or other outdoor venue, or some other place). Those who indicated that they had smoked tobacco

cigarettes at home, at school or work, or at a restaurant or bar, were asked a follow-up question as to whether they had *smoked tobacco cigarettes indoors, outdoors, or both indoors and outdoors* for each of these designated places.

Validated measures were used to examine participants' *intentions to quit smoking*, as well as the *number of past quit attempts* and *length of time since their most recent quit attempt* (for tobacco cigarettes). Participants who indicated that they had any intentions to quit were asked whether they would *use a quit aid*, including a nicotine patch, gum, or lozenge; an e-cigarette; or prescription medication (e.g., 'Zyban', 'Champix').

2.3.3 Vaping behaviours

Participants' *vaping history* was evaluated by asking how long they had been using e-cigarettes daily. Validated measures of cigarette consumption were adapted to the behaviour of e-cigarette use, including: *number of times participants used an e-cigarette (bouts)*, *average number of puffs taken per bout*, and *average duration of use per bout*. In addition, participants' *time to first e-cigarette* and *time since last e-cigarette* were collected, mirroring measures for tobacco cigarettes. Measures of e-cigarette consumption and time to first e-cigarette were collected on the basis of each day as well as for each week in the study, while participants' time since last e-cigarette was collected for each study day.

Several measures were used to collect information regarding characteristics of e-cigarette products used for each week in the study, including: *flavours of e-cigarettes/e-liquids* used (tobacco, menthol/mint, spice, candy, fruit, coffee/drinks/alcohol, other); *type of e-cigarette(s)* used (a disposable e-cigarette, an e-cigarette that uses replaceable pre-filled cartridges, or an e-cigarette that is re-chargeable and has a tank or reservoir that you fill with liquid); and the *brand(s) of e-cigarettes/e-liquids* used. To assess the *nicotine content of e-cigarettes/e-liquids*, participants were asked to indicate whether they had used only e-cigarettes with nicotine, only nicotine-free / non-nicotine e-cigarettes, or some e-cigarettes with nicotine and some nicotine-free / non-nicotine e-cigarettes. Participants who indicated that they had used e-cigarettes containing nicotine were asked to indicate the *concentration/strength of nicotine in their e-cigarettes/e-liquids*.

Participants were asked to indicate *where they used e-cigarettes* for each week in the study (at home, at school or work, at a restaurant or bar, in a vehicle, while walking on the street, in a park

or other outdoor venue, or some other place). For those who indicated that they had used e-cigarettes at home, at school or work, or at a restaurant or bar, they were asked a follow-up question as to whether they had *used e-cigarettes indoors, outdoors, or both indoors and outdoors* for each of these designated places.

Participants' reasons for use of e-cigarettes were examined with respect to the *reason(s) they began to use e-cigarettes daily*, and the *reason(s) they currently use e-cigarettes*. For each of these measures, participants were asked to indicate *all reasons* that applied to them from a list, as well as to select one reason as *the most important reason* for their decisions.

Validated measures for quitting smoking were adapted to the behaviour of e-cigarette use, including: *intentions to quit using e-cigarettes*, as well as the *number of past quit attempts* and *length of time since their most recent quit attempt* (for e-cigarettes).

2.3.4 Nicotine dependence

Nicotine dependence or addiction has been characterized as a cluster of several symptoms, including the following primary criteria: highly controlled or compulsive use, psychoactive effects, and drug-reinforced behavior. Additional criteria include: addictive behavior, often involving stereotypic patterns of use, use despite harmful effects, relapse following abstinence, and recurrent drug cravings; and the observation that dependence-producing drugs often produce tolerance, physical dependence, and pleasant effects (USDHHS, 2010).

Nicotine dependence was measured using the Fagerström Test for Cigarette Dependence (FTCD) and the Nicotine Dependence Syndrome Scale (NDSS). The FTCD is a validated six-item instrument used to measure behavioral and physiological aspects of addiction. The FTCD is a unidimensional measure that shows limited internal consistency, adequate test-retest reliability, modestly correlates with key biomarkers (including levels of carbon monoxide, nicotine, and cotinine), and is a predictor of withdrawal symptoms and successful smoking cessation (Heatherton, Kozlowski, Frecker & Fagerström, 1991; USDHHS, 2010; Fagerström, 2012). The FTCD's first item – time to first cigarette – is a strong predictor of smoking cessation (USDHHS, 2010; Fagerström, 2012).

The NDSS is a valid 19-item instrument used to provide a multidimensional measure of nicotine dependence (Shiffman, Waters, & Hickcox, 2004). The NDSS provides an overall score of

nicotine dependence, as well as five subscale scores relating to: drive (craving and withdrawal, withdrawal avoidance, and subjective compulsion to smoke), priority (preference for smoking over other reinforcers), tolerance (reduced sensitivity to the effects of smoking), continuity (regularity of smoking rate), and stereotypy (invariance of smoking or rigid patterns of tobacco use). The NDSS shows moderate to strong internal consistency, and modest to strong test-retest reliability. In addition, NDSS scores have been associated with number of cigarettes smoked, difficulty in abstaining, and severity of past withdrawal symptoms among smokers who have not quit, while among treatment-seeking smokers, NDSS scores have predicted urges during smoking and during abstinence, acute withdrawal symptoms, and cessation outcome (Shiffman, Waters, & Hickcox, 2004; USDHHS, 2010).

Both measures of nicotine dependence were adapted for e-cigarette use (E-FTCD and E-NDSS, respectively), by substituting the words/phrase 'smoke cigarettes' with 'use e-cigarettes'. All four instruments were used to assess participants' nicotine dependence at baseline. Similar measures for e-cigarettes have been used previously in studies of e-cigarette users (Etter & Eissenberg, 2015; Rass et al., 2015).

2.3.5 Nicotine withdrawal

The brief, 10-item version of the Questionnaire of Smoking Urges (QSU-Brief) is a valid measure of urges and cravings to smoke (Cox, Tiffany, & Christen, 2001). The QSU-Brief provides an overall score reflecting cravings to smoke, as well as scores for two factors that represent distinct expressions of craving: one represents a desire and intention to smoke with smoking perceived as rewarding (Factor 1), while the other represents an anticipation of relief from negative affect with an urgent desire to smoke (Factor 2) (Cox, Tiffany, & Christen, 2001). The QSU-Brief was also adapted to the behaviour of e-cigarette use (E-QSU-Brief), by substituting the words/phrase 'smoke cigarettes' with 'use e-cigarettes'. Given the centrality of cravings to continued cigarette use and relapse (USDHHS, 2010), the QSU-Brief and the E-QSU-Brief were used to evaluate participants' cravings for tobacco cigarettes and e-cigarettes at baseline and following each week in the study.

2.3.6 Self-efficacy

The Smoking Self-Efficacy Questionnaire (SEQ-12) is a valid and reliable 12-item scale used to measure current and former smokers' confidence in their ability to abstain from smoking when

facing internal and external stimuli or barriers (Etter, Bergman, Humair, & Perneger, 2000). Participants are asked to state how sure they are that they could refrain from smoking in various situations. The SEQ-12 consists of two six-item factors, representing internal stimuli (e.g., feeling depressed) and external stimuli (e.g., being with other smokers). The SEQ-12 was also adapted to the behaviour of e-cigarette use (E-SEQ-12), by substituting the words/phrase 'smoke cigarettes' with 'use e-cigarettes'. Both the SEQ-12 and the E-SEQ-12 scales were be applied at baseline and following each week in the study.

2.3.7 Dual use behaviours

Several additional measures were constructed in order to acquire more detail regarding dual use behaviours. First, in order to ascertain the *temporality of dual use behaviours*, participants were asked to indicate which behaviour they began first: smoking cigarettes or using e-cigarettes. Next, dual users were asked which behaviour (smoking cigarettes or using e-cigarettes) they identify with more, as a way of eliciting their *perceived identity with respect to dual use behaviours*. Among those who indicated that they began smoking cigarettes before using e-cigarettes, *change in their daily cigarette consumption* was inferred by asking, "Since you started using e-cigarettes daily, have you changed the amount you use per day?", with response options 'I smoke fewer cigarettes', 'I smoke the same amount of cigarettes', or 'I smoke more cigarettes'.

In addition, *change in participants' daily consumption of e-cigarettes* and *change in the strength of nicotine most commonly used by participants* were examined using the following questions: "Since you started using e-cigarettes daily, have you changed the amount you use per day?", with response options on a bipolar five-step Likert scale ranging from "I use much more" to "I use much less"; and "Since you started using e-cigarettes daily, have you changed the strength of nicotine that you use most?", with response options 'I increased the strength', 'no change in strength', or 'I decreased the strength'. Participants' *perceived addiction to each product* were evaluated using the question: "Do you consider yourself addicted to regular tobacco cigarettes / e-cigarettes?", with response options 'not at all', 'somewhat addicted', or 'very addicted'. Finally, in order to measure participants' *perceived smoking cessation efficacy of e-cigarettes*, participants were asked to indicate whether they thought using e-cigarettes would make it easier to quit smoking cigarettes, with response options 'not at all', 'a little', or 'a lot'.

2.3.8 Perceptions of e-cigarettes

Several questions elicited participants' attitudes of e-cigarettes relative to tobacco cigarettes. The measures used the question stem "Compared to smoking regular tobacco cigarettes, using e-cigarettes is…", and required participants to evaluate the *relative social acceptability, satisfaction, pleasure, harm, and affordability* of e-cigarettes compared to tobacco cigarettes, using bipolar five-step Likert scales (e.g., '... a lot less socially acceptable', 'a little less socially acceptable', 'equally as socially acceptable', 'a little more socially acceptable', or 'a lot more socially acceptable').

2.3.9 Perceived health and subjective effects

Several measures about lung function and breathing were included in the questionnaires. The measures asked participants to reflect on any changes they may have experienced in the past seven days, answering with the responses 'worse than usual', 'no difference', or 'better than usual'. Respiratory health measures asked about any changes in: *experiencing shortness of breath*, *frequency of experiencing cough*, *frequency of experiencing cough with phlegm*, *sounds emanating from the chest*, and *an overall description of lung function*.

Participants were asked a few additional questions about their perceived overall health following each study condition. First, in order to assess participants' *perceived overall health*, they were asked, "In the past seven days, have you noticed any change in your overall health status as a result of not [smoking cigarettes / using e-cigarettes]?", with the following response options: 'worse than usual', 'no difference', 'better than usual'. Second, participants' *negative or positive effects* were examined by asking those who indicated 'worse than usual' or 'better than usual' to explain any negative or positive effects they had experienced in the past week, respectively (open-ended response).

Participants were asked a few questions that prompted them to think about their experiences following each study condition. First, participants' *perceived addiction* was evaluated for each product by asking "Do you consider yourself addicted to [tobacco cigarettes / e-cigarettes]?", with the following response options: 'not at all', 'somewhat addicted', and 'very addicted'. Second, in order to evaluate participants' *perceived difficulty in abstaining from using a particular product*, participants were asked, "Over the past seven days, how easy or difficult was

it to go without [smoking cigarettes / using e-cigarettes]?", indicating their response using a bipolar five-step Likert scale with response options ranging from 'very easy' to 'very difficult'.

An overview of the measures included in each of the study questionnaires is provided in Table 1. Sample copies of the study questionnaires are included in Appendix C.

Table 1: Study questionnaires and measures

Measures	Visit 1 Questionnaire	Visit 2 Questionnaire	Visit 3 Questionnaire	Visit 4 Questionnaire	Daily Diary
Eligibility criteria and sociodemographic information	X				
Smoking and vaping behaviours	X	X	X	X	X[1]
Nicotine dependence [(E-)FTCD; (E-)NDSS]	X				
Nicotine withdrawal [(E-)QSU]	X	X	X	X	
Self-efficacy [(E-)SEQ-12]	X	X	X	X	
Perceptions of e-cigarettes	X	X	X	X	
Perceived health and subjective effects	X	X	X	X	

Notes:
[1] Questions anchored to time frame of one day, rather than a period of one week.

2.3.10 Biomarkers of exposure

Biomarkers of exposure measure the presence of a tobacco or tobacco smoke constituent or their metabolites in the body. Measurement of biomarkers in bodily fluids can be used to quantify exposure to specific substances in various settings, with greater accuracy than can be achieved by self-reported data (WHO, 2007). Several biomarkers of exposure were examined in the current study, as described below.

Carbon monoxide was measured in participants' exhaled breath samples to provide an indication of uptake of tobacco smoke constituents. Given its elimination half-life of approximately four hours, carbon monoxide is a short-term measure of exposure (WHO, 2007). Carbon monoxide is widely used in tobacco research to distinguish smokers from non-smokers: exhaled air carbon monoxide levels of ≥ 8-10 parts per million (ppm) are typically used to identify smokers (SRNT Subcommittee on Biochemical Verification, 2002).

Urinary concentration of *cotinine*, a major proximate metabolite of nicotine, was measured to provide an indication of exposure to nicotine from tobacco smoke. The elimination half-life of urinary cotinine among smokers has been estimated as 16 hours upon smoking cessation (Haley, Sepkovic, & Hofmann, 1989; WHO, 2007). Cotinine is the most widely used biomarker of exposure to nicotine from tobacco smoke, and can also be used to distinguish smokers from non-smokers: urinary cotinine levels of ≥ 50 ng/mL are typically used to identify smokers (SRNT Subcommittee on Biochemical Verification, 2002).

Urinary concentration of *1-hydroxypyrene* (1-HOP) was measured to provide an indication of carcinogen exposure, specifically with respect to exposure to polycyclic aromatic hydrocarbons (PAHs). 1-HOP is the major urinary metabolite of pyrene, a non-carcinogenic component of all PAH mixtures (Hecht, 2002). 1-HOP has a half-life of approximately 19 hours, although estimates vary between 4 and 48 hours (Brandt & Watson, 2003). 1-HOP was examined as a complementary biomarker of tobacco smoke exposure, given that levels of PAHs may not change in similar proportion to levels of other tobacco smoke constituents, and because individuals may be exposed to PAHs from other environmental sources, such as grilled meats (WHO, 2007). Non-smokers are characterized by low levels of PAH exposure, typically at or below 1.4 μmol/mol creatinine, while levels among smokers are approximately 5 times higher (Brandt & Watson, 2003).

Urinary concentration of *NNAL* [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol] was measured at baseline to provide an indication of exposure to the tobacco-specific carcinogen NNK. NNAL (and its glucuronides) are metabolites of NNK, and can be readily detected in human urine (Hecht, 2002). NNAL is only slowly released from the human body after smoking cessation, with a half-life of approximately 40-45 days (Hecht et al., 1999). NNAL can be used to distinguish between smokers and non-smokers, given its high specificity with regard to smoking – detectable levels of NNAL are usually only found in the urine of non-smokers who have been exposed to environmental tobacco smoke. In the literature, levels of total NNAL less than 1 pmol/mL are rarely seen among smokers, whereas the highest levels in non-smokers exposed to environmental tobacco smoke are rarely greater than 0.4 pmol/mL (Hecht, 2002).

Creatinine is a waste product of muscle metabolism. Urinary creatinine measures are often used to adjust or correct for variability in the volume and concentration of urine in spot samples when measuring urinary concentrations of environmental and workplace chemicals or their metabolites (Barr et al, 2005). In the current study, levels of urinary biomarkers (cotinine, 1-HOP, NNAL) were adjusted for *creatinine* by dividing the analyte concentration by the creatinine concentration.

Validated methods were used by Roswell Park Cancer Institute (Buffalo, US) to analyze levels of urinary cotinine (Liang, 2015), urinary 1-HOP (Lankova, Urbancova, Sram, Hajslova & Pulkrabova, 2016), and urinary NNAL (Jacob et al., 2008).

2.3.11 Cognitive testing

A pilot test involving two individuals with a history of dual use was conducted at the University of Waterloo in July 2015. A brief protocol involving two visits to the laboratory and completion of three online questionnaires was used to test core components of the study protocol, including study questionnaires and collection of biological samples. Cognitive interviews were conducted to ensure that study questionnaires had clear instructions and measures. The two pilot participants were remunerated $100 each in appreciation of their participation in the pilot test.

2.4 Analysis

2.4.1 Sample characteristics

Characteristics of dual users were examined using descriptive statistics with respect to: age, sex, ethnicity, education, daily cigarette consumption, and nicotine dependence (using both measures of the FTCD and the NDSS, applied to both tobacco cigarettes and e-cigarettes).

2.4.2 Baseline patterns and perceptions of dual use

Baseline patterns of use of tobacco cigarettes and e-cigarettes, as well as perceptions of e-cigarettes, were examined using exploratory descriptive statistics, without formulation of specific *a priori* hypotheses.

2.4.3 Testing changes in continuous outcomes across study conditions

Changes in several key continuous outcomes were examined across study conditions. The distributions of each continuous outcome were visually examined for any violations from normality, and appropriate transformations were applied, as necessary. Previous research suggests that log transformations may be required for cotinine, 1-HOP, and NNAL values (e.g., Benowitz et al., 2012; Hammond & O'Connor, 2014). For each key outcome, means were computed at baseline and for each study condition. Repeated measures models (using the Linear Mixed Model function in SPSS) were constructed to examine mean differences for each key outcome across study conditions, while accounting for correlated measurements within subjects. Analyses were conducted using SPSS v.24 (Illinois, US) and p-values < 0.05 were considered statistically significant.

2.4.3.1 Exposure to nicotine and compensatory behaviour

Hypothesis 1a: Compared to baseline, consumption of tobacco cigarettes will be significantly higher in the study condition of exclusive use of tobacco cigarettes.

Changes in consumption of tobacco cigarettes were examined by examining changes in mean levels of reported tobacco cigarettes consumed per day in the condition of exclusive use of tobacco cigarettes and dual use at baseline. A repeated measures model was constructed with daily tobacco cigarette consumption as the outcome (Model 1). The model was examined with the following covariates: assigned condition order, and baseline nicotine dependence.

Hypothesis 1b: Compared to baseline, consumption of e-cigarettes will be significantly higher in the study condition of exclusive use of e-cigarettes.

Changes in consumption of e-cigarettes were examined by examining changes in mean levels of reported e-cigarettes consumed per day in the condition of exclusive use of e-cigarettes and dual use at baseline. A repeated measures model was constructed with daily e-cigarette consumption as the outcome (Model 2). The model was examined with the following covariates: assigned condition order, and baseline nicotine dependence.

Hypothesis 1c: Compared to baseline, levels of urinary cotinine will be significantly lower in the study condition of no product use.

Compensatory behaviour was evaluated by examining changes in mean levels of urinary cotinine between each study condition and dual use at baseline. A repeated measures model was constructed with urinary cotinine as the outcome (Model 3). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence, e-cigarette product type, and e-cigarette nicotine content.

2.4.3.2 Exposure to tobacco smoke constituents

Hypothesis 2a: Compared to baseline, levels of exhaled carbon monoxide will be significantly lower in study conditions of exclusive use of e-cigarettes, and of no product use.

Changes in biomarkers of tobacco smoke exposure were examined by comparing differences in mean levels of exhaled carbon monoxide between each study condition and dual use at baseline. A repeated measures model was constructed with exhaled carbon monoxide as the outcome (Model 4). The model was examined with the following covariates: assigned condition order.

Hypothesis 2b: Compared to baseline, levels of urinary 1-HOP will be significantly lower in study conditions of exclusive use of e-cigarettes, and of no product use.

Changes in biomarkers of tobacco smoke exposure were examined by comparing differences in mean levels of urinary 1-HOP (adjusted for urinary creatinine) between each study condition and dual use at baseline. A repeated measures model was constructed with urinary 1-HOP as the outcome (Model 5). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence, e-cigarette product type, and e-cigarette nicotine content.

Hypothesis 2c: Compared to baseline, levels of urinary NNAL will be significantly lower in study conditions of exclusive use of e-cigarettes, and of no product use.

Changes in biomarkers of tobacco smoke exposure were examined by comparing differences in mean levels of urinary NNAL (adjusted for urinary creatinine) between each study condition and dual use at baseline. A repeated measures model was constructed with urinary NNAL as the outcome (Model 6). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence, e-cigarette product type, and e-cigarette nicotine content.

2.4.3.3 Nicotine withdrawal

Hypothesis 3a: Compared to baseline, measures of nicotine withdrawal for tobacco cigarettes will be significantly higher in study conditions of exclusive use of e-cigarettes, and of no product use.

Changes in measures of nicotine withdrawal for tobacco cigarettes were examined by comparing differences in scores for the QSU between each study condition and dual use at baseline. A repeated measures model was constructed with QSU score as the outcome (Model 7). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence.

Hypothesis 3b: Compared to baseline, measures of nicotine withdrawal for e-cigarettes will be significantly higher in study conditions of exclusive use of tobacco cigarettes.

Changes in measures of nicotine withdrawal for e-cigarettes were examined by comparing differences in scores for the E-QSU between each study condition and dual use at baseline. A repeated measures model was constructed with E-QSU score as the outcome (Model 8). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence.

2.4.3.4 Self-efficacy

Hypothesis 4a: Changes in measures of self-efficacy for tobacco cigarettes will depend upon participants' condition order. Compared to baseline, measures of self-efficacy for tobacco cigarettes will be significantly higher in study conditions of exclusive use of e-cigarettes, and of no product use, among participants assigned to Group A; and measures of self-efficacy for tobacco cigarettes will be significantly higher in study conditions of exclusive use of tobacco

cigarettes, of exclusive use of e-cigarettes, and of no product use, among participants assigned to Group B.

Changes in measures of self-efficacy for tobacco cigarettes were examined by comparing differences in scores for the SEQ between each study condition and dual use at baseline. A repeated measures model was constructed with SEQ score as the outcome (Model 9). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence.

Hypothesis 4b: Compared to baseline, measures of self-efficacy for e-cigarettes will be significantly higher in study conditions of exclusive use of tobacco cigarettes, and of no product use.

Changes in self-efficacy for e-cigarettes were examined by comparing differences in scores for the E-SEQ between each study condition and dual use at baseline. A repeated measures model was constructed with E-SEQ score as the outcome (Model 10). The model was examined with the following covariates: assigned condition order, baseline nicotine dependence.

2.4.4 Testing changes in binary outcomes across experimental conditions

Changes in several binary outcomes were examined across study conditions, while accounting for correlated measurements within subjects. For each key outcome, the proportion of participants corresponding to each level of the binary ordinal outcome variables were computed at baseline and for each study condition. Repeated measures models (using the Generalized Linear Mixed Model function in SPSS) were constructed to examine differences in proportions across study conditions. Analyses were conducted using SPSS v.24 (Illinois, US) and p-values < 0.05 were considered statistically significant.

2.4.4.1 Perceived health

Hypothesis 5: Compared to baseline, a significantly greater proportion of participants will report better respiratory health (with respect to experiencing shortness of breath, frequency of experiencing cough, frequency of experiencing cough with phlegm, sounds emanating from the chest, and an overall description of lung function) in study conditions of exclusive use of e-cigarettes, and of no product use.

Changes in perceived respiratory health were examined with respect to five domains: experiencing shortness of breath, frequency of experiencing cough, frequency of experiencing cough with phlegm, sounds emanating from the chest, and an overall description of lung function. Each outcome was modeled as a binary variable (0='worse than usual health' or 'no difference in health'; 1='better than usual health'). Generalized linear mixed models were constructed to test for differences in the proportion of participants who reported better than usual health (compared to those who did not) between each study condition and dual use at baseline, for each of the five domains listed above (Models 11-15). The models were examined with the following covariate: assigned condition order.

2.4.5 Power calculations

Prior to the study, power calculations were conducted for two representative tests: differences in biomarker levels and smoking behaviour across conditions. Data from published studies by McRobbie et al. (2015), Pacifici et al. (2015), and Hecht et al. (2015) were used to estimate means and standard deviations for each of the outcomes. A range of estimates for the correlation between outcome measures across study conditions (0.65, 0.75, and 0.85) were used to estimate power. Two-sided power calculations were conducted assuming 20% loss of sample due to attrition and/or incomplete data and a final sample size of 50 participants, using G*Power v. 3.1 (Heinrich-Heine-Universität Düsseldorf), where alpha = 0.05.

In a within-subjects switching study by McRobbie et al. (2015), exposure to carbon monoxide changed from 23 (SD=11) ppm to 11 (SD=8) ppm among a sample of smokers who took up e-cigarettes but did not quit smoking after a period of four weeks. Using these estimates, the current study provided 80% power to detect a small to medium Cohen's effect size, corresponding to a 15%, 13%, and 11% difference in exhaled carbon monoxide with correlation estimates of 0.65, 0.75, and 0.85, respectively. In addition, McRobbie and colleagues (2015) reported a change in urinary cotinine among this sample of smokers, from 2203 (SD=1734) ng/mL to 1227 (SD=679) ng/mL. A power calculation based on these estimates indicates that the current study provided 80% power to detect a small to medium Cohen's effect size, corresponding to a 26%, 24%, and 22% difference with correlation estimates of 0.65, 0.75, and 0.85, respectively, for urinary cotinine. Hecht et al. (2015) reported levels of exposure to various constituents in samples of smokers versus a sample of e-cigarette users. A comparison of levels

of 1-HOP showed greater exposure among smokers compared to e-cigarette users, at 0.97 (SD=1.21) pmol/mL and 0.38 (SD=0.39) pmol/mL, respectively. Using these estimates, the current study provided 80% power to detect a small to medium Cohen's effect size, corresponding to a 42%, 40%, and 38% difference with correlation estimates of 0.65, 0.75, and 0.85, respectively, for urinary 1-HOP.

Finally, data from a within-subjects switching study by Pacifici et al. (2015) were used to estimate changes in reported daily cigarette consumption. In the study by Pacifici and colleagues (2015), among a subsample of smokers who took up e-cigarettes and were classified as dual users one month later, their reported daily cigarette consumption changed from 23.3 (SD=6.1) to 2.3 (SD=1.5). A power calculation based on these estimates indicates that the current study provided 80% power to detect a small to medium Cohen's effect size, corresponding to a 9% difference across correlation estimates of 0.65, 0.75, and 0.85.

3 RESULTS

3.1 Sample characteristics

Overall, 293 individuals were screened for eligibility to participate in the study. Of these, 60 individuals were deemed eligible and recruited for the study. A summary of the methods used to recruit participants is presented in Appendix D. Among the 60 individuals recruited for the study, three were excluded due to their failure to attend all study visits. In addition, 9 participants were excluded due to very low (< 5 ppm) carbon monoxide levels, as measured at baseline. Although exhaled carbon monoxide levels of ≥ 8-10 ppm are typically used to identify smokers (SRNT Subcommittee on Biochemical Verification, 2002), a slightly more lenient threshold (≥ 5 ppm) was used due to the fact that individuals recruited into the study were established dual users, who exhibit lower levels of carbon monoxide in their breath (Goniewicz et al., 2016). Thus, a total of 48 participants were included in the analyses.

3.1.1 Sociodemographic characteristics

Sociodemographic characteristics of the final sample of 48 dual users are summarized in Table 2. Overall, dual users had a mean age of 35.9 (SD=11.7) years, and a majority were male (70.8%) and self-identified as 'White' (70.8%). Approximately two-thirds (66.7%) of participants were recruited from Toronto, and approximately half of participants were randomized to each of Group A (52.1%) and Group B (47.9%). As shown in Table 2, participants in each group did not differ from one another with respect to key sociodemographic characteristics.

Table 2: Sociodemographic characteristics of dual users, overall and by group

Characteristic		Dual users (n=48)		Group A (n=25)		Group B (n=23)		Test statistic (p-value)[1]
		% (n) or mean (SD)						
Age [years]	Overall	35.9 (11.7)		36.0 (11.4)		35.8 (12.2)		t=0.039 (p=0.969)
	18-24	14.6%	(7)	20.0%	(5)	8.7%	(2)	χ^2=6.740 (p=0.081)
	25-39	56.3%	(27)	44.0%	(11)	69.6%	(16)	
	40-54	20.8%	(10)	32.0%	(8)	8.7%	(2)	
	55+	8.3%	(4)	4.0%	(1)	13.0%	(3)	
Sex	Male	70.8%	(34)	64.0%	(16)	78.3%	(18)	χ^2=1.179 (p=0.278)
	Female	29.2%	(14)	36.0%	(9)	21.7%	(5)	
Ethnicity	White	70.8%	(34)	64.0%	(16)	78.3%	(18)	χ^2=1.179 (p=0.278)
	Other	29.2%	(14)	36.0%	(9)	21.7%	(5)	
Education	High school or less	27.1%	(13)	24.0%	(6)	30.4%	(7)	χ^2=0.943 (p=0.624)
	Technical school/college	35.4%	(17)	32.0%	(8)	39.1%	(9)	
	Any university	37.5%	(18)	44.0%	(11)	30.4%	(7)	
City	Kitchener-Waterloo	33.3%	(16)	24.0%	(6)	43.5%	(10)	χ^2=2.045 (p=0.153)
	Toronto	66.7%	(32)	76.0%	(19)	56.5%	(13)	

Notes:
[1] Differences in means were tested using independent t-tests, while differences in proportions were tested using chi-square tests.

3.1.2 Nicotine dependence

As shown in Table 3, dual users exhibited low to moderate nicotine dependence, with a mean FTCD score of 4.7 (SD=1.9). Nicotine dependence for tobacco cigarettes was greater than for e-cigarettes, at 4.7 (SD=1.9) and 3.0 (SD=2.1), respectively, (t=4.864, p<0.001). This result was reflected in specific items of the FTCD: for instance, a greater proportion of dual users reported smoking tobacco cigarettes (95.8%) versus e-cigarettes (56.2%) within the first hour of waking.

With respect to the NDSS measure, dual users exhibited moderate nicotine dependence, with a mean NDSS score of -0.48 (SD=0.76). Similarly, dual users exhibited greater nicotine dependence for tobacco cigarettes (NDSS -0.48 (SD=0.76)) as compared to e-cigarettes (E-NDSS -1.22 (SD=0.79)), (t=6.657, p<0.001) (see Table 4). When asked about their perceived addiction to each product, almost all dual users indicated they were addicted to tobacco cigarettes (97.9%), but not to e-cigarettes (97.9%) (see Table 5). A McNemar-Bowker test was used to examine participants' perceived addiction to each product. The omnibus test yielded a

significant difference: χ^2=37.000, p<0.001. McNemar post-hoc analyses with Bonferroni adjustment indicated that a significantly greater proportion of participants perceived themselves as addicted to tobacco cigarettes as compared to e-cigarettes (very addicted vs. not at all addicted: χ^2=8.000, p=0.024; very addicted vs. somewhat addicted: χ^2=19.000, p=0.003; and somewhat addicted vs. not addicted: χ^2=10.000, p=0.006).

Table 3: Tobacco cigarette and e-cigarette dependence, as measured by the Fagerström Test for Cigarette Dependence (FTCD), among dual users (n=48)

		Tobacco cigarettes		E-cigarettes	
		% (n) or mean (SD)			
(E-) FTCD	Overall	4.7 (1.9)		3.0 (2.1)	
	0-2 (very low)	9.3%	(4)	35.4%	(17)
	3-4 (low)	34.9%	(15)	34.2%	(13)
	5 (moderate)	20.9%	(9)	2.6%	(1)
	6-7 (high)	27.9%	(12)	18.4%	(7)
	8-10 (very high)	7.0%	(3)	0.0%	(0)
(E-) FTCD Q1: How soon after you wake up do you smoke (use) your first cigarette (e-cigarette)?	Within 5 min	31.3%	(15)	6.3%	(3)
	6-30 min	50.0%	(24)	31.3%	(15)
	31-60 min	14.6%	(7)	18.8%	(9)
	After 60 min	4.2%	(2)	43.8%	(21)
(E-) FTCD Q2: Do you find it difficult to refrain from smoking cigarettes (using e-cigarettes) in places where it is forbidden?	Yes	27.1%	(13)	14.9%	(7)
	No	72.9%	(35)	85.1%	(40)
(E-) FTCD Q3: Which cigarette (e-cigarette) would you hate most to give up?	First in the morning	47.9%	(23)	14.6%	(6)
	All others	45.8%	(22)	85.4%	(35)
(E-) FTCD Q4: How many cigarettes/day (times do you use e-cigarettes/day) do you smoke?	10 or less	29.2%	(14)	58.3%	(28)
	11 to 20	47.9%	(23)	22.9%	(11)
	21 to 30	22.9%	(11)	8.3%	(4)
	31 or more	0.0%	(0)	10.4%	(5)
(E-) FTCD Q5: Do you smoke (use) more frequently during the first hours after waking than during the rest of the day?	Yes	43.8%	(21)	10.6%	(5)
	No	56.3%	(27)	89.4%	(42)
(E-) FTCD Q6: Do you smoke (use) if you are so ill that you are in bed most of the day?	Yes	47.9%	(23)	63.0%	(29)
	No	45.8%	(22)	37.0%	(17)

Notes:
Abbreviations: (E-) FTCD=Fagerström Test for Cigarette Dependence (E=version adapted for e-cigarettes).

Table 4: Tobacco cigarette and e-cigarette dependence, as measured by the Nicotine Dependence Syndrome Scale (NDSS), among dual users (n=48)

	Tobacco cigarettes	E-cigarettes
	Mean (SD)	
(E-) NDSS Overall	- 0.48 (0.76)	- 1.22 (0.79)
(E-) NDSS Drive	- 0.19 (0.95)	- 1.70 (1.18)
(E-) NDSS Stereotypy	- 0.16 (0.78)	0.50 (0.98)
(E-) NDSS Continuity	- 0.66 (1.04)	- 1.05 (1.28)
(E-) NDSS Priority	- 0.68 (0.58)	- 0.55 (0.57)
(E-) NDSS Tolerance	- 0.44 (0.97)	- 0.63 (0.92)

Notes:
Abbreviations: (E-) NDSS=Nicotine Dependence Syndrome Scale (E=version adapted for e-cigarettes).

Table 5: Perceived addiction to tobacco cigarettes and e-cigarettes among dual users (n=48)

		Tobacco cigarettes		E-cigarettes	
		% (n)			
Do you consider yourself addicted to… ?	Not at all	2.1%	(1)	39.6%	(19)
	Somewhat addicted	39.6%	(19)	58.3%	(28)
	Very addicted	58.3%	(28)	2.1%	(1)

3.2 Baseline patterns of use and perceptions among dual users

3.2.1 Patterns of product use

Patterns of use of tobacco cigarettes and e-cigarettes are presented in Table 6. With respect to smoking and vaping histories, participants had smoked and vaped daily for a mean of 17.4 and 1.2 years, respectively. Dual users reported similar rates of daily consumption of tobacco cigarettes and of e-cigarettes ($p=0.09$). Specifically, dual users reported smoking a mean of 13.7 tobacco cigarettes per day and using e-cigarettes 10.9 times (bouts) per day, with a mean of 9.2 puffs per bout, with each bout lasting approximately 7.7 minutes. A greater proportion of dual users reported smoking tobacco cigarettes (97.9%) as compared to e-cigarettes (58.7%) within the first hour of waking ($p<0.001$). In addition, dual users reported a greater number of past quit attempts for tobacco cigarettes versus e-cigarettes ($p=0.006$), and a greater proportion of dual users reported intentions to quit smoking tobacco cigarettes (91.5%) versus e-cigarettes (56.5%) ($p=0.001$). Among those intending to quit smoking tobacco cigarettes (n=43), the vast majority (90.7%) indicated they would consider using e-cigarettes to help them quit, with fewer saying they would consider using nicotine replacement therapy (30.2%) or stop-smoking medications (20.9%).

Table 6: Patterns of use of tobacco cigarettes and e-cigarettes among dual users (n=48)

		Tobacco cigarettes		E-cigarettes		Test statistic (p-value)[1]
		% (n) or mean (SD)				
Duration of daily use [years]		17.4 (12.2)		1.2 (0.9)		t=8.978 (p<0.001)
Times used (bouts) per day[2]		13.7 (5.6)		10.9 (11.4)		t=1.744 (p=0.09)
Number of puffs per bout		-		9.2 (9.4)		-
Duration of bout [minutes]		-		7.7 (9.8)		-
Time to first use	Within 5 min	31.3%	(15)	8.7%	(4)	(p<0.001)
	6-30 min	52.1%	(25)	23.9%	(11)	
	31-60 min	14.6%	(7)	26.1%	(12)	
	After 60 min	2.1%	(1)	41.3%	(19)	
Number of past quit attempts		7.0 (15.4)		0.9 (3.4)		t=2.903 (p=0.006)
Intention to quit	Within the next month	21.3%	(10)	8.7%	(4)	(p=0.001)
	Within 6 months	25.5%	(12)	13.0%	(6)	
	Sometime in the future, beyond 6 months	44.7%	(21)	34.8%	(16)	
	Not intending to quit	8.5%	(4)	43.5%	(20)	

Notes:
[1] Differences in means were tested using paired samples t-tests, while differences in proportions were tested using McNemar tests.
[2] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; "bouts" per day (defined as an instance of at least one puff) for e-cigarettes.

3.2.2 Types of products used

Brands of tobacco cigarettes smoked by dual users are included in Appendix E. Briefly, commonly smoked brands included Belmont (25.0%), Next (20.8%), and First Nations brands (10.4%). Characteristics of e-cigarette products used by dual users are summarized in Table 7. A large majority of dual users reported using tank systems (91.7%) and e-cigarettes with nicotine (93.8%). Common flavours included fruit (50.0%), tobacco (41.7%), and candy (41.7%). As shown in Table 8, among those who reported using e-cigarettes with nicotine (n=45), nicotine concentrations less than or equal to 14 mg/mL were most commonly used (71.1%). Dual users reported using a wide variety of e-cigarette devices and e-liquid brands (see Appendix E).

Table 7: Self-reported e-cigarette product characteristics used by dual users (n=48)

Product characteristic		%	(n)
Product type*	Disposable	6.3%	(3)
	Re-useable	8.3%	(4)
	Tank system	91.7%	(44)
Flavour(s)*	Fruit	50.0%	(24)
	Tobacco	41.7%	(20)
	Candy	41.7%	(20)
	Coffee/drinks/alcohol	20.8%	(10)
	Menthol/mint	18.8%	(9)
	Spice	10.4%	(5)
	Other[1]	2.0%	(1)
Nicotine content	Only e-cigarettes with nicotine	81.3%	(39)
	Only e-cigarettes without nicotine	6.3%	(3)
	Some e-cigarettes with nicotine and some e-cigarettes without nicotine	12.5%	(6)

Notes:
* Proportions may not sum to 100% due to the fact that participants could select multiple response options.
[1] Other flavours included: neutral.

Table 8: Self-reported product nicotine concentrations used, among those who reported using e-cigarettes with nicotine (n=45)

Nicotine concentration	%	(n)
1-8 mg/mL (0.1-0.8%)	40.0%	(18)
9-14 mg/mL (0.9-1.4%)	31.1%	(14)
15-20 mg/mL (1.5-2.0%)	8.9%	(4)
21-24 mg/mL (2.1-2.4%)	6.7%	(3)
25 mg/mL (2.5%) or more	4.4%	(2)
Don’t know	8.9%	(4)

3.2.3 Places of product use

As shown in Table 9, places where tobacco cigarettes and e-cigarettes were commonly used followed a similar pattern, with the greatest rates of use at home, followed by while walking on the street, in a vehicle, at school or work, etc. No significant differences were detected between rates of use of each product at each place.

Table 9: Places of tobacco cigarette and e-cigarette use among dual users (n=48)

Place	Tobacco cigarettes		E-cigarettes		Test statistic (p-value)[1]
	% (n)		% (n)		
At home	93.8%	(45)	100.0%	(48)	(p=0.083)
Indoors	20.0%	(9)	41.7%	(20)	
Outdoors	44.4%	(20)	4.2%	(2)	
Both indoors and outdoors	35.6%	(16)	54.2%	(26)	
While walking on the street	77.1%	(37)	68.8%	(33)	(p=0.388)
In a vehicle	64.6%	(31)	64.6%	(31)	(p=1.000)
At school or work	60.4%	(29)	54.2%	(26)	(p=0.375)
Indoors	3.4%	(1)	15.4%	(4)	
Outdoors	89.7%	(26)	42.3%	(11)	
Both indoors and outdoors	6.9%	(2)	42.3%	(11)	
In a park or other outdoor venue	47.9%	(23)	41.7%	(20)	(p=0.629)
At a restaurant or bar	20.8%	(10)	35.4%	(17)	(p=0.065)
Indoors	0.0%	(0)	11.8%	(2)	
Outdoors	100.0%	(10)	41.2%	(7)	
Both indoors and outdoors	0.0%	(0)	47.1%	(8)	
Other[2]	2.1%	(1)	6.3%	(3)	(p=0.500)

Notes:
* Proportions may not sum to 100% due to the fact that participants could select multiple response options.
[1] Differences in proportions were tested using McNemar tests.
[2] Other places included: friend (1) for tobacco cigarettes; and on public transit (2), at a friend's house (1), at a doctor's office (2), at other offices or in elevators (1) for e-cigarettes.

3.2.4 Reasons for e-cigarette use

Dual users were asked to indicate reasons for their initiation and current use of e-cigarettes. As shown in Table 10, when asked to select all relevant reasons from a list, the most commonly reported reasons for currently using e-cigarettes included: to smoke fewer tobacco cigarettes (79.2%), to help with cravings for tobacco cigarettes (70.8%), and because they are less harmful than smoking tobacco cigarettes (70.8%). Reasons for initiation of e-cigarette use followed a similar pattern. When asked to specify the most important reason for their current use of e-cigarettes, the most commonly reported reasons included: to smoke fewer tobacco cigarettes (25.0%), to quit smoking tobacco cigarettes (20.8%), because they are less harmful than smoking tobacco cigarettes (14.6%), because they cost less money (12.5%), and because respondents liked their taste or flavour (10.4%) (see Table 11). Once again, the most important reasons for initiation of e-cigarette use were generally consistent with those for current use.

Table 10: Potential reasons for initiation and current use of e-cigarettes reported by dual users (n=48)

Reason	Initiation of e-cigarettes		Current use of e-cigarettes	
	% (n)		% (n)	
To help me to smoke fewer cigarettes	75.0%	(36)	79.2%	(38)
They are less harmful to me than smoking	72.9%	(35)	70.8%	(34)
To help me with cravings for cigarettes	70.8%	(34)	70.8%	(34)
I like their taste/flavour	62.5%	(30)	66.7%	(32)
They are less harmful to others around me than smoking	56.3%	(27)	60.4%	(29)
To help me quit smoking	58.3%	(28)	54.2%	(26)
They cost less	50.0%	(24)	47.9%	(23)
I can use them in places where smoking is not allowed	56.3%	(27)	47.9%	(23)
They were recommended by a family/friend	41.7%	(20)	41.7%	(20)
Due to boredom	29.2%	(14)	27.1%	(13)
To reduce stress	29.2%	(14)	20.8%	(10)
They were recommended by a health professional	6.3%	(3)	6.3%	(3)
To control body weight	4.2%	(2)	4.2%	(2)
Other[1]	6.3%	(3)	2.1%	(1)
Don't know	2.1%	(1)	0.0%	(0)

* Proportions may not sum to 100% due to the fact that participants could select multiple response options

[1] Other places included: hobby (1), no cigarettes (1), to more easily smoke e-cigarettes inside during the winter (1) for initiation of e-cigarettes; and hobby (1) for current use of e-cigarettes.

Table 11: The most important reason for initiation and current use of e-cigarettes reported by dual users (n=48)

Reason	Initiation of e-cigarettes		Current use of e-cigarettes	
	% (n)		% (n)	
To help me to smoke fewer cigarettes	18.8%	(9)	25.0%	(12)
To help me quit smoking	27.1%	(13)	20.8%	(10)
They are less harmful to me than smoking	18.8%	(9)	14.6%	(7)
They cost less	12.5%	(6)	12.5%	(6)
I like their taste/flavour	4.2%	(2)	10.4%	(5)
I can use them in places where smoking is not allowed	6.3%	(3)	8.3%	(4)
To help me with cravings for cigarettes	2.1%	(1)	6.3%	(3)
They are less harmful to others around me than smoking	4.2%	(2)	2.1%	(1)
They were recommended by a health professional	0.0%	(0)	0.0%	(0)
They were recommended by a family/friend	0.0%	(0)	0.0%	(0)
Due to boredom	4.2%	(2)	0.0%	(0)
To reduce stress	0.0%	(0)	0.0%	(0)
To control body weight	2.1%	(1)	0.0%	(0)
Other	0.0%	(0)	0.0%	(0)

3.2.5 Dual use characteristics

All dual users in the study sample reported that they began smoking tobacco cigarettes before using e-cigarettes. As shown in Table 12, when asked which behaviour they identified with more – smoking tobacco cigarettes or using e-cigarettes – a majority (60.4%) indicated they identified themselves as a tobacco cigarette smoker, while 37.5% identified themselves as both a tobacco cigarette smoker and an e-cigarette user. From the time they began vaping daily, 37.5% indicated they vape about the same amount, while approximately one-third indicated either vaping more (33.3%) or less (29.2%). Further, from the time they began vaping daily, a majority (75.0%) of respondents reported smoking fewer tobacco cigarettes. Finally, the vast majority (95.8%) of dual users supported the notion that e-cigarettes would make it easier to quit smoking tobacco cigarettes.

Table 12: Dual use characteristics among dual users (n=48)

Characteristic	% (n)	
Which behaviour do you identify yourself with more – smoking or vaping?		
I identify myself as a smoker	60.4%	(29)
I identify myself as a vaper	2.1%	(1)
I identify myself as both a smoker and a vaper	37.5%	(18)
From the time you started vaping daily, have you changed the amount you use per day?		
I use less	29.2%	(14)
I use about the same amount	37.5%	(18)
I use more	33.3%	(16)
From the time you started vaping daily, has the strength of nicotine you use most changed?		
Strength of nicotine has decreased	25.0%	(12)
Strength of nicotine has not changed	64.6%	(31)
Strength of nicotine has increased	10.4%	(5)
From the time you started vaping daily, has the number of tobacco cigarettes you smoke changed?		
Number of tobacco cigarettes has decreased	75.0%	(36)
Number of tobacco cigarettes has not changed	20.8%	(10)
Number of tobacco cigarettes has increased	4.2%	(2)

3.2.6 Perceptions of e-cigarettes

As shown in Table 13, compared to tobacco cigarettes, e-cigarettes were considered more socially acceptable (64.6%), less satisfying (66.7%), less pleasurable (63.8%), less harmful (87.2%), and less expensive (81.3%).

Table 13: Perceptions of e-cigarettes among dual users (n=48)

Perception	% (n)	
Acceptability: Compared to smoking regular tobacco cigarettes, using e-cigarettes is …		
… less socially acceptable	12.5%	(6)
… equally as socially acceptable	22.9%	(11)
… more socially acceptable	64.6%	(31)
Satisfaction: Compared to smoking regular tobacco cigarettes, using e-cigarettes is …		
… less satisfying	66.7%	(32)
… equally as satisfying	22.9%	(11)
… more satisfying	10.4%	(5)
Pleasure: Compared to smoking regular tobacco cigarettes, using e-cigarettes is …		
… less pleasurable	63.8%	(30)
… equally as pleasurable	17.0%	(8)
… more pleasurable	19.2%	(9)
Harm: Compared to smoking regular tobacco cigarettes, using e-cigarettes is …		
… less harmful	87.2%	(41)
… equally as harmful	12.8%	(6)
… more harmful	0.0%	(0)
Cost: Compared to smoking regular tobacco cigarettes, using e-cigarettes is …		
… less expensive	81.3%	(39)
… equally as expensive	14.6%	(7)
… more expensive	4.1%	(2)

3.3 Randomization check

To test whether randomization of participants was successful, several baseline measures were examined by assigned condition order (Group A, Group B). As shown in Table 14, participants in each group did not differ on any of the measures.

Table 14: Key outcomes among study participants at baseline, overall and by group

Characteristic		Dual users (n=48)	Group A (n=25)	Group B (n=23)	Test statistic (p-value)[3]
		mean (SD)			
Times used per day[1]	Tobacco cigarettes	13.7 (5.6)	13.9 (6.1)	13.5 (5.1)	t=0.218 (p=0.828)
	E-cigarettes	11.1 (11.4)	11.5 (12.1)	10.7 (10.8)	t=0.237 (p=0.814)
Urinary cotinine [ng/mL]		1329.4 (783.6)	1173.6 (773.1)	1498.8 (776.0)	t=-1.453 (p=0.153)
Exhaled carbon monoxide [ppm]		17.4 (11.1)	15.6 (9.2)	19.5 (12.8)	t=-1.206 (p=0.234)
Urinary 1-HOP[2] [pg/mg creatinine]		3076.6 (2790.9)	3732.3 (3232.2)	2363.8 (2055.0)	t=1.764 (p=0.085)
Urinary NNAL[2] [pg/mg creatinine]		76.0 (175.6)	64.6 (133.4)	88.3 (214.9)	t=-0.463 (p=0.646)

Notes:
[1] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; 'bouts' per day (defined as an instance of at least one puff) for e-cigarettes.
[2] Arithmetic mean.
[3] Differences in means were tested using independent t-tests.

3.4 Patterns of product use across study conditions

Participants' patterns of use of tobacco cigarettes and e-cigarettes across study conditions are presented in Table 15 (for a detailed daily summary of patterns of product use, see Appendix F). Patterns of use of 'permitted' tobacco cigarettes and e-cigarettes are shown against a white background, while patterns of use of 'not permitted' tobacco cigarettes and e-cigarettes are shown against a grey background in the table below. On average, participants reported using e-cigarettes 2.7 times per day in the condition of *Exclusive use of tobacco cigarettes* and reported smoking 1.9 tobacco cigarettes per day in the condition of *Exclusive use of e-cigarettes*. In the condition of *No product use*, participants reported smoking 2.8 tobacco cigarettes per day and using e-cigarettes 2.7 times per day.

Table 15: Patterns of use of tobacco cigarettes and e-cigarettes across study conditions (n=48)

Product	Variable		Condition			
			Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use
			% (n) or mean (SD)			
Tobacco cigarette	Times used (bouts) per day[1]		13.7 (5.6)	12.3 (6.2)	1.9 (1.8)[2]	2.8 (1.7)[2]
	Time to first use	Within 5 min	31.3%	36.4%	15.4%	12.4%
		6-30 min	52.1%	36.7%	5.1%	12.4%
		31-60 min	14.6%	16.3%	10.3%	5.3%
		After 60 min	2.1%	10.5%	69.2%	69.9%
		Mean (SD)[3]	0.9 (0.7)	1.0 (0.8)	2.6 (0.6)	2.4 (1.0)
	Time since last use [hours]		0.8 (0.6)	4.8 (13.6)	63.7 (37.8)	84.0 (92.5)
E-cigarette	Times used (bouts) per day[1]		11.1 (11.4)	2.7 (1.9)[2]	17.4 (16.0)	2.7 (2.1)[2]
	Number of puffs per bout		9.2 (9.4)	4.5 (5.1)[2]	7.9 (4.8)	3.0 (1.5)[2]
	Duration of bout [minutes]		7.7 (9.8)	2.1 (1.7)[2]	6.7 (5.4)	2.7 (3.7)[2]
	Time to first use	Within 5 min	8.7%	0.0%	27.7%	6.8%
		6-30 min	23.49%	21.7%	37.8%	8.5%
		31-60 min	26.1%	4.3%	20.6%	8.5%
		After 60 min	41.3%	73.9%	13.8%	76.3%
		Mean (SD)[3]	2.0 (1.0)	2.8 (0.6)	1.1 (0.8)	2.5 (0.9)
	Time since last use [hours]		5.0 (7.0)	78.2 (38.1)	1.5 (2.6)	114.6 (90.6)

Notes:
Grey-shaded areas indicate use of 'not permited' products, for each study condition. Measures of patterns of use for 'not permitted' products were obtained through self-reported responses collected from participants' daily diaries, while those for permitted products (white areas) were obtained through self-reported responses collected from scheduled laboratory visits.
[1] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; 'bouts' per day (defined as an instance of at least one puff) for e-cigarettes.
[2] Summary statistics presented for subset of participants who reported using a given product.
[3] Mean time to first use calculated for recoded variable as a continuous measure ranging from 0 (within 5 minutes) to 3 (after 60 minutes).

3.5 Exposure to nicotine and compensatory behaviour

3.5.1 Patterns of use of tobacco cigarettes

To examine whether participants compensated for nicotine by changing their patterns of tobacco cigarette use, several patterns of use were compared across conditions of *Dual use* and of *Exclusive use of tobacco cigarettes* (see Table 16).

Table 16: Patterns of use of tobacco cigarettes across conditions of *Dual use* and *Exclusive use of tobacco cigarettes* (n=48)

Measure of tobacco cigarette use	Condition		Test statistic (p-value)
	Dual use	Exclusive use of tobacco cigarettes	
	Mean (95% CI)		
Times used per day[1]	13.7 (12.1, 15.3)	12.3 (10.5, 14.0)	F=7.888 (p=0.008)
Time to first use[2]	0.9 (0.7, 1.1)	1.0 (0.7, 1.2)	F=1.602 (p=0.213)

Notes:
Abbreviations: CI=confidence interval.
[1] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes.
[2] Mean time to first use calculated for recoded variable as a continuous measure ranging from 0 (within 5 minutes) to 3 (after 60 minutes).

A repeated measures model was conducted to examine daily tobacco cigarette consumption across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The repeated measures model yielded a significant effect of condition (F=7.888, p=0.008): daily tobacco cigarette consumption was significantly higher in the condition of *Dual use* compared to the condition of *Exclusive use of tobacco cigarettes* (mean difference=1.4, 95% CI: 0.4 to 2.4, p=0.008). Baseline nicotine dependence was also significantly associated with daily tobacco cigarette consumption (F=22.941, p<0.001), with higher levels of baseline nicotine dependence associated with greater daily consumption of tobacco cigarettes (β=1.8, 95% CI: 1.0 to 2.5, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=2.999, p=0.091).

A repeated measures model was also conducted to examine time to first tobacco cigarette across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The repeated measures model indicated that there were no statistically significant differences in time

to first tobacco cigarette across study conditions (F=1.602, p=0.213). However, baseline nicotine dependence was significantly associated with time to first tobacco cigarette (F=50.339, p<0.001), with higher levels of baseline nicotine dependence associated with a lower value for time to first tobacco cigarette (β= -0.3, 95% CI: -0.3 to -0.2, p<0.001).

A significant interaction between assigned condition order and condition (F=5.291, p=0.027) was observed. Stratified analyses indicated that the main (null) effect of condition (described above) held for Group B participants (F=0.609, p=0.444). In addition, baseline nicotine dependence was significantly associated with time to first tobacco cigarette (F=16.142, p=0.001), with higher levels of baseline nicotine dependence associated with a lower value for time to first tobacco cigarette (β= -0.2, 95% CI: -0.3 to -0.1, p=0.001).

In contrast, a significant effect of condition was detected for Group A participants (F=5.072, p=0.036): time to first tobacco cigarette was significantly lower in the condition of *Dual use* as compared to the condition of *Exclusive use of tobacco cigarettes* (mean difference=-0.3, 95% CI: -0.6 to -0.1, p=0.036). In addition, baseline nicotine dependence was significantly associated with time to first tobacco cigarette (F=31.584, p<0.001), with higher levels of baseline nicotine dependence associated with a lower value for time to first tobacco cigarette (β= -0.3, 95% CI: -0.3 to -0.2, p<0.001).

3.5.2 Patterns of use of e-cigarettes

To examine whether participants compensated for nicotine by changing their patterns of e-cigarette use, several measures of patterns of use were compared across conditions of *Dual use* and of *Exclusive use of e-cigarettes* (see Table 17).

Table 17: Patterns of use of e-cigarettes across conditions of *Dual use* and *Exclusive use of e-cigarettes* (n=48)

Measure of e-cigarette use	Condition		Test statistic (p-value)
	Dual use	Exclusive use of e-cigarettes	
	Mean (95% CI)		
Times used (bouts) per day[1]	11.1 (7.8, 14.5)	17.4 (12.8, 22.1)	F=10.113 (p=0.003)
Number of puffs per bout	9.2 (6.5, 12.0)	7.9 (6.5, 9.4)	F=1.447 (p=0.236)
Duration of bout [minutes]	7.7 (4.8, 10.6)	6.7 (5.1, 8.3)	F=0.782 (p=0.382)
Time to first use[2]	2.0 (1.7, 2.3)	1.1 (0.9, 1.3)	F=24.004 (p<0.001)

Notes:
Abbreviations: CI=confidence interval.
[1] Times used per day='bouts' per day (defined as an instance of at least one puff) for e-cigarettes.
[2] Mean time to first use calculated for recoded variable as a continuous measure ranging from 0 (within 5 minutes) to 3 (after 60 minutes).

A repeated measures model was conducted to examine daily e-cigarette consumption across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The repeated measures model yielded a significant effect of condition (F=10.113, p=0.003): daily e-cigarette consumption was significantly higher in the condition of *Exclusive use of e-cigarettes* compared to the condition of *Dual use* (mean difference=6.2, 95% CI: 2.3 to 10.1, p=0.003). No significant effect was detected for the interaction of condition and assigned condition order (F=0.010, p=0.921).

A repeated measures model was conducted to examine number of puffs per daily e-cigarette bout across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The model indicated that there were no significant differences in the number of puffs per daily e-

cigarette bout across study conditions (F=1.447, p=0.236), and no significant effect was detected for the interaction of condition and assigned condition order (F=0.746, p=0.393).

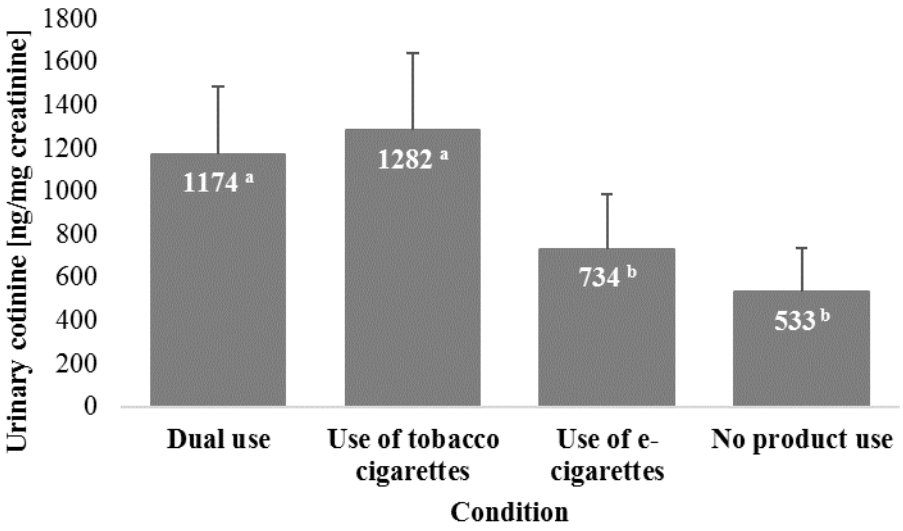
A repeated measures model was conducted to examine the duration of daily e-cigarette bout across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The model indicated that there were no significant differences in the duration of daily e-cigarette bout across study conditions (F=0.782, p=0.382), and no significant effect was detected for the interaction of condition and assigned condition order (F=0.826, p=0.369).

A repeated measures model was also conducted to examine time to first e-cigarette across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. The repeated measures model yielded a significant effect of condition (F=24.004, p<0.001): time to first e-cigarette was significantly lower in the condition of *Exclusive use of e-cigarettes* compared to the condition of *Dual use* (mean difference= -0.9, 95% CI: -1.2 to -0.5, p<0.001). In addition, baseline nicotine dependence was significantly associated with time to first e-cigarette (F=5.291, p=0.027), with higher levels of baseline nicotine dependence associated with a lower value for time to first e-cigarette (β= -0.1, 95% CI: -0.2 to -0.01, p=0.027). No significant effect was detected for the interaction of condition and assigned condition order (F=0.593, p=0.446).

3.5.3 Urinary cotinine

Levels of creatinine-corrected urinary cotinine were tested across study conditions to examine whether participants compensated for nicotine by smoking tobacco cigarettes and/or using e-cigarettes – see Figure 3 (see Appendix G for corresponding table).

Figure 3: Urinary cotinine[1] across study conditions (n=48)



Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

A repeated measures model was conducted to examine urinary cotinine across study conditions, with assigned condition order (Group A, Group B), baseline nicotine dependence (FTCD score), e-cigarette product type (tank system, other), and e-cigarette nicotine content (nicotine present, nicotine absent) as covariates, and an unstructured variance-covariance structure. Measures of urinary cotinine were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented above.

The repeated measures model yielded a significant effect of condition (F=5.788, p=0.002): urinary cotinine was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.6, 95% CI: 1.1 to 2.4, p=0.027), and of *No product use* (mean difference=2.3, 95% CI: 1.3 to 3.9, p=0.004). In addition, urinary cotinine was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the

conditions of *Exclusive use of e-cigarettes* (mean difference=1.7, 95% CI: 1.2 to 2.5, p=0.003), and of *No product use* (mean difference=2.4, 95% CI: 1.5 to 4.0, p=0.001). Baseline nicotine dependence was also significantly associated with urinary cotinine (F=8.366, p=0.006), with higher levels of baseline nicotine dependence associated with higher levels of urinary cotinine (β=1.3, 95% CI: 1.08 to 1.5, p=0.006). No significant effect was detected for the interaction of condition and assigned condition order (F=0.875, p=0.462).

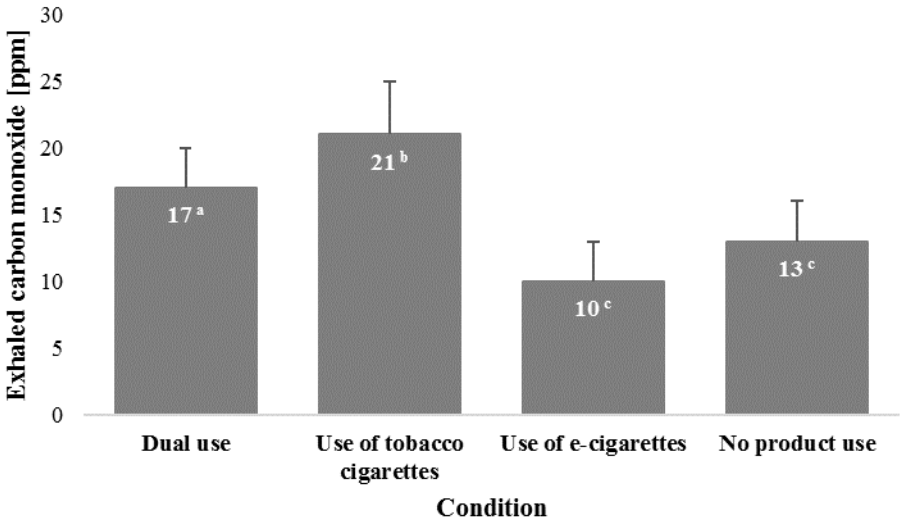
3.6 Exposure to tobacco smoke constituents

Several biomarkers of exposure were examined to determine whether participants' exposure to tobacco smoke constituents changed following product switching.

3.6.1 Exhaled carbon monoxide

Measures of exhaled carbon monoxide are presented across study conditions in Figure 4 (see Appendix G for corresponding table).

Figure 4: Exhaled carbon monoxide across study conditions (n=48)



Notes:
Abbreviations: ppm=parts per million.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.

A repeated measures model was conducted to examine exhaled carbon monoxide across study conditions, with assigned condition order (Group A, Group B), baseline nicotine dependence (FTCD score), e-cigarette product type (tank system, other), and e-cigarette nicotine content (nicotine present, nicotine absent) as covariates, and an unstructured variance-covariance structure. The repeated measures model yielded a significant effect of condition ($F=10.115$, $p<0.001$): exhaled carbon monoxide was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Dual use* (mean difference=3.9, 95% CI: 0.4 to 7.3, $p=0.029$), of *Exclusive use of e-cigarettes* (mean difference=10.7, 95% CI: 6.4 to 15.0, $p<0.001$), and of *No product use* (mean difference=8.4, 95% CI: 4.8 to 12.0, $p<0.001$). In addition, carbon monoxide was significantly higher in the condition of *Dual use* compared to the

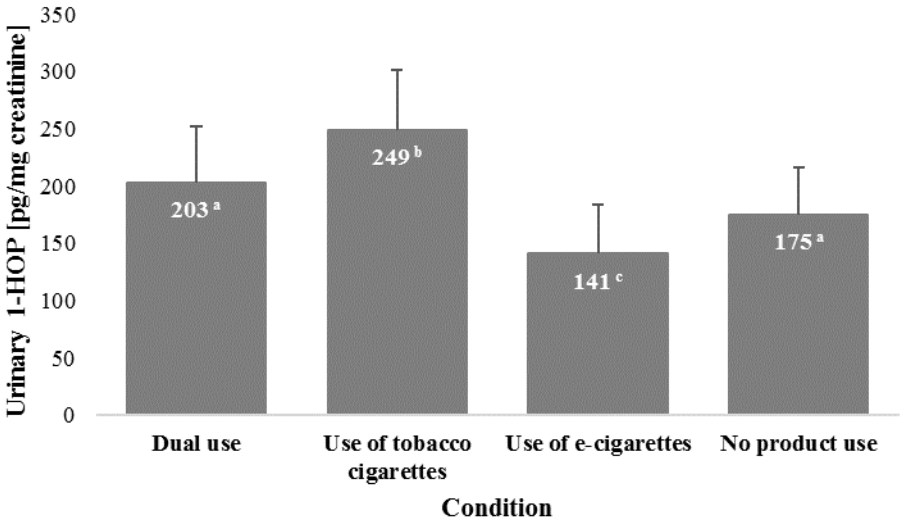
conditions of *Exclusive use of e-cigarettes* (mean difference=6.9, 95% CI: 3.8 to 9.9, p<0.001), and of *No product use* (mean difference=4.6, 95% CI: 1.5 to 7.6, p=0.004).

A significant interaction between assigned condition order and condition (F=3.704, p=0.019) was observed. Stratified analyses indicated that the main effect of condition (described above) generally held for participants randomized to both condition orders (Group A: F=9.383, p<0.001; Group B: F=3.788, p=0.028) (see Appendix H for detailed results).

3.6.2 Urinary 1-hydroxypyrene

Measures of creatinine-corrected urinary 1-hydroxypyrene (1-HOP) are presented across study conditions in Figure 5 (see Appendix G for corresponding table).

Figure 5: Urinary 1-hydroxypyrene[1] across study conditions (n=48)



Notes:
Abbreviations: 1-HOP=1-hydroxypyrene.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

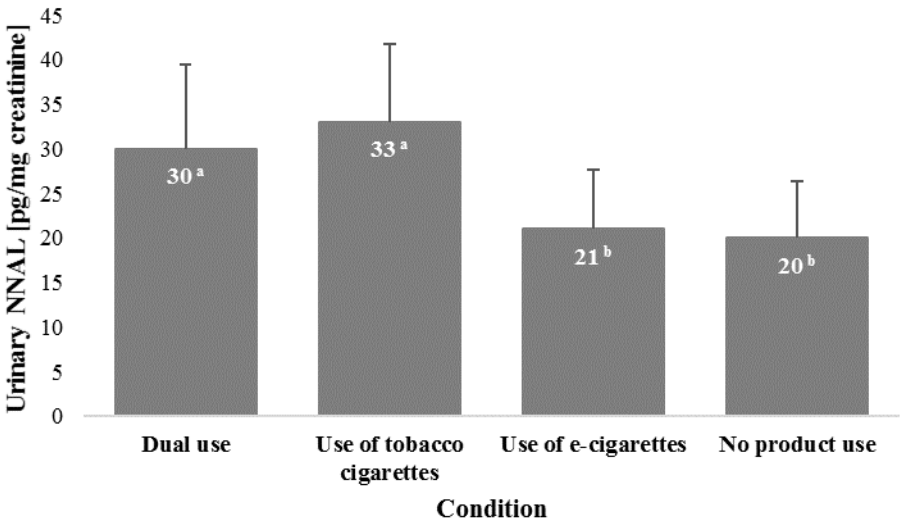
A repeated measures model was conducted to examine urinary 1-HOP across study conditions, with assigned condition order (Group A, Group B), baseline nicotine dependence (FTCD score), e-cigarette product type (tank system, other), and e-cigarette nicotine content (nicotine present, nicotine absent) as covariates, and an unstructured variance-covariance structure. Measures of urinary 1-HOP were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented above.

The repeated measures model yielded a significant effect of condition (F=4.766, p=0.006): urinary 1-HOP was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Dual use* (mean difference=1.3, 95% CI: 1.0 to 1.6, p=0.048), of *Exclusive use of e-cigarettes* (mean difference=1.8, 95% CI: 1.3 to 2.5, p=0.001), and of *No product use* (mean difference=1.4, 95% CI: 1.1 to 1.8, p=0.009). In addition, urinary 1-HOP was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.4, 95% CI: 1.0 to 1.9, p=0.025). Baseline nicotine dependence was also significantly associated with urinary 1-HOP (F=4.377, p=0.043), with higher levels of baseline nicotine dependence associated with higher levels of urinary 1-HOP (β=1.1, 95% CI: 1.0 to 1.3, p=0.043). No significant effect was detected for the interaction of condition and assigned condition order (F=1.883, p=0.148).

3.6.3 Urinary NNAL

Measures of creatinine-corrected urinary NNAL are presented across study conditions in Figure 6 (see Appendix G for corresponding table).

Figure 6: Urinary NNAL[1] across study conditions (n=48)



Notes:
Abbreviations: NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

A repeated measures model was conducted to examine urinary NNAL across study conditions, with assigned condition order (Group A, Group B), baseline nicotine dependence (FTCD score), e-cigarette product type (tank system, other), and e-cigarette nicotine content (nicotine present, nicotine absent) as covariates, and an unstructured variance-covariance structure. Measures of urinary NNAL were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented above.

The repeated measures model yielded a significant effect of condition (F=4.593, p=0.007): urinary NNAL was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.5, 95% CI: 1.2 to 2.0, p=0.002), and of *No product use* (mean difference=1.6, 95% CI: 1.2 to 2.0, p=0.001). In addition, urinary NNAL was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.4, 95% CI: 1.1 to 1.9, p=0.017), and of *No product use* (mean difference=1.5, 95% CI: 1.1 to 2.0, p=0.016). Baseline nicotine dependence was also significantly associated with urinary NNAL (F=13.116, p=0.001), with higher levels of baseline nicotine dependence associated with higher levels of urinary NNAL (β=1.4, 95% CI: 1.1 to 1.6, p=0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=1.260, p=0.301).

3.6.4 Summary

An overview of exposure to tobacco smoke constituents across study conditions is presented in Table 18. Compared to the condition of *Dual use,* mean levels of all biomarkers of exposure among participants declined significantly in the conditions of *Exclusive use of e-cigarettes* and of *No product use*. In contrast, mean levels of exhaled carbon monoxide and urinary 1-HOP were significantly greater in the condition of *Exclusive use of tobacco cigarettes* compared to *Dual use*; although mean levels of urinary NNAL showed a similar trend, this difference was not statistically significant.

Table 18: Summary of biomarkers of exposure across study conditions (n=48)

Biomarker	Condition			
	Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use
	Mean (% change from Dual use)			
Exhaled carbon monoxide[1] [ppm]	17.4	21.1 (+21%)*	10.3 (-41%)*	12.9 (-26%)*
Urinary 1-HOP[2] [pg/mg creatinine]	203.3	249.2 (+23%)*	141.1 (-31%)*	175.1 (-14%)
Urinary NNAL[2] [pg/mg creatinine]	30.3	32.7 (+8%)	21.2 (-30%)*	19.8 (-35%)*

Notes:
Abbreviations: CI=confidence interval; 1-HOP=1-hydroxypyrene; NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Asterisks (*) denote significant differences in biomarker levels compared to the condition of *Dual use*, $p<0.05$.
[1] Arithmetic mean.
[2] Geometric mean.

3.6.5 Sensitivity analyses

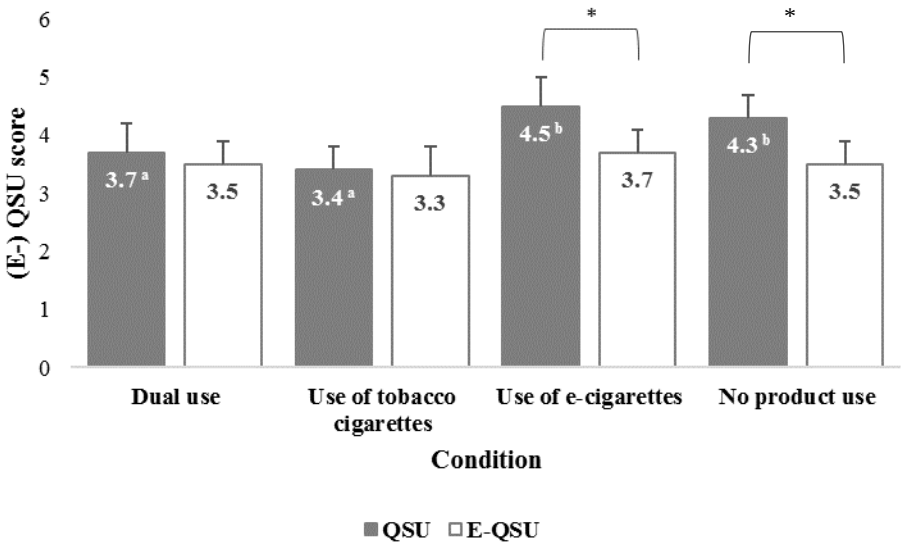
Sensitivity analyses were conducted in an attempt to examine the effect of non-compliance with respect to smoking tobacco cigarettes in the study conditions in which these products were not permitted. The analyses were conducted using two approaches: 1) excluding participants with exhaled carbon monoxide levels greater than 5 ppm in the condition of *No product use* (n=37); and 2) excluding participants who self-reported smoking tobacco cigarettes in the condition of *No product use* (n=28) (see Appendix I for results). Overall, these analyses yielded a pattern of results similar to those outlined above: the exclusion of non-compliant participants resulted in greater differences in biomarkers of exposure across study conditions, despite the use of smaller samples. However, no significant differences in levels of urinary 1-hydroxypyrene were detected across study conditions, likely due to limited statistical power.

3.7 Nicotine withdrawal

To examine changes in nicotine withdrawal experienced by dual users following product switching, measures of urges to smoke tobacco cigarettes were examined across study conditions using the brief version of the Questionnaire of Smoking Urges (QSU). Participants' urges to use e-cigarettes were examined using an adapted version of the QSU (E-QSU), in which the words "smoking cigarettes" were replaced with "use e-cigarettes". The (E-) QSU yields an overall measure of nicotine withdrawal, as well as a Factor 1 score and a Factor 2 score, measuring participants' expectations of positive outcomes from using a particular product, and their expectations of relief from the negative effect of using a particular product, respectively.

Measures of cravings for both tobacco cigarettes and e-cigarettes are presented by study condition in Figure 7 (see Appendix G for corresponding table). Although measures of nicotine withdrawal for tobacco cigarettes and e-cigarettes were similar in each of the conditions of *Dual use* and of *Exclusive use of tobacco cigarettes*, participants reported significantly greater cravings for tobacco cigarettes as compared to e-cigarettes in study conditions of *Exclusive use of e-cigarettes* (t=4.287, p<0.001) and of *No product use* (t=4.470, p<0.001).

Figure 7: Measures of nicotine withdrawal for tobacco cigarettes and e-cigarettes across study conditions (n=48)



Notes:
Abbreviations: QSU=Questionnaire of Smoking Urges; E-=adapted for e-cigarettes.
Asterisks (*) indicate results that are significantly different from one another within a study condition, p<0.05.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

3.7.1 Urges to smoke tobacco cigarettes

A repeated measures model was conducted to examine QSU scores across study conditions, with assigned condition order (Group A, Group B), and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. A repeated measures model examining overall QSU scores yielded a significant effect of condition ($F=6.725$, $p=0.001$): participants reported significantly greater urges to smoke tobacco cigarettes in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.8, 95% CI: 0.3 to 1.2, $p=0.002$), and of *Exclusive use of tobacco cigarettes* (mean difference=1.0, 95% CI: 0.5 to 1.5, $p<0.001$). In addition, participants reported significantly greater urges to smoke tobacco cigarettes in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.6, 95% CI: 0.2 to 1.1, $p=0.009$), and of *Exclusive use of tobacco cigarettes* (mean difference=0.9, 95% CI: 0.4 to 1.4, $p=0.001$) (see Figure 7). No significant effect was detected for the interaction of condition and assigned condition order ($F=0.750$, $p=0.529$).

A repeated measures model examining scores for the QSU Factor 1, which reflect expectations of positive outcomes from smoking tobacco cigarettes (e.g., a cigarette would taste good right now), were also examined across study conditions (see Appendix J). QSU Factor 1 scores showed a similar pattern of results across study conditions, with two exceptions: first, participants' expectations of positive outcomes from smoking tobacco cigarettes were not significantly greater in the condition of *No product use* as compared to the condition of *Dual use*; and second, participants reported significantly greater expectations of positive outcomes from smoking tobacco cigarettes in the condition of *Dual use* as compared to the condition of *Exclusive use of tobacco cigarettes*.

A repeated measures model examining scores for the QSU Factor 2, which reflect expectations of relief from the negative effect of smoking tobacco cigarettes (e.g., I would do almost anything to be able to smoke a cigarette), were also examined across study conditions. QSU Factor 2 scores showed a similar pattern of results across study conditions (see Appendix J).

3.7.2 Urges to use e-cigarettes

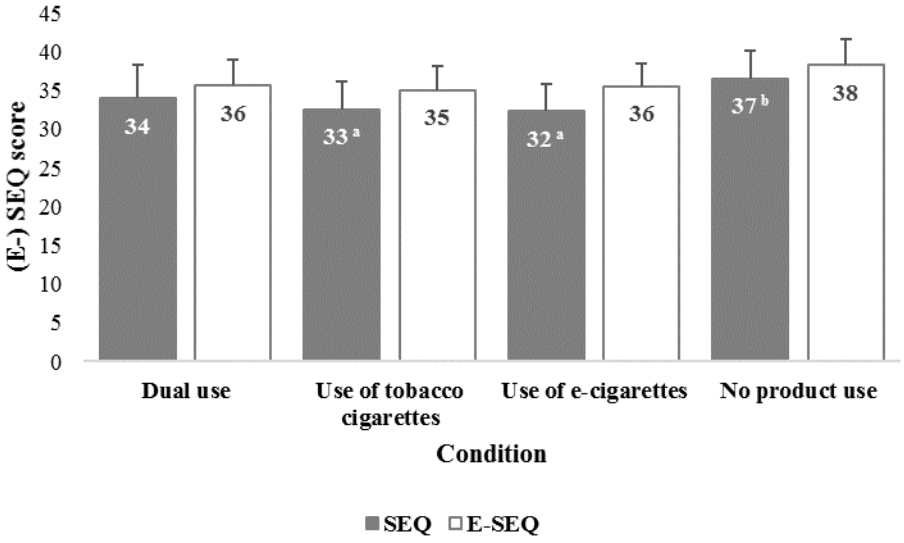
A repeated measures models were conducted to examine E-QSU scores across study conditions, with assigned condition order (Group A, Group B), and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. As shown in Figure 7, there were no statistically significant differences in urges to use e-cigarettes across study conditions for the overall E-QSU measure ($F=0.879$, $p=0.460$). Repeated measures models examining scores for the E-QSU Factor 1 and Factor 2 scores similarly showed no significant differences across study conditions (see Appendix J).

3.8 Self-efficacy

To examine changes in self-efficacy experienced by dual users following product switching, measures of participants' confidence in their ability to abstain from tobacco cigarettes were examined across study conditions using the Smoking Self-Efficacy Questionnaire (SEQ). Participants' self-efficacy to abstain from e-cigarettes was examined using an adapted version of the SEQ (E-SEQ), in which the words "smoking cigarettes" were replaced with "use e-cigarettes". The (E-) SEQ yields an overall measure of self-efficacy, as well as a Factor 1 score and a Factor 2 score, measuring participants' confidence in their ability to abstain from using a particular product when facing internal stimuli and external stimuli, respectively.

Measures of self-efficacy for abstaining from tobacco cigarettes and e-cigarettes are presented by study condition in Figure 8 (see Appendix G for corresponding table). Measures of self-efficacy for e-cigarettes were consistently greater than those for tobacco cigarettes in each study condition, although these differences did not reach statistical significance.

Figure 8: Measures of self-efficacy for abstaining from tobacco cigarettes and e-cigarettes across study conditions (n=48)



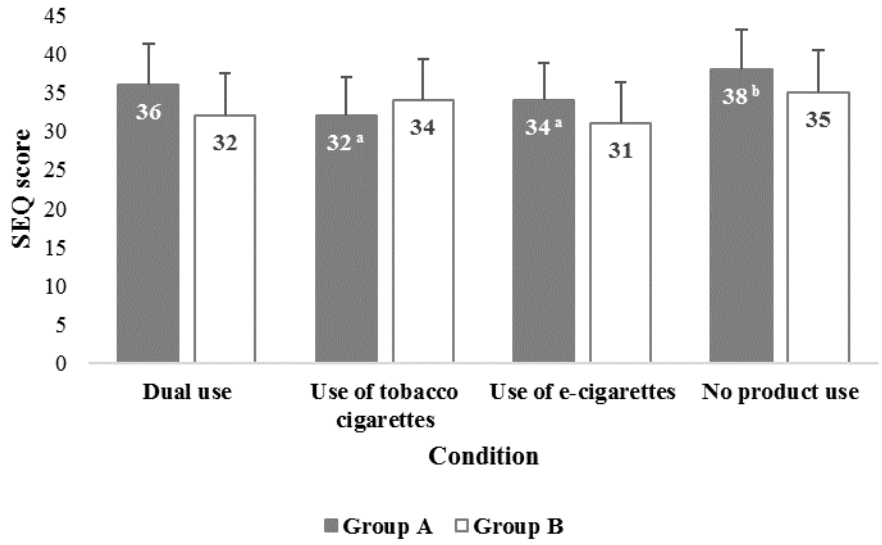
Notes:
Abbreviations: SEQ=Self-Efficacy Questionnaire; E-=adapted for e-cigarettes.
Asterisks (*) indicate results that are significantly different from one another within each study condition, $p<0.05$.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.

3.8.1 Self-efficacy for abstaining from tobacco cigarettes

A repeated measures models were conducted to examine SEQ scores across study conditions, with assigned condition order (Group A, Group B), and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. A repeated measures model examining SEQ scores yielded a significant effect of condition (F=3.419, p=0.026): participants reported significantly greater self-efficacy for abstaining from tobacco cigarettes in the condition of *No product use* as compared to conditions of *Exclusive use of tobacco cigarettes* (mean difference=4.2, 95% CI: 1.3 to 7.1, p=0.006), and of *Exclusive use of e-cigarettes* (mean difference=5.0, 95% CI: 1.5 to 8.5, p=0.006) (see Figure 8).

A significant interaction between assigned condition order and condition (F=3.222, p=0.032) was observed. Stratified analyses indicated that the main effect of condition (described above) held for Group A participants (F=6.466, p=0.003): Group A participants reported significantly greater self-efficacy for abstaining from tobacco cigarettes in the condition of *No product use* as compared to conditions of *Exclusive use of tobacco cigarettes* (mean difference=7.4, 95% CI: 3.7 to 11.0, p<0.001), and of *Exclusive use of e-cigarettes* (mean difference=5.6, 95% CI: 1.2 to 10.0, p=0.015) (see Figure 9). In contrast, there were no significant differences in self-efficacy for abstaining from tobacco cigarettes among Group B participants across study conditions (F=1.383, p=0.276).

Figure 9: Self-efficacy for abstaining from tobacco cigarettes across study conditions, by group (n=48)



Notes:
Abbreviations: SEQ=Self-Efficacy Questionnaire.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.

Repeated measures models examining scores for the SEQ Factor 1 and Factor 2, which reflect participants' confidence in their ability to abstain from smoking when facing internal stimuli (e.g., feeling depressed), and external stimuli (e.g., when having a drink with friends), respectively, were also examined across study conditions (see Appendix K). SEQ Factor 2 scores showed a similar pattern of results across study conditions, while SEQ Factor 1 scores showed no significant differences.

3.8.2 Self-efficacy for abstaining from e-cigarettes

A repeated measures model was conducted to examine E-SEQ scores across study conditions, with assigned condition order (Group A, Group B), and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure. As shown in Figure 8, there were no statistically significant differences in participants' confidence in their ability to abstain from vaping across study conditions ($F=1.867$, $p=0.150$). Repeated measures models examining scores for the E-SEQ Factor 1 and Factor 2 scores similarly showed no significant differences across study conditions (see Appendix K).

3.9 Perceived health and subjective effects

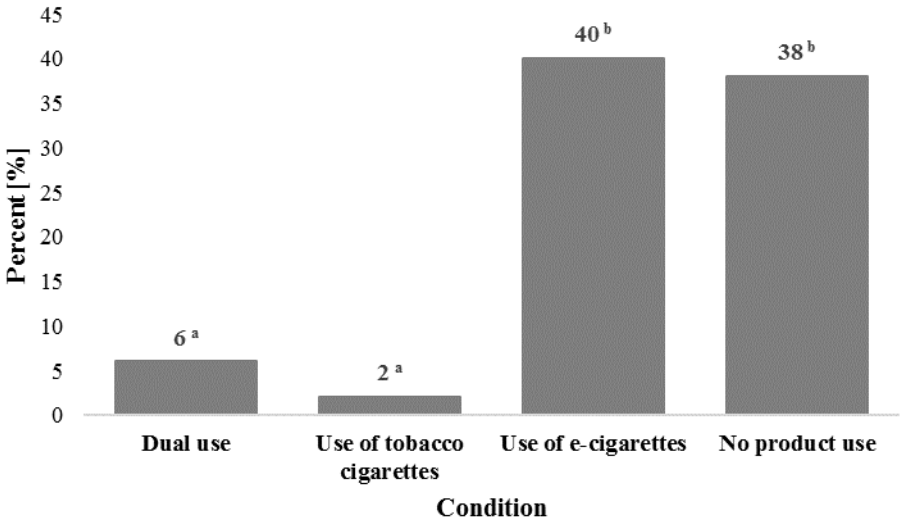
3.9.1 Perceived respiratory health

To examine changes in the perceived health of dual users following product switching, five measures of perceived health were examined across study conditions: experiencing shortness of breath, frequency of experiencing cough, frequency of experiencing cough with phlegm, sounds emanating from the chest, and an overall description of lung function. Each outcome was modeled as a binary variable (0='worse than usual health' or 'no difference in health'; 1='better than usual health'). Repeated measures models were conducted to examine each domain of respiratory health across study conditions, with assigned condition order (Group A, Group B) included as a covariate, and using a diagonal variance-covariance structure.

3.9.1.1 Overall lung function

Participants were asked to indicate whether they perceived a change in their overall lung function in each study condition. Figure 10 shows the proportion of dual users reporting better perceived lung function following each study condition (see Appendix G for corresponding table). In a repeated measures model examining perceived lung function, a significant effect of condition was observed (F=6.778, p<0.001): a greater proportion of participants reported better lung function in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). In addition, a greater proportion of participants reported better lung function in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=0.762, p=0.517).

Figure 10: Proportion of participants reporting better perceived lung function across study conditions (n=48)

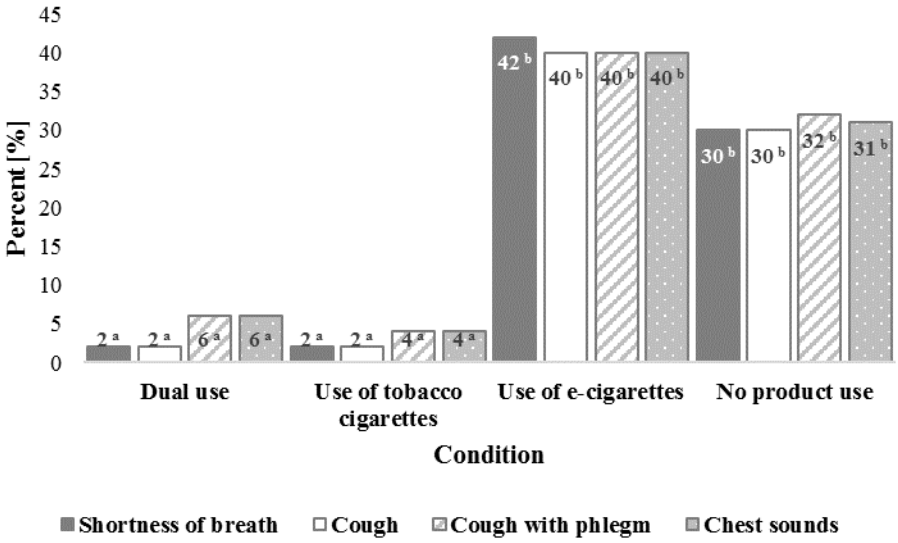


Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.

3.9.1.2 Other respiratory health domains

Participants reported similar improvements in experiencing shortness of breath, cough, cough with phlegm, or sounds emanating from the chest, across study conditions, as shown in Figure 11 (see Appendix G for corresponding table).

Figure 11: Proportion of participants reporting better perceived respiratory health across study conditions (n=48)



Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.

In a repeated measures model examining change in experiencing shortness of breath, a significant effect of condition was observed (F=6.952, p<0.001): a significantly greater proportion of participants reported improvement in experiencing shortness of breath in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). In addition, a significantly greater proportion of participants reported improvement in experiencing shortness of breath in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=1.208, p=0.308).

In a repeated measures model examining change in frequency of experiencing cough, a significant effect of condition was observed (F=6.816, p<0.001): a significantly greater proportion of participants reported improvement in experiencing cough in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). In addition, a significantly greater proportion of participants reported improvement in experiencing cough in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=0.341, p=0.796).

In a repeated measures model examining change in frequency of experiencing cough with phlegm, a significant effect of condition was observed (F=7.561, p<0.001): a significantly greater proportion of participants reported improvement in experiencing cough with phlegm in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). In addition, a significantly greater proportion of participants reported improvement in experiencing cough with phlegm in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.1 to 0.4, p=0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=0.271, p=0.846).

In a repeated measures model examining change in experiencing sounds emanating from the chest, a significant effect of condition was observed (F=6.799, p<0.001): a significantly greater proportion of participants reported improvement in experiencing chest sounds in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.3, 95% CI: 0.2 to 0.5, p<0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.4, 95% CI: 0.2 to 0.5, p<0.001). In addition, a significantly greater proportion of participants reported improvement in experiencing chest sounds in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.2, 95% CI: 0.1 to 0.4, p=0.001), and of *Exclusive use*

of tobacco cigarettes (mean difference=0.3, 95% CI: 0.1 to 0.4, p<0.001). No significant effect was detected for the interaction of condition and assigned condition order (F=0.221, p=0.881).

3.9.2 Perceived overall health

Participants were asked to indicate whether they perceived a change in their overall health in each study condition. Table 19 shows participants' self-reported perceived health by study condition.

Table 19: Changes in perceived health across study conditions (n=48)

	Condition					
	Exclusive use of tobacco cigarettes		Exclusive use of e-cigarettes		No product use	
	% (n)					
Change in overall health as a result of not using e-cigarettes?						
Worse than usual	14.6%	(7)	-	-	2.1%	(1)
No difference	81.3%	(39)	-	-	79.2%	(38)
Better than usual	4.2%	(2)	-	-	18.8%	(9)
Change in overall health as a result of not using tobacco cigarettes?						
Worse than usual	-	-	4.2%	(2)	4.2%	(2)
No difference	-	-	54.2%	(26)	54.2%	(26)
Better than usual	-	-	41.7%	(20)	41.7%	(20)

A McNemar-Bowker test was used to examine changes in participants' perceived health in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *Exclusive use of e-cigarettes*. The omnibus test yielded a significant difference: χ^2=16.571, p=0.001. McNemar post-hoc analyses with Bonferroni adjustment indicated that a significantly greater proportion of participants reported better than usual health (vs. no difference) in the condition of *Exclusive use of e-cigarettes* as compared to the condition of *Exclusive use of tobacco cigarettes* (χ^2=13.000, p=0.003).

Changes in participants' perceived health were also compared in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *No product use*. A McNemar-Bowker test indicated no significant difference in participants' perceived health between these study conditions (χ^2=7.444, p=0.059). Similarly, a McNemar-Bowker test indicated no significant difference in participants'

perceived health in the condition of *Exclusive use of e-cigarettes* as compared to the condition of *No product use* (χ^2=1.400, p=0.706).

Further, participants were asked to consider any negative or positive effects they experienced as a result of abstaining from smoking tobacco cigarettes and/or using e-cigarettes over the course of the study. Participants reported the following negative effects as a result of not using e-cigarettes: body pains (n=1), fatigue (n=1), malaise (n=1), feeling anxious (n=1), feeling depressed (n=1), and feeling angry (n=1). Positive effects resulting from not using e-cigarettes included: increased appetite/eating better (n=1), and having more energy (n=1).

On the other hand, participants reported the following negative effects because of not smoking tobacco cigarettes: suffering from nicotine withdrawal symptoms (n=1), feeling depressed (n=1), and feeling stressed (n=1). Positive effects as a result of not smoking tobacco cigarettes included: having more energy (n=12), feeling better/healthier (n=9), increased appetite/eating better (n=6), engaging in more physical activity (n=5), socializing with friends who don't smoke (n=1), experiencing better mental health (n=3), experiencing fewer cravings for tobacco cigarettes (n=3), increased confidence to quit cigarettes (n=2), improved sense of smell (n=1), and improved sleep (n=1).

3.9.3 Perceived addiction

Participants were asked whether they considered themselves addicted to either tobacco cigarettes or e-cigarettes over the course of the study. Table 20 shows participants' self-reported perceived addiction to each product, by study condition.

Table 20: Perceived addiction to tobacco cigarettes and e-cigarettes across study conditions (n=48)

	Condition					
	Exclusive use of tobacco cigarettes		Exclusive use of e-cigarettes		No product use	
	% (n)					
Do you consider yourself addicted to e-cigarettes?						
Not at all addicted	39.6%	(19)	-	-	41.7%	(20)
Somewhat addicted	52.1%	(25)	-	-	52.1%	(25)
Very addicted	8.3%	(4)	-	-	6.3%	(3)
Do you consider yourself addicted to tobacco cigarettes?						
Not at all addicted	-	-	2.1%	(1)	2.1%	(1)
Somewhat addicted	-	-	35.4%	(17)	41.7%	(20)
Very addicted	-	-	62.5%	(30)	56.3%	(27)

A McNemar-Bowker test was used to examine changes in participants' perceived addiction in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *Exclusive use of e-cigarettes*. The omnibus test yielded a significant difference: χ^2=29.842, p<0.001. McNemar post-hoc analyses with Bonferroni adjustment indicated that a significantly greater proportion of participants perceived themselves as addicted to tobacco cigarettes as compared to e-cigarettes (very addicted vs. not at all addicted: χ^2=11.000, p=0.003; very addicted vs. somewhat addicted: χ^2=11.842, p=0.003; and somewhat addicted vs. not addicted: χ^2=7.000, p=0.048).

Participants' perceived addiction to e-cigarettes was also compared in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *No product use*. A McNemar-Bowker test indicated no significant difference in participants' perceived addiction to e-cigarettes between these study conditions (χ^2=1.077, p=0.584). Similarly, a McNemar-Bowker test indicated no significant difference in participants' perceived addiction to tobacco cigarettes in the condition of *Exclusive use of e-cigarettes* as compared to the condition of *No product use* (χ^2=1.000, p=0.317).

3.9.4 Perceived difficulty in abstaining from product use

Participants were asked to reflect on the difficulty they experienced while abstaining from smoking tobacco cigarettes or from using e-cigarettes over the course of the study. Table 21

shows participants' perceived difficulty in abstaining from using each of these products, by study condition.

Table 21: Perceived difficulty in abstaining from smoking tobacco cigarettes or from using e-cigarettes, across study conditions (n=48)

	Condition					
	Exclusive use of tobacco cigarettes		Exclusive use of e-cigarettes		No product use	
	% (n)					
Over the past week, how easy or difficult was it to go without using e-cigarettes?						
Easy	64.6%	(31)	-	-	54.2%	(26)
Neither easy nor difficult	10.4%	(5)	-	-	2.1%	(1)
Difficult	25.0%	(12)	-	-	43.8%	(21)
Over the past week, how easy or difficult was it to go without smoking cigarettes?						
Easy	-	-	14.6%	(7)	8.3%	(4)
Neither easy nor difficult	-	-	8.3%	(4)	6.3%	(3)
Difficult	-	-	77.1%	(37)	85.4%	(41)

A McNemar-Bowker test was used to examine participants' perceived difficulty in abstaining from product use in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *Exclusive use of e-cigarettes*. The omnibus test yielded a significant difference: χ^2=18.398, p<0.001. McNemar post-hoc analyses with Bonferroni adjustment indicated that a significantly greater proportion of participants reported difficulty (vs. ease) in abstaining from product use in the condition of *Exclusive use of e-cigarettes* as compared to the condition of *Exclusive use of tobacco cigarettes* (χ^2=17.065, p=0.003).

Participants' perceived difficulty in abstaining from using e-cigarettes was also compared in the condition of *Exclusive use of tobacco cigarettes* vs. the condition of *No product use*. A McNemar-Bowker test indicated no significant difference in participants' perceived difficulty in abstaining from using e-cigarettes between these study conditions (χ^2=7.267, p=0.064). Similarly, no significant difference in participants' perceived difficulty in abstaining from smoking tobacco cigarettes was found when comparing the condition of *Exclusive use of e-cigarettes* with the condition of *No product use* (χ^2=4.000, p=0.261).

4 DISCUSSION

4.1 Baseline characteristics and patterns of product use among dual users

4.1.1 Characteristics of dual users

Dual users in this study exhibited low to moderate nicotine dependence for tobacco cigarettes and low nicotine dependence for e-cigarettes. Nicotine dependence for tobacco cigarettes, as measured using the FTCD, among this sample of dual users was greater than that of US dual users surveyed by Rass and colleagues (2015), likely resulting from the inclusion of non-daily smokers reporting lower daily cigarette consumption in the study conducted by Rass and colleagues (2015). When measured using the NDSS, dual users' level of nicotine dependence for tobacco cigarettes fell between that characterizing non-dependent smokers or chippers (NDSS -1.76) and dependent regular smokers, smoking at least 20 cigarettes per day (NDSS 0.12) (Shiffman & Sayette, 2005). Nicotine dependence scores for e-cigarettes were difficult to interpret, as has been noted by other authors, given that some items in the FTCD and NDSS are not well suited for e-cigarettes (e.g., continued product use despite risks) (Etter & Eissenberg, 2015). Nevertheless, comparison of dependence scores for each product (with respect to both the FTCD and NDSS) reflected greater dependence for tobacco cigarettes as compared to e-cigarettes, mirroring respondents' perceived addiction to each product. These findings are consistent with other studies of dual users (Etter & Eissenberg, 2015; Rass et al., 2015), and are supportive of published research suggesting that e-cigarettes have less addictive potential relative to tobacco cigarettes (Etter & Eissenberg, 2015; Goniewicz et al., 2013; Vansickel, Weaver & Eissenberg, 2012).

4.1.2 Patterns of product use among dual users

In the current study, the vast majority of dual users reported using tank system e-cigarette products and e-liquids containing nicotine, with low to moderate nicotine concentrations being the most commonly used. These findings are consistent with other published surveys of dual users (Berg, 2016; Farsalinos, Romagna & Voudris, 2015; Rüther et al., 2016). The consistency of these findings provides further evidence that the restriction on nicotine-containing products in Canada has not prevented individuals from obtaining and using such products (Hammond et al., 2015; Standing Committee on Health, 2015). The reported use of flavoured e-cigarettes/e-liquids

supports previously published findings regarding the popularity of such flavours, and particularly fruit flavours, among e-cigarette users (Shiplo, Hammond & Czoli, 2015).

4.1.3 Dual use behaviour

The findings highlight the dominant role that tobacco cigarettes play among dual users. First, all dual users in the study sample began smoking tobacco cigarettes before taking up e-cigarettes, consistent with a survey of adult US dual users (Rass et al., 2015). Second, although daily consumption of tobacco cigarettes and e-cigarettes were similar, a greater proportion of dual users reported smoking tobacco cigarettes within the first hour of waking, as compared to e-cigarettes. Third, these patterns of use complemented differential scores of nicotine dependence - the results of several measures of nicotine dependence converged to reflect greater dependence for tobacco cigarettes as compared to e-cigarettes. Fourth, dual users perceived e-cigarettes as less satisfying and pleasurable than tobacco cigarettes. Fifth, with respect to their behavioural identity, more respondents self-identified as tobacco cigarette smokers rather than either dual users or e-cigarette vapers.

At the same time, several findings from the current study illustrate the potential of e-cigarettes to compete with, and potentially substitute for, tobacco cigarettes. For instance, the finding that dual users commonly used e-cigarettes and tobacco cigarettes in similar places suggests that e-cigarette use is not confined to settings in which smoking is prohibited. Dual users also reported greater motivation to cease their use of tobacco cigarettes, reflecting a longer-term preference for e-cigarettes, as evidenced by a greater number of past quit attempts and future quit intentions. Furthermore, dual users' most common reasons for initiating and for currently using e-cigarettes included to reduce or quit smoking and as a result of the belief that these products are less harmful than tobacco cigarettes, consistent with other research (Berg, 2016; Etter, 2015; Farsalinos, Romagna & Voudris, 2015; Patel et al., 2016; Rass et al., 2015; Rutten et al., 2015). These findings were further supported by dual users' perceptions of e-cigarettes as less harmful than tobacco cigarettes, which has also been shown in the literature (Farsalinos, Romagna & Voudris, 2015; Rass et al., 2015). Finally, a majority of dual users believed that e-cigarettes would make it easier to quit smoking tobacco cigarettes, and reported smoking fewer tobacco cigarettes from the time they began using e-cigarettes daily, similar to other published studies (Farsalinos, Romagna & Voudris, 2015; Rass et al., 2015; Rutten et al., 2015).

4.1.4 Compensatory behaviour and exposure to nicotine

Dual use vs. exclusive smoking

Compensatory behaviour for nicotine was assessed by examining participants' patterns of product use and levels of urinary cotinine across study conditions in the product switching experiment. In the current study, dual users were able to effectively take in nicotine when they switched from dual use to smoking, as evidenced by their relatively stable cotinine levels. The stability of cotinine levels across dual use and exclusive smoking supports *Hypothesis 1c* and is consistent with published studies examining switching from exclusive smoking to dual use (Pacifici et al., 2015; Meier et al., 2017). This switch does not limit participants' nicotine intake, given that both these behaviours involve use of tobacco cigarettes, which deliver nicotine efficiently (USDHHS, 2010). However, participants' daily tobacco cigarette consumption was not significantly greater when exclusively smoking as compared to when engaging in dual use, in contrast to *Hypothesis 1a*. In fact, study participants reported smoking a greater number of tobacco cigarettes per day when engaging in dual use as opposed to exclusive smoking. However, the magnitude of this difference was modest, and may have been subject to several measurement issues. First, measures of cigarette consumption were based on self-report, which are subject to biases that do not apply to objective measures, such as biomarkers of exposure (discussed below). Second, patterns of dual use were measured retrospectively, prior to participants' entry into the study; as a result, aspects of study participation, such as monitoring and remuneration, may have had an effect on participants' accounts of their behaviour. On the other hand, despite smoking fewer tobacco cigarettes per day when exclusively smoking, participants may have compensated for nicotine by smoking each tobacco cigarette more intensely (Hammond, Fong, Cummings & Hyland, 2005). Due to the fact that daily cigarette consumption is only a crude measure of nicotine intake, it is not clear which of these potential reasons accounts for the study findings.

Dual use vs. exclusive vaping

When comparing the behaviours of dual use and exclusive vaping in the current study, participants' urinary cotinine levels were significantly lower when they exclusively vaped, despite significant increases in self-reported e-cigarette consumption in this study condition. Specifically, participants exhibited compensatory behaviour with respect to e-cigarettes, reporting using e-cigarettes a greater number of times per day as well as using e-cigarettes earlier

in the day, providing support for *Hypothesis 1b.* However, this behavioural change appeared insufficient to maintain stable cotinine levels. This finding contrasts with *Hypothesis 1c* and is inconsistent with several published studies in which smokers were able to achieve similar cotinine levels while using advanced e-cigarette products (Berg et al., 2014; Pacifici et al., 2015). Although the vast majority of dual users in the current study reported using tank systems and e-liquids with nicotine, the nicotine delivery potential of these devices was not tested, and may account for these results. Indeed, similar levels of cotinine among study participants across conditions of exclusive vaping and no product use supports the notion that participants' e-cigarette devices may have been limited in their ability to deliver nicotine. Given that nicotine is the substance that drives tobacco addiction, the inability of dual users to obtain sufficient nicotine exclusively from their e-cigarettes may limit the smoking cessation potential of these devices.

4.1.5 Exposure to tobacco smoke constituents

Dual use vs. exclusive vaping and no product use

Levels of several tobacco smoke exposure biomarkers, including exhaled carbon monoxide, 1-hydroxypyrene, and NNAL, were consistently lower when participants exclusively vaped as compared to when they engaged in dual use, providing support for *Hypotheses 2a, 2b,* and *2c.* Reduction in exposure to carbon monoxide is consistent with published studies examining smokers' switch to use of e-cigarettes (Adriaens et al., 2014; Caponnetto et al., 2013; Cravo et al., 2016; Goniewicz et al., 2016; Litt et al., 2016; McRobbie et al., 2015; O'Connell et al., 2016; Pacifici et al., 2015; van Staden et al., 2013). In addition, reduction in exposure to pyrene supports the findings of Hecht and colleagues (2015) comparing exposure to PAHs among vapers and smokers, as well as the findings of O'Connell and colleagues (2016) examining smokers' exposure to these compounds following their switch to exclusive vaping. Similarly, significant reduction in exposure to the carcinogen NNK supports published comparative analyses (Hecht et al., 2015; Wagener et al., 2016) as well as switching studies (Cravo et al., 2016; O'Connell et al., 2016; Goniewicz et al., 2016).

Biomarkers of exposure were also reduced when participants abstained from both tobacco cigarettes and e-cigarettes, as compared to dual use. Significant reductions were observed for carbon monoxide and NNK biomarkers when participants used neither product; although levels

of 1-HOP also decreased, this difference did not reach statistical significance. In addition, while exposure to all examined tobacco smoke constituents decreased when participants were not permitted to smoke nor vape, exposure did not reduce to nil. Although this is likely the result of some respondents continuing to smoke tobacco cigarettes, as well as slow clearance of some biomarkers, particularly NNAL (Hecht et al., 1999), it may also reflect the presence of contaminants in e-cigarette products, or other sources of environmental exposure, particularly for PAHs (WHO, 2007).

Dual use vs. exclusive smoking

Exposure to carbon monoxide and polycyclic aromatic hydrocarbons was significantly greater when individuals exclusively smoked as compared to when they engaged in dual use (21% and 23%, respectively). With respect to this comparison, a non-significant increase in exposure to NNK was also observed (8%). These findings are generally consistent with two published switching studies. First, in a switching study with 4-week follow-up, McRobbie and colleagues (2015) reported significant reduction in exposure to carbon monoxide among smokers taking up e-cigarettes, with greater reduction observed among exclusive vapers as compared to dual users (80% vs. 52%) (McRobbie et al., 2015). Further, in an industry-sponsored 1-week switching study, O'Connell and colleagues (2016) reported similar findings, with all examined biomarkers showing a decreasing trend with decreasing tobacco cigarette consumption among parallel groups of smokers. Specifically, compared to their baseline smoking behaviour, reduction in exposure to carbon monoxide, PAHs, and NNK, respectively, were observed among smokers who switched to dual use (26-32%, and 25-35%, [NNK exposure value not published]), among smokers who switched to exclusive vaping (89%, 62-69%, and 62-64%), and among smokers who quit tobacco/nicotine products entirely ([carbon monoxide exposure value not published], 70%, and 66%). Notably, greater reduction in exposure was observed in these switching studies when compared with findings from the current study. Factors that may account for these differing results include the motivation of smokers in the study by McRobbie and colleagues (2015) to quit smoking, and the clinical confinement of smokers in the study by O'Connell and colleagues (2016), which may have contributed to greater potential substitution of tobacco cigarettes with e-cigarettes and greater compliance with forced product switching.

To date, only one study has examined tobacco-related biomarkers of exposure in real-world settings. Shahab and colleagues (2017) examined a suite of biomarkers of exposure to TSNAs and volatile organic compounds in several groups of long-term nicotine product users. Cross-sectional comparative analyses indicated that exclusive vaping, but not dual use of tobacco cigarettes and e-cigarettes, was associated with lower levels of exposure to several tobacco constituents, as compared to exclusive smoking (Shahab et al., 2017). Although the authors noted that their statistical power to detect small differences (such as that between dual users and exclusive smokers) was limited, the magnitude of observed differences in exposure were similar to those observed in the current study, at least with respect to NNK exposure. This may reflect the fact that both studies assessed experienced nicotine product users in real-world settings.

Overall, study findings regarding exposure to tobacco smoke constituents are consistent with the product design and properties of e-cigarettes, which do not contain tobacco and do not undergo combustion when used (Bertholon et al., 2013; Besaratinia & Tommasi, 2014), and support research evidence suggesting that use of e-cigarettes is likely to be less harmful than smoking (Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014). Although the current study is unable to discern whether dual users reduce their tobacco cigarette consumption by substitution with e-cigarettes or simply use e-cigarettes alongside their usual smoking to bridge periods of non-smoking, it appears dual users use their products to achieve a desired level of nicotine, consistent with other research (Benowitz, 2001; Shahab et al., 2017). Despite slight reductions in exposure associated with dual use, the findings demonstrate that abstaining from tobacco cigarettes is the most important factor in reducing exposure to toxic smoke constituents. Research evidence indicates that smokers who quit tobacco cigarettes completely reduce their risk of premature death to levels comparable to non-smokers (Doll, Peto, Boreham & Sutherland, 2004; USDHHS, 2010). However, the potential benefits of smoking reduction, as may be the case of dual use, are less clear. Despite the fact that many tobacco smoke constituents, including carbon monoxide, TSNAs, and PAHs, have been implicated in the development of cardiovascular disease and various cancers (IARC, 2004; USDHHS, 2010), evidence regarding how changes in smoking-related biomarkers predict future risk of disease is lacking (USDHHS, 2010). For instance, with respect to cardiovascular disease, epidemiologic evidence demonstrates a strong dose-response relationship between the number of cigarettes smoked per day and cardiovascular risk. However, the relationship is not linear, meaning that even low levels of exposure to tobacco are sufficient

to substantially increase cardiovascular risk (USDHHS, 2010). To date, significant health benefits from reducing the amount of tobacco cigarettes smoked have not been demonstrated with respect to various disease outcomes (USDHHS, 2010). While it is plausible that dual use could reduce individual risk if it results in substantial reductions in smoking, the threshold for meaningful reductions is unclear, particularly given that smokers may compensate for reductions in the number of cigarettes they smoke by smoking each cigarette more intensely (Hammond, Fong, Cummings & Hyland, 2005; USDHHS, 2010). This is generally supported by the current findings, in which the differences between dual use and exclusive smoking were modest. Therefore, dual use is likely to have public health benefit only to the extent that it leads to complete smoking cessation.

4.1.6 Nicotine withdrawal and self-efficacy

In the current study, participants experienced significantly greater cravings for tobacco cigarettes when they were not permitted to use these products. This finding supports *Hypothesis 3a*, and indicates that dual users perceived smoking tobacco cigarettes as a desirable and rewarding behaviour, and also anticipated relief from nicotine withdrawal (Cox, Tiffany & Christen, 2001). This finding contrasts with other studies examining smokers' switch to use of e-cigarettes, in which smokers' cravings either declined (Goniewicz et al., 2016), or did not change (Meier et al., 2017; Wagener et al., 2014). When compared to the current study, these switching studies involved different design parameters, such as the study length and the type of e-cigarette products used: the studies by Meier et al. (2017) and by Goniewicz et al. (2016) examined first-generation products for one- and two-weeks, respectively, while Wagener and colleagues (2014) evaluated use of a second-generation product for a one-week period. Participants in these studies also differed with respect to their intentions to quit smoking tobacco cigarettes: while Goniewicz et al. (2016) studied smokers who may have intended to quit, the study by Wagener and colleagues (2014) examined smokers not intending to quit smoking. However, it is not entirely clear whether these factors account for these inconsistent results.

Changes in participants' self-efficacy for abstaining from smoking tobacco cigarettes depended on the order in which they experienced study conditions, providing partial support for *Hypothesis 4a.* Participants who were assigned to a 'step-wise' sequence of product switching – from dual use at baseline to exclusive smoking, to exclusive vaping, and finally to use of neither product –

experienced no significant changes in their self-efficacy with respect to tobacco cigarettes. In contrast, the self-efficacy of participants who were assigned to a more challenging sequence of product switching – from dual use at baseline to exclusive vaping, to exclusive smoking, and finally to use of neither product – reflected this challenge, decreasing non-significantly following their first and second product switches, and then increasingly significantly in the final week of the study. Overall, at the end of the product-switching experiment, the self-efficacy of participants assigned to both sequences did not differ significantly from their baseline values, which is consistent with the findings of other switching studies involving smokers not intending to quit (Meier et al., 2017; Wagener et al., 2014).

Participants reported no changes in cravings for e-cigarettes and self-efficacy to abstain from using e-cigarettes across study conditions. In contrast to *Hypothesis 3b*, these findings indicate that dual users did not experience marked changes in either their desire to vape or nicotine withdrawal symptoms with respect to these products. Further, in contrast to *Hypothesis 4b*, participants were confident in their ability to abstain from vaping, even when they were not permitted to use e-cigarettes. These findings were supported by participants' subjective experiences throughout the study, in which they perceived themselves as more addicted to tobacco cigarettes versus e-cigarettes, and perceived greater difficulty in abstaining from smoking as compared to vaping. Overall, the study findings show that dual users are comfortable both using and abstaining from e-cigarettes, and may reflect the lower addictive potential of these products (Etter & Eissenberg, 2015; Goniewicz et al., 2013; Vansickel, Weaver & Eissenberg, 2012).

4.1.7 Perceived health

Dual users reported that their respiratory health significantly improved when they abstained from smoking tobacco cigarettes. Participants consistently reported improvement in experiencing shortness of breath, cough, cough with phlegm, sounds emanating from the chest, and in perceived lung function in conditions in which they were not permitted to smoke, providing support for *Hypothesis 5*. Additional health improvements associated with not smoking included having more energy, feeling better/healthier, increased appetite/eating better, engaging in more physical activity, experiencing better mental health, experiencing fewer cravings for tobacco cigarettes, increased confidence to quit cigarettes, improved sense of smell, and improved sleep.

These findings are consistent with other published studies, in which smokers switching to use of e-cigarettes similarly reported experiencing health improvements, particularly respiratory health, with few reports of adverse effects associated with vaping (Adriaens et al., 2014; Berg et al., 2014; Caponnetto et al., 2013; Cibella et al., 2016; Goniewicz et al., 2016; Polosa et al., 2014; van Staden et al., 2013). Overall, the study findings demonstrate that abstaining from smoking tobacco cigarettes is associated with significant improvements in perceived health, with many of these benefits experienced very quickly after a change in behaviour, even within a week-long period.

4.2 Limitations and strengths

The current study faced several limitations, the first of which is the study's use of a non-probability-based sample. However, a comparison of characteristics of the current study's sample with a nationally representative data indicate that daily dual users in the current study resembled those in the Canadian population (CTADS [data not published], 2015). The current study sample reported similar daily tobacco cigarette consumption as Canadian daily dual users at large (13.7 vs. 13.0 cigarettes per day), although daily dual users in the current study exhibited greater dependence (mean Heaviness of Smoking Index 2.8 vs. 1.8), given that they reported smoking their first tobacco cigarette earlier in the day (83.4% vs. 75.8% reported smoking their first tobacco cigarette within 30 minutes) (CTADS [data not published], 2015). Although a greater proportion of Canadian daily dual users report intentions to quit smoking in the next six months as compared to the current study sample (81.3% vs. 46.8%), it is important to note that an exclusion criterion of the current study was that potential participants not have serious intentions to quit smoking in the next six months. With respect to sociodemographic characteristics, the current study sample was younger (mean age 35.9 years vs. 48.7 years), and consisted of a greater proportion of males (70.8% vs. 61.9%) (CTADS [data not published], 2015). These differences in sociodemographic characteristics also differentiate the current sample of daily dual users from samples of dual users surveyed in the US (Rass et al., 2015; Rutten et al., 2015). Overall, daily dual users in the current study appear to resemble those in the Canadian population at large, indicating that potential biases stemming from participant recruitment may not overly influence the study findings.

Next, dual users' patterns of use of both tobacco cigarettes and e-cigarettes were based on self-reported data, which are subject to various biases. Although self-reported measures of tobacco cigarette consumption used in population surveys have been shown to be valid and reliable (Hatziandreu et al., 1989; Ramo, Hall, & Prochaska, 2011), the data may nevertheless be subject to social desirability bias, given that participants were asked to consciously monitor their behaviour in a context in which smoking is increasingly perceived as socially undesirable. With respect to use of e-cigarettes, although measures of patterns of use were selected based upon a review of the literature, and are reflected in a recently published list of core items recommended for assessing e-cigarette use (Pearson et al., 2017b), they nevertheless face potential limitations. For instance, self-reported measures of the number of daily bouts of e-cigarette use and number of puffs per bout may be subject to recall bias. One challenge associated with measuring e-cigarette use is posed by the physical properties of e-cigarettes themselves: unlike tobacco cigarettes, which have a distinct beginning and end point, e-cigarettes can last several days before they need to be re-filled or replaced (Pearson et al., 2017a). In addition, qualitative research has indicated that much vaping behaviour is not consciously tracked, at least among novice users (Kim, Davis, Dohack, & Clark, 2017). Indeed, a study comparing self-reported puffing frequency collected via ecological momentary assessment (EMA) to objective data collected by a Bluetooth-enabled e-cigarette device indicated that vaping participants significantly under-reported their e-cigarette puffs (Pearson et al., 2017a). Given that EMA reduces recall bias by collecting behavioural information in the time and place where the behaviour occurs (Pearson et al., 2017a), these findings may imply that self-reported measures collected using surveys may be subject to even greater under-reporting. Overall, measures of consumption of tobacco cigarettes and e-cigarettes in the current study may be subject to various biases, potentially resulting in under-reported values. However, these limitations are tempered with the study's use of biomarkers of exposure, which provide more robust measures with which to examine product switching behaviour.

Measures used to assess e-cigarette use were limited in several other ways. For instance, the current study did not collect data regarding the quantity of e-liquid dual users consumed. Although the potential value of this measure is not yet well understood (Pearson et al., 2017b), such information may have contributed to our understanding of the relationship between smoking and vaping behaviours among dual users, and may have informed interpretations of

compensatory behaviour in the product-switching experiment. In addition, several measures used to assess nicotine dependence, nicotine withdrawal, and self-efficacy were adapted from the smoking literature and applied to e-cigarettes, but have yet to be validated for this purpose. Therefore, these results should be interpreted with caution.

The study's product-switching experiment also faced several limitations, one of which relates to its naturalistic design. Unlike other switching studies, the current study did not confine participants to a laboratory setting. As a result, participants' adherence to the study protocol was not absolute. Biomarker data reflected this lack of compliance, particularly in the conditions in which participants were not permitted to smoke tobacco cigarettes. This is particularly relevant for the final study condition of no product use, which was expected to be the most challenging for study participants. The use of non-permitted tobacco cigarettes was monitored throughout the study, and sensitivity analyses showed that accounting for 'cheating' adjusted the levels of biomarkers of exposure in the expected direction. Although 'cheating' undermines the internal validity of the study to some extent, it also enables the study to reflect what product-switching behaviour might look like in real-world conditions, which was the primary objective of the current study.

In addition, dietary and environmental sources of exposure to polycyclic aromatic hydrocarbons and carbon monoxide were not assessed in the study, limiting the extent to which exposure to these constituents can be attributed to intake of tobacco smoke; however, assessment of NNAL exposure provides a source of tobacco-specific exposure against which the findings may be interpreted. The study was also limited in its examination of biomarkers of exposure: although three biomarkers of exposure to tobacco smoke constituents were examined, there are many others that could have been assessed. In addition, the study did not assess constituents specific to e-cigarette aerosol, meaning the results reflect only a limited examination of human-level exposure to tobacco cigarettes and e-cigarettes. Finally, although analyses relating to the product-switching experiment may have been impacted by the modest sample size, the detection of significant differences in several outcomes across study conditions reflects sufficient statistical power.

Despite these limitations, the current study has several notable strengths. The current study is the first to examine detailed patterns and perceptions of use of dual users of tobacco cigarettes and e-

cigarettes in the Canadian context. An additional strength of the study is its use of complementary measures for assessment of behavioural use of both tobacco cigarettes and e-cigarettes. Such a distinction may aid in understanding the ways in which e-cigarettes may affect smoking behaviour, and reflects the tobacco/nicotine market's recent evolution (Benowitz & Goniewicz, 2013; Zeller, 2012). Furthermore, the study is strengthened by its use of objective measures of exposure. All biomarkers assessed in the current study have been recommended for use in studies of tobacco use and harm (WHO, 2007), and in contrast to laboratory animal models and smoking machines, provide valid measures of body-level exposure that take into account user characteristics. A final strength of the study is its enhanced external validity, reflected in its naturalistic design and inclusion of experienced dual users using their own products. These features enable the study to capture realistic interactions between e-cigarette users and their devices, meaning the study findings are likely to be more reflective of user populations and products in today's market.

4.3 Future research

Future research may consider several key areas. As noted above, there are few standardized behavioural assessments for the emerging behaviour of e-cigarette use. Although researchers have begun to consolidate measures (Pearson et al., 2017b), more work is needed to develop valid and reliable measures that assess this behaviour accurately and in a way that can inform the development of policy. For instance, it is not yet known what frequency or level of e-cigarette use is relevant to behavioural and health outcomes (Pearson et al., 2017b). In addition, the diversity of tobacco/nicotine products presents challenges for measuring nicotine dependence. Although some researchers (e.g., Fagerström, 2012) have recommended the development and use of measures to assess dependence to specific products – thereby acknowledging the role played by psychosocial and physical properties other than nicotine in determining dependence – others have pointed out that dependence to other drugs, such as opioids, is not typically measured in product-specific terms, such as for heroin and prescription opioids (e.g., Rass et al., 2015). Thus, it will be important for researchers to select measures carefully, and share their learnings to advance the field.

Future research should assess a wider range of biomarkers of exposure among a larger sample of established dual users to examine potential health effects. Although some e-cigarette product

characteristics were examined in the current study, the sample size and low variability limited the extent to which the association of such characteristics with nicotine intake and exposure to key constituents could be examined. In addition, the long-term health effects of e-cigarette use need to be evaluated in longitudinal observation studies. Although evidence to date suggests that the health risks of e-cigarettes are comparable to those of nicotine replacement therapy (Grana, Benowitz & Glantz, 2014; Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014; Shahab et al., 2017), such research would help firmly establish the risk profile of e-cigarettes, and may potentially inform a harm reduction strategy for nicotine.

The current study did not evaluate the effectiveness of e-cigarettes in supporting smoking cessation and/or reduction, which remains a central question in understanding the potential public health impact of these products. Although several longitudinal cohort studies and randomized controlled trials have been conducted to date (McRobbie, Bullen, Hartmann-Boyce & Hajek, 2014; Hartmann-Boyce et al., 2016), further research involving advanced products is needed to evaluate the cessation potential of these devices (Lopez & Eissenberg, 2015).

Data regarding dependence and patterns of use among smokers and vapers in the Canadian context is scarce. Although the current study sheds some light on dual use behaviour in this context, research using nationally representative samples would greatly contribute to our understanding of smoking, vaping, and dual use behaviours. Robust longitudinal data assessing these user populations and their characteristics over time will also help ascertain whether dual use sustains smoking or promotes cessation. As the nicotine market continues to evolve—and an increasing number of Canadians report dual use of combustible and non-combustible nicotine products—future research should examine the behaviours and perceptions of tobacco/nicotine product users to understand the public health implications of the shifting product market.

4.4 Policy implications

Findings from the current study can inform policy pertaining to e-cigarettes in Canada in several ways. For instance, the findings suggest that dual use behaviour is similar to that in other jurisdictions, despite Canada's restrictive regulatory framework for these products. Consistent with a body of research evidence (Hamilton et al., 2015; Hammond et al., 2015; Reid et al., 2017), these findings demonstrate that the current restriction on nicotine-containing e-cigarettes is a restriction in name only, which has not prevented individuals from obtaining and using such

products (Hammond et al., 2015). This underscores the need for a new regulatory framework for e-cigarettes, supporting recommendations made by Canadian legislators (Standing Committee on Health, 2015; Standing Senate Committee on Social Affairs, Science and Technology, 2017). Although several provinces have developed policies to address this issue (Province of British Columbia, 2015; Province of Manitoba, 2015; Province of Newfoundland and Labrador, 2016; Province of New Brunswick, 2015; Province of Nova Scotia, 2014; Province of Ontario, 2015; Province of Prince Edward Island, 2015; Province of Quebec, 2015), stakeholders anticipate that forthcoming legislation introduced in the Senate in November 2016 may better address and regulate both nicotine- and non-nicotine-containing vaping products (Parliament of Canada, 2016).

The study findings support other research demonstrating that complete smoking cessation is the best option to reduce health risks associated with smoking over the long term. Although exclusive vaping is associated with significant reduction in exposure to tobacco smoke constituents, dual use is not likely to result in reduced potential health risks, due to the magnitude of harm associated with even low levels of tobacco cigarette consumption. Therefore, smokers – including those concurrently using e-cigarettes – should be encouraged to completely quit tobacco cigarettes in order to avoid harm. These findings have direct implications for public health policy and practice. First, public health authorities should acknowledge differences in risk between smoking and exclusive e-cigarette use and communicate this clearly to the general public. Communicating the relative risk of e-cigarettes and tobacco cigarettes should focus on two salient points: 1) e-cigarettes are not harmless, but they are less harmful than smoking tobacco cigarettes; and 2) using e-cigarettes while smoking may not necessarily reduce health risks, and consumers should stop smoking to maximize any health benefit. Although the communication of relative risk information is fraught with difficulties, public health authorities must rise to this challenge for several reasons: because consumers have a right to be accurately informed of product risks (Kozlowski & Edwards, 2005; Kozlowski & Sweanor, 2016); because the rapid growth of the e-cigarette market in recent years means e-cigarettes are likely here to stay (Benowitz & Goniewicz, 2013); and because in the absence of evidence-based communication from such authorities, consumers' reliance on industry-sponsored marketing, media, and anecdotal evidence is likely to increase (Zeller & Hatsukami, 2009).

Relative health risk communication regarding e-cigarettes and tobacco cigarettes can also inform clinical practice. E-cigarettes represent a challenge for the medical community, as health care professionals are increasingly encountering patients with questions about vaping, but have limited scientific evidence to inform their practice (Palazzolo, 2013; Orellana-Barrios, Payne, Mulkey & Nugent, 2015). Currently, health professionals may be limited in the clinical recommendations they provide regarding the cessation potential of e-cigarettes to smokers (McRobbie, Bullen, Hartmann-Boyce & Hajek, 2014; Hartmann-Boyce et al., 2016). However, findings from the current study, together with evidence regarding the long-term health effects of e-cigarettes (Shahab et al., 2017), may help them have more productive conversations with those patients who already use e-cigarettes. Relative risk communication, such as that noted above, delivered by health professionals, can help ensure that patients are adequately informed of products' relative risks, and may encourage smokers using e-cigarettes to quit smoking.

Finally, the relative risks of e-cigarettes and tobacco cigarettes can inform broad regulatory measures, such as product availability and access, labelling, marketing, and pricing. Public health authorities can implement regulations that are proportional to product risk, thereby creating market differentials that can help shift smokers away from use of tobacco cigarettes (Zeller & Hatsukami, 2009). The development of such evidence-based policies would better address the substantial risks of tobacco cigarettes and have greater potential to benefit public health.

5 CONCLUSIONS

The findings suggest that dual use behaviour is similar to that in other jurisdictions, despite Canada's restrictive regulatory framework for these products. Although dual users seem primarily motivated to use e-cigarettes for health reasons, tobacco cigarettes remain an important component of nicotine use. In addition, tobacco cigarettes appear superior to e-cigarettes in their ability to deliver nicotine. Although abstaining from smoking tobacco cigarettes elicits cravings, it is also associated with significant improvements in perceived respiratory health. Consistent with other research, results from the current study demonstrate that abstaining from tobacco cigarettes is the most important factor in reducing exposure to toxic smoke constituents. Therefore, dual use is likely to have public health benefit only to the extent that it leads to complete smoking cessation.

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APPENDICES

Appendix A: Recruitment materials

Figure A1: Sample recruitment flyer

RESEARCH STUDY:

ADULTS USING CIGARETTES AND E-CIGARETTES

UNIVERSITY OF WATERLOO

The School of Public Health at the University of Waterloo is conducting a 3 week study to understand how smokers use e-cigarettes, including how e-cigarettes affect nicotine levels. We are currently recruiting adults 18 or older who use both cigarettes and e-cigarettes.

Over the 3-week study period, participants will be asked to:

- Abstain one week from cigarettes, one week from e-cigarettes and one week from both
- Visit our lab 4 times at the University of Waterloo campus (45min each visit)
- Complete a questionnaire and provide a urine and expired breath sample at each visit
- Complete a brief online questionnaire every day for the duration of the study

All information is kept confidential.

Remuneration may be up to $295 for participation in the study.

Please call: 519-888-4567 ext. 38549, or email: smokingstudy@uwaterloo.ca
for more information

This study has received clearance through a University of Waterloo Research Ethics Committee.

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Figure A2: Sample recruitment advertisement

Appendix B: Informed consent

Study information letter and informed consent form

INFORMATION LETTER

Title of Project: Smoking Study

Principal Investigator:

Dr. David Hammond (PhD), School of Public Health & Health Systems

University of Waterloo

519-888-4567 ext. 36462 dhammond@uwaterloo.ca

Please read this Information Letter and Consent Form carefully and ask as many questions as you like before deciding whether to participate in this research study.

INTRODUCTION

You have been asked to participate in a research project entitled: *Smoking Study*. You are being approached to participate in this study because you are a current cigarette smoker and a current user of electronic cigarettes (e-cigarettes) or another form of vapourized nicotine.

The purpose of this study is to examine behaviours related to the use of cigarettes and e-cigarettes among adults in Ontario. Your participation will help the investigators to examine if and how smokers use e-cigarettes, including how e-cigarette use may affect nicotine uptake.

This study is being conducted by researchers at the University of Waterloo, and is funded by a grant from the Ontario Ministry of Health and Long Term Care (MOHLTC). About 100 participants will be included in the study. Each participant will be involved with the study for 3 weeks.

PROCEDURE

If you agree to participate in this study, you will be asked to visit the lab at the University of Waterloo for a total of 4 visits over a 3 week period. Each visit to the lab will last approximately 45 minutes and will take place in a small group setting. Over the 3 week period, participants will be asked to refrain from using cigarettes or e-cigarettes or both products, in a random order.

Visit 1

During Visit 1, you will be asked to complete online questionnaires about your smoking and vaping history, any previous quit attempts, level of nicotine dependence, cravings and symptoms of nicotine withdrawal, and a few questions about your lung health. These questionnaires will take approximately 20 minutes to complete.

We will ask all participants to provide a urine sample, following the same procedure used in a doctor's office. This urine sample will be analyzed in a laboratory at the Roswell Park Cancer Institute for levels of nicotine and chemicals from tobacco products. No other tests will be conducted and the sample will be destroyed after it is analyzed.

We will also ask you to provide a breath sample to measure the amount of carbon monoxide in your lungs. This procedure consists of you blowing into a new, sterile mouthpiece that is connected to a hand-held unit. You will then be provided with instructions for Week 1 and told which product(s) to refrain from using for that week.

Visit 2

During Visit 2, you will be asked to complete an online questionnaire about your smoking and vaping behaviours over the past week. The questionnaire will take approximately 20 minutes to complete. In addition, you will be asked to provide a urine sample and a breath sample, following the same procedures as in your previous visit. You will then be provided with instructions for Week 2 and told which product(s) to refrain from using for that week.

Visit 3

During Visit 3, you will be asked to complete an online questionnaire about your smoking and vaping behaviours over the past week. The questionnaire will take approximately 20 minutes to complete. In addition, you will be asked to provide a urine sample and a breath sample, following the same procedures as in your previous visit. You will then be provided with instructions for Week 3 and told which product(s) to refrain from using for that week. For Week 3, we will provide you with resources to help you refrain from using cigarettes and e-cigarettes, if you are interested.

Visit 4

During Visit 4, you will be asked to complete an online questionnaire about your smoking and vaping behaviours over the past week. The questionnaire will take approximately 20 minutes to complete. In addition, you will be asked to provide a final urine sample and a breath sample, following the same procedures as in your previous visit. At the end of the study, you will receive a feedback letter about the study, and, if you are interested, resources to help you quit smoking.

Daily Diaries

During all 3 weeks of the study period, participants will be asked to complete brief online daily diaries about their smoking and vaping behaviours at the end of each day (after 9pm). The daily diaries will take approximately 5 minutes to complete.

POSSIBLE RISKS AND DISCOMFORTS

The risks from taking part in this study are no greater than the risks associated with regular smoking or regular use of e-cigarettes. There is very minimal risk in giving urine and exhaled breath samples. Breathing into the device to measure carbon monoxide should pose no concern as the mouthpiece will be new and sterile. Collection of urine is a non-invasive procedure that does not require direct assistance. We will be using universal precautions while handling the urine samples, following the same procedure used in a doctor's office.

Completing the online daily diaries, and providing your biological samples on time will be very important. We will keep the daily diaries as brief as possible to minimize any inconvenience. If you do not complete the tasks in a timely fashion, you will not be allowed to participate in the remainder of the study.

Coming to the laboratory at the time you are scheduled for your visits is also important. We will do everything we can to accommodate your schedule. Visits will be made in the evening, or for those who work during the evening, we will try to schedule you during convenient daytime hours.

You may experience withdrawal symptoms when asked to refrain from using certain products, particularly in Week 3 of the study period, when you will be asked to refrain from both cigarettes and e-cigarettes. In order to assist you in Week 3, we will provide you with resources to help you refrain from using cigarettes and e-cigarettes, if you are interested.

POSSIBLE BENEFITS

By participating, you will help researchers better understand how smokers use different nicotine and tobacco products. The findings will also be used to help inform regulations on tobacco products and e-cigarettes. We also have information on smoking cessation resources, should these be of interest to you.

FINANCIAL CONSIDERATIONS

In appreciation of your time and to cover the cost of parking or transit, you will receive the following amounts for your participation:

Visit	Remuneration Amount
Visit 1	$50 (cash)
Visit 2	$70 (cash or Interac e-transfer)
Visit 3	$75 (cash or Interac e-transfer)
Visit 4	$100 (cash or Interac e-transfer)
Total	$295

In total, you will receive $295 for your participation in the study. You will receive $50 after Visit 1, $70 at the end of Visit 2, $75 at the end of Visit 3, and $100 after the final Visit. Although the Visit 1 amount will be provided as cash, the remaining amounts can be provided as cash or as an Interac e-transfer, whichever you prefer. The amount received is taxable. It is your responsibility to report this amount for income tax purposes.

OWNERSHIP AND DOCUMENTATION OF YOUR URINE SAMPLES

Your urine samples that are collected over the course of the study will be sent to the lab for testing. Testing will only be conducted for components of tobacco and nicotine products. The samples will be the property of the scientists doing the study. The samples will be labelled only

with your study ID number in order to protect your privacy. The samples will be destroyed after the study is completed.

CONFIDENTIALITY

All of the information you provide in this study will be kept strictly confidential. For your protection, we will assign you a number that will be used to label all information, including any urine samples. Personal information, such as your name and contact information, will be kept in a separate file that is locked away. No personal information such as your name or contact details will be kept on the urine samples, and your samples will be destroyed after we conduct the analyses: they will not be used for any other purposes than examining levels of nicotine and chemicals from tobacco smoke. All paper records will be stored in a secure facility at the University of Waterloo, and destroyed after 7 years. Electronic copies of your survey data will not contain any personal identifiers and will be encrypted and stored in password-protected files on a secure server and retained for a period of 7 years. Only the research team will have access to the data. You will not be identifiable in any publications or presentations resulting from this study.

WITHDRAWAL FROM STUDY

You are free to choose to whether or not to participate in this study, and may refuse to answer any specific questions. You can also choose to stop being a part of the study at any time. If you do choose to stop participating before the end of the study, you will still be remunerated a certain amount of money depending on when you withdraw (see remuneration chart in Section 5 of this document). Any data already collected may be used in the study, unless you contact the researcher to have it deleted.

ETHICS REVIEW

This project has been reviewed by and received ethics clearance through a University of Waterloo Research Ethics Committee. Should you have any comments or concerns resulting from your participation in this study, please contact the Chief Ethics Officer, Office of Research Ethics at 519-888-4567 ext. 36005 or by email at maureen.nummelin@uwaterloo.ca.

AVAILABLE SOURCES OF INFORMATION

If you have any questions later or if you require additional information about the study, please feel free to contact research staff at: 519-888-4567 ext.38549 or via email at smokingstudy@uwaterloo.ca.

CONSENT FORM

Title of Project: Smoking Study

Principal Investigator:

Dr. David Hammond (PhD), School of Public Health & Health Systems

University of Waterloo

519-888-4567 ext. 36462 dhammond@uwaterloo.ca

I have read the information presented in the information letter. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and to request any additional details I wanted. I understand the purposes, procedures and risks of the research described in the project. I understand that I will be asked to refrain from using cigarette or e-cigarettes or both products at certain points throughout the study. I understand that I will be asked to complete online daily diaries at the end of each day of the study period. I understand that I will be asked to attend 4 scheduled visits to the lab at the University of Waterloo, at which I will be asked to complete online questionnaires and provide urine and exhaled breath samples.

I am aware that I may withdraw from the study without penalty at any time by advising the researchers of this decision. In appreciation of my time and to cover the cost of parking or transit, I am aware that I will be provided with $50 today. I am aware that I will be provided with $70 following Visit 2, $75 following Visit 3, and $100 following Visit 4, which will be sent to me as an Interac e-transfer, unless I request to pick it up as cash from the lab. If I do not attend the scheduled lab visits, or complete the online daily diaries, I am aware that I will be discontinued from the study.

This project has been reviewed by, and received ethics clearance through a University of Waterloo Research Ethics Committee. I understand that if I have any comments or concerns resulting from my participation in this study, I may contact the Chief Ethics Officer, Office of Research Ethics at 519-888-4567 ext. 36005.

With full knowledge of all foregoing, I agree, of my own free will to participate in this study, and provide urine and exhaled breath samples.

☐YES ☐NO

I give permission that my urine and exhaled breath samples can be analyzed for levels of nicotine and chemicals from tobacco products.

☐YES ☐NO

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

_____ _____

Participant Name (Please Print) Date

_____

Participant Signature

_____ _____

Witness Name (Please Print) Date

_____

Witness Signature

Appendix C: Study questionnaires

Visit questionnaires

Questionnaires were completed by participants at each of four scheduled visits to the laboratory.

The Visit 1 questionnaire was completed by all participants at baseline.

Visit 1 questionnaire

LOG IN
Please enter your participant ID: _____ [insert] **Please enter your email address: _____ [insert]**

SOCIODEMOGRAPHIC INFORMATION	
To start, we would like to ask you a few questions about yourself to make sure we have interviewed a true cross-section of people. Please be assured that all your responses will be kept entirely confidential.	
Gender	What is your gender? 1. Male 2. Female 3. Other 77. Don't know 88. Refused
Age	How old are you? ___ years 77. Don't know 88. Refused
Height	What is your height? ___ ft ___ inches OR ___ cm 77. Don't know 88. Refused
Weight	What is your weight? ___ lbs OR ___ kg 77. Don't know 88. Refused
Education	What is the highest level of formal education that you have completed? 1. Grade school or some high school 2. Completed high school 3. Technical or trade school or community college (some or completed) 4. Some university (no degree)

	5. Completed university degree 6. Post-graduate degree 77. Don't know 88. Refused
Ethnicity	People in Canada come from many racial and cultural groups. Do you consider yourself to be: *[Please check all that apply]* 1. White 2. South Asian (e.g., East Indian, Pakistani, Sri Lankan) 3. Chinese 4. Black 5. Filipino 6. Latin American 7. Arab 8. Southeast Asian (e.g., Vietnamese, Cambodian, Malaysian, Laotian) 9. West Asian (e.g., Iranian, Afghan) 10. Korean 11. Japanese 12. Aboriginal (e.g., First Nations, Métis, Inuk/Inuit) 13. Other: ___ [open-ended text] 77. Don't know 88. Refused

SMOKING BEHAVIOURS	
Next, we would like to ask you some questions about your behaviours and experiences related to smoking cigarettes – you might recognize some of these questions from our previous telephone conversation.	
V1.smokingstatus1	Do you **smoke cigarettes** every day, occasionally, or not at all? 1. Every day 2. Occasionally 3. Not at all 77. Don't know 88. Refused
V1.smokingstatus2	**Progammer note: Ask only if V1.smokingstatus1=2 or 3.** Just to confirm, do you **smoke cigarettes** everday or less than everyday? 1. Every day 2. Less than every day 77. Don't know 88. Refused
V1.smokingstatus.terminate	**Progammer note: If V1.smokingstatus2=2:** Unfortunately, because you do not smoke cigarettes every day, you are not eligible to participate in the study. Please return the iPad to the Research Assistant. Thank you.
V1.smoketime	How long have you been **smoking cigarettes** daily? ___ months OR ___ years 77. Don't know 88. Refused

V1.DD.cig.CPD	How many **cigarettes did you smoke** today? ___ [open-ended text] 77. Don't know 88. Refused
V1.DD.cig.wake	**Progammer note: If V1.DD.cig.CPD>0, ask:** How soon after waking today did you **smoke** your first **cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V1.cig.CPD	In the past 7 days, on average, how many **cigarettes** did you **smoke** per day? ___ [open-ended text] 77. Don't know 88. Refused
V1.cig.wake	In the past 7 days, on average, how soon after waking did you **smoke** your first **cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V1.cig.lastcig	How long has it been since you last **smoked a cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused
V1.cig.brand	Please specify the usual brand of **cigarettes** you **smoke** (include any specific flavours or varieties): ___ [open-ended text] 77. Don't know 88. Refused
V1.cig.where	Please specify where you **smoked cigarettes** in the past 7 days. *[Please check all that apply]* 1. At home 2. At school or work 3. At a restaurant or bar 4. In a vehicle 5. While walking on the street 6. In a park or other outdoor venue 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V1.cig.home	**Programmer Note: Ask only if V1.cig.where=1.**

	In the past 7 days, when you **smoked cigarettes** at home, did you **smoke** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.cig.work	**Programmer Note: Ask only if V1.cig.where=2.** In the past 7 days, when you **smoked cigarettes** at school or work, did you **smoke** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.cig.restbar	**Programmer Note: Ask only if V1.cig.where=3.** In the past 7 days, when you **smoked cigarettes** at a restaurant or bar, did you **smoke** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.cig.everquit	How many times, if ever, have you ever tried to **quit smoking**? ___ [open-ended text] 77. Don't know 88. Refused
V1.cig.lastquit	**Progammer note: If V1.cig.everquit>0, ask:** How long ago did your most recent serious quit attempt (for regular **tobacco cigarettes**) end? ___ days ago OR ___ months ago OR ___ years ago 77. Don't know 88. Refused
V1.cig.planquit	Are you seriously planning to **quit smoking**: 1. Within the next month? 2. Within the next 6 months? 3. Sometime in the future, beyond 6 months? 4. I am not planning to quit 77. Don't know 88. Refused
V1.cig.quitmethod	**Programmer Note: Ask only if V1.cig.planquit=1-3.** If you were to **quit smoking**, would you consider using any of the following products to help you quit? 1. Nicotine patch, gum, or lozenge? Yes / No / Don't know 2. E-cigarette? Yes / No / Don't know 3. Prescription medication (e.g., Zyban, Champix)? Yes / No / Don't know

FTCD	
Please answer the following questions based on your behaviours in general.	
V1.FTCD1	How soon after you wake up do you **smoke** your first **cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V1.FTCD2	Do you find it difficult to refrain from **smoking cigarettes** in places where it is forbidden? 1. Yes 2. No 77. Don't know 88. Refused
V1.FTCD3	Which **cigarette** would you most hate to give up? 1. The first one in the morning 2. All others 77. Don't know 88. Refused
V1.FTCD4	How many **cigarettes** do you **smoke** per day? 1. 10 or less 2. 11-20 3. 21-30 4. 31 or more 77. Don't know 88. Refused
V1.FTCD5	Do you **smoke cigarettes** more frequently during the first hours after waking than the rest of the day? 1. Yes 2. No 77. Don't know 88. Refused
V1.FTCD6	Do you **smoke cigarettes** when you are so ill that you are in bed most of the day? 1. Yes 2. No 77. Don't know 88. Refused

NDSS				
Please answer the following questions based on your behaviours <u>in general</u>. **Select the number that indicates how well the following statements describe you:**				
1. After not **smoking cigarettes** for a while, I need to **smoke a cigarette** to relieve feelings of restlessness and irritability.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
2. Whenever I go without **smoking cigarettes** for a few hours, I experience craving.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
3. After not **smoking cigarettes** for a while, I need to **smoke a cigarette** in order to keep myself from experiencing any discomfort.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
4. When I'm really craving **a cigarette**, it feels like I'm in the grip of some unknown force that I cannot control.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
5. I feel a sense of control over my **cigarette smoking**. I can "take it" or "leave it" at any time.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
6. I tend to avoid restaurants that don't allow **cigarette smoking**, even if I would otherwise enjoy the food.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
7. Sometimes I decline offers to visit with my **non-smoking** friends because I know I'll feel uncomfortable if I **smoke cigarettes**.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
8. Even if traveling a long distance, I'd rather not travel by airplane because I wouldn't be allowed to **smoke cigarettes**.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
9. Since the time when I became a regular **cigarette smoker**, the amount I **smoke** has either stayed the same or has decreased somewhat.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
10. Compared to when I first started **smoking cigarettes**, I need to **smoke** a lot more now in order to get what I really want out of it.				

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

11. Compared to when I first started **smoking cigarettes**, I can **smoke** much, much more now before I start to feel nauseated or ill.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

12. It's hard to estimate how many **cigarettes** I **smoke** per day because the number often changes.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

13. My **smoking** pattern is very irregular throughout the day. It is not unusual for me to **smoke** many **cigarettes** in an hour, then not have another one until hours later.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

14. The number of **cigarettes** I **smoke** per day is often influenced by other factors – how I'm feeling, what I'm doing, etc.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

15. I **smoke cigarettes** at different rates in different situations.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

16. My **smoking** is not much affected by other things. I **smoke cigarettes** about the same amount whether I'm relaxed or working, happy or sad, alone or with others, etc.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

17. My **cigarette smoking** is fairly regular throughout the day.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

18. I **smoke cigarettes** consistently and regularly throughout the day.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

19. I **smoke cigarettes** about the same amount on weekends as on weekdays.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

QSU-Brief						
Please answer the following questions based on your thoughts and behaviours <u>today</u>. **Select the number that indicates how well the following statements describe you:**						
1. I would like to **smoke a cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
2. I have a desire to **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
3. Nothing would be better than **smoking a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
4. If it were possible, I probably would **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
5. I could control things better right now if I could **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
6. All I want right now is to **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
7. I have an urge to **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
8. **A cigarette** would taste good right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
9. I would do almost anything to be able to **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**

Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

10. **Smoking a cigarette** would make me less depressed.

1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

SEQ-12

The following are some situations in which certain people might be tempted to <u>smoke cigarettes</u>.
Please indicate whether you are sure that you could *go without* <u>smoking cigarettes</u> in each situation.

1. When I feel nervous

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

2. When I feel depressed

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

3. When I am angry

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

4. When I feel very anxious

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

5. When I want to think about a difficult problem

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

6. When I feel the urge to **smoke cigarettes**

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

7. When having a drink with friends

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

8. When celebrating something				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
9. When drinking beer, wine, or other spirits				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
10. When I am with **cigarette smokers**				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
11. After a meal				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
12. When having coffee or tea				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

VAPING BEHAVIOURS	
Next, we would like to ask you some questions about your behaviours and experiences related to <u>using e-cigarettes</u> – you might recognize some of these questions from our previous telephone conversation.	
V1.vapingstatus1	Do you **use e-cigarettes** every day, occasionally, or not at all? 1. Every day 2. Occasionally 3. Not at all 77. Don't know 88. Refused
V1.vapingstatus2	**Progammer note: Ask only if V1.vapingstatus1=2 or 3.** Just to confirm, do you **use e-cigarettes** everyday or less than everyday? 1. Every day 2. Less than every day 77. Don't know 88. Refused
V1.vapingstatus.terminate	**Progammer note: If V1.vapingstatus2=2:** Unfortunately, because you do not use e-cigarettes every day, you are not eligible to participate in the study.

	Please return the iPad to the Research Assistant. Thank you.
V1.vapetime	How long have you been **using e-cigarettes** daily? ___ months OR ___ years 77. Don't know 88. Refused
V1.ecig.reasons.initiation.all	What are the reason(s) you began to **use e-cigarettes** daily? Please check all the reasons that apply. *[Please check all that apply]* 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know 88. Refused
V1.ecig.reasons.initiation.most	What is the most important reason you began to **use e-cigarettes** daily? Please select one reason. 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know 88. Refused
V1.DD.ecig.times	How many times did you **use an e-cigarette** today? ___ [open-ended text] 77. Don't know 88. Refused
V1.DD.ecig.puffs	**Progammer note: If V1.DD.ecig.times>0, ask:**

	On average, for each time you **used an e-cigarette** today, how many puffs did you take? ___ Puffs 77. Don't know 88. Refused
V1.DD.ecig.length	**Progammer note: If V1.DD.ecig.times>0, ask:** On average, for each time you **used an e-cigarette** today, how long did you use it for? ___ Minutes 77. Don't know 88. Refused
V1.DD.ecig.wake	**Progammer note: If V1.DD.ecig.times>0, ask:** How soon after waking today did you **use** your first **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V1.ecig.times	In the past 7 days, on average, how many times did you **use an e-cigarette** per day? ___ [open-ended text] 77. Don't know 88. Refused
V1.ecig.puffs	In the past 7 days, on average, for each time you **used an e-cigarette**, how many puffs did you take? ___ Puffs 77. Don't know 88. Refused
V1.ecig.length	In the past 7 days, on average, for each time you **used an e-cigarette**, how long did you use it for? ___ Minutes 77. Don't know 88. Refused
V1.ecig.wake	In the past 7 days, on average, how soon after waking did you **use** your first **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V1.ecig.lastecig	How long has it been since you last **used an e-cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused
V1.ecig.flavour	Please indicate the flavour(s) of the **e-cigarette(s)/e-liquid** you **used** in the past 7 days. *[Please check all that apply]*

	1. Tobacco 2. Menthol/mint 3. Spice 4. Candy 5. Fruit 6. Coffee/drinks/alcohol 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V1.ecig.type	What type of **e-cigarette(s)** have you **used** in the past 7 days? *[Please check all that apply]* 1. A disposable e-cigarette 2. An e-cigarette that uses re-placeable pre-filled cartridges 3. An e-cigarette that is re-chargeable and has a tank or reservoir that you fill with liquid 77. Don't know 88. Refused
V1.ecig.device.brand	**Programmer Note: Ask only if V1.ecig.type=1 or 2.** What brand(s) of **e-cigarette** have you **used** in the past 7 days? 1. ___ [open-ended text] 2. Don't know 88. Refused
V1.ecig.ejuice.brand	**Programmer Note: Ask only if V1.ecig.type=3.** What brand(s) of **e-liquid** have you **used** in the past 7 days? 1. ___ [open-ended text] 2. Don't know 88. Refused
V1.ecig.nic	What type of **e-cigarettes** did you **use** in the past 7 days? 1. Only e-cigarettes with nicotine 2. Only nicotine-free / non-nicotine e-cigarettes 3. Some e-cigarettes with nicotine and some nicotine-free / non-nicotine e-cigarettes 4. Don't know 88. Refused
V1.ecig.nic.conc	**Progammer note: Ask only if V1.ecig.nic=1 or 3.** What was the concentration/strength of nicotine in your **e-cigarette**? 1. 1-8 mg/mL (0.1-0.8%) 2. 9-14 mg/mL (0.9-1.4%) 3. 15-20 mg/mL (1.5-2.0%) 4. 21-24 mg/mL (2.1-2.4%) 5. 25 mg/mL (2.5%) or more 77. Don't know 88. Refused
V1.ecig.where	Please specify where you **used e-cigarettes** in the past 7 days. *[Please check all that apply]* 1. At home 2. At school or work 3. At a restaurant or bar

	4. In a vehicle 5. While walking on the street 6. In a park or other outdoor venue 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V1.ecig.home	**Programmer Note: Ask only if V1.ecig.where=1.** In the past 7 days, when you **used e-cigarettes** at home, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.ecig.work	**Programmer Note: Ask only if V1.ecig.where=2.** In the past 7 days, when you **used e-cigarettes** at school or work, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.ecig.restbar	**Programmer Note: Ask only if V1.ecig.where=3.** In the past 7 days, when you **used e-cigarettes** at a restaurant or bar, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V1.ecig.reasons.cu.all	What are the reason(s) you currently **use e-cigarettes**? Please check all the reasons that apply. *[Please check all that apply]* 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know

	88. Refused
V1.ecig.reasons.cu.most	What is the most important reason you currently **use e-cigarettes**? Please select one reason. 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know 88. Refused
V1.ecig.everquit	How many times, if ever, have you ever tried to **quit using e-cigarettes**? ___ [open-ended text] 77. Don't know 88. Refused
V1.ecig.lastquit	**Progammer note: If V1.ecig.everquit>0, ask:** How long ago did your most recent serious quit attempt (for **e-cigarettes**) end? ___ days ago OR ___ months ago OR ___ years ago 77. Don't know 88. Refused
V1.ecig.planquit	Are you seriously planning to **quit using e-cigarettes**: 1. Within the next month? 2. Within the next 6 months? 3. Sometime in the future, beyond 6 months? 4. I am not planning to quit 77. Don't know 88. Refused

E-FTCD	
Please answer the following questions based on your behaviours in general.	
V1.EFTCD1	How soon after you wake up do you **use** your first **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know

	88. Refused
V1.EFTCD2	Do you find it difficult to refrain from **using e-cigarettes** in places where it is forbidden? 1. Yes 2. No 77. Don't know 88. Refused
V1.EFTCD3	Which **e-cigarette** would you <u>most</u> hate to give up? 1. The first one in the morning 2. All others 77. Don't know 88. Refused
V1.EFTCD4	How many times do you **use** an **e-cigarette** per day? 1. 10 or less 2. 11-20 3. 21-30 4. 31 or more 77. Don't know 88. Refused
V1.EFTCD5	Do you **use e-cigarettes** more frequently during the first hours after waking than the rest of the day? 1. Yes 2. No 77. Don't know 88. Refused
V1.EFTCD6	Do you **use e-cigarettes** when you are so ill that you are in bed most of the day? 1. Yes 2. No 77. Don't know 88. Refused

E-NDSS				
Please answer the following questions based on your behaviours <u>in general</u>. **Select the number that indicates how well the following statements describe you:**				
20. After not **using e-cigarettes** for a while, I need to **use an e-cigarette** to relieve feelings of restlessness and irritability.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
21. Whenever I go without **using e-cigarettes** for a few hours, I experience craving.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
22. After not **using e-cigarettes** for a while, I need to **use an e-cigarette** in order to keep myself from experiencing any discomfort.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
23. When I'm really craving **an e-cigarette**, it feels like I'm in the grip of some unknown force that I cannot control.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
24. I feel a sense of control over my **vaping**. I can "take it" or "leave it" at any time.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
25. I tend to avoid restaurants that don't allow **vaping**, even if I would otherwise enjoy the food.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
26. Sometimes I decline offers to visit with my **non-vaping** friends because I know I'll feel uncomfortable if I **use e-cigarettes**.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
27. Even if traveling a long distance, I'd rather not travel by airplane because I wouldn't be allowed to **use e-cigarettes**.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
28. Since the time when I became a regular **e-cigarette user**, the amount I **vape** has either stayed the same or has decreased somewhat.				
1 Not At All True	**2** Somewhat True	**3** Moderately True	**4** Very True	**5** Extremely True
29. Compared to when I first started **using e-cigarettes**, I need to **vape** a lot more now in order to get what I really want out of it.				

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

30. Compared to when I first started **using e-cigarettes**, I can **vape** much, much more now before I start to feel nauseated or ill.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

31. It's hard to estimate how many **e-cigarettes** I **use** per day because the number often changes.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

32. My **vaping** pattern is very irregular throughout the day. It is not unusual for me to **use** many **e-cigarettes** in an hour, then not have another one until hours later.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

33. The number of **e-cigarettes** I **use** per day is often influenced by other factors – how I'm feeling, what I'm doing, etc.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

34. I **use e-cigarettes** at different rates in different situations.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

35. My **vaping** is not much affected by other things. I **use e-cigarettes** about the same amount whether I'm relaxed or working, happy or sad, alone or with others, etc.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

36. My **e-cigarette vaping** is fairly regular throughout the day.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

37. I **use e-cigarettes** consistently and regularly throughout the day.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

38. I **use e-cigarettes** about the same amount on weekends as on weekdays.

1	2	3	4	5
Not At All True	Somewhat True	Moderately True	Very True	Extremely True

E-QSU-Brief						
Please answer the following questions based on your thoughts and behaviours <u>today</u>. **Select the number that indicates how well the following statements describe you:**						
11. I would like to **use an e-cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
12. I have a desire to **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
13. Nothing would be better than **using an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
14. If it were possible, I probably would **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
15. I could control things better right now if I could **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
16. All I want right now is to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
17. I have an urge to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
18. **An e-cigarette** would taste good right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
19. I would do almost anything to be able to **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**

Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

20. **Using an e-cigarette** would make me less depressed.

1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

E-SEQ-12

The following are some situations in which certain people might be tempted to <u>use e-cigarettes</u>.
Please indicate whether you are sure that you could *go without* <u>using e-cigarettes</u> in each situation.

13. When I feel nervous

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

14. When I feel depressed

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

15. When I am angry

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

16. When I feel very anxious

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

17. When I want to think about a difficult problem

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

18. When I feel the urge to **use e-cigarettes**

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

19. When having a drink with friends

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

20. When celebrating something				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
21. When drinking beer, wine, or other spirits				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
22. When I am with **e-cigarette users**				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
23. After a meal				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
24. When having coffee or tea				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

DUAL USE BEHAVIOURS	
Next, we would like to ask you some questions about <u>both</u> your <u>cigarette smoking</u> and <u>use of e-cigarettes</u>. Please pay careful attention to the behaviours asked about in each question.	
V1.productorder	Which behaviour did you begin <u>first</u>, **smoking cigarettes** or **using e-cigarettes**? 1. I began smoking cigarettes first 2. I began using e-cigarettes first 77. Don't know 88. Refused
V1.identity	Which behaviour do you identify yourself with more, **smoking cigarettes** or **using e-cigarettes**? 1. I identify myself more as a cigarette smoker 2. I identify myself more as an e-cigarette user 3. Both a cigaretet smokers and an e-cigarette user 4. Neither 77. Don't know 88. Refused
V1.vapechange	Since you started **using e-cigarettes** daily, have you changed the amount you **use** per day? 1. I use much more 2. I use a little more

	3. I use about the same amount 4. I use a little less 5. I use much less 77. Don't know 88. Refused
V1.vapenic	Since you started **using e-cigarettes** daily, have you changed the strength of nicotine that you use most? 1. I increased the strength 2. No change in strength 3. I decreased the strength 77. Don't know 88. Refused
V1.vapeCPD	**Programmer Note: Ask only if V1.productorder=1.** Since you started **using e-cigarettes** daily, has the number of **cigarettes** you **smoke** changed? 1. I smoke fewer cigarettes 2. I smoke the same amount of cigarettes 3. I smoke more cigarettes 77. Don't know 88. Refused
V1.cig.selfcaddict	Do you consider yourself addicted to **regular tobacco cigarettes**? 1. Not at all 2. Somewhat addicted 3. Very addicted 77. Don't know 88. Refused
V1.ecig.selfaddict	Do you consider yourself addicted to **e-cigarettes**? 1. Not at all 2. Somewhat addicted 3. Very addicted 77. Don't know 88. Refused
V1.cig.easy.quit	Do you think **using e-cigarettes** would make it <u>easier</u> to quit **smoking cigarettes**? 1. Not at all 2. A little 3. A lot 77. Don't know 88. Refused

OTHER BEHAVIOURS	
Next, we would like to ask you some questions about other behaviours – you might recognize some of these questions from our previous telephone conversation.	
V1.ATP	<u>In the past 7 days</u>, have you used any other tobacco products, such as kreteks, bidis, cigars, pipe tobacco, smokeless tobacco or hookah/waterpipe?

	[Please check all that apply] 1. Kreteks 2. Bidis 3. Cigars 4. Pipe tobacco 5. Smokeless tobacco 6. Hookah/waterpipe 7. Other: ___ [open-ended text] 8. I have not used any other tobacco product in the past 7 days 77. Don't know 88. Refused
V1.ATP.terminate	**Programmer Note: If V1.ATP= not equal to 8:** Unfortunately, because you have used other tobacco products in the past 7 days, you are not eligible to participate in the study. Please return the iPad to the Research Assistant. Thank you.
V1.NRT	In the past 7 days, have you used any nicotine replacement therapy products, such as the patch, gum, inhaler, or lozenges? 1. Yes 2. No 3. Don't know 88. Refused
V1.NRT.terminate	**Programmer Note: If V1.NRT=1:** Unfortunately, because you have used nicotine replacement therapy products in the past 7 days, you are not eligible to participate in the study. Please return the iPad to the Research Assistant. Thank you.
V1.SSM	In the past 7 days, have you used any medications, such as "Zyban", "Wellbutrin", or "Champix", to help you quit smoking? 1. Yes 2. No 3. Don't know 88. Refused
V1.SSM.terminate	**Programmer Note: If V1.SSM=1:** Unfortunately, because you have used stop-smoking medications in the past 7 days, you are not eligible to participate in the study. Please return the iPad to the Research Assistant. Thank you.
V1.counselling	In the past 7 days, have you participated in any group or individual counselling programs to help you quit smoking? 1. Yes 2. No 3. Don't know 88. Refused
V1.counselling.terminate	**Programmer Note: If V1.counselling=1:** Unfortunately, because you have participated in smoking cessation counselling programs in the past 7 days, you are not eligible to participate in the study. Please return the iPad to the Research Assistant. Thank you.

PERCEPTIONS OF E-CIGARETTES	
We would like to ask you some questions about your opinion regarding <u>e-cigarettes</u>. There is no right or wrong answer – we are simply interested in your thoughts.	
V1.ecig.accept	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less socially acceptable 2. … a little less socially acceptable 3. … equally as socially acceptable 4. … a little more socially acceptable 5. Using e-cigarettes is … a lot more socially acceptable 77. Don't know 88. Refused
V1.ecig.satisf	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less satisfying 2. … a little less satisfying 3. … equally as satisfying 4. … a little more satisfying 5. Using e-cigarettes is … a lot more satisfying 77. Don't know 88. Refused
V1.ecig.pleasure	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less pleasurable 2. … a little less pleasurable 3. … equally as pleasurable 4. … a little more pleasurable 5. Using e-cigarettes is … a lot more pleasurable 77. Don't know 88. Refused
V1.ecig.harm	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less harmful 2. … a little less harmful 3. … equally as harmful 4. … a little more harmful 5. Using e-cigarettes is … a lot more harmful 77. Don't know 88. Refused
V1.ecig.cost	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less expensive 2. … a little less expensive 3. … equally as expensive 4. … a little more expensive 5. Using e-cigarettes is … a lot more expensive 77. Don't know 88. Refused

RESPIRATORY HEALTH	
We would like to ask you about your lung function and breathing. Please note, the following questions specifically ask about changes in the past 7 days. For example, many smokers experience shortness of breath; if this has not changed for you in the past 7 days, please respond "no difference".	
V1.HC.short.breath	In the past 7 days, have you noticed any change in experiencing shortness of breath? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V1.HC.cough.freq	In the past 7 days, have you noticed any change in how often you cough? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V1.HC.phlegm	In the past 7 days, have you noticed any change in how often you cough up phlegm? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V1.HC.chest.sound	In the past 7 days, have you noticed any change in how your chest sounds, such as wheezing or whistling? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V1.HC.overall.lung	Overall, in the past 7 days, would you describe your lung function as: 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused

EXIT	
V1.exit	Thank you for completing the questionnaire. Please return the iPad to the Research Assistant.

Visit 2-4 questionnaires

Participants completed the Visit 2 questionnaire following Week 1, and the Visit 3 questionnaire following Week 2, as per their condition order (Group A or Group B).
A sample Visit 2 questionnaire is included below for participants assigned to Group A (equivalent to the Visit 3 questionnaire for participants assigned to Group B).

The Visit 2 questionnaire for participants assigned to Group B as well as the Visit 3 questionnaire for participants assigned to Group A were similarly structured to the sample below, with the only difference being that questions regarding smoking behaviours (permitted) and the QSU are presented before questions regarding vaping behaviours (not permitted) and the E-QSU.

The Visit 4 questionnaire was completed by all participants at the end of the study period. The Visit 4 questionnaire was similarly structured to the sample below, with the only difference being that use of both tobacco cigarettes and e-cigarettes was not permitted. Questions that were asked at Visit 4 with respect to both smoking cigarettes and using e-cigarettes are denoted by an asterisk.

LOG IN
Please enter your participant ID: _____ [insert] **Please enter your email address: _____ [insert]**

DAILY DIARY (DAY 8)	
We would like to ask you some questions about your behavior and experiences <u>today, up until your current visit to the lab.</u>	
V2.D8.ecig.times	How many times did you **use an e-cigarette** <u>today</u>? ___ [open-ended text] 77. Don't know 88. Refused
V2.D8.ecig.puffs	**Progammer note: If V2.D8.ecig.times>0, ask:** On average, <u>for each time</u> you **used an e-cigarette** <u>today</u>, how many puffs did you take? ___ Puffs 77. Don't know

	88. Refused
V2.D8.ecig.length	**Progammer note: If V2.D8.ecig.times>0, ask:** On average, <u>for each time</u> you **used an e-cigarette** <u>today</u>, how long did you use it for? ___ Minutes 77. Don't know 88. Refused
V2.D8.ecig.wake	**Progammer note: If V2.D8.ecig.times>0, ask:** How soon after waking <u>today</u> did you **use** your <u>first</u> **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V2.D8.cig.CPD	How many **cigarettes did you smoke** <u>today</u>? ___ [open-ended text] 77. Don't know 88. Refused
V2.D8.cig.wake	**Progammer note: If V2.D8.cig.CPD>0, ask:** How soon after waking <u>today</u> did you **smoke** your <u>first</u> **cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V2.D8.cig.lastcig	How long has it been since you <u>last</u> **smoked a cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused

VAPING BEHAVIOURS (PERMITTED)	
Next, we would like to ask you some questions about your behavior and experiences <u>in the past 7 days.</u>	
V2.ecig.times	<u>In the past 7 days</u>, on average, how many times did you **use an e-cigarette** <u>per day</u>? ___ [open-ended text] 77. Don't know 88. Refused
V2.ecig.puffs	<u>In the past 7 days</u>, on average, <u>for each time</u> you **used an e-cigarette**, how many puffs did you take? ___ Puffs 77. Don't know 88. Refused

V2.ecig.length	In the past 7 days, on average, for each time you **used an e-cigarette**, how long did you use it for? ___ Minutes 77. Don't know 88. Refused
V2.ecig.wake	In the past 7 days, on average, how soon after waking did you **use** your first **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
V2.ecig.lastecig	How long has it been since you last **used an e-cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused
V2.ecig.flavour	Please indicate the flavour(s) of the **e-cigarette(s)/e-liquid** you **used** in the past 7 days. *[Please check all that apply]* 1. Tobacco 2. Menthol/mint 3. Spice 4. Candy 5. Fruit 6. Coffee/drinks/alcohol 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V2.ecig.type	What type of **e-cigarette(s)** have you **used** in the past 7 days? *[Please check all that apply]* 1. A disposable e-cigarette 2. An e-cigarette that uses re-placeable pre-filled cartridges 3. An e-cigarette that is re-chargeable and has a tank or reservoir that you fill with liquid 77. Don't know 88. Refused
V2.ecig.device.brand	**Programmer Note: Ask only if V2.ecig.type=1 or 2.** What brand(s) of **e-cigarette** have you **used** in the past 7 days? 1. ___ [open-ended text] 2. Don't know 88. Refused
V2.ecig.ejuice.brand	**Programmer Note: Ask only if V2.ecig.type=3.** What brand(s) of **e-liquid** have you **used** in the past 7 days? 1. ___ [open-ended text] 2. Don't know 88. Refused

V2.ecig.nic	What type of **e-cigarettes** did you **use** in the past 7 days? 1. Only e-cigarettes with nicotine 2. Only nicotine-free / non-nicotine e-cigarettes 3. Some e-cigarettes with nicotine and some nicotine-free / non-nicotine e-cigarettes 4. Don't know 88. Refused
V2.ecig.nic.conc	**Progammer note: Ask only if V2.ecig.nic=1 or 3.** What was the concentration/strength of nicotine in your **e-cigarette**? 1. 1-8 mg/mL (0.1-0.8%) 2. 9-14 mg/mL (0.9-1.4%) 3. 15-20 mg/mL (1.5-2.0%) 4. 21-24 mg/mL (2.1-2.4%) 5. 25 mg/mL (2.5%) or more 77. Don't know 88. Refused
V2.ecig.where	Please specify where you **used e-cigarettes** in the past 7 days. *[Please check all that apply]* 1. At home 2. At school or work 3. At a restaurant or bar 4. In a vehicle 5. While walking on the street 6. In a park or other outdoor venue 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V2.ecig.home	**Programmer Note: Ask only if V2.ecig.where=1.** In the past 7 days, when you **used e-cigarettes** at home, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V2.ecig.work	**Programmer Note: Ask only if V2.ecig.where=2.** In the past 7 days, when you **used e-cigarettes** at school or work, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V2.ecig.restbar	**Programmer Note: Ask only if V2.ecig.where=3.** In the past 7 days, when you **used e-cigarettes** at a restaurant or bar, did you **use** them indoors or outdoors? 1. Indoors 2. Outdoors

	3. Both indoors and outdoors 77. Don't know 88. Refused
V2.ecig.reasons.cu.all	In the past 7 days, what were the reason(s) you **used e-cigarettes**? *[Please check all that apply]* 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know 88. Refused
V2.ecig.reasons.cu.most	In the past 7 days, what was the most important reason you **used e-cigarettes**? Please select one reason. 1. I like their taste / flavour 2. They are less harmful to me than smoking 3. They are less harmful to others around me than smoking 4. To help me with cravings for cigarettes 5. To help me quit smoking 6. To help me to smoke fewer cigarettes 7. They cost less 8. They were recommended by a health professional 9. They were recommended by a family/friend 10. I can use them in places where smoking is not allowed 11. Due to boredom 12. To reduce stress 13. To control body weight 14. Other reason – please specify: _____ [open-ended] 77. Don't know 88. Refused
V2.ecig.selfaddict	Do you consider yourself addicted to **e-cigarettes**? 1. Not at all 2. Somewhat addicted 3. Very addicted 77. Don't know 88. Refused
V2.cig.easy.quit	Do you think **using e-cigarettes** would make it easier to quit **smoking cigarettes**?

	1. Not at all 2. A little 3. A lot 77. Don't know 88. Refused

E-QSU-Brief						
Please answer the following questions based on your thoughts and behaviours <u>today</u>. Select the number that indicates how well the following statements describe you:						
21. I would like to **use an e-cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
22. I have a desire to **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
23. Nothing would be better than **using an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
24. If it were possible, I probably would **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
25. I could control things better right now if I could **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
26. All I want right now is to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
27. I have an urge to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

28. **An e-cigarette** would taste good right now.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

29. I would do almost anything to be able to **use an e-cigarette** right now.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

30. **Using an e-cigarette** would make me less depressed.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

E-SEQ-12

The following are some situations in which certain people might be tempted to <u>use e-cigarettes</u>.
Please indicate whether you are sure that you could *go without* <u>using e-cigarettes</u> in each situation.

25. When I feel nervous

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

26. When I feel depressed

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

27. When I am angry

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

28. When I feel very anxious

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

29. When I want to think about a difficult problem

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

30. When I feel the urge to **use e-cigarettes**

1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
31. When having a drink with friends				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
32. When celebrating something				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
33. When drinking beer, wine, or other spirits				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
34. When I am with **e-cigarette users**				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
35. After a meal				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
36. When having coffee or tea				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

SMOKING BEHAVIOURS (NOT PERMITTED)	
V2.cig.use	Over the past 7 days, we asked you to NOT **smoke cigarettes**. We know this may have been a very difficult thing to ask of you. It's really, really important that we know about any **cigarettes** you may have **smoked**. Over the past 7 days (since your last visit to the lab), did you **smoke any cigarettes**? 1. Yes 2. No 77. Don't know 88. Refused
V2.cig.report	**Programmer Note: Ask only if V2.cig.use=1.**

	Thank you for letting us know. Did you report all the **cigarettes** you **smoked** in the past 7 days in the online daily diaries? 1. Yes 2. No 77. Don't know 88. Refused
V2.cig.cheat	**Programmer Note: Ask only if V2.cig.report=2.** Please tell us how many **cigarettes** you **smoked** on each day in the past 7 days. Please include **ALL** the **cigarettes** you **smoked**, even if you already reported them in the online daily diaries. Day 1 (night after your last visit to the lab): ___ Day 2: ___ Day 3: ___ Day 4: ___ Day 5: ___ Day 6: ___ Day 7 (today, before your visit to the lab): ___ 77. Don't know 88. Refused
V2.cig.brand	**Programmer Note: Ask only if V2.cig.use=1.** Please specify the brand of **cigarettes** you **smoked** in the past 7 days (include any specific flavours or varieties): ___ [open-ended text] 77. Don't know 88. Refused
V2.cig.where	**Programmer Note: Ask only if V2.cig.use=1.** Please specify where you **smoked cigarettes** in the past 7 days. *[Please check all that apply]* 1. At home 2. At school or work 3. At a restaurant or bar 4. In a vehicle 5. While walking on the street 6. In a park or other outdoor venue 7. Other: ___ [open-ended text] 77. Don't know 88. Refused
V2.cig.home	**Programmer Note: Ask only if V2.cig.use=1 AND V2.cig.where=1.** In the past 7 days, when you **smoked cigarettes** at home, did you **smoke** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V2.cig.work	**Programmer Note: Ask only if V2.cig.use=1 AND V2.cig.where=2.** In the past 7 days, when you **smoked cigarettes** at school or work, did you **smoke** them indoors or outdoors?

	1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V2.cig.restbar	**Programmer Note: Ask only if V2.cig.use=1 AND V2.cig.where=3.** In the past 7 days, when you **smoked cigarettes** at a restaurant or bar, did you **smoke** them indoors or outdoors? 1. Indoors 2. Outdoors 3. Both indoors and outdoors 77. Don't know 88. Refused
V2.cig.selfaddict	Do you consider yourself addicted to **regular tobacco cigarettes**? 1. Not at all 2. Somewhat addicted 3. Very addicted 77. Don't know 88. Refused

QSU-Brief						
Please answer the following questions based on your thoughts and behaviours today. Select the number that indicates how well the following statements describe you:						
31. I would like to **smoke a cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
32. I have a desire to **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
33. Nothing would be better than **smoking a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
34. If it were possible, I probably would **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
35. I could control things better right now if I could **smoke a cigarette**.						

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

36. All I want right now is to **smoke a cigarette**.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

37. I have an urge to **smoke a cigarette**.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

38. **A cigarette** would taste good right now.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

39. I would do almost anything to be able to **smoke a cigarette** right now.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

40. **Smoking a cigarette** would make me less depressed.

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

SEQ-12

The following are some situations in which certain people might be tempted to <u>smoke cigarettes</u>.
Please indicate whether you are sure that you could *go without* <u>smoking cigarettes</u> in each situation.

37. When I feel nervous

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

38. When I feel depressed

1	2	3	4	5
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

39. When I am angry

1	2	3	4	5

Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
40. When I feel very anxious				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
41. When I want to think about a difficult problem				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
42. When I feel the urge to **smoke cigarettes**				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
43. When having a drink with friends				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
44. When celebrating something				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
45. When drinking beer, wine, or other spirits				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
46. When I am with **cigarette smokers**				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
47. After a meal				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure
48. When having coffee or tea				
1	**2**	**3**	**4**	**5**
Not at all sure	Not very sure	More or less sure	Fairly sure	Absolutely sure

OTHER BEHAVIOURS	
Next, we would like to ask you some questions about other behaviours – you might recognize some of these questions from our previous telephone conversation.	
V2.ATP	In the past 7 days, have you used any other tobacco products, such as kreteks, bidis, cigars, pipe tobacco, smokeless tobacco or hookah/waterpipe? *[Please check all that apply]* 1. Kreteks 2. Bidis 3. Cigars 4. Pipe tobacco 5. Smokeless tobacco 6. Hookah/waterpipe 7. Other: ___ [open-ended text] 8. I have not used any other tobacco product in the past 7 days 77. Don't know 88. Refused
V2.ATP.cheat	**Programmer Note: Ask only if V2.ATP= not equal to 8.** Please tell us how many times you used an other tobacco product (such as kreteks, bidis, cigars, pipe tobacco, smokeless tobacco or hookah/waterpipe), in the past 7 days. Day 1 (night after your last visit to the lab): ___ Day 2: ___ Day 3: ___ Day 4: ___ Day 5: ___ Day 6: ___ Day 7 (today, before your visit to the lab): ___
V2.NRT	In the past 7 days, have you used any nicotine replacement therapy products, such as the patch, gum, inhaler, or lozenges? 1. Yes 2. No 3. Don't know 88. Refused
V2.NRT.cheat	**Programmer Note: Ask only if V2.NRT=1.** Please tell us how many times you used a nicotine replacement therapy product (such as the patch, gum, inhaler, or lozenges), in the past 7 days. in the last 7 days. Day 1 (night after your last visit to the lab): ___ Day 2: ___ Day 3: ___ Day 4: ___ Day 5: ___ Day 6: ___ Day 7 (today, before your visit to the lab): ___
V2.NRT.terminate	**Programmer Note: If V2.NRT=1**

	Unfortunately, because you have used nicotine replacement therapy products within the study period, we can no longer have you participate in the study. Please return the iPad to the Research Assistant. Thank you.
V2.SSM	In the past 7 days, have you used any medications, such as "Zyban", "Wellbutrin", or "Champix", to help you quit smoking? 1. Yes 2. No 3. Don't know 88. Refused
V2.SSM.terminate	**Programmer Note: If V2.SSM=1:** Unfortunately, because you have used stop-smoking medications within the study period, we can no longer have you participate in the study. Please return the iPad to the Research Assistant. Thank you.
V2.counselling	In the past 7 days, have you participated in any group or individual counselling programs to help you quit smoking? 1. Yes 2. No 3. Don't know 88. Refused
V2.counselling.terminate	**Programmer Note: If V2.counselling=1:** Unfortunately, because you have participated in smoking cessation counselling programs within the study period, we can no longer have you participate in the study. Please return the iPad to the Research Assistant. Thank you.

PERCEPTIONS OF E-CIGARETTES	
We would like to ask you some questions about your opinion regarding e-cigarettes. There is no right or wrong answer – we are simply interested in your thoughts.	
V2.ecig.accept	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less socially acceptable 2. … a little less socially acceptable 3. … equally as socially acceptable 4. … a little more socially acceptable 5. Using e-cigarettes is … a lot more socially acceptable 77. Don't know 88. Refused
V2.ecig.satisf	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less satisfying 2. … a little less satisfying 3. … equally as satisfying 4. … a little more satisfying 5. Using e-cigarettes is … a lot more satisfying 77. Don't know 88. Refused
V2.ecig.pleasure	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is…

	1. Using e-cigarettes is … a lot less pleasurable 2. … a little less pleasurable 3. … equally as pleasurable 4. … a little more pleasurable 5. Using e-cigarettes is … a lot more pleasurable 77. Don't know 88. Refused
V2.ecig.harm	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less harmful 2. … a little less harmful 3. … equally as harmful 4. … a little more harmful 5. Using e-cigarettes is … a lot more harmful 77. Don't know 88. Refused
V2.ecig.cost	Compared to smoking regular tobacco cigarettes, **using e-cigarettes** is… 1. Using e-cigarettes is … a lot less expensive 2. … a little less expensive 3. … equally as expensive 4. … a little more expensive 5. Using e-cigarettes is … a lot more expensive 77. Don't know 88. Refused

RESPIRATORY HEALTH	
We would like to ask you about your lung function and breathing. Please note, the following questions specifically ask about <u>changes</u> in the <u>past 7 days</u>. For example, many smokers experience shortness of breath; if this has not changed for you in the past week, please respond "no difference".	
V2.HC.short.breath	<u>In the past 7 days</u>, have you noticed any change in experiencing shortness of breath? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V2.HC.cough.freq	<u>In the past 7 days</u>, have you noticed any change in how often you cough? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V2.HC. phlegm	<u>In the past 7 days</u>, have you noticed any change in how often you cough up phlegm? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused

V2.HC.chest.sound	In the past 7 days, have you noticed any change in how your chest sounds, such as wheezing or whistling? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V2.HC.overall.lung	Overall, in the past 7 days, would you describe your lung function as: 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V2.HC.gh.cig1*	In the past 7 days, have you noticed any change in your overall health status as a result of not **smoking cigarettes**? 1. Worse than usual 2. No difference 3. Better than usual 77. Don't know 88. Refused
V2.HC.gh.cig2*	**Programmer Note: Ask only if V2.HC.gh.cig1=1.** You've indicated that your overall health status in the past 7 days has been worse than usual as a result of not **smoking cigarettes**. Please briefly explain any negative effects you have experienced in the past week: ___ [open-ended text]
V2.HC.gh.cig3*	**Programmer Note: Ask only if V2.HC.gh.cig1=3.** You've indicated that your overall health status in the past 7 days has been better than usual as a result of not **smoking cigarettes**. Please briefly explain any positive effects you have experienced in the past 7 days: ___ [open-ended text]

EXPERIENCES OVER THE PAST WEEK	
V2.cig.difficulty*	Over the past 7 days, how easy or difficult was it to go without **smoking cigarettes**? 1. Very easy 2. Somewhat easy 3. Neither easy nor difficult 4. Somewhat difficult 5. Very difficult 77. Don't know 88. Refused
V2.cig.reflect*	Did your experience over the past 7 days change how you think about your **cigarette smoking**? *[Please write a response below]* ___ [open-ended text]

	77. Don't know 88. Refused
V2.ecig.reflect*	Did your experience <u>over the past 7 days</u> change how you think about your **use of e-cigarettes**? *[Please write a response below]* ___ [open-ended text] 77. Don't know 88. Refused

EXIT	
V2.exit	Thank you for completing the questionnaire. Please return the iPad to the Research Assistant.

Daily diaries

Daily diaries were completed by participants for each day (Days 1-7) in each of the three seven-day study periods (Weeks 1-3), corresponding to participants' condition order (Group A or Group B). A sample daily diary is included below for participants assigned to Group A for Week 1 (equivalent to that for participants assigned to Group B for Week 2).

Daily diaries for participants assigned to Group B for Week 1 and for participants assigned to Group A for Week 2 were similarly structured to the sample below, with the only difference being that questions regarding smoking behaviours (permitted) and the QSU were presented before questions regarding vaping behaviours (not permitted) and the E-QSU.

Daily diaries for all participants for Week 3 were similarly structured to the sample below, with the only difference being that use of both tobacco cigarettes and e-cigarettes was not be permitted.

LOG IN
Please complete the daily diary <u>at the end of each day</u> (after 9pm). **Please enter your participant ID: _____ [insert]** **Please enter your email address: _____ [insert]**
Programmer Note: If Daily Diary=1: **We would like to ask you some questions about your behavior and experiences <u>since your last visit to the lab</u> (do not include anything from before your visit).**
Programmer Note: If Daily Diary=2-7: **We would like to ask you some questions about your behavior and experiences <u>today.</u>**

VAPING BEHAVIOURS (PERMITTED)	
DD.ecig.times	How many times did you **use an e-cigarette** <u>today</u>? ___ [open-ended text] 77. Don't know 88. Refused

DD.ecig.puffs	**Progammer note: If DD.ecig.times>0, ask:** On average, for each time you **used an e-cigarette** today, how many puffs did you take? ___ Puffs 77. Don't know 88. Refused
DD.ecig.length	**Progammer note: If DD.ecig.times>0, ask:** On average, for each time you **used an e-cigarette** today, how long did you use it for? ___ Minutes 77. Don't know 88. Refused
DD.ecig.wake	**Progammer note: If DD.ecig.times>0, ask:** How soon after waking today did you **use** your first **e-cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes 4. After 60 minutes 77. Don't know 88. Refused
DD.ecig.lastecig	How long has it been since you last used an **e-cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused

E-QSU-Brief						
Programmer Note: Ask only if Daily Diary=2.						
Please answer the following questions based on your thoughts and behaviours today. **Select the number that indicates how well the following statements describe you:**						
41. I would like to **use an e-cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
42. I have a desire to **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
43. Nothing would be better than **using an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

44. If it were possible, I probably would **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
45. I could control things better right now if I could **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
46. All I want right now is to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
47. I have an urge to **use an e-cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
48. **An e-cigarette** would taste good right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
49. I would do almost anything to be able to **use an e-cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
50. **Using an e-cigarette** would make me less depressed.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

SMOKING BEHAVIOURS (NOT PERMITTED)	
DD.cig.CPD	How many **cigarettes did you smoke** <u>today</u>? ___ [open-ended text] 77. Don't know 88. Refused
DD.cig.wake	**Progammer note: If DD.cig.CPD>0, ask:** How soon after waking <u>today</u> did you **smoke** your <u>first</u> **cigarette**? 1. Within 5 minutes 2. 6-30 minutes 3. 31-60 minutes

	4. After 60 minutes 77. Don't know 88. Refused
DD.cig.lastcig	How long has it been since you last **smoked a cigarette**? ___ minutes OR ___ hours OR ___ days 77. Don't know 88. Refused

QSU-Brief						
Programmer Note: Ask only if Daily Diary=2.						
Please answer the following questions based on your thoughts and behaviours today. **Select the number that indicates how well the following statements describe you:**						
51. I would like to **smoke a cigarette** as soon as possible.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
52. I have a desire to **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
53. Nothing would be better than **smoking a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
54. If it were possible, I probably would **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
55. I could control things better right now if I could **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
56. All I want right now is to **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

57. I have an urge to **smoke a cigarette**.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
58. **A cigarette** would taste good right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
59. I would do almost anything to be able to **smoke a cigarette** right now.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree
60. **Smoking a cigarette** would make me less depressed.						
1	**2**	**3**	**4**	**5**	**6**	**7**
Strongly Disagree	Disagree	Disagree Somewhat	Undecided	Agree Somewhat	Agree	Strongly Agree

EXIT 1 (Day 1-6)	
DD.exit1	**Programmer note: If Daily Diary=Day 1-6.** Thank you for completing the daily diary. Please remember to complete the daily diary tomorrow night, at the end of the day. If you have any questions, please let us know. You can reach us at smokingstudy@uwaterloo.ca or 519-888-4567 ext. 38549.

EXIT 2 (Day 7)	
DD.exit2	**Programmer note: If Daily Diary=Day 7.** Thank you for completing the daily diary. We look forward to seeing you for your visit tomorrow. If you have any questions, please let us know. You can reach us at smokingstudy@uwaterloo.ca or 519-888-4567 ext. 38549.

Appendix D: Participant recruitment statistics

Table A1: Methods used for participant recruitment

Method of recruitment		Kitchener-Waterloo		Toronto		Total	
		No. of individuals screened	No. of individuals recruited	No. of individuals screened	No. of individuals recruited	No. of individuals screened	No. of individuals recruited
Print newspaper advertisements	24 Hours	-	-	77	16	77	16
	Metro	-	-	40	8	40	8
	The Record	10	4	-	-	10	4
	Subtotal	10	4	117	24	127	28
Online advertisement	Facebook	46	6	36	6	82	12
	Kijiji	12	1	9	5	21	6
	Other	0	0	3	3	3	3
	Subtotal	58	7	48	14	106	21
Print flyers		11	1	-	-	11	1
Vape shops		6	1	4	1	10	2
Unspecified referral		18	3	21	5	39	8
Total		103	16	190	44	293	60

Appendix E: Products used by dual users

Table A2: Tobacco cigarette brands smoked by dual users (n=48)

Brand*	% (n)	
Belmont	25.0%	(12)
Next	20.8%	(10)
First Nations	10.4%	(5)
Canadian	6.3%	(3)
du Maurier	6.3%	(3)
Pall Mall	4.2%	(2)
Phillip Morris	4.2%	(2)
Players	4.2%	(2)
Other[1]	18.8%	(9)
Not stated	4.2%	(2)

Notes:
* Proportions may not sum to 100% due to the fact that participants could report smoking multiple tobacco cigarette brands.
[1] Other brands included: John Player Standard, Kam, LD, Macdonald, Marlboro, Peter Jackson, Studio, Super slim, and Viceroy.

Table A3: E-cigarette device and e-liquid brands used by dual users (n=48)

Brand*		% (n)	
Device	Vapor	2.1%	1
	180 smoke	2.1%	1
	E-got	2.1%	1
	Dune	2.1%	1
	Joy tec	2.1%	1
E-liquid	Walk of shame	2.1%	1
	Mylk	2.1%	1
	Vape north	2.1%	1
	The vapoist	2.1%	1
	Pony Boy	2.1%	1
	Vjuice	2.1%	1
	Ego-t	2.1%	1
	Cosmic fog	2.1%	1
	Filmore	2.1%	1
	Mothers earth	2.1%	1
	360 brand	2.1%	1
	Maven	2.1%	1
	Badlands	2.1%	1
	12 monkeys	2.1%	1
	Sweet water liquids	2.1%	1
	Kilo	2.1%	1
	Rocochette	2.1%	1
	Moshi	2.1%	1
	VaporNorth.com	2.1%	1
	Cloud Panda	2.1%	1
	416 Vapes	2.1%	1
	Liquidtronic	2.1%	1
	Blu	2.1%	1
	Candy	2.1%	1
	Turkish tobacco	2.1%	1
	Dune	2.1%	1
	Self-made liquid	2.1%	1

Liquid made by friend	2.1%	1

Notes:

* Proportions may not sum to 100% due to the fact that participants could report using multiple e-cigarette brands.

Appendix F: Patterns of product use across study conditions

Table A4: Daily patterns of use of tobacco cigarettes and e-cigarettes across study conditions (n=48)

Condition: Exclusive use of tobacco cigarettes														
Product	**Variable**		**Day 1**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7**	
	% (n) or mean (SD)															
Tobacco cigarette	Times used (bouts) per day[a], among all participants		8.3 (6.0)		11.6 (6.6)		12.2 (7.1)		12.6 (6.6)		12.9 (6.1)		12.7 (7.2)		12.4 (7.3)	
	Time to first use, among all participants	Within 5 min	26.3%	(10)	36.4%	(16)	37.8%	(17)	40.4%	(19)	43.8%	(21)	29.8%	(14)	38.6%	(17)
		6-30 min	31.6%	(12)	36.4%	(16)	40.0%	(18)	34.0%	(16)	33.3%	(16)	44.7%	(21)	36.4%	(16)
		31-60 min	15.8%	(6)	13.6%	(6)	11.1%	(5)	19.1%	(9)	16.7%	(8)	17.0%	(8)	20.5%	(9)
		After 60 min	26.3%	(10)	13.6%	(6)	11.1%	(5)	6.4%	(3)	6.3%	(3)	8.5%	(4)	4.5%	(2)
	Time since last use [hours], among all participants		12.6 (42.9)		11.6 (41.9)		6.4 (34.5)		0.66 (0.9)		3.7 (17.6)		4.4 (17.9)		2.6 (7.5)	
E-cigarette	Times used (bouts) per day[a], among all participants		0.6 (1.4)		0.5 (1.7)		0.3 (1.1)		0.4 (1.7)		0.4 (0.9)		0.5 (1.6)		0.5 (1.2)	
	Times used (bouts) per day[a], among those who used e-cigarettes		3.0 (1.9)		3.6 (3.2)		2.8 (1.9)		4.0 (3.7)		2.1 (1.0)		3.1 (2.8)		2.5 (1.6)	
	Number of puffs per bout, among those who used e-cigarettes		3.6 (2.1)		6.1 (6.3)		3.8 (1.0)		7.0 (7.3)		6.1 (6.0)		5.8 (5.8)		5.0 (6.3)	
	Duration of bout [minutes], among those who used e-cigarettes		6.7 (9.2)		3.1 (2.2)		2.6 (1.5)		3.6 (1.3)		2.8 (3.1)		2.8 (1.7)		1.6 (1.5)	
	Time to first use, among those who used e-cigarettes	Within 5 min	0.0%	(0)	0.0%	(0)	0.0%	(0)	0.0%	(0)	0.0%	(0)	0.0%	(0)	0.0%	(0)
		6-30 min	50.0%	(4)	16.7%	(1)	20.0%	(1)	20.0%	(1)	12.5%	(1)	12.5%	(1)	16.7%	(1)
		31-60 min	12.5%	(1)	0.0%	(0)	0.0%	(0)	0.0%	(0)	0.0%	(0)	12.5%	(1)	0.0%	(0)
		After 60 min	37.5%	(3)	83.3%	(5)	80.0%	(4)	80.0%	(4)	87.5%	(7)	75.0%	(6)	83.3%	(5)
	Time since last use [hours], among all participants		14.7 (12.9)		34.2 (21.9)		54.9 (29.5)		73.1 (36.8)		88.5 (47.2)		103.7 (55.8)		120.0 (65.7)	

Notes:

[1] Summary statistics collected for Day 1 do not reflect a full 24-hour period.

[2] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; 'bouts' per day (defined as an instance of at least one puff) for e-cigarettes.

Condition: Exclusive use of e-cigarettes														
Product	**Variable**		**Day 1**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7**	
	% (n) or mean (SD)															
Tobacco cigarette	Times used (bouts) per day[a], among all participants		0.7 (1.4)		0.5 (1.4)		0.3 (0.7)		0.3 (0.7)		0.7 (3.0)		0.8 (1.9)		0.8 (1.7)	
	Times used (bouts) per day[a], among those who used tobacco cigarettes		2.2 (1.8)		2.5 (2.1)		1.3 (1.0)		1.5 (1.0)		4.3 (6.7)		2.7 (2.8)		2.4 (2.1)	
	Time to first use, among those who used tobacco cigarettes	Within 5 min	42.9%	(6)	10.0%	(1)	0.0%	(0)	11.1%	(1)	14.3%	(1)	7.7%	(1)	12.5%	(2)
		6-30 min	14.3%	(2)	0.0%	(0)	0.0%	(0)	0.0%	(0)	14.3%	(1)	7.7%	(1)	0.0%	(0)
		31-60 min	21.4%	(3)	10.0%	(1)	0.0%	(0)	11.1%	(1)	14.3%	(1)	7.7%	(1)	6.3%	(1)
		After 60 min	21.4%	(3)	80.0%	(8)	100.0%	(9)	77.8%	(7)	57.1%	(4)	76.9%	(10)	81.3%	(13)
	Time since last use [hours], among all participants		11.7 (11.7)		28.6 (17.4)		45.7 (27.7)		66.3 (37.7)		81.3 (46.8)		83.4 (60.4)		89.9 (72.7)	
E-cigarette	Times used (bouts) per day[a], among all participants		11.9 (15.8)		16.1 (16.7)		18.2 (16.9)		16.5 (17.4)		16.9 (16.6)		17.9 (18.1)		17.4 (15.4)	
	Number of puffs per bout, among all participants		10.3 (12.0)		7.5 (4.6)		8.3 (6.2)		7.8 (5.3)		7.8 (4.6)		7.6 (4.8)		8.2 (5.4)	
	Duration of bout [minutes], among all participants		7.0 (7.0)		6.7 (6.2)		5.8 (4.2)		6.2 (4.3)		6.4 (4.4)		5.8 (4.1)		6.6 (6.5)	
	Time to first use, among all participants	Within 5 min	19.0%	(8)	29.8%	(14)	21.3%	(10)	33.3%	(16)	30.4%	(14)	25.5%	(12)	33.3%	(16)
		6-30 min	19.0%	(8)	40.4%	(19)	53.2%	(25)	31.3%	(15)	43.5%	(20)	38.3%	(18)	37.5%	(18)
		31-60 min	11.9%	(5)	23.4%	(11)	19.1%	(9)	29.2%	(14)	15.2%	(7)	31.9%	(15)	12.5%	(6)
		After 60 min	50.0%	(21)	6.4%	(3)	6.4%	(3)	6.3%	(3)	10.9%	(5)	4.3%	(2)	16.7%	(8)
	Time since last use [hours], among all participants		5.3 (31.1)		1.1 (2.7)		0.8 (1.9)		1.4 (3.8)		2.0 (5.1)		2.2 (7.4)		1.9 (4.1)	

Notes:

[1] Summary statistics collected for Day 1 do not reflect a full 24-hour period.

[2] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; 'bouts' per day (defined as an instance of at least one puff) for e-cigarettes.

Condition: No product use														
Product	**Variable**		**Day 1**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7**	
	% (n) or mean (SD)															
Tobacco cigarette	Times used (bouts) per day[a], among all participants		1.0 (2.1)		0.6 (1.2)		0.7 (1.3)		0.6 (1.3)		1.0 (2.5)		1.2 (2.1)		2.1 (2.9)	
	Times used (bouts) per day[a], among those who used tobacco cigarettes		2.8 (2.7)		2.0 (1.3)		2.7 (1.2)		2.4 (1.4)		3.1 (3.5)		3.1 (2.3)		4.0 (2.9)	
	Time to first use, among those who used tobacco cigarettes	Within 5 min	25.0%	(4)	0.0%	(0)	16.7%	(2)	15.4%	(2)	12.5%	(2)	16.7%	(3)	4.2%	(1)
		6-30 min	25.0%	(4)	21.4%	(3)	8.3%	(1)	7.7%	(1)	0.0%	(0)	11.1%	(2)	12.5%	(3)
		31-60 min	0.0%	(0)	7.1%	(1)	0.0%	(0)	0.0%	(0)	12.5%	(2)	5.6%	(1)	8.3%	(2)
		After 60 min	50.0%	(8)	71.4%	(10)	75.0%	(9)	76.9%	(10)	75.0%	(12)	66.7%	(12)	75.0%	(18)
	Time since last use [hours], among all participants		53.1 (76.4)		56.5 (73.5)		73.8 (78.6)		87.8 (86.3)		98.2 (103.1)		102.1 (117.0)		105.1 (126.3)	
E-cigarette	Times used (bouts) per day[a], among all participants		0.4 (0.9)		0.5 (1.6)		0.5 (1.1)		0.6 (1.8)		0.8 (2.3)		0.6 (1.8)		0.6 (1.6)	
	Times used (bouts) per day[a], among those who used e-cigarettes		2.1 (0.9)		3.6 (2.6)		2.3 (1.3)		3.4 (2.8)		4.3 (3.7)		4.1 (3.1)		4.0 (1.8)	
	Number of puffs per bout, among those who used e-cigarettes		3.0 (1.6)		4.3 (1.8)		3.7 (2.1)		3.0 (1.4)		2.6 (1.3)		3.1 (1.8)		4.1 (1.2)	
	Duration of bout [minutes], among those who used e-cigarettes		2.0 (1.5)		2.4 (1.8)		3.0 (2.8)		2.8 (3.0)		2.8 (3.0)		6.9 (10.7)		6.7 (10.4)	
	Time to first use, among those who used e-cigarettes	Within 5 min	20.0%	(2)	14.3%	(1)	0.0%	(0)	11.1%	(1)	0.0%	(0)	0.0%	(0)	0.0%	(0)
		6-30 min	30.0%	(3)	0.0%	(0)	10.0%	(1)	0.0%	(0)	11.1%	(1)	0.0%	(0)	0.0%	(0)
		31-60 min	0.0%	(0)	0.0%	(0)	0.0%	(0)	22.2%	(2)	11.1%	(1)	14.3%	(1)	14.3%	(1)
		After 60 min	50.0%	(5)	85.7%	(6)	90.0%	(9)	66.7%	(6)	77.8%	(7)	85.7%	(6)	85.7%	(6)
	Time since last use [hours], among all participants		70.2 (80.9)		77.3 (78.0)		101.8 (87.0)		108.4 (95.3)		124.5 (99.9)		142.0 (106.0)		157.8 (117.6)	

Notes:

[1] Summary statistics collected for Day 1 do not reflect a full 24-hour period.

[2] Times used per day=cigarettes per day, in the past 7 days, for tobacco cigarettes; 'bouts' per day (defined as an instance of at least one puff) for e-cigarettes.

Appendix G: Key outcomes across study conditions

Table A5: Key continuous outcomes across study conditions (n=48)

Outcome	Condition				Test statistic (p-value)
	Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use	
	Mean (95% CI)				
Urinary cotinine[1] [ng/mg creatinine]	1174.4 (859.4, 1604.7)[a]	1282.0 (925.3, 1776.2)[a]	733.7 (478.4, 1125.1)[b]	533.2 (326.6, 870.6)[b]	F=5.788 (p=0.002)
Exhaled carbon monoxide[1] [ppm]	17.4 (14.2, 20.7)[a]	21.1 (17.4, 24.9)[b]	10.3 (7.5, 13.2)[c]	12.9 (10.2, 15.6)[c]	F=10.115 (p<0.001)
Urinary 1-HOP[2] [pg/mg creatinine]	203.3 (153.9, 268.7)[a]	249.2 (197.2, 315.1)[b]	141.1 (98.3, 202.5)[c]	175.1 (134.3, 228.2)[a]	F=4.766 (p=0.006)
Urinary NNAL[2] [pg/mg creatinine]	30.3 (20.9, 43.7)[a]	32.7 (24.0, 44.7)[a]	21.2 (14.5, 31.6)[b]	19.8 (13.5, 28.8)[b]	F=4.593 (p=0.007)
QSU	3.7 (3.2, 4.1)[a]	3.4 (3.0, 3.9)[a]	4.5 (4.0, 4.9)[b]	4.3 (3.9, 4.8)[b]	F=6.725 (p=0.001)
QSU: Factor 1	4.4 (4.0, 4.8)[a,c]	3.9 (3.5, 4.4)[b]	5.1 (4.7, 5.5)[c]	5.0 (4.5, 5.4)[c]	F=6.229 (p=0.001)
QSU: Factor 2	3.0 (2.5, 3.4)[a]	3.0 (2.5, 3.4)[a]	3.8 (3.3, 4.3)[b]	3.7 (3.2, 4.2)[b]	F=6.658 (p=0.001)
E-QSU	3.5 (3.1, 3.9)	3.3 (2.8, 3.7)	3.7 (3.3, 4.0)	3.5 (3.1, 3.9)	F=0.879 (p=0.460)
E-QSU: Factor 1	4.1 (3.7, 4.6)	3.8 (3.3, 4.3)	4.4 (4.1, 4.8)	4.1 (3.6, 4.5)	F=1.615 (p=0.200)
E-QSU: Factor 2	2.8 (2.4, 3.3)	2.7 (2.2, 3.2)	2.9 (2.6, 3.3)	3.0 (2.6, 3.4)	F=0.474 (p=0.702)
SEQ	34.0 (30.3, 37.7)	32.6 (29.1, 36.1)[a]	32.3 (28.8, 35.7)[a]	36.5 (32.8, 40.1)[b]	F=3.419 (p=0.026)
SEQ: Factor 1	17.3 (15.3, 19.2)	16.5 (14.6, 18.3)	16.3 (14.5, 18.1)	18.1 (16.2, 19.9)	F=1.708 (p=0.180)
SEQ: Factor 2	16.8 (14.6, 18.9)	16.1 (14.2, 18.1)[a]	16.0 (14.0, 17.9)[a]	18.4 (16.3, 20.4)[b]	F=4.145 (p=0.012)
E-SEQ	35.6	35.0	35.5	38.3	F=1.867

	(32.2, 38.9)	(31.9, 38.1)	(32.5, 38.4)	(35.0, 41.5)	(p=0.150)
E-SEQ: Factor 1	18.3 (16.5, 20.2)	18.3 (16.6, 19.9)	17.5 (15.9, 19.2)	19.4 (17.7, 21.2)	F=2.352 (p=0.086)
E-SEQ: Factor 2	17.3 (15.4, 19.0)	16.7 (15.1, 18.4)	17.9 (16.3, 19.6)	18.8 (17.0, 20.6)	F=2.192 (p=0.103)

Notes:
Abbreviations: CI=confidence interval; 1-HOP=1-hydroxypyrene; NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; QSU=Questionnaire of Smoking Urges; SEQ=Self-Efficacy Questionnaire; E-=measure adapted to use of e-cigarettes.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
[1] Arithmetic mean.
[2] Geometric mean.

Table A6: Key binary outcomes across study conditions (n=48)

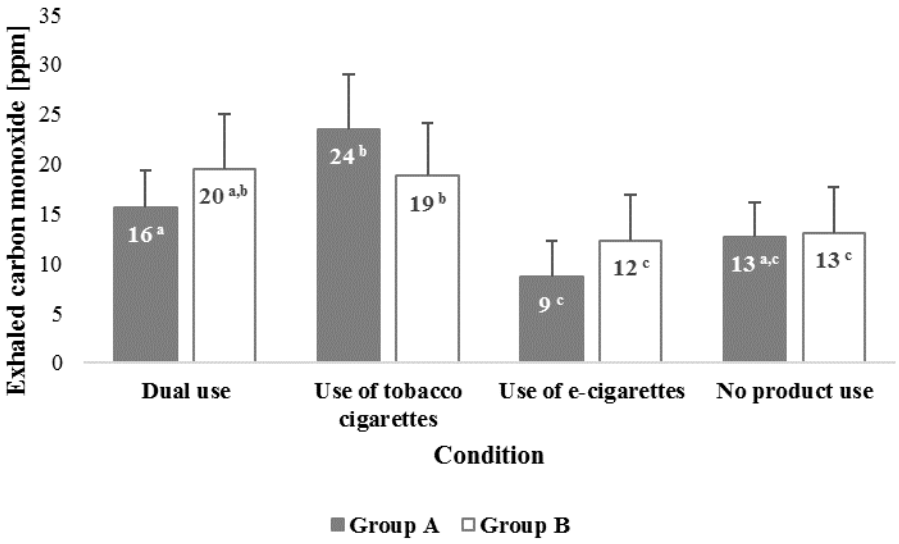
Outcome	Condition				Test statistic (p-value)
	Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use	
	% (n)				
Change in experiencing shortness of breath					
Worse than usual or no difference	97.9% (47)	97.9% (47)	58.3% (28)	70.2% (33)	F=6.952 (p<0.001)
Better than usual	2.1% (1)[a]	2.1% (1)[a]	41.7% (20)[b]	29.8% (14)[b]	
Change in frequency of cough					
Worse than usual or no difference	97.9% (46)	97.9% (47)	60.4% (29)	70.2% (33)	F=6.816 (p<0.001)
Better than usual	2.1% (1)[a]	2.1% (1)[a]	39.6% (19)[b]	29.5% (14)[b]	
Change in frequency of cough with phlegm					
Worse than usual or no difference	93.6% (44)	95.8% (46)	59.6% (28)	68.1% (32)	F=7.561 (p<0.001)
Better than usual	6.4% (3)[a]	4.2% (2)[a]	40.4% (19)[b]	31.9% (15)[b]	
Change in chest sounds, such as wheezing or whistling					
Worse than usual or no difference	93.6% (44)	95.8% (46)	59.6% (28)	68.8% (33)	F=6.799 (p<0.001)
Better than usual	6.4% (3)[a]	4.2% (2)[a]	40.4% (19)[b]	31.3% (15)[b]	
Change in overall lung function					
Worse than usual or no difference	93.6% (44)	97.9% (47)	59.6% (28)	62.5% (30)	F=6.778 (p<0.001)
Better than usual	6.4% (3)[a]	2.1% (1)[a]	40.4% (19)[b]	37.5% (18)[b]	

Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.

Appendix H: Interaction effects of key outcomes across study conditions

Stratified analyses were conducted to examine exhaled carbon monoxide across study conditions by assigned condition order (see Figure A3). Repeated measures models were conducted to examine exhaled carbon monoxide across study conditions, with baseline nicotine dependence (FTCD score), e-cigarette product type (tank system, other), and e-cigarette nicotine content (nicotine present, nicotine absent) as covariates, and an unstructured variance-covariance structure, separately for participants assigned to each condition order (Group A, Group B).

Figure A3: Exhaled carbon monoxide across study conditions, by group (n=48)



Notes:
Abbreviations: ppm=parts per million.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

The repeated measures model examining exhaled carbon monoxide for Group A participants yielded a significant effect of condition (F=9.383, p<0.001): exhaled carbon monoxide was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Dual use* (mean difference=9.1, 95% CI: 4.0 to 14.3, p=0.002), of *Exclusive use of e-cigarettes* (mean difference=15.8, 95% CI: 9.2 to 22.4, p<0.001), and of *No product use* (mean difference=11.5, 95% CI: 6.4 to 16.7, p<0.001). In addition, carbon monoxide was significantly higher in the condition of *Dual use* compared to the condition of *Exclusive use of e-cigarettes* (mean difference=6.7, 95% CI: 2.6 to 10.8, p=0.003). However, exhaled carbon monoxide was

not significantly different between the conditions of *Dual use* and *No product use* (mean difference=2.4, 95% CI: -1.3 to 6.1, p=0.190).

The repeated measures model examining exhaled carbon monoxide for Group B participants also yielded a significant effect of condition (F=3.788, p=0.028): exhaled carbon monoxide was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=6.8, 95% CI: 1.9 to 11.7, p=0.009), and of *No product use* (mean difference=5.8, 95% CI: 0.6 to 11.1, p=0.032). In addition, carbon monoxide was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=7.6, 95% CI: 2.7 to 12.6, p=0.004), and of *No product use* (mean difference=6.6, 95% CI: 1.7 to 11.5, p=0.011). However, exhaled carbon monoxide was not significantly different between the conditions of *Exclusive use of tobacco cigarettes* and *Dual use* (mean difference=-0.8, 95% CI: -4.8 to 3.2, p=0.679).

Appendix I: Sensitivity analyses

Sensitivity analyses were conducted in an attempt to examine the effect of non-compliance with respect to use of tobacco cigarettes. The first approach involved excluding participants with exhaled carbon monoxide levels greater than 5 ppm in the condition of *No product use* (n=37). A summary of biomarkers of exposure across study conditions among this sub-sample is presented in Table A7.

Table A7: Biomarkers of exposure across study conditions, among participants with exhaled carbon monoxide levels less than 5 ppm in the condition of *No product use* (n=11)

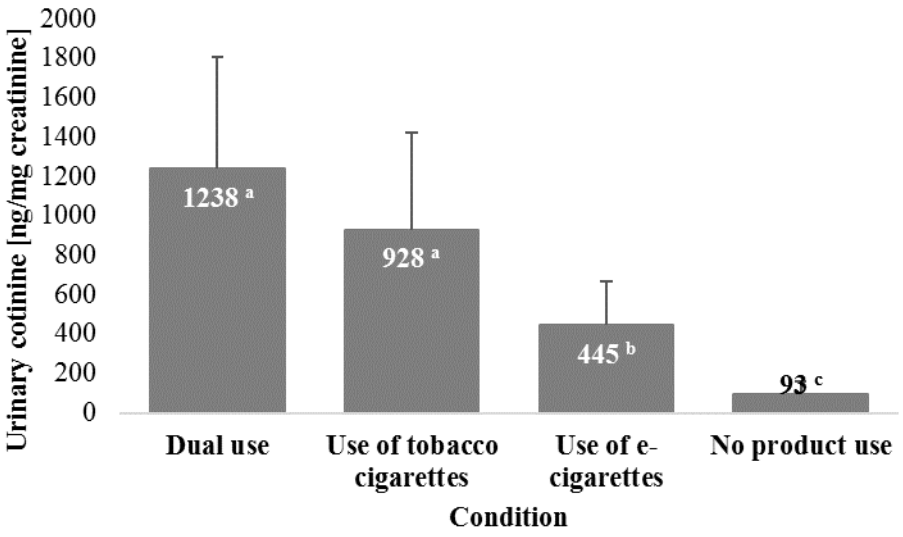
Biomarker	Condition				Test statistic (p-value)
	Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use	
	Mean (95% CI)				
Urinary cotinine[2] [ng/mg creatinine]	1238.2 (667.9, 2295.6)[a]	927.7 (430.5, 1998.9)[a]	445.0 (224.1, 884.1)[b]	93.0 (28.3, 305.9)[c]	F=9.350 (p=0.004)
Exhaled carbon monoxide[1] [ppm]	14.4 (9.7, 19.1)[a]	14.8 (9.1, 20.4)[a]	4.6 (2.7, 6.4)[b]	3.3 (2.5, 4.2)[b]	F=7.769 (p=0.007)
Urinary 1-HOP[2] [pg/mg creatinine]	99.6 (55.8, 177.7)	157.9 (99.4, 250.6)	75.3 (32.5, 174.3)	105.3 (66.2, 167.5)	F=1.485 (p=0.283)
Urinary NNAL[2] [pg/mg creatinine]	26.5 (13.8, 51.1)[a]	29.2 (14.6, 58.4)[a]	11.5 (6.5, 20.2)[b]	8.7 (4.6, 16.4)[b]	F=4.529 (p=0.034)

Notes:
Abbreviations: CI=confidence interval; 1-HOP=1-hydroxypyrene; NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Asterisks (*) denote significant differences in biomarker levels compared to the condition of *Dual use*, p<0.05.
[1] Arithmetic mean.
[2] Geometric mean.

Urinary cotinine

A repeated measures model was conducted to examine urinary cotinine across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary cotinine were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A4).

Figure A4: Urinary cotinine[1] across study conditions (n=11)



Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

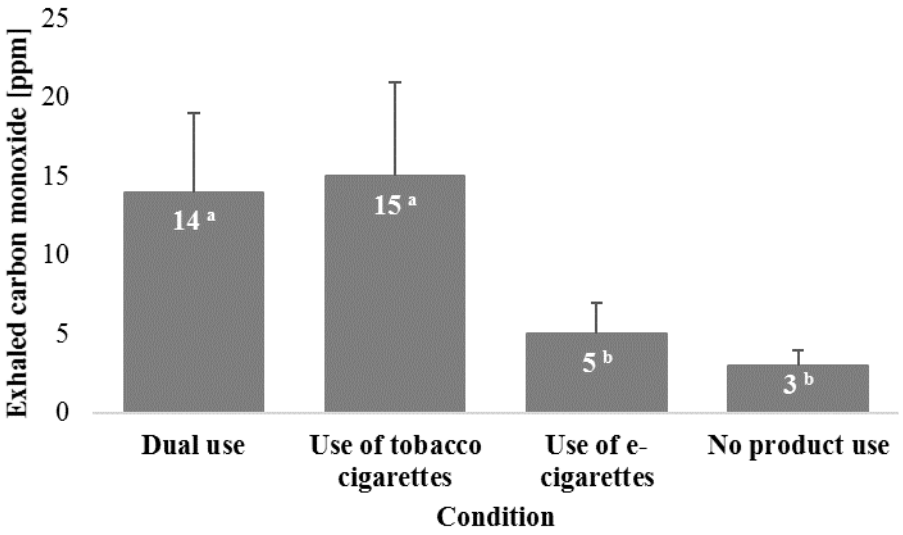
The repeated measures model yielded a significant effect of condition (F=9.350, p=0.004): urinary cotinine was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=2.7, 95% CI: 1.7 to 4.4, p=0.001), and of *No product use* (mean difference=14.0, 95% CI: 2.8 to 70.8, p=0.005). In addition, urinary cotinine was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=2.0, 95% CI: 0.5 to 4.5, p=0.075), and of *No product use* (mean difference=10.4, 95% CI: 2.4 to 45.7, p=0.006). Finally, urinary cotinine was significantly higher in the condition of *Exclusive use of e-cigarettes* compared to the condition of *No product use* (mean difference=5.1, 95% CI: 1.1 to 23.0, p=0.037). No

significant effect was detected for the interaction of condition and assigned condition order (F=0.875, p=0.462).

Exhaled carbon monoxide

Levels of exhaled carbon monoxide across study conditions are presented in Figure A5. A repeated measures model was conducted to examine exhaled carbon monoxide across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure.

Figure A5: Exhaled carbon monoxide across study conditions (n=11)



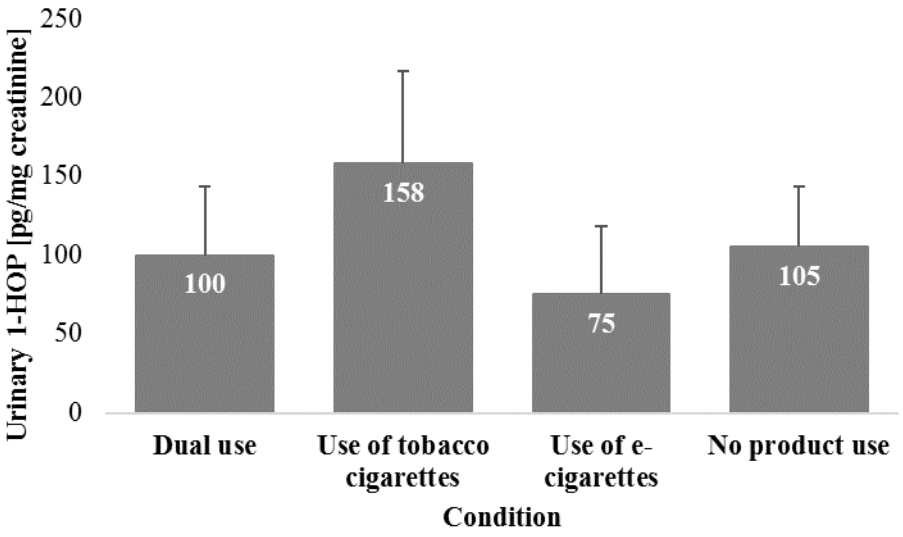
Notes:
Abbreviations: ppm=parts per million.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

The repeated measures model yielded a significant effect of condition (F=7.769, p=0.007): exhaled carbon monoxide was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=10.0, 95% CI: 3.6 to 16.4, p=0.007), and of *No product use* (mean difference=11.5, 95% CI: 4.9 to 18.0, p=0.003). In addition, carbon monoxide was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=9.6, 95% CI: 3.6 to 15.5, p=0.007), and of *No product use* (mean difference=11.0, 95% CI: 5.4 to 16.6, p=0.002). No significant effect was detected for the interaction of condition and assigned condition order (F=0.432, p=0.736).

Urinary 1-hydroxypyrene

A repeated measures model was conducted to examine urinary 1-HOP across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary 1-HOP were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A6).

Figure A6: Urinary 1-hydroxypyrene[1] across study conditions (n=11)



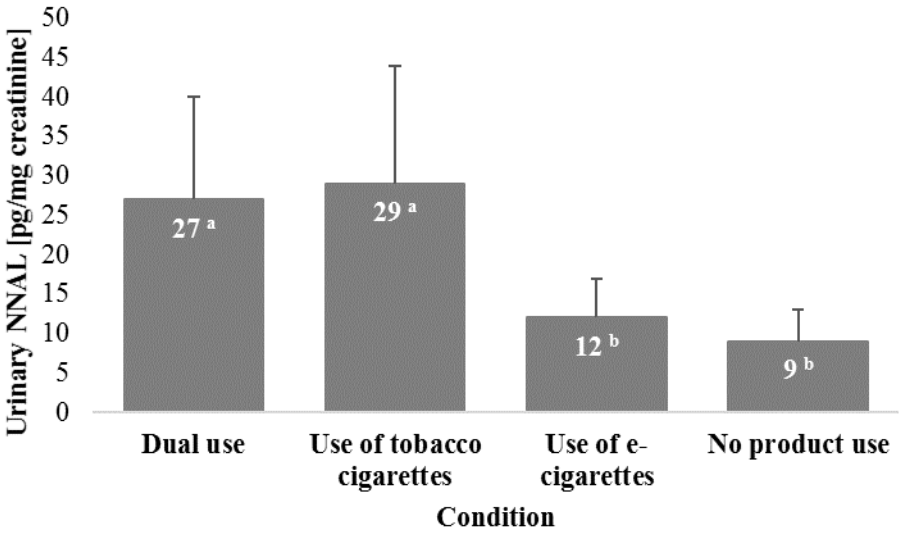
Notes:
Abbreviations: 1-HOP=1-hydroxypyrene.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

The repeated measures model indicated no significant differences in urinary 1-HOP across study conditions (F=1.485, p=0.283). However, a significant effect was detected for assigned condition order (F=21.281, p=0.002), with Group A participants exhibiting greater levels of 1-HOP compared to Group B participants (β=2.1, 95% CI: 1.4 to 3.1, p=0.002). In addition, baseline nicotine dependence was significantly associated with urinary 1-HOP (F=8.776, p=0.021), with higher levels of baseline nicotine dependence associated with higher levels of urinary 1-HOP (β=1.1, 95% CI: 1.0 to 1.2, p=0.021). No significant effect was detected for the interaction of condition and assigned condition order (F=2.910, p=0.101).

Urinary NNAL

A repeated measures model was conducted to examine urinary NNAL across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary NNAL were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A7).

Figure A7: Urinary NNAL[1] across study conditions (n=11)



Notes:
Abbreviations: NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

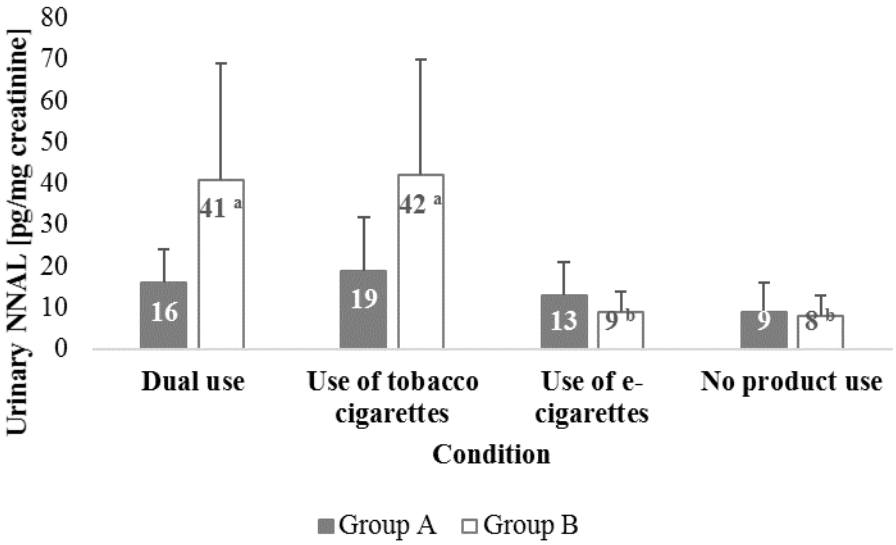
The repeated measures model yielded a significant effect of condition (F=4.529, p=0.034): urinary NNAL was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=2.8, 95% CI: 1.3 to 6.1, p=0.016), and of *No product use* (mean difference=3.3, 95% CI: 1.6 to 7.0, p=0.006). In addition, urinary NNAL was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=2.4, 95% CI: 1.2 to 4.9, p=0.017), and of *No product use* (mean difference=2.9, 95% CI: 1.4 to 6.0, p=0.009). A significant effect was detected for assigned condition order (F=45.343, p<0.001), with Group A participants exhibiting greater levels of NNAL compared to Group B participants (β=4.9, 95% CI: 2.8 to 8.5,

p<0.001). Baseline nicotine dependence was also significantly associated with urinary NNAL (F=60.357, p<0.001), with higher levels of baseline nicotine dependence associated with higher levels of urinary NNAL (β=1.5, 95% CI: 1.4 to 1.8, p<0.001).

A significant effect was detected for the interaction of condition and assigned condition order (F=4.783, p=0.034). Stratified analyses indicated that the main effect of condition held for Group B participants (F=8.541, p=0.021): urinary NNAL was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=4.5, 95% CI: 1.9 to 10.5, p=0.006), and of *No product use* (mean difference=5.0, 95% CI: 2.0 to 13.0, p=0.007). In addition, urinary NNAL was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=4.4, 95% CI: 2.0 to 9.6, p=0.005), and of *No product use* (mean difference=4.9, 95% CI: 2.0 to 11.9, p=0.006). In addition, baseline nicotine dependence was significantly associated with urinary NNAL (F=32.684, p=0.005), with higher levels of baseline nicotine dependence associated with higher levels of urinary NNAL (β=1.6, 95% CI: 1.3 to 2.0, p=0.005) (see Figure A8).

In contrast, no significant differences in urinary NNAL were detected across study conditions for Group A participants (F=0.212, p=0.883). However, baseline nicotine dependence was significantly associated with urinary NNAL (F=1.993, p=0.001), with higher levels of baseline nicotine dependence associated with higher levels of urinary NNAL (β=1.5, 95% CI: 1.5 to 1.6, p=0.001) (see Figure A8).

Figure A8: Urinary NNAL[1] across study conditions, by group



Notes:
Abbreviations: NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

The second approach involved excluding participants who self-reported smoking tobacco cigarettes in the condition of *No product use* (n=28). A summary of biomarkers of exposure across study conditions among this sub-sample is presented in Table A8.

Table A8: Biomarkers of exposure across study conditions, among participants who did not report smoking tobacco cigarettes in the condition of *No product use* (n=20)

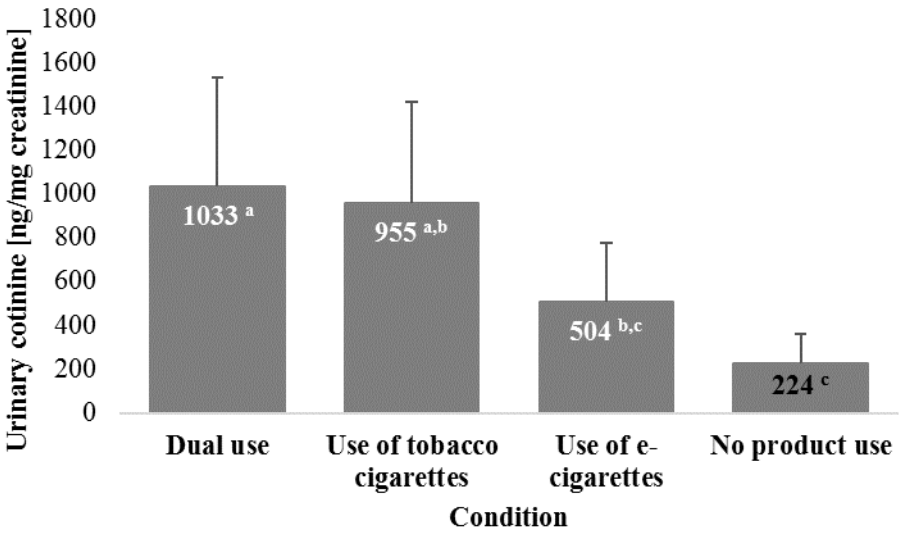
Biomarker	Condition				Test statistic (p-value)
	Dual use	Exclusive use of tobacco cigarettes	Exclusive use of e-cigarettes	No product use	
	Mean (95% CI)				
Urinary cotinine[2] [ng/mg creatinine]	1032.5 (533.2, 1999.4)[a]	954.6 (487.0, 1870.7)[a,b]	504.3 (231.8, 1097.2)[b,c]	223.7 (85.3, 586.7)[c]	F=3.413 (p=0.041)
Exhaled carbon monoxide[1] [ppm]	16.9 (12.5, 21.4)[a]	17.5 (12.7, 22.4)[a]	11.8 (6.7, 16.8)[b]	10.7 (5.9, 15.5)[b]	F=3.558 (p=0.042)
Urinary 1-HOP[2] [pg/mg creatinine]	191.7 (125.7, 292.2)	232.8 (178.9, 302.8)	138.5 (84.1, 227.9)	142.6 (91.7, 221.8)	F=2.462 (p=0.098)
Urinary NNAL[2] [pg/mg creatinine]	36.3 (21.0, 62.8)[a]	33.1 (18.3, 59.9)[a]	21.0 (11.0, 40.0)[b]	18.0 (9.6, 33.6)[b]	F=3.476 (p=0.039)

Notes:
Abbreviations: CI=confidence interval; 1-HOP=1-hydroxypyrene; NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Asterisks (*) denote significant differences in biomarker levels compared to the condition of *Dual use*, p<0.05.
[1] Arithmetic mean.
[2] Geometric mean.

Urinary cotinine

A repeated measures model was conducted to examine urinary cotinine across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary cotinine were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A9).

Figure A9: Urinary cotinine[1] across study conditions (n=20)



Notes:
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

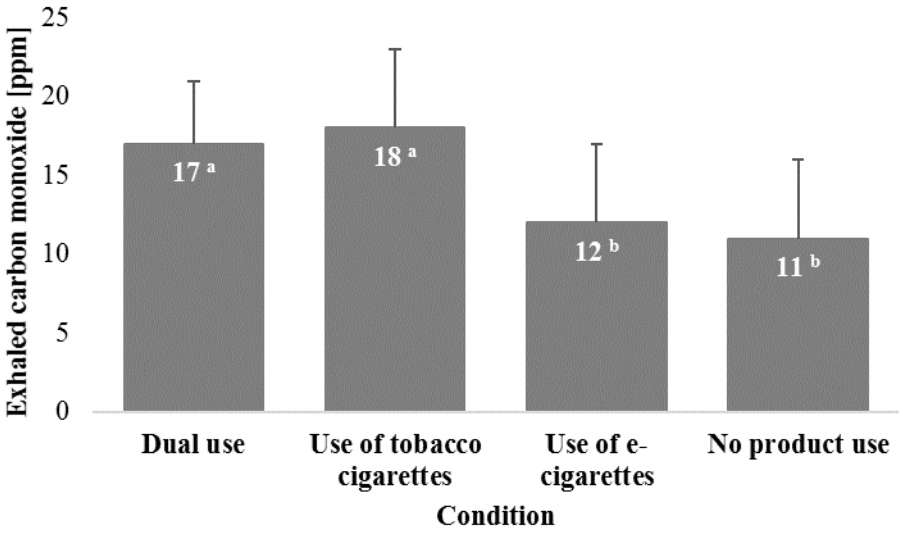
The repeated measures model yielded a significant effect of condition (F=3.413, p=0.041): urinary cotinine was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=2.1, 95% CI: 1.1 to 4.3, p=0.034), and of *No product use* (mean difference=5.3, 95% CI: 1.6 to 17.2, p=0.009). In addition, urinary cotinine was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the condition of *No product use* (mean difference=4.7, 95% CI: 1.7 to 13.5, p=0.006); the contrast between the condition of *Exclusive use of tobacco cigarettes* and the condition of *Exclusive use of e-cigarettes* was borderline significant (mean difference=1.9, 95% CI: 1.0 to 3.8, p=0.058). Similarly, the contrast between the condition of *Exclusive use of e-cigarettes* and the condition of

No product use was borderline significant (mean difference=2.5, 95% CI: 1.0 to 6.3, p=0.055). In addition, baseline nicotine dependence was significantly associated with urinary cotinine (F=5.401, p=0.035), with higher levels of baseline nicotine dependence associated with higher levels of urinary cotinine (β=1.6, 95% CI: 1.0 to 2.4, p=0.035). No significant effect was detected for the interaction of condition and assigned condition order (F=0.705, p=0.563).

Exhaled carbon monoxide

Levels of exhaled carbon monoxide across study conditions are presented in Figure A10. A repeated measures model was conducted to examine exhaled carbon monoxide across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score) as covariates, and an unstructured variance-covariance structure.

Figure A10: Exhaled carbon monoxide across study conditions (n=20)



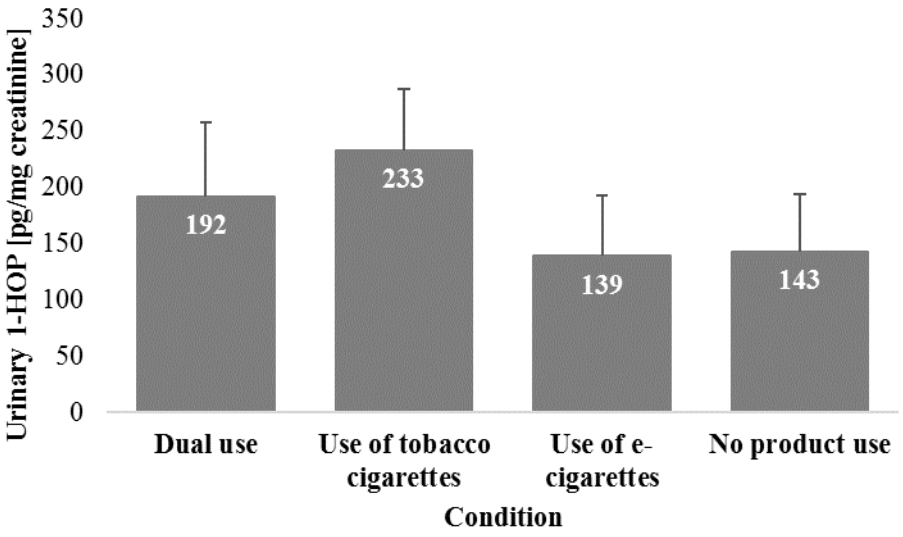
Notes:
Abbreviations: ppm=parts per million.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

The repeated measures model yielded a significant effect of condition (F=3.558, p=0.042): exhaled carbon monoxide was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=6.9, 95% CI: 2.3 to 11.6, p=0.006), and of *No product use* (mean difference=6.8, 95% CI: 1.2 to 12.5, p=0.021). In addition, carbon monoxide was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=6.9, 95% CI: 0.7 to 13.1, p=0.032), and of *No product use* (mean difference=6.8, 95% CI: 1.8 to 11.9, p=0.011). No significant effect was detected for the interaction of condition and assigned condition order (F=0.413, p=0.746).

Urinary 1-hydroxypyrene

A repeated measures model was conducted to examine urinary 1-HOP across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary 1-HOP were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A11).

Figure A11: Urinary 1-hydroxypyrene[1] across study conditions (n=20)



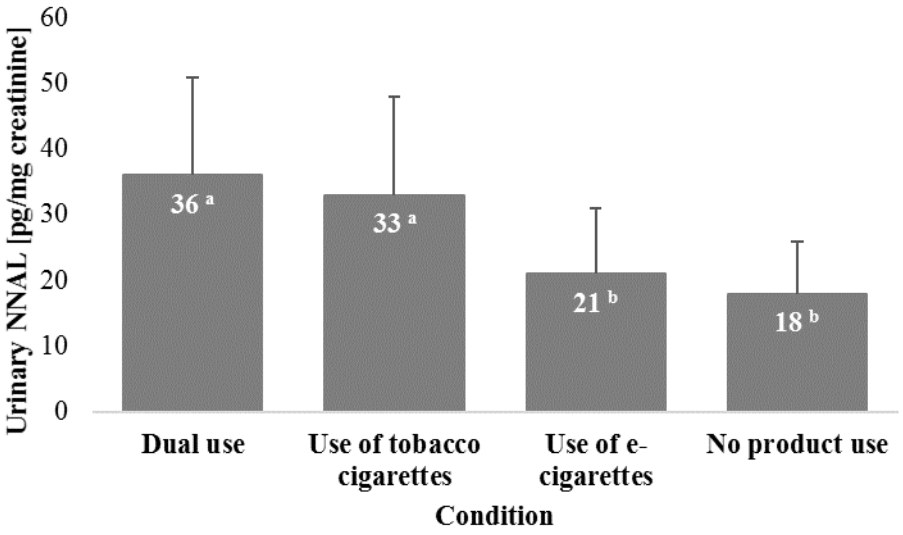
Notes:
Abbreviations: 1-HOP=1-hydroxypyrene.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

The repeated measures model indicated no significant differences in urinary 1-HOP across study conditions ($F=2.462$, $p=0.098$). However, a significant effect was detected for assigned condition order ($F=5.366$, $p=0.035$), with Group A participants exhibiting greater levels of 1-HOP compared to Group B participants ($\beta=1.9$, 95% CI: 1.1 to 3.3, $p=0.035$). In addition, baseline nicotine dependence was significantly associated with urinary 1-HOP ($F=10.283$, $p=0.006$), with higher levels of baseline nicotine dependence associated with higher levels of urinary 1-HOP ($\beta=1.3$, 95% CI: 1.1 to 1.5, $p=0.006$). No significant effect was detected for the interaction of condition and assigned condition order ($F=2.183$, $p=0.130$).

Urinary NNAL

A repeated measures model was conducted to examine urinary NNAL across study conditions, with assigned condition order (Group A, Group B) and baseline nicotine dependence (FTCD score), and an unstructured variance-covariance structure. Measures of urinary NNAL were adjusted for creatinine and log-transformed for analyses to ensure approximate normality; geometric means in original units are presented below (see Figure A12).

Figure A12: Urinary NNAL[1] across study conditions (n=20)



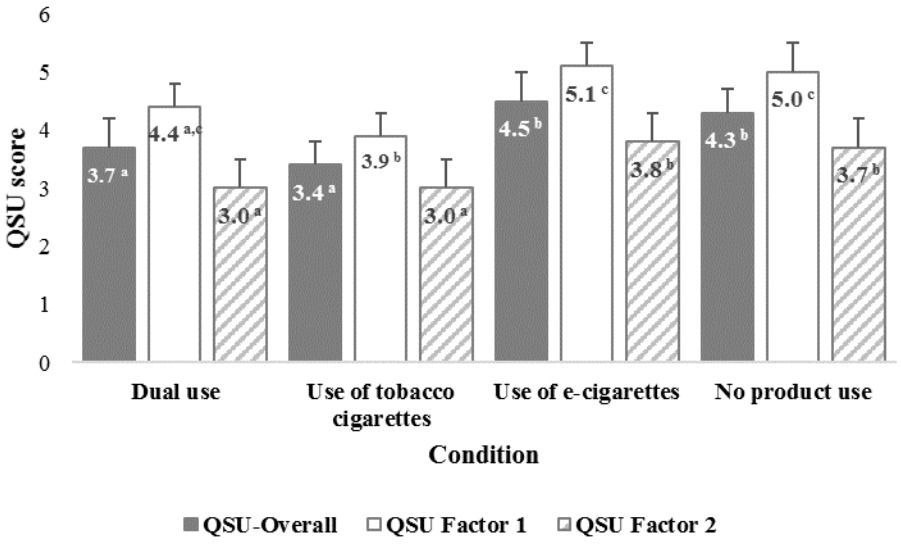
Notes:
Abbreviations: NNAL=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.
[1] Geometric means, expressed in original units.

The repeated measures model yielded a significant effect of condition (F=3.476, p=0.039): urinary NNAL was significantly higher in the condition of *Exclusive use of tobacco cigarettes* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.6, 95% CI: 1.0 to 2.6, p=0.038), and of *No product use* (mean difference=1.8, 95% CI: 1.1 to 3.0, p=0.015). In addition, urinary NNAL was significantly higher in the condition of *Dual use* compared to the conditions of *Exclusive use of e-cigarettes* (mean difference=1.8, 95% CI: 1.1 to 2.7, p=0.013), and of *No product use* (mean difference=2.0, 95% CI: 1.3 to 3.1, p=0.006). No significant effect was detected for the interaction of condition and assigned condition order (F=1.465, p=0.262).

Appendix J: Additional findings: Nicotine withdrawal

Measures of nicotine withdrawal for tobacco cigarettes across study conditions are presented in Figure A13.

Figure A13: Measures of nicotine withdrawal for tobacco cigarettes across study conditions (n=48)



Notes:
Abbreviations: QSU=Questionnaire of Smoking Urges.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

QSU-Factor 1

Scores for the QSU Factor 1, which reflect expectations of positive outcomes from smoking tobacco cigarettes (e.g., a cigarette would taste good right now), were also examined across study conditions. The repeated measures model yielded a significant effect of condition (F=6.229, p=0.001): participants reported significantly greater expectations of positive outcomes from smoking tobacco cigarettes in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.7, 95% CI: 0.2 to 1.2, p=0.008), and of *Exclusive use of tobacco cigarettes* (mean difference=1.2, 95% CI: 0.6 to 1.7, p<0.001). In addition, participants reported significantly greater expectations of positive outcomes from smoking tobacco cigarettes in the condition of *No product use* as compared to the condition of *Exclusive use of tobacco cigarettes* (mean difference=1.0, 95% CI: 0.4 to 1.6, p=0.001), as well as in the

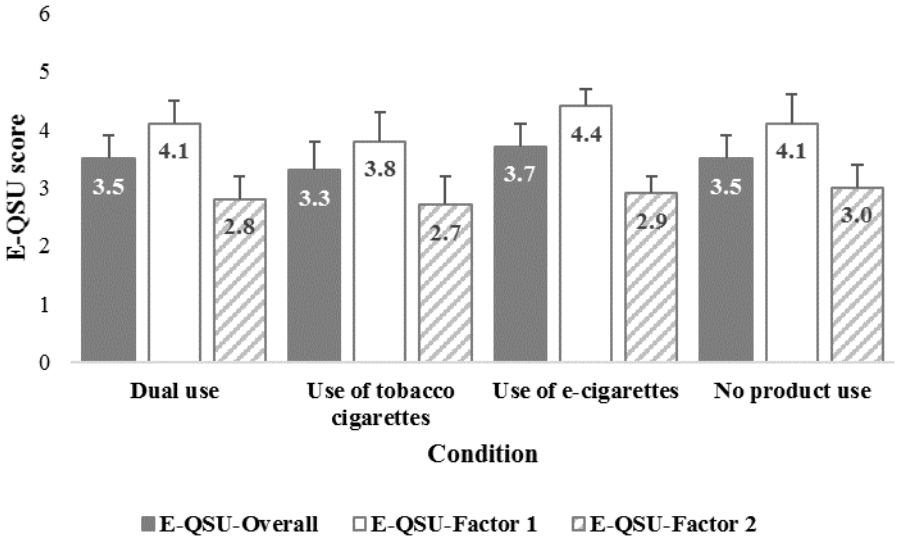
condition of *Dual use* as compared to the condition of *Exclusive use of tobacco cigarettes* (mean difference=0.5, 95% CI: 0.0 to 0.9, p=0.039) (see Figure A13).

QSU-Factor 2

Scores for the QSU Factor 2, which reflect expectations of relief from the negative effect of smoking tobacco cigarettes (e.g., I would do almost anything to be able to smoke a cigarette right now), were also examined across study conditions. The repeated measures model yielded a significant effect of condition (F=6.658, p=0.001): participants reported significantly greater expectations of relief from the negative effect of smoking tobacco cigarettes in the condition of *Exclusive use of e-cigarettes* as compared to conditions of *Dual use* (mean difference=0.8, 95% CI: 0.3 to 1.3, p=0.001), and of *Exclusive use of tobacco cigarettes* (mean difference=0.8, 95% CI: 0.4 to 1.3, p=0.001). In addition, participants reported significantly greater expectations of relief from the negative effect of smoking tobacco cigarettes in the condition of *No product use* as compared to conditions of *Dual use* (mean difference=0.8, 95% CI: 0.3 to 1.3, p=0.002), and of *Exclusive use of tobacco cigarettes* (mean difference=0.8, 95% CI: 0.3 to 1.2, p=0.002) (see Figure A4). Baseline nicotine dependence was also significantly associated with QSU Factor 2 scores (F=5.664, p=0.022), with higher levels of baseline nicotine dependence associated with greater expectations of relief from the negative effect of smoking tobacco cigarettes (β=0.2, 95% CI: 0.0 to 0.4, p=0.022) (see Figure A13).

Measures of nicotine withdrawal for e-cigarettes across study conditions are presented in Figure A14.

Figure A14: Measures of nicotine withdrawal for e-cigarettes across study conditions (n=48)



Notes:
Abbreviations: E-QSU=Questionnaire of Smoking Urges, adapted for e-cigarettes.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.

E-QSU-Factor 1

Scores for the E-QSU Factor 1, which reflect expectations of positive outcomes from using e-cigarettes (e.g., an e-cigarette would taste good right now), were also examined across study conditions. The repeated measures model indicated no statistically significant differences in expectations of positive outcomes from using e-cigarettes across study conditions ($F=1.615$, $p=0.200$) (see Figure A14).

E-QSU-Factor 2

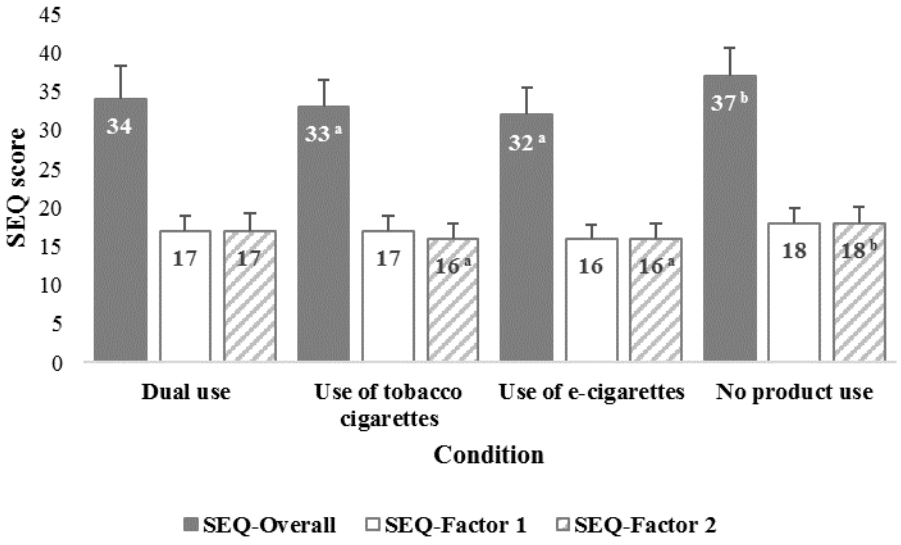
Scores for the E-QSU Factor 2, which reflect expectations of relief from the negative effect of using e-cigarettes (e.g., I would do almost anything to be able to use an e-cigarette right now), were also examined across study conditions. The repeated measures model indicated no statistically significant differences in expectations of relief from the negative effect of using e-cigarettes across study conditions ($F=0.474$, $p=0.702$) (see Figure A14). However, assigned condition order showed an overall significant effect ($F=5.531$, $p=0.024$): Group A participants

expressed significantly greater expectations of relief from the negative effect of using e-cigarettes as compared to Group B participants (β=0.8, 95% CI: 0.1 to 1.5, p=0.024). Baseline nicotine dependence was also significantly associated with E-QSU Factor 2 scores (F=5.207, p=0.028), with higher levels of baseline nicotine dependence associated with greater expectations of relief from the negative effect of using e-cigarettes (β=0.2, 95% CI: 0.0 to 0.4, p=0.028).

Appendix K: Additional findings: Self-efficacy

Measures of self-efficacy for abstaining from tobacco cigarettes across study conditions are presented in Figure A15.

Figure A15: Measures of self-efficacy for abstaining from tobacco cigarettes across study conditions (n=48)



Notes:
Abbreviations: SEQ=Self-Efficacy Questionnaire.
Conditions with different superscript letters were significantly different from one another, p<0.05.
Error bars indicate upper limits of 95% confidence intervals.

SEQ-Factor 1

Scores for the SEQ Factor 1, which reflect participants' confidence in their ability to abstain from smoking when facing internal stimuli (e.g., feeling depressed), were also examined across study conditions. The repeated measures model indicated no statistically significant differences in participants' confidence in their ability to abstain from smoking tobacco cigarettes when facing internal stimuli across study conditions (F=1.708, p=0.180) (see Figure A15).

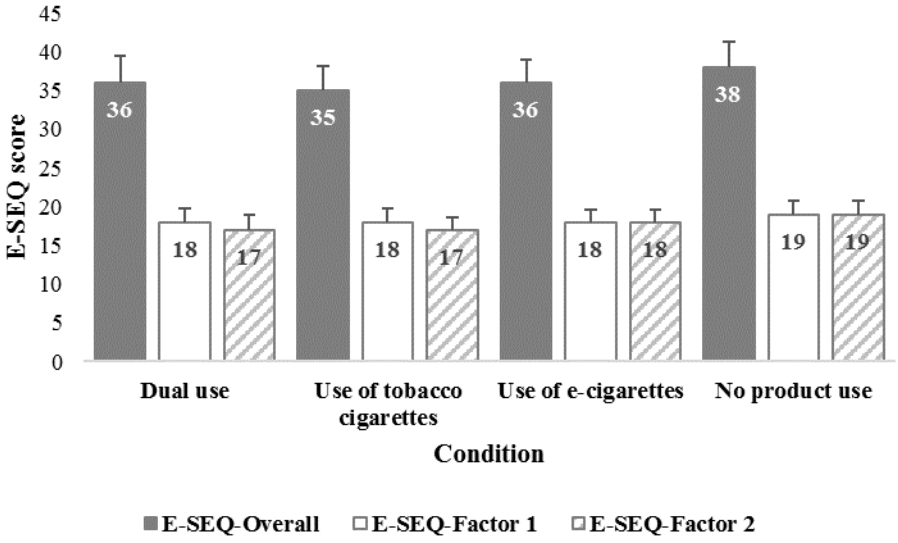
SEQ-Factor 2

Scores for the SEQ Factor 2, which reflect participants' confidence in their ability to abstain from smoking when facing external stimuli (e.g., when having a drink with friends), were also examined across study conditions. The repeated measures model yielded a significant effect of condition (F=4.145, p=0.012): participants reported significantly greater confidence in their ability to abstain from smoking tobacco cigarettes when facing external stimuli in the condition

of *No product use* as compared to conditions of *Exclusive use of tobacco cigarettes* (mean difference=2.4, 95% CI: 0.9 to 3.9, p=0.003), and of *Exclusive use of e-cigarettes* (mean difference=2.9, 95% CI: 0.9 to 4.8, p=0.005) (see Figure A15).

Measures of self-efficacy for abstaining from e-cigarettes across study conditions are presented in Figure A16.

Figure A16: Measures of self-efficacy for abstaining from e-cigarettes across study conditions (n=48)



Notes:
Abbreviations: E-SEQ=Self-Efficacy Questionnaire, adapted for e-cigarettes.
Conditions with different superscript letters were significantly different from one another, $p<0.05$.
Error bars indicate upper limits of 95% confidence intervals.

E-SEQ-Factor 1

Scores for the E-SEQ Factor 1, which reflect participants' confidence in their ability to abstain from vaping when facing internal stimuli (e.g., feeling depressed), were also examined across study conditions. The repeated measures model indicated no statistically significant differences in participants' confidence in their ability to abstain from vaping when facing internal stimuli across study conditions ($F=2.352$, $p=0.086$) (see Figure A16).

E-SEQ-Factor 2

Scores for the E-SEQ Factor 2, which reflect participants' confidence in their ability to abstain from vaping when facing external stimuli (e.g., being with other vapers), were also examined across study conditions. The repeated measures model indicated no statistically significant differences in participants' confidence in their ability to abstain from vaping when facing external stimuli across study conditions ($F=2.192$, $p=0.103$) (see Figure A16).