DOCTOR OF PHILOSOPHY, POPULATION HEALTH SCIENCES

A COMPARISON OF ELECTRONIC CIGARETTE REGULATION AND ASSOCIATED INFLUENCING FACTORS IN THE US AND THE UK: CONTEXTUAL SIMILARITIES AND POTENTIAL REGULATORY IMPLICATIONS FOR NIGERIA

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Abstract

Background

Tobacco smoking (TS) is the leading preventable cause of premature mortality and morbidity in the world. The World Health Organisation's (WHO) 2021 report on the global tobacco epidemic focused on addressing new and emerging products including e-cigarettes and highlighted dangers of e-cigarettes to youths. Countries with a large proportion of young people like Nigeria are likely to consider regulating e-cigarettes. The US and UK are two countries that can be said to be leading the way in communicating or promoting through research and policy the risks and benefits of e-cigarettes to public health. Comparing both countries' e-cigarette policies and regulations can provide some valuable lessons for Nigerian regulators as they look to embark on their e-cigarette regulatory journey.

Aim

This PhD project aims to compare the US and UK e-cigarette regulatory policies and public health initiatives and policies, to inform policy approaches in the context of Nigeria.

Methods

This PhD project, which comprised three empirical studies, used a multimethod qualitative approach. Study one involved purposive sampling and collection of primary data through interviews of 4 UK-based participants (between February to November 2022) and collation of secondary data through conference audio recordings (4 US and 5 UK recording) from the conference series - 'E-cigarette Summit: Science, Regulation and Public Health' (between November 2017 to May 2021); thematic analysis was carried out for all the data. Study two involved collation of secondary data (Twitter™ data) across 4 time periods (25th April 2014 to 8th August 2014, 10th May 2016 to 23rd August 2016, 2nd January 2016 to 17th April 2016, and 20th May 2016 to 2nd September 2016) that corresponds with pre- and- post e-cigarette regulatory period in the US and the UK; thematic and sentiment analysis was carried out on the data using Atlas.Ti. Study three involved purposive sampling and collection of primary data through interview of 4 Nigerian-based participants (between November 2022 to February 2023), with thematic analysis carried out using Nvivo.

Results

This PhD project found that the US and the UK had similar regulatory measures with respect to Notification, Warning labelling, and Child safety packaging of e-cigarettes. By contrast the

two countries had different regulatory measures with respect to Classification, Flavours, Nicotine concentration, General safety, Age of sale, and Advertising of e-cigarettes. Study one found that Existing regulatory frameworks, Guidance from available evidence, and Public health considerations, were the main factors that determined e-cigarette regulations in the US and the UK. Study two found six themes/ topics that were discussed by Twitter™ users in relation to e-cigarette regulations during the pre- and- post e-cigarette regulatory period in the US and the UK. The six themes are: Updates (or clarification) on e-cigarette regulations; E-cigarettea as a public health concern; E-cigarettes as a smoking cessation aid; Opposition to e-cigarette regulations and policies; Growing use and popularity of e-cigarettes; and Research on e-cigarettes. The Twitter™ discussions and associated sentiments of Twitter™ users in three of themes (E-cigarette as a public health concern, E-cigarette as a smoking cessation aid, Opposition to e-cigarette regulations and policies) were of a nature that had the potential to influence regulators' regulatory decisions through reputational theory, whereby regulators respond to patient activism or media pressure to protect their reputation in the public sphere. Study three found six factors with the potential to influence e-cigarette regulation in Nigeria. These comprise: existing regulatory framework; research evidence; public health considerations; economic considerations; infrastructural insufficiency; and role of industry.

Conclusion

Regulating e-cigarettes with existing national regulations and policies are a quick means of imposing e-cigarette regulations but can bring in ineffective and non-targeted e-cigarette regulatory measures. Whatever approach is used in developing e-cigarette regulations, nations could maximize benefits by ensuring responsive regulations i.e., ongoing monitoring and promptly responding to e-cigarette related public health concerns. Although collection of research evidence should be done objectively, application of e-cigarette research evidence should be context-based with appropriate weighing of risks:benefits of regulatory measures. Nigerian (and other) e-cigarette regulators should be cautious of and prevent external factors such as media pressure and actions of commercial actors that may unduly influence e-cigarette regulatory decisions.

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List of Abbreviations

AIDS- Acquired Immune Deficiency Syndrome

APCON - Advertising Practitioners' Promotion Council of Nigeria

APPH - Appropriate for the Protection of Public Health

ASA - Advertising Standards Authority

ASH - Action for Smoking and Health

BAT - British America Tobacco

CDC - Centre for Disease Control and Prevention

CDC- US Centre for Disease Control and Prevention

CMR - Carcinogenic, Mutagenic, or Toxic for Reproduction

CRUK- Cancer Research UK

CTP - Centre for Tobacco Products

DH - Department of Health

DHSC – Department of Health and Social Care

ECJ - European Court of Justice

EMA- European Medicines Agency

ENDS - Electronic Nicotine Delivery System

ENHANCED – Enhancing Dental Health Advice

EU – European Union

EVALI- E-cigarette and Vaping Associated Lung Injuries

FCCPC - Federal Competition and Consumer Protection Commission

FCTC - Framework Convention on Tobacco Control

FDA - Food and Drug Administration

FDCA - Federal Food, Drug, and Cosmetic Act 1938

FMOH - Federal Ministry of Health

FMS - Faculty of Medical Sciences

FSPTCA - Family Smoking Prevention and Tobacco Control Act 2009

FTND - Fagerström Test for Nicotine Dependence

GATS - Global Adult Tobacco Survey

GDP – Gross Domestic Product

GRAS - Generally Recognized as Safe

HCA- Health Care Professionals

HCC - House of Commons (Science and Technology Select) Committee

HCE - Office of Health Communication and Education

LOQ - Limit of Qualification

MDO - Marketing Denial Order

MEP – Member of European Parliament

MHRA - Medicines and Healthcare products Regulatory Agency

MRTP - Modified Risk Tobacco Product

NAFDAC - National Agency for Food and Drug Administration and Control

NASEM - National Academy of Sciences, Engineering and Medicine

NATOCC - National Tobacco Control Committee

NHS-SR - NHS Health Scotland representative

NI – Northern Ireland

NICE - National Institute for Health and Care Excellence

NIH - National Institutes of Health

NIHR – National Institute of Health Research

NPRM - Notice of Proposed Rulemaking

NRT - Nicotine Replacement Therapies

NTCA - National Tobacco Control Act, 2015

NTCR - National Tobacco Control Regulations, 2019

OHID - Office for Health Improvement and Disparities

ONS - Office of National Statistics

OTC - Over- The- Counter

PHE – Public Health England

PIR - Post-Implementation Review

PMTA - Premarket Tobacco product Application

PPP - Purchasing Power Parity

REC - Research Ethics Committee

SON - Standards Organisation of Nigeria

THC – Tetrahydrocannabinol

TPD - Tobacco Products Directive and Related Products 2016

TRPR – Tobacco and Related Product Regulations

TS - Tobacco Smoking

TVPA -Tobacco and Vaping Products Act

UK – United Kingdom

UKHSA - UK Health Security Agency

UNTH - University of Nigeria Teaching Hospital

US – United States of America

VAT - Value Added Tax

WHO - World Health Organisation

WTO – World Trade Organisation

Chapter 1. Background

1.1 Introduction

Reducing tobacco smoking is a priority public health concern for many countries around the world, because it remains the leading preventable cause of premature mortality and morbidity in the world (1). The advent of electronic cigarettes (e-cigarettes) has added a new dynamic to the discussions about tobacco control measures. Although e-cigarettes do not contain tobacco, their role in affecting tobacco smoking has been the subject of many public health debates (2). Some public health experts consider e-cigarettes to have the potential to compromise decades of public health efforts by acting as a gateway to traditional cigarettes and thereby driving smoking rates up, while others view them as an effective smoking cessation tool with the potential to drive smoking rates down (2). This division amongst public health experts and researchers has led to considerable variation in regulatory approaches to e-cigarettes around the world (3).

A member of the Nigerian Ministry of Health has reliably informed me informally that Nigeria has begun to consider regulation of e-cigarettes for the protection of public health. It is likely to be weighing up different regulatory approaches and policies to use for optimal benefit and to meet Nigeria's regulatory needs. The World Health Organisation (WHO) has stated that countries without regulation of e-cigarettes leave themselves 'particularly vulnerable to the activities of tobacco and related industries'(4)(pg. 21). Nigeria has a young population with approximately 43% under the age of 15 years (5) and should be vigilant to protect a new generation of Nigerians against nicotine addiction and tobacco smoking with their associated health problems. Nigeria is also a gateway to the African market as it is the the most populous country in Africa. Therefore, conducting research that could inform Nigeria's e-cigarette regulatory decision making is of great importance because regulation of e-cigarettes in Nigeria has the potential to influence public health outcomes not only in Nigeria itself but also in the wider African region. My research attempts to inform e-cigarette policy approaches in the context of Nigeria by comparing the US and UK e-cigarette regulatory policies and public health initiatives and policies to one another and to potential determinant factors of e-cigarette regulations in Nigeria.

Nigeria is a party to the WHO Framework Convention for Tobacco Control (FCTC) (6) and as such is likely to align itself to the guidance from WHO FCTC when regulating e-cigarettes. The

WHO FCTC governing body, Conference of the Parties (COP), has provided guidance on the regulation of tobacco and nicotine products since 2008 (7). The COP activities and reporting around e-cigarette regulation to date are summarised in Figure 1 below. Following these activities, the primary focus of WHO's 2021 report (4) on the global tobacco epidemic was on new and emerging products including e-cigarettes. The report recommended that e-cigarettes should be strictly regulated for maximum protection of public health as they are addictive and because children and adolescents who use them can double their risk of smoking cigarettes (4). In the remaining sections of Chapter 1, I present the background to the entire study.

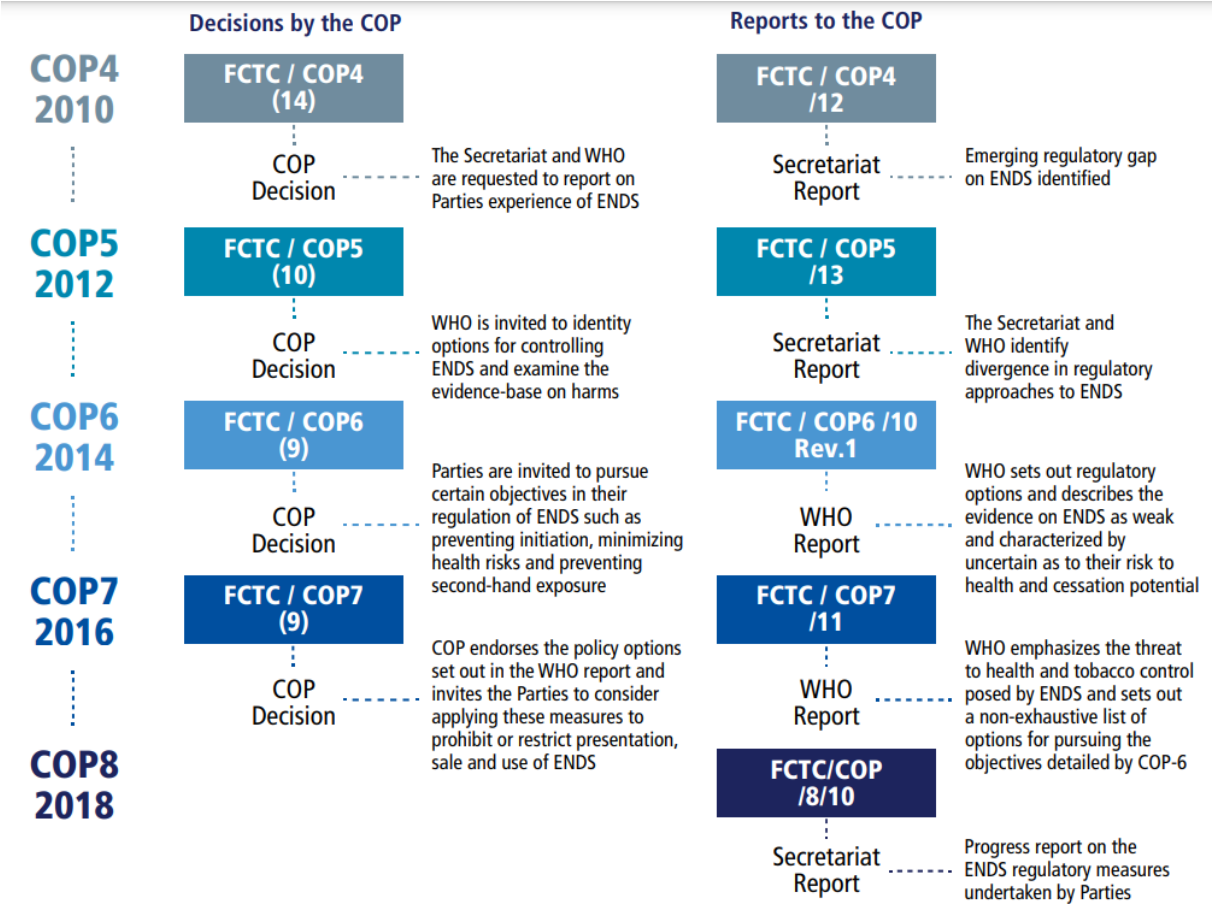


Figure 1: Timeline of e-cigarette reports from parties and decisions by COP
Source: Adopted from WHO report on the global tobacco epidemic 2021(4)

1.2 Rationale for conducting this study

The WHO report on the global tobacco epidemic 2021 (4)(pg. 31) recommends addressing e-cigarettes as part of tobacco control strategies based on seven outlined points:

- Article 5.2 of the WHO FCTC and FCTC/COP7 decisions obliges Parties to implement effective measures aimed at preventing and reducing tobacco consumption, nicotine addiction and exposure to tobacco smoke.
- Nicotine present in e-cigarettes is highly addictive posing the risk of nicotine addiction, including among children and adolescents.
- Nicotine in e-cigarettes can have deleterious impacts on brain development, making e-cigarettes harmful especially for children and adolescents.
- E-cigarettes are marketed in flavours that specifically target children and young adults.
- The use of e-cigarettes mimics the hand to mouth action associated with conventional smoked tobacco products and so may risk renormalizing smoking behaviour, particularly among younger populations.
- E-cigarettes generate an aerosol that looks similar to tobacco smoke making it difficult to tell if a person is smoking a tobacco product or using an e-cigarette.
- E-cigarettes are marketed and promoted by the tobacco and related industries, employing many established tactics to target their products at young people.

The majority of the above concerns relate to the exposure to nicotine and the initiation of smoking (following on from vaping) in youth. Note that, with regards to the likelihood of subsequent smoking initiation by young people who had ever used e-cigarettes, the systematic review and meta-analysis (8) WHO presents in the 2021 report on the tobacco epidemic, and other data available from reviewed studies (9-13) only shows an association between use of e-cigarette and subsequent smoking. None of the cited studies demonstrate a causal relationship or even that vaping is the primary factor leading to subsequent smoking; the Report on the Scientific Basis of Tobacco Product Regulation: Seventh Report of a WHO Study Group has acknowledged this (14).

Nonetheless, it would still be advisable for countries to take a cautious approach in regulation of e-cigarettes following WHO recommendations. Nigeria, as a party to WHO FCTC, is likely to now consider regulating e-cigarettes which have already found their way into the Nigerian market, presumably through importation. A 2021 cross-sectional survey (15) showed that e-cigarettes are currently being used in Nigeria with a prevalence of 7.9% among 949 respondents aged 15-35 years that were surveyed. In 2018, Chris McAllister, the Managing Director of British America Tobacco (BAT) Nigeria, stated that the company plans

to launch their world leading range of e-cigarettes in Nigeria 'in the near future' (16). Although BAT has not launched its range of e-cigarettes in Nigeria to date (April 2024), it is likely that BAT would aim to do so because Nigeria is the most populous country in Africa and serves as a gateway to the wider African market. It is therefore vital to regulate e-cigarettes in Nigeria for the protection of public health.

Comparing cross-country experiences is a useful way of developing policy instruments for problem-solving in a particular country because it provides guidance on what to do and what not to do. This is achieved through: comparing different ways of managing similar problems; understanding how government institutions operate within their environment; and understanding how the policies adopted in one country can have important implications for other countries (17). A comparison of e-cigarette national regulatory approaches in Canada, US, UK, France, Australia and New Zealand, concluded that Europe and the US appear to be leading the way towards e-cigarette policies that acknowledge governments' responsibility to impose public health regulatory controls (18). The above comparative study (18) suggested that, amongst the countries compared, the US regulations were the most permissive; those in Canada and New Zealand, the most conservative; those in Canada, Australia and New Zealand were easily bypassed through Internet imports and lenient enforcement; and European health agencies were paving the way for Member States (UK was then part of the EU) to take appropriate steps to regulate e-cigarettes according to their own jurisdictions. However, since that study was published there have been some changes to regulations in some of those countries. Most recent among such changes is the regulatory change by the Australian Therapeutic Goods Administration announcing that, effective from 1st January 2024, the importation of disposable vapes irrespective of nicotine content or therapeutic claims will be prohibited (19), and also, from 1st April 2024, the importation of all non-therapeutic vapes will be prohibited (19).

In Europe, the UK has had at least a decade of experience with e-cigarette use which makes it a viable option for cross-country comparison. It is plausible that Nigeria may look to the UK when developing e-cigarette policy because it is an English-speaking country like Nigeria, ensuring ease of comparability and transfer or exchange of knowledge. Other reasons include that Nigeria has a commonwealth/ colonial tie with the UK, and like Nigeria, the UK is a party to the WHO FCTC.

The US, which also appears to be leading the way in e-cigarette policy, is another viable

option for cross-country comparison because it, similarly (to the UK), has at least a decade of experience with e-cigarette use, is an English-speaking country, and has a long-standing trade relationship with Nigeria, but has taken a different approach to the UK in regulation of e-cigarettes. Australia is another country that could have been added for comparison due to its distinct regulatory approach. In Australia, therapeutic vapes (i.e., e-cigarettes that contain nicotine and for which the manufacturer has made a therapeutic claim) are permissible for smoking cessation and the management of nicotine dependence, under prescription and supervision of a health practitioner (19). Also, vapes that do not contain nicotine, or any other medicine, and do not make therapeutic claims, may be supplied by retailers generally, including vape stores, subject to state or territory law (19). However, I do not anticipate that Nigeria would look to Australia for regulatory guidance, as historically, Nigeria has tended to look to either the UK or the US for the reasons already highlighted above. Nigeria is also unlikely to look towards other African countries that currently regulate e-cigarettes because those countries have had less than a decade's experience with e-cigarettes and may not provide similar capital institutional knowledge to the US and the UK.

If Nigeria tends towards following WHO's guidance on e-cigarettes, they are likely to look towards the US as a model country with respect to regulation and policies. This is because, despite the US not being a ratified member of the WHO FCTC, the US public health agencies (similarly to WHO) advise that e-cigarettes are addictive, can harm the adolescent brain, and that children and adolescents who use them can double their risk of smoking cigarettes (20). The US regulation of e-cigarettes therefore focuses on preventing initiation of children into nicotine use through e-cigarettes. Nigeria may have similar priorities and may adopt a similar regulatory focus to the US because of Nigerian population's demographics. In 2021, about 43.29 percent of Nigeria's total population were children under the age of 15 and therefore in the at-risk age-group (5), warranting caution with e-cigarettes. However, focusing on the prevention of adolescent uptake of nicotine takes away focus from helping current adult smokers quit smoking (an important public health priority). Smoking prevalence is considerably lower among people aged 15 years and older in Nigeria (2.7%) compared to the US (16.6%) and in the UK (13.2%)(21). Nonetheless, for those adults who smoke, e-cigarettes have been shown (22) to be more effective than Nicotine Replacement Therapies (NRTs) which are currently recommended in Nigeria for helping adult smokers quit. Therefore, Nigerian regulators may decide to explore the use of e-cigarettes for smoking cessation, in

which case they are likely to look towards the UK as a model. However, a potential limitation is that e-cigarettes are relatively expensive in Nigeria (23) precluding the possibility of using them for smoking cessation. One of the objectives of my research was to gather the views of potential stakeholders in Nigerian e-cigarette regulation as to what they were likely to prioritise in their regulatory policies – deterring initiation of vaping in youth and adults naïve to smoking, supporting adult smokers to quit, or a combination of the two.

Clearly there are potential aspects of e-cigarette regulation that Nigeria could take from the regulation of e-cigarettes in the US and the UK. Both of these countries have long-standing and respected regulatory agencies that can provide capital institutional knowledge, beneficial in terms of policy development. Nigeria could learn from what the US and the UK did in terms of regulation (and why they did it), and the implications and consequences (both positive and negative) of what they did. It is therefore important to compare regulations and policies around e-cigarette use in the US versus the UK, to enable identification of the differences, similarities and determining factors of e-cigarette regulations in both countries. The Nigerian regulatory environment can then be explored to identify what determinant factors found in the US and or the UK exist in the context of Nigeria and are potential determinant factors for e-cigarette regulations in Nigeria. The findings from this study may then inform Nigerian e-cigarette regulators on regulatory approaches and policies to use for optimal benefit and to meet the country's regulatory needs, as it looks to begin its journey with e-cigarette use and regulation.

1.3 Aims and Objectives

In this PhD project I aimed to compare US and UK e-cigarette regulatory policies and public health initiatives and policies, to inform policy approaches in the context of Nigeria. To achieve this aim, I had three objectives:

1. To describe the similarities and differences between e-cigarette regulation and policies in the US and the UK.
2. To explore the determining factors of the policies and regulation of e-cigarettes in the US and the UK.

3. To understand the similarities and differences between contextual factors in Nigeria versus factors identified as determining the regulatory and policy approach to e-cigarette in the US and the UK.

A structured literature review (presented in Section 1.8) was used to gain understanding and describe the similarities and differences between e-cigarette regulation and policies in the US and the UK (Objective 1). I then carried out three related empirical studies to achieve Objective 2 and 3, with the findings drawn together in Chapter 6 of this thesis. The three studies are:

1. Factors Influencing E-Cigarette Regulation and Policies in the US and the UK (Chapter 3)
2. The Values and Sentiments of the Public Towards Electronic Cigarettes and their Regulation in the US and the UK (Chapter 4)
3. Potential Determinant Factors of Electronic Cigarette Regulation in Nigeria (Chapter 5)

The methods used in each of these empirical studies are elaborated in respective chapters.

1.4 Prevalence and Burden of Tobacco Smoking globally, and more specifically in the US, the UK and Nigeria

1.4.1 Prevalence and Burden of Tobacco Smoking Globally

According to the World Health Organisation, 1.3 billion people use tobacco worldwide, and in 2020, this figure represented 22.3% of the global population (36.7% of all men and 7.8% of the world's women)(1). Tobacco use appears to be decreasing in all the regions of the world, but at a slower rate in the African region with the estimated lowest average rate at around 18% in 2000 and 10% in 2020 (21). However, the African region has maintained the lowest average rate of tobacco use in the world (see Figure 2 below). The South-East Asia Region is estimated to have the highest average rate of tobacco use amongst WHO regions, at around 50% in 2000 and 29% in 2020 (21).

'Current' smokers in this context are people who, at the time they participated in a survey about tobacco smoking, reported smoking 'every day' or 'some days.'

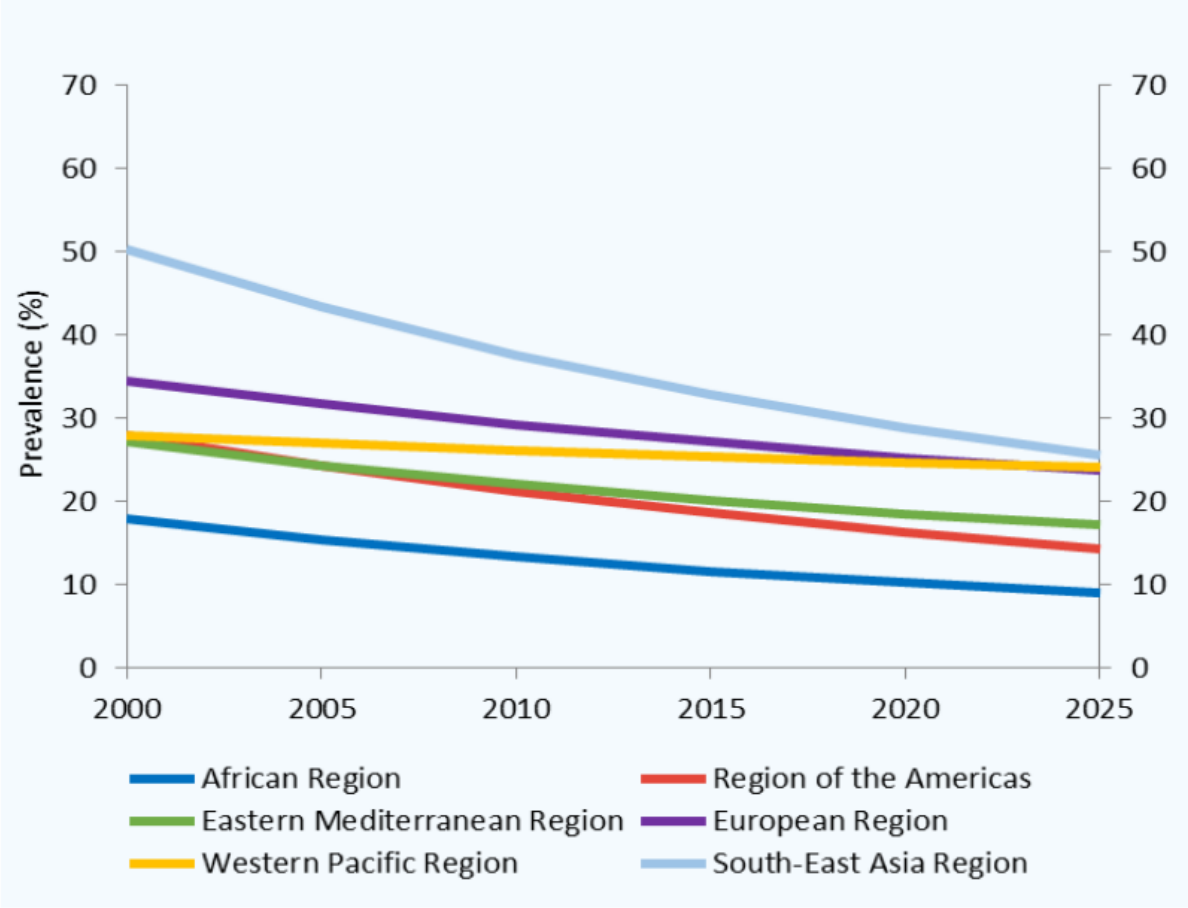


Figure 2: Trends in tobacco use within WHO regions from 2000 to 2025
Source: Adopted from WHO (21)

Tobacco use remains the leading cause of preventable premature mortality and morbidity in the world (1). Tobacco kills up to half of its users, translating to more than 8 million people each year. Of these, more than 7 million deaths are the result of direct tobacco use while around 1.2 million are the result of non-smokers being exposed to second-hand smoke. Over 80% of the world's 1.3 billion tobacco users live in low- and middle-income countries (1). The burden of tobacco smoking includes not only tobacco-related illness and death but also economic impacts. Economic costs of tobacco smoking includes health care costs for treating the diseases caused by tobacco use as well as the lost human capital that results from tobacco-attributable morbidity and mortality (1). The burden flows down even to the basic unit of society – i.e., families – by contributing to poverty, when household spending is diverted from basic needs, such as food and shelter, to tobacco.

The addictiveness of tobacco makes it difficult to stop this consumption and spending behaviour (1). The World Health Organisation (WHO), through its Framework Convention on Tobacco Control (FCTC), suggests that countries should implement tobacco taxation and

should impose restrictions on packaging, labelling, promotion, sponsorship and advertisement to control tobacco smoking (6). However, the most progress has been made since 2007 when the WHO introduced MPOWER as a tool to help countries implement WHO FCTC measures (4). MPOWER is an acronym for: M - Monitor tobacco use and prevention policies; P - Protect people from tobacco smoke; O - Offer help to quit tobacco use; W - Warn about the dangers of tobacco; E - Enforce bans on tobacco advertising, promotion, and sponsorship; R- Raise taxes on tobacco. 5.6 billion people (over 70% of the world's population) are now covered by at least one MPOWER measure being met at the highest level of achievement, compared to only 1 billion people (15% of the world's population) before 2007 (24). See Figure 3 below for the percentage increases in coverage of people with the MPOWER measures. As a result of MPOWER measures being rolled out across 195 countries and the increasing coverage of people, the prevalence of smoking worldwide is expected to steadily reduce. The Global Tobacco Control Progress Hub[1] is a useful live platform for monitoring countries progress on MPOWER measures and adherence to WHO FCTC; as of July 2023, it ranks UK (4th of 195) above the US (78th of 195) and Nigeria (131st of 195) in terms of progress with MPOWER measures. Table 1 below shows the years of MPOWER achievement for the three respective countries.

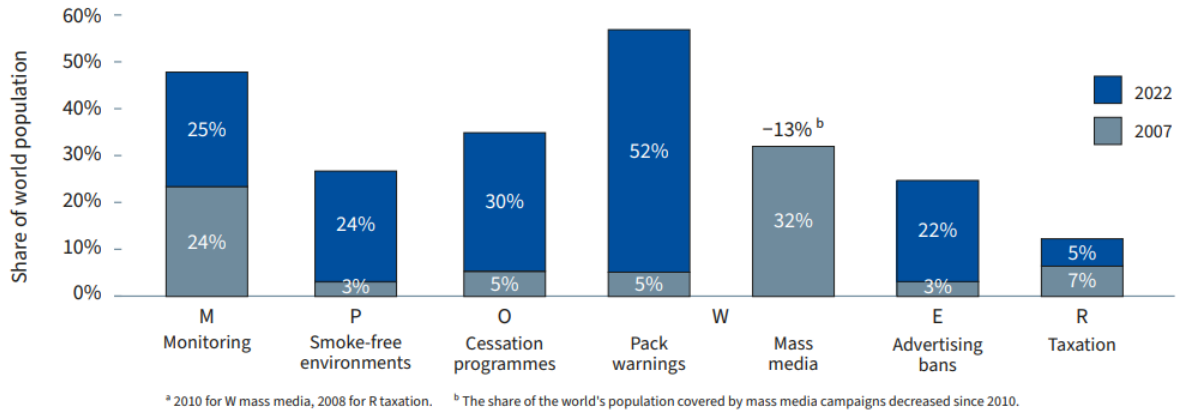


Figure 3: Increase in MPOWER worldwide coverage from 2007 to 2022.
Source: WHO Report on the Global Tobacco Epidemic, 2023 (24) - https://iris.who.int/bitstream/handle/10665/372043/9789240077164-eng.pdf?sequence=1 (accessed 14/01/2024)

[1] See https://public.tableau.com/app/profile/globalprogresshub/viz/WHO-FCTC-Dashboard-June-28/CountryLandingPage (accessed 10/08/2023)

Countries	Monitor tobacco use and Prevention policies	Protect people from tobacco smoke	Offer help to quit tobacco use	Warn about the dangers of tobacco	Enforce bans on tobacco advertising, promotion, and sponsorship
US	2007		2008	2020	
UK	2007	2006		2016	
Nigeria				2019	2015

Table 1: Year of highest level of achievement of MPOWER measures in the US, UK, and Nigeria

Source: Adopted from WHO report on global tobacco epidemic 2021 (4)

Across the world, tobacco is used in various forms and there are several tobacco products including waterpipe tobacco, cigars, cigarillos, heated tobacco, roll-your-own tobacco, pipe tobacco, bidis and kreteks, and smokeless tobacco products. However, tobacco smoking, which includes cigarette smoking, appears to be a popular form of tobacco use.

The global number of tobacco smokers aged 15 years and older in 2000 was estimated at 1.13 billion and is projected to decline to around 0.96 billion by 2025, based on countries' current prevalence and trends in population size. While the global number of smokers aged 15 years and older is consistently declining in the Region of the Americas, the European Region, and the South-East Asia Region, the rate of decline is slower in the African Region and the Eastern Mediterranean Region (21). As of 2020, the WHO age-standardized estimates of current tobacco smoking prevalence rate among people aged 15 years and older was low in Nigeria (both sexes 2.9%: Male 5.5%; Female 0.3%) compared to the US (both sexes 23.0%: Male 28.4%; Female 17.5%) and the UK (both sexes 15.4%: Male 17.3%; Female 13.5%) (21). However, note that the above rates could be distorted (under- or over-estimated) because of when and how data were collected. For example, the first and only national tobacco survey conducted to date in Nigeria is the Global Adult Tobacco Survey (GATS) collected in 2012 (25).

Cigarette smoking is the most common form of tobacco use worldwide. According to WHO 2020 age-standardized estimates, current cigarette smoking prevalence rate among people aged 15 years and older were 2.7% in Nigeria; 16.6% in the US; and 13.2% in the UK (21).

1.4.2 Prevalence and Burden of Tobacco Smoking in the US Context

In the US, in 2021, an estimated 28.3 million people aged 18 years and above (11.5% of population) currently smoked cigarettes (26); discrepancies between this prevalence rate and that reported on page 10 may be due to the different age-groups considered or may be an artefact of how data were collected. Adult men (13.1%) were more likely to be current smokers than were adult women (10.1%). Adults aged 45-64 years (14.9%) had the highest prevalence of smoking followed by 25-44-year-olds (12.6%), 65 years and older (8.3%), while those aged 18–24 years (5.3%) had the lowest prevalence (26). Smoking rates in the US have experienced a statistically significant decline of more than 9.4 percentage points from 2005 (when overall prevalence of current smoking was 20.9%) to 2021. Nonetheless, tobacco smoking remains the single largest preventable cause of mortality and morbidity, killing more than 480,000 people each year, and with more than 16 million Americans living with a smoking-related disease (26). Smoking kills more people than alcohol, AIDS, car accidents, illegal drugs, murders and suicides combined. Of all the young people who become new smokers each year, almost a third will ultimately die as a result. In addition, smokers lose a decade of life on average because of their smoking. For every person who dies from smoking, at least 30 more live with serious smoking-caused disease and disability (27). Smoking is the leading preventable cause of preterm birth (birth <37 gestational weeks), and smoking in pregnancy remains a leading modifiable cause of poor birth outcomes (e.g. preterm birth, low birth weight, perinatal mortality), with approximately 360,000–500,000 smoke-exposed infants born yearly (28). In terms of economic burden, smoking-related illness in the US gives rise to a total annual public and private health care expenditure of $241.4 billion (27).

1.4.3 Prevalence and Burden of Tobacco Smoking in the UK Context

In the UK, in 2022, an estimated 6.4 million (12.9%) people aged 18 years and above currently smoked cigarettes. Based on estimates from the Annual Population Survey (APS), this is the lowest proportion of current smokers since such records began in 2011 (29). In the UK, in 2022, the prevalence of smoking was higher amongst men (14.6%) than amongst women (11.2%) (29). The age-bands used in reporting are not directly comparable to those used for US data. In the UK, the prevalence of current smoking in 2022 was highest amongst those aged 25-34 years (16.3%), compared with those aged 35-44 years (14.5%), 45-54 years

(14.3%), 55-64 years (13.6%), 18-24 years (11.6%), and 65 years and over who had the lowest prevalence (8.3%)(29). Even though smoking rates are going down, tobacco smoking remains the leading preventable cause of illness and premature death, killing around 74,600 people in England in 2019 (30). In the UK, smoking in pregnancy causes up to 5,000 miscarriages, 300 perinatal deaths and around 2,200 premature births each year (31). Second hand smoke also causes around 165,000 cases of disease in children every year (32). In 2015, in England alone, the total estimated smoking-related cost to the NHS was £2.6 billion (33); as of 2019 there was a cost of £720 million a year in social care to local authorities(34).

1.4.4 Prevalence and Burden of Tobacco Smoking in the Nigerian Context

WHO estimates that as of 2020, in Nigeria 2.7% of people aged 15 years and older smoked cigarettes, with at a higher rate among men (5.1%) than women (0.2%) (21). Use of tobacco is not confined to commercially produced cigarettes in Nigeria. Other common forms of tobacco vary from rolled cigarettes, through shredded tobacco being inserted into pipes for smoking to finely pulverized tobacco for inhalation (referred to as snuff)(25). In 2020, tobacco was estimated to kill 246 men and 64 women every week in Nigeria, with more than 16,100 people dying from tobacco-related diseases yearly (35). Although economic costs of smoking in Nigeria are not known, as at 2020, a smoker in Nigeria would have to spend 6.03% of their average income (measured by per capita GDP) to purchase ten of the most popular cigarettes to smoke daily each year, and this prevents many families from rising out of poverty (35).

1.5 E-cigarettes: Smoking cessation and Public Health

1.5.1 Harm Reduction Approach and E-cigarettes

The harms of tobacco smoking (TS) are well established in the literature. Several measures, including tobacco taxation and regulation and restrictions on packaging, labelling, promotion, sponsorship and advertisement, as suggested in the WHO Framework Convention on Tobacco Control (6), have been adopted by many countries seeking to control TS. Despite these measures, 22.3% (1.3 billion people) of the global population still used tobacco in 2020 (1).

There are 98 hazardous smoke components in tobacco cigarettes e.g. chromium VI, formaldehyde, hydrazine, aniline, acrylonitrile, etc. (36); these cause cancer, respiratory and cardiovascular diseases. However, it is nicotine, which is not one of these hazardous components, that is the substance in cigarettes that keeps people hooked on smoking, since nicotine is highly addictive.

Because of the addictive nature of nicotine, researchers have, over time, shifted their focus from studying conventional cigarettes to studying nicotine. The concept of a *Harm Reduction Approach*, which surfaced in the 1990s in response to the spread of Acquired Immune Deficiency Syndrome (AIDS) among injected drug users (37), is now being used in tobacco control. Within the tobacco control context, it refers to an approach whereby alternative means for nicotine delivery that do not include (burning) tobacco are promoted for use by smokers as an alternative to conventional cigarettes. This approach is based on the premise that the nicotine replacement product is less harmful than tobacco smoking but satisfies the smoker's urge for nicotine uptake. In public health, *harm reduction approaches* allow people to engage in risky activities, but with reduced risk due to safety measures (e.g., wearing a crash helmet for motor cycling) or safer alternatives (e.g., using nicotine replacement therapy or e-cigarettes instead of tobacco cigarettes) (38). [Other examples include, using a seatbelt when driving, instead of totally avoiding driving; applying sunscreen when out in the sun, instead of staying indoors on sunny days; wearing protective headgear on a construction site or to play contact sports such as rugby; and responsible drinking, i.e., staying within recommended limits for units of alcohol per week, or consuming low alcohol products, as opposed to becoming teetotal.] It is important to emphasize that with the use of e-cigarettes in harm reduction, the risk is not eliminated as the nicotine contained in most e-cigarettes is not a completely safe substance.

In the context of reducing harms from nicotine addiction, inventors have produced alternative means for nicotine delivery that do not expose the user to the toxic components of TS, in a bid to reduce the health burden of TS. NRT – e.g., nicotine gums, inhalers and patches – which first emerged in the 1980s, have been adopted by many countries as smoking cessation aids (39, 40). The first NRT (Nicorette gum) to be licensed as a medicine in the US was in 1984 (41). In the UK, NRT, which can now be purchased over- the- counter (OTC) from pharmacies, supermarkets and at other outlets, was licensed as a medicine and became available on prescription in 2001, allowing smokers to purchase NRT at a reduced or

zero cost depending on income level (42). More recent innovations, e.g. vape pens and e-cigarettes, are still being explored and debated as a prospect for smoking cessation (43). Others (e.g. Heat not Burn (HnB), e-hookahs, e-cigars, e-pipes) are just considered as alternatives to TS (44), but not advocated for smoking cessation. The focus of my research is on e-cigarettes.

1.5.2 What are E-cigarettes?

An E-cigarette is an electronic vaping device that is handheld and produces for inhalation an aerosol formed by heating an e-liquid. This is achieved by using a battery-powered heating coil which is activated by a switch or by suction as the user sucks on the mouthpiece of the device. The e-liquid contains one or more humectants (propylene glycol, glycerol or glycerine), usually together with flavourings (e.g., tobacco, mint, fruit) and (usually) nicotine (in various doses)(45). E-cigarettes do not necessarily contain nicotine or any pharmacologically active substance. The type of e-cigarettes whose e-liquid contains nicotine are referred to as nicotine-containing e-cigarettes, and it is this type that are generally considered as an aid to smoking cessation (45).

E-cigarettes have evolved considerably over the last decade with a wide variety of products on offer. At the simple end of the scale there are disposable single use devices, whereas at the sophisticated end there are modifiable devices which can be controlled from the user's smart phone (46). The modern e-cigarette is often credited to Hon Lik, a Chinese pharmacist who invented the product in 2003, and whose design was patented internationally in 2007 (Electronic Atomization Cigarette: US 20070267031 A1), subsequently becoming commercially available in Europe and the US in 2007, but not widely used until 2012 (47, 48).

Figure 4: Different types of Electronic Cigarettes
Source: The US Food and Drug Administration (49)

E-cigarettes can have a range of designs and appearance (Figure 4*)* but typically contain a power source (most usually a lithium battery), a heating element, and a reservoir/cartridge for the 'e-liquid' (50). For self-activated versions, such as JUUL devices, when the user inhales the negative pressure closes a switch, turning on the heater, which turns some of the liquid into an aerosol, which is then inhaled (50). In other models, the atomizer is triggered manually by pressing and holding an on/off switch which raises the temperature of the atomizer to vaporize the e-liquid drawn from the cartridge/ reservoir (51). As e-cigarettes were viewed as producing vapour, it led to their colloquial name of 'vapes', with users referred to as 'vapers' and the action of using an e-cigarette being termed 'vaping'(52).

However, e-cigarettes actually produce aerosol rather than vapour. In some countries, such as the US, and in some literature, including the WHO report (24), e-cigarettes are referred to as Electronic Nicotine Delivery System (ENDS). Therefore, the term 'ENDS' is used interchangeably with 'e-cigarettes' in some sections of this thesis.

1.5.3 The Prospects and Concerns around E-cigarettes

By and large, the discussion amongst public health experts and researchers about the place of e-cigarettes in public health circles around whether e-cigarettes present a positive potential to aid smokers quit TS (22, 53), or a negative potential to lead non-smokers (particularly children and adolescents) to TS (the so called 'gateway theory') (8-10). For those who favour the stance that e-cigarettes have the potential to aid attempts to quit smoking, they argue that the goal is for people to stop TS completely because of the harmful health effects. However, they recognise that people find it difficult to stop because of an addiction to the nicotine which, on its own, is not responsible for the established health harms that results from smoking. Therefore, it is argued, that if cigarettes are substituted with an alternative form of nicotine delivery that is safer and effective for smoking cessation (as is the case of e-cigarettes(22)), it will enable achievement of the overall goal of preventing the harms of smoking, even for those who fail to overcome their addiction to nicotine. On the other hand, for those who are of the opinion that e-cigarettes will lead non-smokers to take up smoking, their argument is that e-cigarettes make vaping appealing, especially to youths, through advertisements, flavours, and presentation of e-cigarettes as safe products (54). This leads naïve non-smokers to take up e-cigarettes and to get addicted to nicotine, with the possibility of switching to conventional cigarettes, either for a new type of 'high', exploration, or other reasons.

Individual researchers (55, 56), organisations (57, 58) and governments (59, 60) have expressed varying opinions on the place of e-cigarettes in public health and have sometimes provided evidence to support their viewpoint. However, the expression of opinions has taken different shapes, from messages publicised to policies implemented. Such policies lie on a spectrum that ranges from promotion of e-cigarettes as a smoking cessation aid (as is the case in the UK) to complete bans on e-cigarettes in countries such as Australia and Brazil. One of the most recent countries to ban e-cigarettes was India whose health minister stated that it is in the public interest to ensure vaping does not become an 'epidemic' among young

people (61). The World Health Organisation (WHO) congratulated the Indian government stating that 'It is a strong and definitive step to protect its citizens, especially the youth and children, from the increasing risk of nicotine-addiction' (62). With respect to Health Care Professionals (HCPs) who have a role to play in guiding patients to make evidence- based decisions regarding the use of e-cigarettes, a systematic review (63) found that they held diverse views about the efficacy of e-cigarettes. Some expressed wariness over their potential health effects, with their endorsement of e-cigarettes seemingly largely dependent on patient health status, the presence of other competing risk factors and patient preferences.

More generally, the WHO has taken a cautious approach to e-cigarettes which is reflected in their press release following a Question and Answer series about e-cigarettes in January 2020 (64) and in their 2021 report (4). In the Q&A series, in response to the question 'Are e-cigarettes and other vaping products dangerous?' WHO stated, amongst other claims, that 'Evidence reveals that these products are harmful to health and are not safe', and that '…there is a growing body of evidence in some settings that never-smoker minors who use ENDS at least double their chance of starting to smoke conventional tobacco cigarettes later in life' (64)(p.1). These assertions were rapidly challenged. Some research experts, via the Science Media Centre in London, responded to this press release with statements along the lines of 'Practically all the factual statements in it (*WHO press release*) are wrong. There is no evidence that vaping is 'highly addictive' – less than 1% of non-smokers become regular vapers. Vaping does not lead young people to smoking – smoking among young people is at all-time low. There is no evidence that vaping increases risk of heart disease or that it could have any effect at all on bystanders' health' (65)(p.1). This goes to show the contested opinions on this topic.

Looking into the WHO report (14) that compiles and summarises the evidence referred to in the WHO press release, the conclusions about the toxicity of e-cigarettes are based mainly on empirical evidence from *in vitro* chemical and toxicological studies of rats (66-71). The authors of the report conclude that e-cigarettes are not completely harmless but are generally less dangerous than cigarettes. Regarding the likelihood of subsequent smoking initiation by young people who had ever used ENDS, the WHO report acknowledged that, even though the data available from reviewed studies (10-13) shows an association between experimental use of ENDS and subsequent experimental smoking, those studies do not

provide evidence of a causal relationship or even that the experimental smoking is due mostly to previous ENDS use (14).

While NRTs are recommended in many countries' guidelines for quitting smoking, evidence suggests that e-cigarettes are more cost efficient and effective than NRT for smoking cessation (22, 72). Perhaps in countries where NRTs are recommended but e-cigarettes are not endorsed, there is still a lack of country-specific evidence on acceptability, effectiveness, and cost-effectiveness of e-cigarettes. In the UK where such data are collected, evidence suggests that many smokers have used e-cigarettes to quit – and to quit completely, not just for use in combination with smoking (dual use)(53, 59). In England alone, estimates suggest that e-cigarettes may well help 70,000 smokers quit each year (73).

In the US, e-cigarettes have caused concerns because of a steady increase in adolescent use and its reported association with respiratory injury, including acute eosinophilic pneumonia, organizing pneumonia, acute respiratory distress syndrome, and hypersensitivity pneumonitis (50). E-cigarettes were even implicated in a crisis that was termed EVALI (E-cigarette and Vaping Associated Lung Injuries) that involved a total of 2,807 hospitalized cases or deaths in US states, districts and territories (74). (Subsequent investigations have identified that this illness was related to products containing vitamin E acetate (74), an additive substance in some Tetrahydrocannabinol (THC) containing products, which are not permitted under UK regulations).

1.6 E-cigarette regulation: Global context

Within the context of this thesis, regulation refers to 'a specific set of commands - where regulation involves the promulgation of a binding set of rules to be applied by a body devoted to this purpose' (75)(p.3). E-cigarettes have been met with different reactions in different countries, with some countries regulating them broadly, some regulating more specifically or only focusing on certain aspects, and others having no regulations in place yet.

Internationally, as of 2021 WHO (4) reported that 79 countries had adopted one or more legislative measures to regulate e-cigarettes, and 32 countries have banned the sale of e-cigarettes completely, making a total of 111 countries which regulate e-cigarettes in some way. There are still 84 countries that neither ban nor regulate e-cigarettes through any means (4)(pg. 21). Internationally, e-cigarette regulations are driven by three main

contrasting principles - upholding consumer product standards; limiting access, addictiveness or attractiveness of e-cigarettes for youths and non-smokers; and facilitating e-cigarette use for smoking cessation by adults (76). Campus *et al.* (77) placed the options for regulation and incentivization of e-cigarettes in a spectrum ranging from health protection measures at one end, to harm reduction measures at the other end (see Figure 5 below). At the health protection end of the spectrum, policies are prohibitive (including complete bans on e-cigarettes) and aim to prevent new users from becoming addicted to nicotine. At the harm reduction end of the spectrum, policies are less restrictive and involve positive financial incentives to promote switching from tobacco cigarettes to a less harmful product (i.e., e-cigarettes) with the aim of reducing the more harmful toxicological effects of smoking tobacco cigarettes.

Figure 5: Spectrum of e-cigarette regulation and incentivization
Source: Adopted from Campus *et al.(77)*

In 2016, a study (51) found that, worldwide, e-cigarettes are regulated in a range of ways: by using existing regulations that primarily relates to tobacco products; by enacting new policies to regulate e-cigarettes; or by using a combination of new/amended and existing regulation. The study also showed that common policies included a minimum-age-of-purchase, indoor-use (vape-free public places) bans and marketing restrictions, with a few countries applying a tax to e-cigarettes (51). A regularly updated e-cigarette policy scan (78) shows that, as of April 2024, 132 identified countries or other jurisdictions worldwide regulate or ban e-cigarettes. This number is more than the 111 countries reported in the 'WHO report on the global tobacco epidemic 2021'(4) because the WHO report (4)

accounted for a snapshot in time (2021) while the e-cigarette policy scan website is regularly updated with the April 2024 update being presented here.] According to the policy scan (78), as of April 2024, sales of e-cigarettes are regulated in 110 countries, sale of all types of e-cigarettes is banned in 31 countries, and four countries (Jamaica, Japan, Mexico, and Switzerland) prohibit the sale of nicotine-containing e-cigarettes. Fifty-six of these countries (or jurisdictions) have a minimum age restriction for the purchase and/or use of e-cigarettes. In 55 countries permitting the sale of e-cigarettes, there are other regulations around sale such as marketing authorization requirements, cross-border sale restrictions/regulations, restrictions in venues where they can be sold, or other constraints. Seventy-eight countries prohibit or regulate advertising, promotion, or sponsorship of e-cigarettes, while six of these countries apply the advertising restrictions only to e-cigarettes that contain nicotine or that are regulated as medicines. Thirty-eight countries have regulations on child safety packaging, 51 countries mandate the placement of health warnings on e-cigarette packaging, Israel requires plain packaging for all e-liquids, and Uruguay prohibits brands/patents for e-cigarettes. Thirty-nine countries regulate the amount (concentration/volume) of nicotine in e-liquids, 39 countries do not permit the use of ingredients (other than nicotine) that pose a risk to human health, in heated or unheated form, in nicotine-containing e-liquid or regulate flavours in e-liquid. Thirty-four countries: regulate the quality of nicotine and other ingredients used to manufacture the e-liquid; require products to pass safety and quality evaluation; or have instituted other safety-related regulations for e-cigarettes. Forty-three countries have regulations that require manufacturers/retailers to notify the competent authority prior to introducing e-cigarettes to the market, as well as to submit an annual report of sales and other specified information. Sixty-eight countries (explicitly or as implied in the law) prohibit or restrict the use of e-cigarettes in public places. Thirty-five countries/jurisdictions tax e-cigarettes (78).

As indicated above, a total of 35 countries (26.5% of all countries or jurisdictions with some regulation in place) have a ban either on all e-cigarettes or only those containing nicotine. Of the 35 countries, 19 are in Asia, five in South America, six in Africa, two in Central America and North America, and one (Switzerland) in Europe. In Australia, nicotine is classified as a restricted poison if it is not used for therapeutic purposes. Therapeutic vapes are permissible under prescription for smoking cessation while vapes that do not contain nicotine, or any other medicine, and do not make therapeutic claims, may be supplied as legal consumer

products by retailers generally, including vape stores, subject to state or territory law (19). However, because marketing of e-cigarettes is banned in Australia, the advertising, promotion, sponsorship, and recreational use of e-cigarette are inherently prohibited (78). In Brazil, e-cigarettes are classified as tobacco products, and a resolution prohibits their sale, advertisement, distribution, and importation (78).

All EU member states (countries) have at least one e-cigarette regulation in place that is in line with the Tobacco Products Directive (TPD). After the TPD came out in 2014, all EU countries were required to transpose the TPD into national law by 2016 (79). The TPD which regulates nicotine-containing e-cigarettes and refill containers (except medicinal e-cigarette products), generally covered: aspects of minimum standards for the safety and quality of all e-cigarettes and refill containers; provision of information to consumers so that they can make informed choices; and protection of children from starting to use e-cigarettes. Regulation of e-cigarettes in the UK is discussed in Section 1.8 below.

In Canada, e-cigarettes (regardless of nicotine content) are regulated as vaping products under the Tobacco and Vaping Products Act (TVPA). They are also subject to either the Canadian Food and Drugs Act (FDA) or the Canada Consumer Products Safety Act, depending on the presence of therapeutic claims. For vaping products subject to the Canadian FDA, manufacturers must obtain marketing authorization from Health Canada prior to sale. Under the TVPA, marketing and sale of e-cigarettes that contain certain additives (such as amino acids, caffeine, colouring agents, essential fatty acids, glucuronolactone, probiotics, taurine, vitamins and mineral nutrients) is prohibited. There are also restrictions on the marketing of flavours used in vaping liquids. Flavours used in e-liquids cannot be marketed in a way that appeal to youth (including marketing suggestive of confectionery, desserts, cannabis, soft drinks or energy drinks). Canada limits the amount of nicotine to less than 66 mg/mL under the consumer safety legislation (oral toxicity) (78). Regulation of e-cigarettes in the US is discussed in Section 1.8 below.

In Japan, non-nicotine e-cigarettes are currently not regulated, while nicotine-containing e-cigarettes are classified as medicinal products and are regulated under the Japanese pharmaceutical affairs law. Therefore, marketing approval for the sale, advertisement, manufacture, importation and distribution of e-cigarettes must be sought under this law (78).

In China, where e-cigarettes were invented, online sales, sales to minors (under age of 18), and sales or use of e-cigarettes around public places where minors gather (e.g., schools, kindergartens, youth activity centres etc.) are banned (78).

In the African continent, only nine countries currently (April 2024) regulate e-cigarettes and regulations vary amongst these nations. In South Africa, nicotine-containing e-cigarettes are regulated by the Medicines Control Council as Schedule 3 medicines i.e., they can only be sold at pharmacies and purchased with a prescription. Gambia classifies e-cigarettes as electronic nicotine delivery systems (ENDS). The sale, offer for sale, possession, distribution, importation of nicotine-containing and non-nicotine e-cigarettes are prohibited. Mauritius's public health regulations, passed in 2022, prohibit the manufacture, importation, distribution, and sale of e-cigarettes in the country. The use of e-cigarettes is also banned in all public places. In Senegal, Law No. 2014-14 prohibits direct or indirect advertisement and promotion of tobacco, tobacco products, and tobacco derivatives, which is interpreted to include e-cigarettes. In Seychelles, the Tobacco Control Act prohibits the manufacture, importation, supply, display, distribution, or sale of imitation tobacco products. Togo's tobacco control law classifies nicotine-containing e-cigarettes as derivative products. The law prohibits provision to under 18 years, advertising, and promotion, smoking in public places/transport outside of designated areas. There are also paid duties/fees without tax exemptions, with e-cigarettes taxed at a ceiling of 45 percent. In Uganda, the Tobacco Control Act 2015 classifies e-cigarettes as ENDS (as in Gambia). The Act prohibits the sale, offer for sale, distribution, importation, manufacture, or processing of nicotine-containing and non-nicotine e-cigarettes. It also prohibits e-cigarettes from being brought into the country. Cabo Verde banned the sale of e-cigarettes, and its use in some public places. Ethiopia similarly banned the sales of e-cigarettes (78).

1.7 E-cigarette regulation: Overview of divergence in regulatory approaches in the US versus the UK

In the UK, e-cigarettes were initially regulated under the Tobacco Product Directive (TPD) by the European Medicines Agency (EMA) until 2016. The TPD was then transposed into UK law as the Tobacco and Related Products Regulations 2016 (TRPR), regulated by the Medicines and Healthcare products Regulatory Agency (MHRA). The TPD allowed some flexibility for countries to determine certain aspects of their regulations such as minimum age of sale and

use in public places, and these aspects of regulation were devolved to the four nations of the UK (80). Post-Brexit, the TPD continues to apply to Northern Ireland (NI) because of the then NI Protocol, and this may continue with the current Windsor Framework that replaced the NI protocol (81).

In the case of the US, e-cigarettes are regulated under a generic regulation (Federal Food, Drug, and Cosmetic Act 1938 (FDC Act) amended by the Family Smoking Prevention and Tobacco Control Act 2009 (FSPTCA)) for tobacco products. Although e-cigarettes are currently regulated by the FSPTCA – a regulation first proposed in 2000 but which only came into force in 2009 – e-cigarettes did not come into the US market until about 2010. Therefore, this general tobacco product regulation (FSPTCA) was originally produced without particular attention to the uniqueness of e-cigarettes. However, during the institution of FSPTCA, the FDA was made the competent authority for regulation of tobacco products. Therefore, when e-cigarettes emerged and their use became popular, the FDA provided clarification that e-cigarettes or Electronic Nicotine Delivery Systems (ENDS) (as referred to in US regulatory context) were a tobacco product subject to FSPTCA and FDA regulatory jurisdiction. This can be seen in the 2016 Deeming Tobacco Products to Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act (herein referred to as 'Final Rule').

Whilst the US largely concerns itself with e-cigarette uptake by individuals who would not otherwise smoke, and frames e-cigarettes as posing a risk to non-smoking children and young people, the UK focuses primarily on existing tobacco smokers and is concerned with reducing smoking prevalence and addressing health inequalities (of smoking related death and morbidity rates between the rich and poor in the UK) by helping tobacco smokers reduce consumption or, ideally, quit (82). For example, a critical review with qualitative synthesis (83), aimed at identifying planned regulations targeting e-cigarettes in the US, showed that there was a consensus among policymakers to implement youth protection measures in e-cigarette regulation. The US Centre for Disease Control and Prevention (CDC) currently states that e-cigarettes are unsafe and claims that they can harm adolescent brain development (84). Conversely, the UK National Institute for Health and Care Excellence (NICE) has partially updated its guidelines (85) to reflect the use of e-cigarettes as a tool for smoking cessation in current smokers. NICE is an executive non-departmental public body, of the Department of Health and Social Care (DHSC) that evaluates new health technologies

for NHS use, considering clinical effectiveness and value for money to produce useful and usable guidance, helping health and care practitioners deliver the best care (86). On 19th August 2015, Public Health England (PHE) published a report stating that the current best estimate was that e-cigarettes are at least 95% less harmful to health than tobacco cigarettes (87). PHE was an executive agency of the DHSC, with operational autonomy, that provided government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific expertise and support (88).

The difference in how the US and the UK approach e-cigarettes probably originates from their divergent policy response to smoking. The US focused on controlling tobacco use through preventing initiation and addiction, while the UK by contrast, although also interested in preventing initiation and addiction, additionally explored a harm reduction approach that involves the use of safer alternatives (to burnt tobacco) to wean people off tobacco smoking.

It would appear that these differing responses have shaped the research that informed the policy around e-cigarettes in both countries. For example, in the US, the tobacco regulatory research funding priorities of the National Institutes of Health (NIH) include toxicity, addiction, and health effects of ENDS, but there is no consideration of effectiveness of ENDS in smoking cessation (89). In the UK, by contrast, Cancer Research UK (CRUK) is funding projects, via the Tobacco Advisory Group project fund, with foci including safety and health effects (including in the longer term) of ENDS, their use by different populations, environment for sale, effects of regulation, and role of e-cigarettes in cessation amongst others (90). The National Institute of Health Research has also funded and continues to fund research on the effectiveness of ENDS in promoting smoking cessation. The result of these divergent research foci is currently seen in the CDC's overarching message of e-cigarettes being unsafe and the Office for Health Improvement and Disparities (OHID) promoting its use for smoking cessation (84, 91). OHID is an executive agency of the DHSC that brings together expert advice, analysis and evidence with policy development and implementation to shape and drive health improvement and equalities priorities for government (92).

Note also that while the US classifies e-cigarettes as a tobacco product, the UK classifies them as a medicinal or consumer product (51). This divergence leads to challenges in communication e.g., an increase in e-cigarette use can be interpreted as an increase in tobacco use in the US but not in the UK. Irrespective of the difference in how both countries

classify e-cigarettes, the US and the UK regulate e-cigarettes through similar regulatory institutions, providing the opportunity not only for contrasting differences, but also for comparing similarities, and understanding how they both arrived at their respective (divergent) regulatory policies.

In the US, e-cigarettes are regulated under the Family Smoking Prevention and Tobacco Control Act 2009, by the Food and Drug Administration (FDA). In the UK, e-cigarettes are regulated under the Tobacco and Related Products Regulations 2016 (TRPR), by the Medicines and Healthcare products Regulatory Agency (MHRA). Prior to 2016, when the TRPR came into force, e-cigarettes were regulated in the UK under the Tobacco Product Directive (TPD), by the European Medicines Agency (EMA) - the regulatory institution for member states of the European Union (EU). The TPD had to be transcribed into UK law to give the MHRA full regulatory authority to enforce e-cigarette regulation in the UK, hence the adoption of TRPR in 2016. Because of the association between TPD and TRPR (TRPR was transcribed from TPD, and e-cigarettes were first regulated under TPD before TRPR in the UK), contextualisation of e-cigarettes regulation in the UK may reflect e-cigarette regulation in the EU, since both regulatory instruments are intertwined. Post-BREXIT, TRPR has been amended by The Tobacco Products and Nicotine Inhaling Products (Amendment etc.) (EU Exit) Regulations 2019 (93) and 2020 (94). The latest (June 2023) House of Commons research briefing (95) on the regulation of e-cigarettes shows that national regulations have gone beyond what is in the TPD and TRPR. Additional national regulations include: devolved nations taking steps to address the sale of e-cigarettes to under 18s; the Welsh Government attempting to extend smokefree legislation to nicotine products; some organisations and businesses restricting the use of e-cigarettes on their premises (95); and the English government proposing to ban the use of disposable vapes with effect from April 2025 (96).

1.8 Comparison of E-cigarette regulation between the US and the UK

This section presents the findings of literature review aimed to achieve Objective 1 of this PhD study - ‘To describe the similarities and differences between e-cigarette regulation and policies in the US and the UK.

To carry out the literature review, I started by searching for grey literature from government and organisational websites to identify the regulations and policy approaches to e-cigarettes

in the US and the UK. I then searched for published literature from an online database (PubMed) to identify articles and relevant referenced studies that complement understanding of the rationale for policy approaches to e-cigarettes in the US and the UK. The PubMed database was first searched on 10/01/2020 and has been frequently searched whenever new data covering the research topic was required. The following search terms, adapted from the UK Electronic Cigarette Research Forum (UKECRF) search strategy, were used:

E-cigarette*[title/abstract] OR electronic cigarette*[title/abstract] OR ecig[title/abstract] OR (nicotine AND (vaporizer OR vaping OR vapourizer OR vaporiser OR vapouriser))

Based on the titles and abstracts, studies on e-cigarettes that were relevant to the research topic were identified. Only peer-reviewed primary studies, review articles and systematic reviews were included. Studies funded by the tobacco industry were excluded. Published literature was also sourced from repositories (such as the UKECRF monthly research briefing).

Through my engagement with the literature, and my reading of the primary regulatory documents in the US and the UK i.e., the FSPTCA and TRPR respectively, I identified nine (9) main regulatory areas in the US and the UK regulations. The 9 areas comprise: Classification; Registration/Notification; Health warning labelling; Ingredients and Flavours; Nicotine volume/concentration; General safety; Child safety packaging; Minimum age of sale; and Advertising/Promotion/Sponsorship. These 9 areas are presented in section 1.8.2 to 1.8.10 as topic headings for discussion of findings from the literature review. Tables are used to aid comparison of the US versus the UK regulations in the 9 respective regulatory areas.

There is an online scanner[2] by Global Tobacco Control which enables online comparison of e-cigarette policies between countries. This online scanner has ten policy domains for England (UK) (see Table 2). Sales and Tax are the two UK domains from the online scanner not discussed in depth in this study. The online scanner has eight policy domains for US (see Table 2). Sales, Importation, and Distribution are the three US domains from the online scanner not discussed in depth in this study. Sales, Importation, and Distribution are partly covered in my discussions around Notification, Minimum age of sale, and Promotion of e-

[2] See https://globaltobaccocontrol.org/en/policy-scan/e-cigarettes/country-comparison (accessed 24/08/2023)

cigarettes. Taxation, which did not figure at all in the US and UK regulatory documents that were reviewed, will be discussed in section 6.1.10.

Study policy domains	Online scanner UK domains	Online scanner US domains
Registration/ Notification	Reporting/Notification	Reporting/Notification
Health warning labelling	Health warning labelling	Health warning labelling
Child safety packaging	Child safety packaging	Child safety packaging
Minimum age of sale	Minimum age of sale	Minimum age of sale
Advertising/ Promotion/ Sponsorship	Advertising/ Promotion/ Sponsorship	Advertising/ Promotion/ Sponsorship
Ingredients and Flavours	Ingredients and Flavours	
Nicotine volume/ concentration [a]	Nicotine volume/ concentration	
General safety [b]	Safety/ Hygiene	
Classification		
	Sales	Sale
		Importation
	Tax	
		Distribution
[a] only explicit in UK regulation [b] only explicit in UK regulation		

Table 2: Comparison between literature review and online scanner policy domains

Since in this section I compare US and UK e-cigarette regulations, it is important to set out the relevant regulatory context and terms used in the discussions.

1.8.1 Description of terms and context

In this section, the US and the UK are compared and treated as national entities with single e-cigarette regulations. However, due to their political systems, both entities devolve some legislative powers, and this gives room for localised variations in national regulations. For instance, the US is made up of fifty state governments, each with the authority to make their

own health regulations in the context of their local populations' health challenges. Similarly, the UK is made up of four nations – England, Scotland, Wales, and Northern Ireland – with their own independent health authorities capable of instituting regulations applicable to their local jurisdictions. Noted below are key local regulatory variations from the national e-cigarette regulation in the US and the UK.

In the US, while there is yet to be a national (federal) regulation prohibiting indoor use of e-cigarettes, some individual state and regional governments have included e-cigarettes in existing indoor smoking bans (97). Twenty-two State, Commonwealth and Territory laws restrict e-cigarette use in 100% smoke-free venues, while 13 State, Commonwealth and Territory laws restrict e-cigarette use in other venues. In addition, 970 local laws in the US restricts e-cigarette use in 100% Smoke-free venues, while 709 local laws restrict e-cigarette use in other venues (98). Also, 33 out of 50 states of the US had already implemented Tobacco 21 laws (laws increasing the minimum age of purchase of tobacco products from 18 to 21 years) before a national Tobacco 21 law was enacted on 20th December 2019 (99). On the other hand, the four nations of the UK (England, Scotland, Wales, and Northern Ireland) are regulated by the TRPR, but Scotland has its own additional regulation for the purchase and use of e-cigarettes (referred to as Nicotine Vapour Products in Scotland) which came into force on 1st April 2017. The Scottish e-cigarette regulation which restricts the sale of single use nicotine-free products (a rule not covered in the TRPR) is the Health (Tobacco, Nicotine etc. and Care) (Scotland) Act 2016 (100).

It is also important to set out the distinctions in terminology between a regulation, an Act, a directive, and a policy in terms of their legal connotation. Since there may be variations in the legal interpretation of these terms across countries, the meaning of these terms in the US, the UK, and the European Union (EU) are described below.

In the US, *federal laws* are bills that have passed both Houses of Congress, have been signed by the president (therefore passed over the president's veto) or are allowed to become law without the president's signature. The federal laws are also individually referred to as *Acts* and are arranged by subject in the United States Code. *Regulations* are rules made by executive departments and agencies, and are arranged by subject in the Code of Federal Regulations (101). A *policy* is a document published by the government to clarify regulations or suggest voluntary actions. A *policy* could clarify the language in a regulation, explain how a Department interprets a regulation, and/or suggest voluntary actions to be taken by

entities outside the Federal Government (102). The FDCA, FSPTCA and Tobacco 21 Act 2019 are US Acts, whereas the Final Rule is a regulation made by the FDA and the 'FDA enforcement policy on unauthorized flavoured cartridge-based e-cigarettes, 2020' is a policy enforced by the FDA.

In the UK, an *Act* is a Bill that has been approved by both the House of Commons and the House of Lords and been given Royal Assent by the Monarch (103). Secondary legislation is law created by ministers (or other bodies) under powers given to them by an *Act* of Parliament (primary legislation). Secondary legislation is also known as 'delegated' or 'subordinate' legislation and often takes the form of a statutory instrument (SI) (104). The TRPR is a statutory instrument.

Within the European Union (EU), a *regulation* is a binding legislative act that must be applied in its entirety across the EU. By contrast, a *directive* is a legislative act that sets out a goal that all EU countries must achieve. However, it is up to the individual countries to devise their own laws on precisely how to reach these goals, i.e., to transpose the directive into national law (105). The Tobacco Product Directive (TPD) is an EU directive that entered into force on 19 May 2014 and became applicable in EU countries on 20 May 2016 (106).

In this section, e-cigarette regulations in the US and the UK were compared with the primary focus being on the main e-cigarette regulatory documents of the US and the UK. These are, respectively, the Food, Drug, and Cosmetic Act (FDCA), as amended by the Family Smoking Prevention and Tobacco Control Act (FSPTCA) for the US, and the Tobacco and Related Products Regulations 2016 (TRPR) for the UK.

Within the US, other regulatory documents that complemented the above-mentioned regulations, in respect of e-cigarette regulation, were the Child Nicotine Poisoning Prevention Act of 2015 and Tobacco 21 Act of 2019. The Child Nicotine Poisoning Prevention Act of 2015 provided regulations regarding child safety packaging of e-cigarettes, while the Tobacco 21 Act of 2019 provided regulations regarding minimum age of sale for e-cigarettes. In the UK, another key regulatory document was the Children and Young Persons (Sale of Tobacco Etc.) Order 2007 (107).

The main regulatory agencies responsible for regulating e-cigarette in the US and the UK are, respectively, the US Food and Drug Administration (FDA), and the UK Medicines and Healthcare products Regulatory Agency (MHRA). Two main documents set out the evidence

and opinions that guided the FDA and the MHRA in their regulatory approaches to e-cigarettes.

For the US, the main document was the 'Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products'(108). This shows the FDA's thinking about e-cigarettes at year 2016, in response to questions posed to them by the public through comments to a Notice of Proposed Rulemaking (NPRM) issued by the FDA. A notice of proposed rulemaking is a notice in the US Federal Register that announces the intent of an agency to promulgate a particular rule, giving the public an opportunity for public comment; it is often the first time the public becomes aware of an agency's proposed rule (109). The FDA issued this NPRM when it set out to enact new regulations and amend previous ones involving e-cigarettes.

For the UK, the majority of the TRPR was a transposition of the TPD which generally covered: aspects of minimum standards for the safety and quality of all e-cigarettes and refill containers; provision of information to consumers so that they can make informed choices; and protection of children from starting to use e-cigarettes (110). However, the UK still had some aspects of regulation that could be determined at a national level (i.e., within the four nations of the UK respectively). Such aspects comprise: smoke-free environments; domestic advertising; domestic sales; age restrictions; nicotine–free cigarettes; and flavourings of e-cigarettes (111). So, Public Health England (PHE) was commissioned in 2014 (following the EU Directive TPD) to assess and produce a report to update and expand on the evidence of the implications of e-cigarettes for public health. Therefore the document considered as setting forth the rationale for additional (to TPD requirements) e-cigarette regulations or policies in England was 'Electronic Cigarettes - A report commissioned by Public Health England'(112). Public Health England (PHE) was an executive agency of the Department of Health that began operating on 1st April 2013 and was replaced on 1st October 2021 by the UK Health Security Agency and the Office for Health Improvement and Disparities. While PHE operated, it was responsible for supporting the public to protect and improve their health, for protecting England's health, for preparing for public health emergencies, for sharing information and expertise with local authorities and the NHS, and for conducting research and collecting data (113). These PHE's responsibilities were met by similar agencies

in the devolved nations i.e., Public Health Scotland, Public Health Wales and the Public Health Agency in Northern Ireland. However, because the TPD applied to the four nations of the UK, and the PHE report was commissioned by the DHSC, their findings informed a UK-wide policy approach to regulation of e-cigarette through the TRPR.

Note that, based on the regulations and their supporting documents as listed above, I have drawn some inferences on the rationale behind specific aspects of e-cigarette regulations in the US and the UK. In the tables that follow, I consider only what is in the TRPR, and therefore applicable across all four nations of the UK.

1.8.2 Classification

Comparator	US Regulation	UK Regulation
Classification	Tobacco product	Consumer or Medicinal product

Table 3: Classification of E-cigarette in the US and the UK Regulations

As can be seen in Table 3 above, e-cigarettes are classified as Tobacco products in the US, and as Consumer or Medicinal products in the UK. In the UK, if a manufacturer makes a medical claim that an e-cigarette product can be used for medicinal purpose, such as for the treatment of nicotine addiction (i.e., relieve or prevent craving and nicotine withdrawal symptoms when tobacco smokers wish to quit or reduce smoking), such a product would need to be licensed as a medicinal product before authorisation for sale in the UK market. To date (April 2024), Voke and e-Voke are the only e-cigarettes that have been granted marketing authorisations by MHRA (114). However, neither of these products entered the UK market, perhaps because of the complexity of the process[3]. For example, the manufacturers of Voke (British American Tobacco) appeared to have favoured the lower regulatory hurdles for bringing e-cigarettes to the market as a consumer product when this route became available in 2016, than pursuing the medicinal route (115).

Where an e-cigarette product does not contain nicotine or no medicinal claim has been made, such a product can be brought into the UK market as a consumer product but must be notified to MHRA and adhere to the TRPR.

[3] See- https://www.gov.uk/guidance/licensing-procedure-for-electronic-cigarettes-as-medicines

In the US, the FSPTCA defines the term 'tobacco product' as 'any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product)' (116). In 2016, the FDA clarified that 'tobacco products' includes 'all products that meet the statutory definition, such as cigarettes, cigarette tobacco, roll-your-own tobacco, smokeless tobacco, cigars, pipe tobacco, waterpipe tobacco, electronic nicotine delivery systems (ENDS) (including e-cigarettes), and other novel tobacco products such as certain dissolvable products and gels.' These 'products' further include 'components and parts of the newly deemed products, including pipes, e-liquids, atomizers, batteries, cartomizers (atomizer plus replaceable fluid-filled cartridge), tank systems, flavours for e-liquids, vials that contain e-liquids, programmable software, flavour enhancers for waterpipe tobacco, waterpipe cooling attachments, water filtration base additives, flavoured waterpipe tobacco charcoals, and waterpipe bowls, valves, hoses, and heads' (108)(p. 28976). Therefore, in the US, an e-cigarette is classified as a tobacco product, because the e-liquid contains nicotine, which is, in most instances, a derivative of tobacco.

Similarly, the TRPR defines a 'tobacco product' as 'a product that can be consumed and consists, even partly, of tobacco' (110). However, the TRPR goes on specifically to define 'electronic cigarette' as 'a product that can be used for the consumption of nicotine-containing vapour via a mouth piece, or any component of that product, including a cartridge, a tank and the device without cartridge or tank (regardless of whether the product is disposable or refillable by means of a refill container and a tank, or rechargeable with single use cartridges); and is not a medicinal product or medical device' (110).

1.8.2.1 Classification in the US Context

As noted above, the FDC Act classifies all products that contain tobacco or its derivatives as 'tobacco products'(117). However, the FDC Act was drafted at a time (1938) many decades before e-cigarettes were invented; it was amended in 2009 by the Family Smoking Prevention and Tobacco Control Act (FSPTCA) (116). With the emergence of e-cigarettes around 2010 and in recognition of their marked difference from conventional cigarettes, in terms of mechanism of operation and product constituents, there were doubts in the US among e-cigarette manufacturers and the public as to whether the classification in the

FSPTCA applied to e-cigarettes. In an attempt to clarify this confusion, the FDA provided a policy brief on 25th April 2014 through a Notice of Proposed Rulemaking (NPRM) titled 'Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products' (108). After the publication of the NPRM, and a collection of comments, a 'Final Rule' was enacted on 10th May 2016, setting out clarifications and amendments to the FSPTCA.

In the Final Rule, the FDA expressed the belief that there was an expanding market of products sold under several different names that meet the FDC Act definition of 'tobacco products,' including e-cigarettes, e-cigars, e-hookahs, vape pens, personal vaporizers and electronic pipes (108). Components and parts, such as e-liquids, tanks, cartridges, pods, wicks, and atomizers, were also seen as subject to FDA's authority (109). However, the FDA did not see an advantage in defining individual categories of tobacco products for purposes of the Final Rule. On the contrary, the FDA believed that deeming all such products to be 'tobacco products' would help ensure that novel and future tobacco products were introduced into the market in an appropriate and efficient manner (108). Notwithstanding this rule, the FDA did not dismiss the possibility of issuing a specific definition later if they determined that doing so was appropriate (108). The FDA also stated that the FDC Act only describes the statutory definition of 'cigarette' as established by Congress but does not classify cigarettes as a combusted product. Therefore, for purposes of the regulations in the 'Final Rule', the FDA did not believe it was necessary to distinguish between vapourised products and combusted products. Besides, as the FDA claims, there are some e-cigarettes that are heated to a high enough level to cause combustion of the e-liquid (108). Note that classifying e-cigarettes as tobacco products is not a universal phenomenon (only 62 countries worldwide classify e-cigarettes as tobacco products, tobacco related products, tobacco imitation, tobacco derivatives, or tobacco surrogates), as some countries such as the UK (as described above) and Japan refers to e-cigarettes as consumer or medicinal products respectively (78). To date (April 2024), Nicotine and Tobacco Research (a renowned peer-reviewed journal devoted exclusively to the study of nicotine and tobacco) has not had an explicit policy on how e-cigarettes should be described internationally. Notwithstanding, it is

fundamentally necessary that scientific journals and researchers should ensure that the terms they use are clear and unambiguous (118).

1.8.2.2 Classification in the UK Context

In the UK, the classification of e-cigarettes followed considerations of the potential public health impact, rather than an adoption of regulatory classification used for other tobacco products as seen in the US. Some of these considerations are noted in the aforementioned policy brief or report commissioned by PHE (112), which reviewed available evidence around e-cigarettes. The authors of the report stated that, although at the time of publication in 2014, there was insufficient evidence of the effectiveness of e-cigarettes as a smoking cessation tool, many people in the UK were using e-cigarettes to successfully quit smoking each year (112). This highlights the perceived public health impact of e-cigarettes and sets the scene for consideration on regulatory classification. By mode of operation, e-cigarettes are an alternative means of nicotine delivery and they were therefore considered with respect to their potential as a smoking cessation tool, similar to Nicotine Replacement Therapies (NRTs) which were already regulated (as medicinal products) by that time.[4] Therefore, in classifying e-cigarettes, it is plausible that UK regulators were more likely to look at how NRTs were classified rather than how conventional cigarettes were classified. A natural conclusion from the PHE report (94) would have been to regulate e-cigarettes as a medicinal product rather than as a tobacco product. This was even affirmed at a later date in the 2018 (post-regulation) House of Commons Science and Technology Committee Policy Brief (59); in this document, it was suggested that a medically licensed e-cigarette could assist smoking cessation efforts by making it easier for medical professionals to discuss and recommend such products as a stop smoking treatment with patients. However, it seems that a major barrier to this route to regulation was the MHRA's medical authorisation process itself. To license e-cigarettes as medicinal products, the proposed e-cigarette product should meet the Medicines Regulations' standards of quality, safety and efficacy, and the usual quality and safety standards for consumer e-cigarettes that have been developed by national and international standards organisations, where relevant. Also, the proposed e-cigarette product might need to comply with the UK Medical Device Regulations,

[4] Nicotine Replacement Therapies (NRTs) have been regulated as medicinal products in the UK since 2001, and thus regulated in the US since 1984.

depending on the design of the product (119). As Dr Ian Jones from Japan Tobacco International (expert witnesses in the House of parliament inquiry on e-cigarette) elaborated in point 41 of the report (59), the medical licence approval route would have required putting a hold on the manufacture and sales of e-cigarette products until the end of the license approval process for each individual product. With e-cigarette innovation changing so fast, the product may have evolved significantly before the end of the approval process (59). It is clear that there would have been very significant cost and effort involved alongside the loss of valuable time within which e-cigarettes could have led more people to quit cigarettes. With these challenges in mind, regulating e-cigarettes as a consumer product, rather than a medicinal product, was the most plausible and pragmatic approach to continue to promote smoking cessation by ensuring consumers' ongoing access to these products.

1.8.2.3 Summary of difference between classification of e-cigarette in the US and the UK regulations with respect to possible influential factors

The evidence presented from regulatory documents and policy briefs showed that the US and the UK followed different pathways to classifying e-cigarettes in regulation. The US utilised an already existing legal framework (FSPTCA) for classifying e-cigarettes, but the UK developed a new legal framework which took into account the peculiar nature of e-cigarettes and the legal and public health impact of any adopted classification. In other words, while the US retrospectively looked at a legal ruling that could be deemed to cover e-cigarettes in terms of classification, the UK prospectively considered the implications of adoption of a legal framework in view of their public health objective (smoking cessation through use of e-cigarette as a quit smoking aid). Note, however, that while the above-mentioned rationales were the primary focus in the US and UK respectively, they were not the sole consideration. For example, the US did take into account public health concerns; however, their public health position was that e-cigarettes are a potential gateway to smoking for youth and smoking-naïve adults. Regulating e-cigarettes in the same way as other tobacco products fits this narrative. The UK, on the other hand, also considered

previous regulation, namely the EU TPD, a directive that similarly classifies e-cigarettes as consumer products.[5]

[5] Note that not all EU member states classify e-cigarettes as either medicinal or consumer products. Germany for instance, classifies both nicotine containing and non-nicotine containing e-cigarettes as 'tobacco related products'.

1.8.3 Registration/ Notification

Comparator	US Regulation	UK Regulation
Registration/ Notification	An application for review of a new tobacco product must be made to the Secretary and must contain the following content. a. full reports of all information, published or known to, or which should reasonably be known to, the applicant, concerning investigations which have been made to show the health risks of such tobacco product and whether such tobacco product presents less risk than other tobacco products. b. a full statement of the components, ingredients, additives, and properties, and of the principle or principles of operation, of such tobacco product. c. a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such tobacco product. d. such samples of such tobacco product and of components thereof as the Secretary may reasonably require. e. an identifying reference to any tobacco product standard that exist in the US which would be applicable to any aspect of such tobacco product, and either adequate information to	A producer who supplies or intends to supply electronic cigarettes or refill containers must notify the Secretary of State in accordance with the TRPR regulation. A notification must contain the following information (so far as relevant to the product concerned); a. Toxicological data regarding the product's ingredients (including in heated form) and emissions, referring to their effects on the health of consumers when inhaled and considering, amongst other things, any addictive effect. b. A list of all ingredients contained in, and emissions resulting from the use of, the product by brand and variant name, including quantities. c. A description of the production process and a declaration that the production process ensures conformity with the requirements of this Part d. A description of the components of the product including, where applicable, the opening and refill mechanism of the electronic cigarette or refill

show that such aspect of such tobacco product fully meets such tobacco product standard or adequate information to justify any deviation from such standard; f. specimens of the labelling proposed to be used for such tobacco product; and Such other information relevant to the subject matter of the application as the Secretary may require.	container. e. Information on the nicotine dose and uptake when consumed under normal or reasonably foreseeable conditions. f. A declaration that the producer bears full responsibility for the quality and safety of the product when supplied and used under normal or reasonably foreseeable conditions. g. The name and contact details of the person who manufactures the product, the importer (if applicable) and, if neither is based in a member State (England, Wales, Scotland, Northern Ireland), a responsible person within a member State;

Table 4: Registration/ Notification requirements for E-cigarettes in the US and the UK Regulations

As presented in Table 4 above, the FSPTCA and TRPR both require the Secretary of the state to be notified of any new e-cigarette product or tobacco product (as generically referred to in the FSPTCA). However, the registration/ notification of such products entails different requirements for the FSPTCA and TRPR respectively, albeit with some similarities. The points of similarity include: a) a report of health risk to the consumer from using the product; b) a description of ingredients used, components of the product, and mechanism of operation (including samples of such products as per FSPTCA regulation); c) a description of methods used in the production process. Two components of the FSPTCA are not covered in the TRPR.

The first is a requirement to show that registrants have met or can justify deviation from meeting any other tobacco product standard in the US that applies to their product. The second requirement is to provide specimens of the labelling proposed for use for the related product. On the other hand, there are two components of the TRPR that are not covered in the FSPTCA. One is the requirement to provide information on the nicotine dose and uptake when consumed under normal or reasonably foreseeable conditions. The other is the requirement to provide a declaration that the producer bears full responsibility for the quality and safety of the product when supplied and used under normal or reasonably foreseeable conditions.

1.8.3.1 Registration/ Notification in the US Context

In the FDC Act, a Premarket Tobacco Product Application (PMTA) is required to be submitted for authorisation by the FDA before any tobacco product is introduced in the US. The PMTA ensures that the safety and health risks of products (when used according to manufacturer's intention) coming into the US market are well known. Like many other FSPTCA regulations, the FDA have stated that, regardless of the type of product (and its potential risks and benefits), all tobacco products must go through the PMTA pathway and meet all the requirements for a premarket authorization in the FDC Act (108). However, it seems to me that the FDA had other ENDS-specific considerations that warranted caution over the introduction of potentially harmful products to the US market. Since ENDS products contain nicotine, the FDA were concerned that their introduction may result in overall public health harm if individuals who would not have initiated tobacco use in the absence of ENDS ultimately graduated to combusted products (though scientific data regarding this hypothesis is unclear) (108). There were also concerns about dual use of ENDS in conjunction with combusted products. Therefore, it seems that, from experience of regulating other tobacco products, the FDA used a registration/ notification requirement (PMTA) as a tool to monitor ENDS products and to stop products that pose a public health risk from entering the market.

1.8.3.2 Registration/ Notification in the UK Context

In the UK, the requirement for notification was a direct transposition from the TPD to the TRPR. In the TPD, all tobacco products are required to be notified to the competent authority. This seems a sensible mechanism to put in place to prevent manufacturers from adding ingredients or components to e-cigarettes to make them more addictive to non-smokers, or that may increase the risk from their use.

1.8.3.3 Summary of difference between registration/ notification requirements for e-cigarettes in the US and the UK regulations with respect to possible influential factors

In the US, the major reason for a registration/ notification requirement for e-cigarettes was safety concerns, whereas the UK was legally mandated to transpose notification requirements from the TPD to the TRPR. However, the authorities in both countries wished to put in place a safeguard to prevent products that pose substantial public health risks from entering their country. The evidence suggest that the US was speculative in their concerns that e-cigarettes can lead naïve users to eventual smoking of combustible products. By contrast, UK monitoring data (59) suggested that there was no causal relationship between use of e-cigarettes and eventual smoking and therefore the gateway argument received less emphasis. The evidence suggest that UK safety concerns were not definitive; rather, they reflected the lack of adequate data to ascertain the overall short and long-term effects of e-cigarette use. Notwithstanding the difference in safety concerns, the experienced regulatory agencies in both countries took a generic precautionary measure of requiring registration/ notification for products to prevent entry of harmful products and to allow withdrawal from the market of products that subsequently prove harmful.

1.8.4 Health warning labelling

Comparator	US Regulation	UK Regulation
Health warning labelling	Beginning on 10th August 2018, the product packages and advertisements of all newly regulated covered tobacco products must bear the following warning statement: **'WARNING: This product contains nicotine. Nicotine is an addictive chemical.'** This required warning statement on package labels must also appear directly on the package, and be clearly visible underneath any cellophane or other clear wrapping as follows: a. Be located in a conspicuous and prominent place on the two 'principal display panels' of the package. b. Comprise at least 30 percent of each of the principal display panels. c. Be printed in at least 12-point font size and must occupy the greatest possible proportion of the warning label area set aside for the required text. d. Be printed in conspicuous and legible **Helvetica bold** or **Arial bold** type or other similar sans serif fonts and in black text on a white background or white text on	1. Each unit packet electronic cigarette or refill container pack must carry a health warning consisting of the text: **'This product contains nicotine which is a highly addictive substance'.** 2. The health warning must— a. appear on both the front and back surfaces of the unit packet and any container pack. b. cover 30% of the area of each of those surfaces, calculated in relation to the area of the surface concerned when the pack is closed. c. be in **black Helvetica bold** type on a white background. d. be in a font size which ensures that the text occupies the greatest possible proportion of the surface area reserved for it; and e. Appear at the centre of that area. 3. The health warning must be parallel to the main text on the surface concerned.

a black background in a manner that contrasts by typography, layout, or colour, with all other printed material on the package; e. Be capitalized and punctuated f. Be centred in the warning area in which the text is required to be printed and positioned such that the text of the required warning statement and the other information on the principal display panels have the same orientation If the tobacco product manufacturer submits a self-certification statement to FDA that the newly regulated tobacco product does not contain nicotine (and that the manufacturer has data to support this assertion), then an alternate statement must be used on product packages and advertisements: **'This product is made from tobacco.'**	4. Each unit packet of the electronic cigarette or refill container must include a leaflet with information on— a. instructions for use and storage of the product, including a reference that the product is not recommended for use by young people and non-smokers. b. contra-indications. c. warnings for specific risk groups. d. possible adverse effects. e. addictiveness and toxicity. 5. Each unit packet and any container pack must include— a. a list of all ingredients contained in the product set out in descending order by weight. b. an indication of the nicotine content of the product and the delivery per dose. c. the batch number; and d. A recommendation to keep the product out of reach of children.

Table 5: Health warning label requirement for E-cigarettes in the US and the UK Regulations

From June 2009, when the FDA began to regulate tobacco products through the FSPTCA (an amendment of the Food, Drug, and Cosmetic Act (FDC)), until May 2016, US labelling regulations only covered cigarettes and smokeless tobacco, i.e., the products that were prevalent at the time. However, in the FDA's Deeming Regulations for E-Cigarettes, Cigars, and All Other Tobacco (108) (often referred to in this study as 'Final Rule'), that took effect from May 2016, regulatory requirements were introduced for labelling of Electronic Nicotine Delivery Systems (ENDS) products, hookah tobacco, cigarette tobacco and roll-your-own tobacco products as shown in Table 5 above. In the UK, the TRPR, which has specific regulations for e-cigarettes, includes specific regulatory requirements for labelling of e-cigarettes.

Whilst the Final Rule and the TRPR have similar requirements in terms of the text, font characteristics, and surface area covered by their health warning label, there are differences in the component areas covered by both regulations. For example, the Final Rule only requires a health warning label on the product package, whereas the TRPR, in addition to the health warning label, also requires inclusion of a list of ingredients, details of nicotine content and a child safety warning (to minimise the risk of accidental poisoning). The TRPR also mandates provision of a leaflet or package insert with information on the principles of use of the product and safety warnings.

1.8.4.1 Health warning labelling in the US Context

In the Final Rule, the FDA noted that some research studies were considered before issuing the health warning labelling of deemed tobacco products including e-cigarettes. The main studies considered by the FDA were those in the 2014 Surgeon General's Report that reported the risks associated with nicotine (108). The studies in the 2014 Surgeon General's Report (120) were *in vivo* animal studies conducted on rats and mice between 1945 to 1995, looking at acute toxicity of nicotine. The 2014 Surgeon General's Report suggested that nicotine at high enough doses has acute toxicity and adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth (120). The report also suggested that nicotine exposure during fetal development has lasting adverse consequences for brain development and that nicotine exposure during adolescence may also have lasting adverse consequences for brain

development (120). Review articles had also suggested that nicotine can have detrimental effects on the cardiovascular system and potentially disrupt the central nervous system (121, 122). The FDA also clarified that, although researchers recognize that the effects from nicotine exposure by inhalation are unlikely to be responsible for the high prevalence of tobacco-related death and disease in the US, nicotine is not completely harmless (123, 124). Furthermore, although nicotine has not been shown to cause the chronic disease associated with tobacco use, the FDA claimed that it did not have sufficient data to be able to conclude that consumers of ENDS are inhaling only nicotine, and are not being exposed to other chemicals or toxicants (108). In addition, the FDA claimed that, although ENDS probably do not deliver the same level of toxicants as cigarettes, there are (potential) dangers associated with ENDS use and that exhaled aerosol is not simply 'water vapor,' as some believe (108).

The FDA was also concerned about the addictiveness of inhaled nicotine from a non-combustible product such as e-cigarettes. They acknowledged that the inhalation of nicotine without the production of combustion is of less risk to a user than the inhalation of nicotine delivered by smoke from combusted tobacco products. However, they stated that limited data suggest that the pharmacokinetic properties of inhaled nicotine can be similar to the properties of nicotine delivered by combusted tobacco products. Therefore, inhaled nicotine from a non-combustible product may be as addictive as inhaled nicotine delivered by combusted tobacco products (108). This concern is what is reflected in the e-cigarette's health warning label 'WARNING: This product contains nicotine. Nicotine is an addictive chemical.'

1.8.4.2 Health warning labelling in the UK Context

The TPD mandates member countries to include one of the following health warnings in their regulation of e-cigarette: 'This product contains nicotine which is a highly addictive substance. It is not recommended for use by non-smokers'; or 'This product contains nicotine which is a highly addictive substance'. The UK used the latter warning statement when it transposed the TPD to the TRPR.

It is important to note that although the warning label is simply a function of the transposition of the TPD to the TRPR, the warning statement is also a summative representation of the evaluation of nicotine in the context of the UK. In a report

commissioned by PHE, entitled 'Electronic cigarettes' (112), which contributes towards e-cigarette policy framework in the UK, the author highlighted that, since nicotine is the addictive substance in tobacco cigarettes, nicotine delivery from e-cigarettes is essential if e-cigarettes are to be effective for smoking cessation or harm reduction. This report (112), which also evaluated the risk of e-cigarettes relative to cigarettes using data available at the time, found that, aside from minor and transient adverse effects at the point of absorption, nicotine is not a significant health hazard. A referenced observational study of human data concluded that nicotine does not cause serious adverse health effects such as acute cardiac events, coronary heart disease or cerebrovascular disease (125), and cited epidemiological evidence from the International Agency for Research on Cancer Working group shows that nicotine is not carcinogenic (126). The conclusion of the report was therefore that doses of nicotine delivered by electronic cigarettes are extremely unlikely to cause significant short or long-term adverse events (112).

With regards to the addictiveness of e-cigarettes, the PHE report (112), published in 2014, stated that data on the arterial nicotine levels achieved by e-cigarettes were not available at the time. However, what was then known is that there are three key elements that influence nicotine delivery from e-cigarette vapour to the human body. Firstly, the nicotine content in the cartridge, which determines the amount of nicotine vapourised; secondly, the efficacy of vaporization, which affects levels of nicotine transferred from a cartridge into aerosol; and thirdly, the bioavailability of nicotine, which determines the dose and speed of absorption of nicotine from the aerosol and subsequent transfer into the blood stream and hence to nicotine receptors in the brain (127). All of these characteristics vary across brands, manufacturers and product designs (112). Given the above mechanisms of action, it was not yet clear at the time of reporting (76) whether electronic cigarettes produce vapour that is sufficiently fine to reach the alveoli, but available pharmacokinetic data at the time suggested that absorption is primarily from the upper airway, is slower than absorption from a cigarette, and achieves systemic venous blood levels of similar order of magnitude to a conventional NRT inhalator (128). Cigarette smoking delivers nicotine throughout the lungs and leads to absorption into both the systemic venous circulation, via the oropharynx and large airways, and the pulmonary circulation, via the small airways and alveoli. The latter route of absorption generates a rapid peak in systemic arterial nicotine levels and hence rapid delivery to the brain (121). A year later (i.e. in 2015), an updated report (129)

commissioned by PHE confirmed that cigarlike[6] e-cigarettes deliver lower levels of nicotine than tobacco cigarettes (130-132) especially to novice users (128, 133, 134). Vapers obtain slightly more nicotine from e-cigarettes with practice, but compared to combustible cigarettes, nicotine delivery is low and slow (131). Tank systems deliver nicotine more efficiently, somewhat faster than cigarlike but still slower than cigarettes (135-137).

1.8.4.3 Summary of health warning label requirement for e-cigarettes in the US and the UK regulations with respect to possible influential factors

Both the US and the UK adopted a health warning that labels nicotine as an addictive substance. It is an internationally accepted fact that nicotine is an addictive substance, rendering it the component of tobacco cigarettes that makes it hard for smokers to quit. As the addictive nature of nicotine is well established in the literature, and nicotine is present in most e-cigarettes, both the US and the UK considered the potential health hazards of nicotine in e-cigarettes. The US focussed on the absolute risk of e-cigarettes and drew on *in vivo* animal studies suggesting that the fetal, cardiovascular, and neurological harms of e-cigarettes were derived mostly from the nicotine therein. The UK, in its evidence base, focussed on the relative risk of e-cigarettes compared to tobacco cigarettes and cited human observational studies suggesting nicotine as delivered by electronic cigarettes is extremely unlikely to cause significant health hazards to users. However, the US did not adopt a health warning that communicated the absolute risk of e-cigarette use, and the UK did not additionally (to TPD requirements) adopt a health warning that communicated the relative risk of e-cigarettes compared to tobacco cigarettes. Instead, in their health warning labels, both countries placed the emphasis on nicotine being an addictive substance. For the UK it was simply a case of transposing the required statement in the TPD to the TRPR, while in the US, nicotine-containing tobacco product health warnings were simply applied to e-cigarettes.

[6] There are four types of e-cigarettes namely, Cig-A-Like, Vape Pen, Mod, and Mechanical Mods. Cigarlike are about the size and shape of a traditional cigarette and are often coloured to look like one.

1.8.5 Ingredients/ Flavours

Comparator	US Regulation	UK Regulation
Ingredients/ Flavours	According to FDA policy directive on 2nd January 2020, companies to cease manufacture, distribution, and sale of any flavoured, cartridge-based ENDS product (other than a tobacco- or menthol-flavoured ENDS product);	1. Nicotine-containing liquid in an electronic cigarette or refill container must not contain any - a. vitamins or other additives that create the impression that a tobacco product has a health benefit or presents reduced health risks. b. caffeine, taurine or other additives and stimulant compounds that are associated with energy and vitality. c. additives which have colouring effects on emissions d. additives that have CMR (carcinogenic, mutagenic, or toxic for reproduction) properties in unburnt form; or e. Additives in quantities that increase, to a significant or measurable degree, the toxic or addictive effect or CMR properties of the product when it is consumed. 2. Nicotine-containing liquid in an electronic cigarette or refill container- a. must be manufactured using only ingredients of high purity. b. must not contain substances other than the ingredients notified under regulation 31, unless present in trace levels, where such trace levels are technically unavoidable during manufacture; and c. Must not include ingredients (except for nicotine) which pose a risk to human health in heated or unheated form.

Table 6: Ingredients and Flavour restrictions for E-cigarettes in the US and the UK Regulations

In terms of regulatory restrictions of ingredients and flavours prohibited in e-cigarettes, the FSPTCA does not contain a list of such ingredients or flavours; it only mandates manufacturers to disclose to the public any tar, nicotine, and other smoke constituents contained in their product. By contrast, the TRPR is specifically prescriptive on the ingredients prohibited in e-cigarettes, as can be seen in Table 6 above. This includes vitamins and stimulants. Additives that are associated with energy and vitality are prohibited in e-cigarettes. Ingredients that have colouring effects on emissions, or have CMR (carcinogenic, mutagenic, or toxic for reproduction) properties in unburnt form are also prohibited.

Although the FSPTCA appears deficient in aspects of regulation related to prohibited ingredients and flavours, it is plausible that this may be due to a lack of contextualised evidence (possibly owing to the novelty of e-cigarettes) to guide such e-cigarette policies in the US at the time (enactment of the FSPTCA in 2009). However, with emergence of research evidence over time, a more recent (January 2020) FDA policy directive prohibits any further manufacture, distribution, and sale of any flavoured, cartridge-based ENDS product (other than a tobacco- or menthol-flavoured ENDS product) because such flavours were considered to be appealing to children.

1.8.5.1 Ingredients/ Flavours in the US Context

The FDA stated that, although they did not currently have sufficient data about e-cigarettes and similar products to fully determine what effects they have on the public health, there were identified concerns regarding the toxicants in e-liquid, the exhaled aerosol and the nicotine delivery from e-cigarettes (108). The FDA identified some studies that showed these concerns as seen below.

Firstly, cited *in vitro* laboratory studies had shown that e-liquids contain nicotine, propylene glycol, glycerine, tobacco specific nitrosamines, tobacco alkaloids, carbonyls, ethylene glycol, diacetyl, and acetyl propionyl (138-140). Some studies had suggested that flavoured e-liquids contain chemicals that could be dangerous to consumers when inhaled. For example, in one study where 159 e-liquids with sweet flavours, such as toffee, chocolate, and caramel, were tested, 74 percent of the samples were found to contain diacetyl or acetyl propionyl (141), both of which pose known inhalation risks (142). Furthermore, amongst the study samples that contained diacetyl or acetyl propionyl, nearly half of the e-liquids had a potential to

expose users to levels that exceed recommended workplace limits for breathing these chemicals (141). Another study, in which researchers analysed 51 types of flavoured e-cigarettes for total mass of diacetyl, 2,3-pentanedione, and acetoin, found that 39 of the 51 flavoured e-cigarettes contained diacetyl, 23 contained 2,3-pentanedione and 46 contained acetoin above the laboratory limit of detection, at concentrations ranging from limit of qualification (LOQ) to 239mg/ e-cigarette for diacetyl, 64mg/e-cigarette for 2,3-pentanedione and 529 mg/e-cigarette for acetoin (143). However, this study utilised convenience sampling and so may not be representative of the types of e-liquids available to users at the time. One other study on flavoured e-liquids analysed 30 e-cigarette liquids and found that some flavours, including cotton candy and bubble gum, contained aldehydes, a class of chemicals that can cause respiratory irritation and airway constriction (144). In that study, two flavours (dark chocolate and wild cherry) were particularly noted to expose e-cigarette users to more than twice the recommended workplace safety limit for the aldehydes vanillin and benzaldehyde (144). Similarly, *in vitro* laboratory tests showed that cinnamon-flavoured e-liquids contain a chemical, cinnamaldehyde, which is highly toxic to human cells (145). With the wide variability of concentrations of constituents in the flavours of current ENDS products, the FDA admitted that it may not be possible to account for the constituents in the flavoured e-liquids without a regulatory standard (108).

Secondly, chemicals such as nicotine, carbonyls, tobacco specific nitrosamines, heavy metals, and volatile organic compounds have been identified in e-cigarette aerosols through laboratory testing (138-140, 146-148). However, lower levels of toxicants are observed in e-cigarette aerosols than in combusted tobacco smoke (148). For example, across several Japanese brands evaluated in a self-published web site, under some conditions of use, ENDS released 1/50th of the level of formaldehyde released by cigarettes (149). The highest level detected was six times lower than the level in cigarette smoke (149). A clinical investigation comparing the levels of toxicants and carcinogen metabolites in the urine of e-cigarette users and combusted cigarette users found that e-cigarette users had significantly lower levels of all evaluated toxicants, which included acrolein and crotonaldehyde (150). Nevertheless, specific product design parameters, such as voltage, can affect toxicant deliveries (151). For example, some ENDS devices, when operated at certain power levels, have been reported to deliver more formaldehyde than other ENDS products or conventional cigarettes, which can affect public health (151-153). One study reported that,

in a laboratory testing environment, increasing the voltage from 3.2 to 4.8 volts increased formaldehyde, acetaldehyde, and acetone levels from 4-fold to over 200-fold (151). Similarly, another study reported that ENDS devices operated at 5 volts delivered a mean mass of formaldehyde per 10 puff sample that was greater than the estimated average delivery of formaldehyde in conventional cigarettes. No formaldehyde-releasing agents were detected when ENDS were operated at 3.3 volts (153). A subsequent peer reviewed article on 5 variable-power ENDS devices found large variations in formaldehyde delivery across devices (152). The first device yielded more formaldehyde than combustible cigarettes at every power level tested, and the second device delivered more formaldehyde at the highest power level tested; the remaining three devices delivered less formaldehyde than combustible cigarettes at all power levels tested (152). The same research found that aldehyde delivery varied by 750-fold from one ENDS device to another (152).

The FDA also stated their view that the belief that aerosol is safe, based on certain components such as propylene glycol and glycerine being 'generally recognized as safe' (GRAS), is false (108). They emphasized that such food additives are only referred to as GRAS in relation to their intended use as a component or otherwise affecting the characteristics of any food (as can be seen in section 201(s) of the FDC Act). E-liquid is not a food or intended for ingestion; therefore, the fact that propylene glycol and glycerine have been designated GRAS for food does not necessarily mean that these components are safe for inhalation.

The FDA did acknowledge that the aerosol exhaled by users of some e-cigarettes and similar electronic apparatus may not pose as much harm as smoke emitted from combusted tobacco products. For example, the FDA agreed with a study (69) that found that exhaled aerosol from ENDS users is potentially less hazardous than second-hand smoke from combusted cigarettes. However, given that studies did indicate that both nicotine and other toxicants are found in the exhaled aerosol, the FDA concluded that limiting exposures must be considered; they therefore disagreed with the study author's conclusion that exposure to aerosol (vapor) 'pose(s) no apparent concern'(108)(p.29032).

1.8.5.2 Ingredients/ Flavours in the UK Context

In the UK, the regulation of ingredients in e-cigarette was transposed from the TPD to TRPR. However, all the available evidence at the time of regulation supported the need for such regulatory restrictions to some ingredients in e-cigarettes such as vitamins and additives.

A report commissioned by PHE and published in 2015, entitled 'E-cigarettes: an evidence update'(129), which contributed towards e-cigarette policy framework in the UK, presented results of their evaluation as discussed below.

Similar to the studies presented by the FDA, in the 2014 PHE report (112), a cited *in vitro* study showed that e-cigarettes contain toxic substances, including small amounts of formaldehyde and acetaldehyde, which are carcinogenic to humans (148) and that, in some cases, vapour contains traces of carcinogenic nitrosamines and of some toxic metals such as cadmium, nickel and lead (148). It was concluded that, although levels of these substances are much lower than those in conventional cigarettes (148), regular exposure over many years is likely to present some degree of health hazard, though the magnitude of this effect is difficult to estimate (112).

With regards to the effect of voltage on toxicants released by e-cigarettes, the PHE update report (129) assessed a laboratory-based study which examined third generation e-cigarettes at maximum power and using puffs lasting 3-4 seconds. The study found that, if inhaled in this way throughout the day, the levels of formaldehyde generated would exceed formaldehyde levels in cigarette smoke between five and 15 times (153). The PHE report noted that in this study the e-cigarettes were puffed by a puffing machine at a higher power and longer puff duration than vapers normally use; it was therefore possible that the e-liquid was overheated to the extent that it was releasing novel thermal degradation chemicals (129). Such overheating can happen during vaping when the e-liquid level is low or the power is too high for a given e-cigarette coil or puff duration (129). Vapers call this phenomenon 'dry puff', and it is instantly detected due to a distinctive harsh and acrid taste (note that this can be detected by vapers, but not by puffing machines) (154). This poses no danger to either experienced or novice vapers because dry puffs are aversive and are avoided rather than inhaled (129). A subsequent study tested the hypothesis that the previous study (153) had used dry puffs (155). In this follow-on study (155) all seven vapers received dry puffs and could not use the device at the settings used in the previous report (153). When further machines were tested at the dry puff setting, formaldehyde was

released at levels reported in the previous study (153). However, at normal settings, there was no or negligible formaldehyde release (155).

As noted above, in the 'Final Rule'(108), the FDA claimed that there are toxicants such as acrolein and crotonaldehyde in e-cigarettes, referencing a study (150) where vapers had much lower levels of acrolein and crotonaldehyde in urine than smokers. This had raised concerns as to whether dual users (i.e., those who smoke and vape) may be at an increased risk from exposure to these toxicants in both cigarettes and e-cigarettes combined. The PHE report (129) acknowledged that study (165) but countered the FDA's concern by citing a study funded by the MHRA which examined changes in acrolein levels in smokers who switched to exclusive e-cigarette use and in those who continued to smoke while also using e-cigarettes (dual users) (156). The latter study (156) showed a substantial decrease in acrolein intake in smokers who switched to EC, but it also found a significant decrease in acrolein intake in dual users. This was because dual users reduced their smoke intake as indexed by exhaled carbon monoxide levels (156). Also, normal vaping generated negligible aldehyde levels (156). PHE concluded that, although in principle e-liquid can be heated to a temperature which leads to a release of aldehydes, the resulting aerosol is aversive to vapers and so poses no health risk (129).

1.8.5.3 Summary of ingredients and flavour restrictions for e-cigarettes in the US and the UK regulations with respect to possible influential factors

Both the US and the UK examined a range of research studies on the risk potential of e-liquid ingredients and flavouring, with findings from this research apparently influencing how they regulated these aspects of e-cigarettes. However, due to the novelty of e-cigarettes at the time of regulation and to the wide variety of flavours and range of ingredients available in e-cigarettes, it appeared that there was inadequate evidence to determine the risk of all the ingredients and flavours found therein. This limited the regulators' ability to wholly specify individual flavour and ingredient restrictions from the onset. However, irrespective of their different approaches, in the light of ongoing research and monitoring, both countries were able to place needed restrictions in the context of country-specific emerging public health concerns. For example, in the US, there was an increasing public health concern that certain e-cigarette flavours, such as bubble-gum, attracted naïve non-smoking children to use e-cigarettes (157). As a result, in January 2020, the FDA issued a directive prohibiting

manufacture, distribution and sale of any flavoured, cartridge-based ENDS product (other than a tobacco- or menthol-flavoured ENDS product) (157). The UK took a different approach from the onset of regulation by placing a blanket restriction on vitamins, stimulants, and additives that are either associated with energy and vitality, have colouring effects on emissions, appear to present reduced health risks, or have CMR (carcinogenic, mutagenic, or toxic for reproduction) properties in unburnt form (158).

1.8.6 Nicotine volume/ concentration

Comparator	**US Regulation**	**UK Regulation**
Nicotine volume/ concentration	Not regulated	1. Nicotine-containing liquid which is presented for retail sale must be in— a. A dedicated refill container in a volume not exceeding 10 millilitres; or b. A disposable electronic cigarette, a single use cartridge, or a tank, in a volume not exceeding 2 millilitres. 2. The capacity of the tank of a refillable electronic cigarette must not exceed 2 millilitres. 3. Nicotine-containing liquid which is presented for retail sale in an electronic cigarette or refill container must not contain nicotine in excess of 20 milligrams per millilitre.

Table 7: Nicotine volume and concentration for E-cigarettes in the US and the UK Regulations

In terms of nicotine volume and concentration, while the FSPTCA is silent on regulation of this aspect of e-cigarettes, the TRPR is prescriptive on what is permissible within this domain. As seen in Table 7 above, the TRPR specifies a maximum nicotine concentration of 20 milligrams per millilitre (mg/ml) in an e-cigarette and that disposable e-cigarettes (or cartridge) and refill containers should contain no more than 2 millilitres and 10 millilitres of nicotine-containing liquid, respectively.

1.8.6.1 Nicotine volume/ concentration in the US and UK Context

It was the TPD, which was transposed to the TRPR in the UK, that set out the requirements for nicotine volume and concentration. In the interests of free trade, this was an aspect of the TPD that could not be changed during transposition across the EU member states. Also, it seemed that, even if the UK had been legally able to change the directive on nicotine volume and concentration in the TRPR, regulators were less likely to do that for the reason explained hereafter. For a novel product such as an e-cigarette that has nicotine as its major constituent, it would be ideal to limit the concentration and volume of nicotine the product contains. An important consideration is whether e-cigarettes are used as a smoking cessation tool or for recreational purposes.

Where e-cigarettes are to be used for smoking cessation, it would seem reasonable to set the maximum concentration allowed at a level at or below that found in a typical cigarette. The amount of nicotine in a single cigarette varies between 6 and 28mg/ml (159). Therefore, a typical pack of cigarettes contains 120 - 560mg/ml of nicotine concentration. Anecdotal claims from dual users of e-cigarettes and tobacco cigarettes suggest that the number of puffs a user obtains from using up the e-liquid in a single e-cigarette cartridge (containing 2 millilitres of e-liquid) equates to the number of puffs from a pack of cigarettes. It can therefore be inferred that, in terms of nicotine concentration in e-cigarettes which are limited to 20mg/ml, a user would be getting considerably less nicotine (i.e., 3- or 14-times less nicotine than in the weakest and strongest cigarettes respectively) from a single e-cigarette cartridge than from 20 cigarettes. However, this calculation does not account for the possibility that e-cigarette users may be using more than one e-cigarette cartridge, either to get the same nicotine hit as they would from smoking or because e-cigarettes are readily accessible. For instance, there are no statutory restrictions on indoor use in public places in England, Wales, and Scotland, though many organisations nonetheless impose bans on vaping indoors. Available pharmacokinetic data suggests that absorption of nicotine from e-cigarettes is primarily via the upper airway and is therefore slower than from a combustible cigarette (128). Several studies have also shown that e-cigarettes deliver lower levels of nicotine than cigarettes (130-132). Since nicotine is the addictive substance that keeps people smoking, if e-cigarettes are to be used to wean people out of smoking, they should logically present a lower concentration of the addictive substance, nicotine.

Similarly, it seemed reasonable that, where e-cigarettes are mostly used for recreational purposes, it is also important to limit the level of nicotine concentration, to minimise the risk of addiction and to prevent an epidemic of chronic use. For example, in the US where there is no regulatory restriction on the concentration of e-cigarettes, there was a sharp increase in e-cigarette use from 11.7% to 20.8% among high school students and from 3.3% to 4.9% among middle school students in a single year, from 2017 to 2018 (20). This increase was largely attributed to the popularity of JUUL which is the most commonly sold e-cigarette in the US, with an estimated 72.1% e-cigarette market share as of August 2018 (160). The popularity of JUUL devices has been attributed to its trendy design, high nicotine concentration, and appeal to youth. JUUL advertises a much higher nicotine concentration of 59mg/ml compared to other e-cigarette solutions, which typically range from 0 to 24mg/ml (160) with an average of 22.3 mg/ml for second-generation e-cigarettes, and 4.1 mg/ml for third-generation e-cigarettes (161). JUUL uses liquid nicotine refills called 'pods', which contain at least as much nicotine as a pack of cigarettes (20). Conversely, over the same period in the UK, where nicotine concentration in e-cigarettes is restricted to 20mg/ml, regular use of e-cigarettes remained low with 1.7% of 11 to 18 year olds in the UK reporting at least weekly use in 2018 compared to 0.4% among 11 year olds and 2.6% among 18 year olds in 2017 (91). However, the UK is now experiencing increased use of e-cigarettes; Trading Standards raised concerns in January 2023 that the number of children accessing e-cigarettes are increasing with some shops illicitly selling vaping products to children (162) . Action on Smoking and Health (ASH) has subsequently reported in June 2023 that the current use of e-cigarettes amongst 11- 17 year olds stands at 7.6% (163). As disposable vapes are the most commonly used e-cigarettes among children and pose environmental problems, the UK and Scottish governments have now (April 2024) proposed a ban on the sale of disposable vapes in England, Wales and Scotland from April 2025 (164).

1.8.6.2 Summary of nicotine volume and concentration for e-cigarettes in the US and the UK regulations with respect to possible influential factors

At the time when e-cigarette regulations were being first established in the US and the UK, evidence to support any regulatory limitations or permissions regarding nicotine concentration was unavailable. The US regulation therefore remained silent on regulation of nicotine concentration. The UK, on the other hand, placed restrictions (limitation to

20mg/ml) on nicotine concentration to comply with the TPD and ensure free trade, but also possibly to make sure that the nicotine concentration in e-cigarettes is no more than that in conventional cigarettes. This inference is based on suggestions around the time of e-cigarette regulations in EU (2014), such as those seen in a review (165), that nicotine reduction policy will be very likely to increase tobacco cessation efforts.

1.8.7 General safety

Comparator	US Regulation	UK Regulation
General safety	No specific tobacco product regulation relating to considerations within this section (e.g., protection against breakage and leakage, tamper-evident, adulteration)	1. An electronic cigarette must be able to deliver a dose of nicotine at consistent levels under normal conditions of use. 2. An electronic cigarette or refill container must be tamper-evident; and protected against breakage and leakage. 3. A product is tamper-evident if it has one or more indicators or barriers to entry which, if breached or missing, can reasonably be expected to provide visible evidence that the product (or its packaging) has been opened. 4. An electronic cigarette or refill container must have a mechanism for ensuring re-filling without leakage (unless it is a disposable electronic cigarette). 5. A product has a mechanism for ensuring re-filling without leakage if the mechanism— a. entails— i. the use of a refill container possessing a securely attached nozzle at least 9 millimetres long which is narrower than, and slots comfortably into, the opening of the tank of the electronic cigarette, and ii. in the case of refill containers, a flow control mechanism that emits no more than 20 drops of refill liquid per minute when placed vertically and subjected only to atmospheric pressure at a temperature between 15 and 25 degrees Celsius: or b. Operates by means of a docking system which only releases refill liquids into the tank of an electronic cigarette when the electronic cigarette and refill container are connected.

Table 8: General safety requirements for E-cigarettes in the US and the UK Regulations

Perhaps due to the generic nature of the FSPTCA (i.e., regulatory instrument for all tobacco products, which covers diverse types of products including ENDS, rather than e-cigarettes in particular), there are no specific safety guidance that pertains to the peculiar specifications of e-cigarettes in US regulations. By contrast, the TRPR contains regulations that specify safety measures relevant to the unique nature of e-cigarettes available at the time of enactment. These include requirements for e-cigarettes to be tamper-evident and protected against breakage and leakage as evidenced by specified mechanisms in place. Table 8 above shows that the UK also has other general safety requirements mandated by the TRPR.

1.8.7.1 General safety in the US and UK Context

The TPD required that e-cigarettes and refill containers are child- and tamper-proof, are protected against breakage and leakage and have a mechanism that ensures refilling without leakage. This were transposed to the TRPR. These requirements were sensible for a couple of reasons discussed below.

For a novel product such as an e-cigarette, with significant public health implications (both positive and negative), a cautious regulatory approach was needed in my view. Therefore, it seems to me that a conscious effort to reduce regulatory loopholes for industry, market, or individual exploitation was important. To ensure this, proactively ensuring that e-cigarette products are always used in the way intended by the manufacturer and approved by the regulatory agency could be considered an ideal situation. One such way to ensure this is through tamper-evident regulations, protecting such products against tampering, breakage, and leakage. An example for why these sorts of regulations is important is the so-called E-cigarette and Vaping Associated Lung Injuries (EVALI) outbreak in the US which led to 2,807 cases of hospitalisation or deaths by mid-February. A common denominator for all affected patients was that they used e-cigarettes that had refillable chambers or interchangeable cartridges to vape tetrahydrocannabinol (THC) vaping concentrates or oils, which were all purchased on the street (166). Since there was no tamper-evident regulation in the US, this sort of manipulation of e-cigarette products was not constrained. Indeed, this manipulation was (and still is) common in the US; it is referred to by vapers as ‘dripping’, to imply the direct dripping of vape liquids onto the heated coils for inhalation (50). Vapers drip because it produces a thicker cloud of vapour, better flavour taste, a stronger throat hit, or to satisfy curiosity (167). However, dripping has the potential to increase the harms from vaping as it

involves higher temperatures, leading to higher amounts of nicotine delivered (50), and may expose users to high levels of carbonyl compounds (151). The practice of dripping has not yet been reported in the UK, possibly due to the existence of tamper-evident rules.

Other aspects of safety that the FDA were (at the time of regulation) concerned about was overheating, exploding batteries, and accidental nicotine poisoning which the FDA stated was increasing in the wake of growing e-cigarette use (108). The UK's regulation on protection against breakage and leakage was a measure that can be said to have addressed the issue of accidental nicotine poisoning. In contrast, the US regulation did not have protection against breakage and leakage, but the Pre- Market Tobacco Authorisation (PMTA) can be said to be a useful way of preventing e-cigarettes with concerning characteristics from coming into the US market.

1.8.7.2 Summary of general safety requirements for e-cigarettes in the US and the UK regulations with respect to possible influential factors

Both the US and the UK have shown a consideration of the safety of e-cigarette use in their policy briefs. However, although the US were concerned with safety issues such as overheating, exploding batteries and accidental nicotine poisoning, they did not impose regulations protecting against breakage and leakage, tampering, or adulteration in response to those concerns. This might perhaps be due to the adoption of a generic regulation primarily used to regulate other 'tobacco products' such as tobacco cigarettes which are a considerably different in design and mode of operation from e-cigarette devices. On the other hand, the UK, which communicated fewer e-cigarette specific safety concerns, transposed TPD directives on protection against breakage and leakage, tampering, and adulteration and to ensure that e-cigarette products are always used the way intended by the manufacturer and approved by the regulatory agency. Perhaps this was not only done to abide by legal provisions of the TPD, but also to prevent the UK population from experiencing the sort of safety issues (such as accidental nicotine poisoning) that had been reported in the US or other countries.

1.8.8 Child safety packaging

Comparator	US Regulation	UK Regulation
Child safety	The Child Nicotine Poisoning Prevention Act of 2015 requires child-resistant packaging for nicotine-containing e-liquid containers.	An electronic cigarette or refill container must be child resistant.

Table 9: Child Safety Packaging for E-cigarettes in the US and the UK Regulations

As seen in Table 9 above, the FSPTCA and TRPR both mandate e-cigarette companies to consider child safety via child-resistant packaging or other unspecified means but neither describes the mechanisms for implementation or assessment of adherence. Note also that the FSPTCA does not set out its own rules but points instead to adherence to the Child Nicotine Poisoning Prevention Act of 2015 which requires child-resistant packaging for nicotine-containing e-liquid containers. The Child Nicotine Poisoning Prevention Act of 2015 is an Act that requires special packaging for liquid nicotine containers, and for other purposes. In the Act, the term `liquid nicotine container' means a package from which nicotine in a solution or other form is accessible through normal and foreseeable use by a consumer and that is used to hold soluble nicotine in any concentration.

1.8.8.1 Child safety packaging in the US Context

The CDC reported more than 2,400 calls to U.S. poison control centres for e-liquid exposure between September 2010 and February 2014 (168). In another study of 1,700 e-liquid exposures reported to U.S. poison control centres from June 2010 through September 2013, children 5 years of age or younger represented the largest proportion of e-liquid exposures and the group with the greatest increase in exposures per month in the first three quarters of 2013 (169). Studies show that nicotine in sufficient concentrations, either when ingested or in contact with the skin, can result in serious or fatal poisoning and is concerning (170, 171). Nicotine has also been used in suicide attempts (129). Although completed suicides using e-liquids are extremely rare, suicide attempts with large amounts of pesticides containing nicotine sulphate often succeed (172). In cases when adults drank up to 1,500mg of nicotine in e-liquid, the result was vomiting and recovery within a few hours (173), but higher doses have proved fatal. For example, in one case where 3,950mg of nicotine was

found in the gastric contents of a victim who seem to have drunk three vials of e-liquid totalling over 10,000mg of nicotine, the outcome was fatal (173). Another fatal outcome was from an intravenous injection of unknown quantity of e-liquid (174). Symptoms of nicotine toxicity include nausea, vomiting, seizures, coma, cardiovascular instability, respiratory arrest, and sometimes death. Regardless of the incidence of nicotine poisoning in comparison to poisonings attributed to other household products, the dramatic rise in nicotine poisoning from e-liquid exposures was very concerning to the FDA (108).

1.8.8.2 Child safety packaging in the UK Context

The requirement for e-cigarettes and refill containers to be childproof originated from the TPD which was transposed to TRPR. Research evidence and reports also backed this regulatory mechanism.

A 2015 PHE report (129) on e-cigarettes showed that PHE was not oblivious to the reported incidents of nicotine and e-liquid poisoning in the US, especially affecting children. In this report (129) the authors stated that they were aware of three published case studies of small children who drank e-liquid. In the first case study, a two-year old was admitted to hospital with vomiting, ataxia, and lethargy, and was discharged after 24 hours of observation (175). The second case involved an 18-month old girl who drank 24mg nicotine in e-liquid, vomited and was irritable, but recovered fully within about an hour (176). The third case was a 30-month old child suspected to have ingested e-liquid (quantity was uncertain), but was asymptomatic with all clinical observations reported to be normal (177). The PHE report (129) noted that an increase in e-cigarette use had unfortunately been met with an increase in calls to poison centres to report accidental exposures. Nonetheless, they went on to note that none of these accidents resulted in any serious harm. The PHE report (129) did not indicate that there were any similar calls to poison centres following exposure to NRT, but the report highlighted that in comparison, related calls remained lower than calls following similar exposure to tobacco (168). The authors of the PHE report (129) explained that serious nicotine poisoning was normally avoided because relatively low doses of nicotine cause nausea and vomiting, which stops users from further intake. E-liquid normally comes in 10ml bottles containing up to 360mg of nicotine; these quantities, when used as intended, pose no risk to vapers. Nonetheless, the 2015 PHE report (129) recommended e-liquids should have ‘childproof’ packaging to prevent small children, who

may find the colours and flavouring appealing, from drinking it. It was noted that all e-liquids seen in the UK and globally up to the time of the 2015 PHE report, were sold in child-resistant packaging (129). Therefore, this requirement is likely to be acceptable practice within the e-cigarette industry.

1.8.8.3 Summary of child safety packaging for e-cigarettes in the US and the UK regulations with respect to possible influential factors

The US regulation on child safety packaging was possibly influenced by case studies and reports they cited to acknowledge that nicotine use presents the possibility of accidental exposure and poisoning. Whereas, in the UK, it was the TPD that determined the regulation on child safety packaging.

The bright packaging of e-cigarettes and coloured e-liquids increases the potential for accidental exposure and poisoning as it may make e-cigarette products more attractive to inquisitive toddlers and children. Both the US and the UK confirmed that there had been an increase in calls to poison centres to report accidental exposures to nicotine since the introduction of e-cigarettes, with this increase attributed to ingestion of e-liquids. However, the UK added that such calls remained lower than calls following similar exposure to tobacco, and that accidental nicotine exposure rarely resulted in any serious harm. Nevertheless, both the US and the UK regulations require child-resistant packaging for e-cigarettes and nicotine-containing e-liquid containers.

1.8.9 Minimum age of sale

Comparator	US Regulation	UK Regulation
Minimum age of sale	Sale to minors (amended from 18 years to 21 years on 20/12/2019 through the 'Tobacco 21' or 'T21' legislature) is prohibited. Retailers must verify age of customers under 27 years (via photo identification) before sale can be made. Sale via vending machine is restricted to adult-only facilities	Prior to, or at the time of sale, the retailer's age verification system confirms that the consumer's age is not lower than the minimum age applicable for the purchase of the product in the member State in which the consumer is located. The referred minimum age is currently 18 years in England, Wales, Scotland, and Northern Ireland.

Table 10: Age restriction for sales of E-cigarettes in the US and the UK Regulations

Prior to the Tobacco 21 Act that was enacted and took effect on 20th of December 2019, the US and the UK had similar age-related restriction on sale of e-cigarettes, namely a minimum age of sale of 18 years old. However, the TRPR does not directly stipulate 18 years of age as the minimum age of sale of e-cigarettes; rather it adopts the minimum age applicable for the purchase of the product in the member State in which the consumer is located. Currently, all four member states of the UK (England, Scotland, Wales, and Northern Ireland) set 18 years of age as the minimum age for the purchase of tobacco and related products, and so by inference, the TRPR can be interpreted to mean that 18 years is the minimum age of sale of e-cigarettes across the UK. This interpretation could change if any member state chooses to change their minimum age of sale for e-cigarettes, perhaps in response to public health concerns within that region. A responsive change to regulation is seen in the Tobacco 21 Act which changed the minimum age of sale of e-cigarettes in the US from 18 years to 21 years due to a rising number of smokers among young people. This change was based on a gateway theory, whereby use of e-cigarettes eventually leads to smoking. In other words, increasing the number of young vapers will lead to an increasing number of that age-group becoming smokers. As can be seen in Table 10 above, both the FSPTCA and TRPR recommends a verification system to confirm the age of consumers at point of sale.

1.8.9.1 Minimum age of sale in the US Context

FDA was (at the time of initial regulation) and still is concerned about the rise in ENDS use among youth and young adults as well as the trends in dual use of ENDS and combusted products in both youth and adults (178). In 2019, approximately one in four youths (23.0%) had used a tobacco product during the past 30 days, representing approximately three in ten high school students (31.2%) and one in eight middle school students (12.5%) (179). According to a 2019 survey, since 2014, e-cigarettes had been the most used tobacco product among youths with 27.5% of high school students (4.1 million) and 10.5% of middle school students (1.2 million) reporting use in the past 30 days (179). Drawing on *in vivo* animal studies, the US Surgeon General had stated that adolescents appear to be particularly vulnerable to the adverse effects of nicotine on the central nervous system (120). An outbreak in the US that was termed 'E-cigarette and Vaping Associated Lung Injuries (EVALI)' started in mid-August and had led to 2,807 cases of hospitalisation or deaths by mid-February 2020 (74). As of 14th January 2020, of the 2,668 hospitalized EVALI cases or deaths reported to CDC, 52% were between 13 to 24 years, with a median age of 24 years and a range of 13-85 years. The EVALI outbreak, which involved respiratory injuries such as acute eosinophilic pneumonia, organizing pneumonia, acute respiratory distress syndrome and hypersensitivity pneumonitis (50), was initially reported to have resulted from use of e-cigarettes. Investigations later revealed that the illnesses were related to products purchased on the street containing vitamin E acetate, an additive substance in some Tetrahydrocannabinol (THC) (166). Nevertheless, at the peak of the outbreak (September 2019) there was public outcry and pressure to implement regulations reducing youth access to ENDS products. A study by Friedman (180) had already concluded that reducing e-cigarette access increases smoking among 12 to 17 year olds. Therefore, the evidence to support an increase in minimum age of sale of e-cigarettes alone was lacking. However, e-cigarettes are classified as tobacco products in the US, and an increase in minimum age of sale of tobacco products from 18 years to 21 years had previously been shown to be an effective means of reducing youth smoking initiation (181, 182). Hence, on 20th December 2019, the President of the US signed legislation amending the FDC Act, to raise the federal minimum age for sale of all tobacco products from 18 to 21 years. This legislation which is known as 'Tobacco 21' or 'T21' was immediately effective from the day of passing into law. It was the increased use of e-cigarettes among young people and the EVALI crisis that gave

momentum and urgency to passing into law of the Tobacco 21 Act that affects all tobacco products including e-cigarettes.

1.8.9.2 Minimum age of sale in the UK Context

The TRPR requires the vendors to verify that the consumer's age is not lower than the minimum age applicable for the purchase of the product in the member State in which the consumer is located. Therefore, regulation of the minimum age of sale for e-cigarettes and other tobacco or tobacco related products is devolved to the respective nations of the UK. However, the Children and Young Persons (Sale of Tobacco Etc.) Order 2007 (107) sets the minimum age of sale of tobacco products at 18 years in the UK. Since the TRPR regulates tobacco products and subject to this existing minimum age of sale requirement, UK nations applied this requirement to e-cigarettes which are tobacco related products and part of the TRPR.

In the UK, evidence from studies, and monitoring data that showed the trends of e-cigarette use, supported the decision to maintain the minimum age of sale of e-cigarettes at 18 years. A 2014 PHE report (112) stated that data for the UK, as suggested by a smoking toolkit study (183) demonstrated trends in use of e-cigarettes similar to those in the US, and concluded that e-cigarette use, having increased rapidly over the previous two years, had stabilised at the time of reporting at around 17% (184). Action on Smoking and Health (ASH) estimated that in 2014 about 1.3 million people in the UK used electronic cigarettes, and around 400,000 people had completely replaced smoking with electronic cigarettes (57). E-cigarettes were primarily used by current and former smokers, and only about 0.5% of never smokers in Great Britain had tried the product (185).

With regards to youth e-cigarette use, a 2015 PHE report (129) showed that regular e-cigarette use among youth was rare, with around 2% using at least monthly and 0.5% weekly. At that time, e-cigarette use among young people remained lower than among adults, although a minority (13%) of British youth reported having tried e-cigarettes in 2015 (129). Also, whilst there was some experimentation with e-cigarettes among never smoking youth, prevalence of use (at least monthly) among never smokers was 0.3% or less in 2015 (129).

All the evidence (at the time of original e-cigarette regulation in the UK) suggested that e-cigarette use in the UK was predominantly amongst former and current adult smokers, but rarely among youths and children. Therefore, no additional age-related access restriction was considered other than the default 18 years minimum age of sale restriction for products deemed to pose some harm to users. E-cigarettes are deemed to pose some harm to users because they contain nicotine which is addictive and has potential for harm if abused. With the recent increase in use of disposable vapes among young people, the UK and Scottish governments have recently proposed a ban on the sale of disposable vapes in England, Wales and Scotland with effect from April 2025 (164).

1.8.9.3 Summary of age restriction for sales of e-cigarettes in the US and the UK regulations with respect to possible influential factors

In both the US and the UK, age restrictions imposed for use of tobacco products were applied to e-cigarettes. It is not clear to me from the documents supporting regulations whether this was because, at the time of regulation, e-cigarettes were treated as a tobacco product or because a legal age (usually 18 years or older) of use is the default for any products (e.g., alcohol) containing addictive substances or deemed to pose some harm to users. Legally, in most jurisdictions, a person 18 years or older is considered an adult and can make autonomous decisions affecting their lives; they are of the age when they are deemed to have the mental capacity to do so in the absence of any health disability. Default restrictions are set to protect children ('minors') who are by virtue of age and mental maturity vulnerable to manipulation and the making of irrational decisions. This perceived duty of public institutions and governments to protect their young or children influenced the age restriction for sales of e-cigarettes. This is evidently the case in the US as the Tobacco 21 law that increased the minimum age of sale of tobacco products from 18 years to 21 years was implemented to reduce youth smoking initiation.

1.8.10 Advertising/ Promotion/ Sponsorship

Comparator	US Regulation	UK Regulation
Advertising/ Promotion/ Sponsorship	For cigarette tobacco, roll-your-own tobacco, and covered tobacco products (which includes e-cigarettes), it is unlawful for any such tobacco product manufacturer, packager, importer, distributor, or retailer of the tobacco product to advertise or cause to be advertised within the United States any tobacco product unless each advertisement bears the required warning statement.	1. No person may in the course of a business publish, or procure the publication of, an electronic cigarette advertisement in a newspaper, periodical or magazine. 2. No person may in the course of a business sell, offer for sale or otherwise make available to the public a newspaper, periodical or magazine containing an electronic cigarette advertisement. 3. The above points do not apply— a. to a newspaper, periodical or magazine which is intended exclusively for professionals in the trade of electronic cigarettes or refill containers; or b. To a newspaper, periodical or magazine which is printed and published in a third country (not a member State or EEA state) and is not principally intended for the Union market (the market of one or more member States) 4. No person may during a business include, or procure the inclusion of, an electronic cigarette advertisement in an information society service provided to a recipient in the United Kingdom. 5. No service provider established in the United Kingdom may in the course of a business include an electronic cigarette advertisement in an information society service provided to a recipient in an EEA State other than the United Kingdom (‘a non-UK-EEA-State’).

Table 11: Advertising/ Promotion/ Sponsorship for E-cigarettes in the US and the UK Regulations

The FSPTCA only prohibits advertisement of all tobacco products (including e-cigarettes) if they do not bear the required warning statement in the format described in Table 11. On the contrary, the TRPR prohibits publication or procurement of publication of advertisement, sales or offer of sales of e-cigarettes in any newspaper, periodical, magazine, or information society service within the UK. Although not part of the TRPR, Ofcom (UK's communications regulator) also prohibits the advertisements for e-cigarettes and refill containers in broadcast television and radio services, as well as programme sponsorship which has the aim or effect of promoting such products. These prohibitions follow the direction of the Secretary of State for Health to Ofcom under section 321(6) of the Communications Act 2003 in order to implement provisions of the TPD.

1.8.10.1 Advertising/ Promotion/ Sponsorship in the US Context

The FDA have acknowledged that some individual smokers may potentially use ENDS to transition away from combustible tobacco products (108). Prospective studies, of varying duration, examining the efficacy of e-cigarettes as cessation devices suggest their potential to decrease combustible cigarette use as well as to promote abstinence from combustible cigarettes (156, 186-189). However, the FDA also cited contradictory evidence from a year-long study of 5,128 20-year-old Swiss men which found that, even after adjusting for nicotine dependence, individuals who were smokers at the start of the study and who reported e-cigarette use at the end of the study were more likely to still be smoking and more likely to have made one or more unsuccessful quit attempts at the end of the year than individuals who were smokers at the start and who reported no e-cigarette use (190). The FDA stated their belief that data from long-term population level studies, such as the PATH Study, will help to provide information about the overall population health impacts of ENDS. The FDA therefore clarified that ENDS are not an FDA-approved cessation product. Any ENDS manufacturer wishing to make a cessation claim, or otherwise market its product for therapeutic purposes, must apply for their ENDS to be marketed as a medical product (108). The FDA emphasized that Section 911 of the FDC Act requires the FDA to assess Modified Risk Tobacco Product claims for specific products. Therefore, until an FDA evaluation verifies e-cigarettes to be as claimed by the manufacturers, they cannot be advertised, sold or distributed for use to reduce harm or the risk of tobacco-related disease

associated with commercially marketed tobacco products, as stated in section 911 of the FDC Act (108).

1.8.10.2 Advertising/ Promotion/ Sponsorship in the UK Context

In the UK, regulation on advertising, promotion, and sponsorship of e-cigarettes was determined by the TPD. In addition, Ofcom prohibits the advertisements for e-cigarettes and refill containers in broadcast television and radio services.

According to PHE, e-cigarettes do not produce smoke so the well-documented effects of passive exposure of others to cigarette smoke (191) are (clearly) not relevant (112). E-cigarettes appeal to smokers by mimicking the sensation and appearance of smoking a cigarette, and by their market positioning as lifestyle rather than medical products. This clearly gives e-cigarettes a potential to reduce the prevalence of smoking in the UK if promoted as a smoking cessation aid (112). PHE noted that the challenges are to harness that potential and to maximise the benefits whilst minimising risks. In terms of risks, a major concern is that e-cigarettes and tobacco cigarettes are similar in appearance. Therefore, there is a risk that the advertising, sponsorship, celebrity endorsement and portrayals in film and other media of e-cigarettes can mislead people into taking up smoking. In this area there is considerable scope for promotion of nicotine use to young people, representing a significant concern (112). It is perhaps due to these concerns that e-cigarettes were governed by the voluntary agreement (192) between Department of Health and the tobacco industry prior to the institution of TRPR in 2016. More specifically, the agreement stated that advertising must be socially responsible, must not promote any design, imagery or logo that might be associated with a tobacco brand or show the use of a tobacco product in a positive light, must make clear that the product is an e-cigarette and not a tobacco product, must not undermine quit tobacco messaging, and must not contain health or medicinal claims unless the product is licensed as a medicinal product (129). I believe that these same concerns are likely to have influenced the TRPR with regards advertising, promotion, and sponsorship.

1.8.10.3 Summary of Advertising/ Promotion/ Sponsorship for e-cigarettes in the US and the UK regulations with respect to possible influential factors

In the US, the main concern with advertising and promotion was that companies might market e-cigarettes as smoking cessation products in the absence of what FDA considered to

be sufficient evidence of their efficacy in smoking cessation, and the fact that e-cigarettes were and are not an FDA approved cessation product. Surprisingly, therefore, the FDA, though warning against such claims and presenting a synthesis of different types or research studies and systematic reviews to support their position, did not impose any specific restrictions to the effect. Therefore, advertising of all tobacco products (including e-cigarettes) is permissible in the US with the only criterion being that an appropriate warning label is used. On the other hand, in the UK, the main concern was the similarity in appearance between electronic and tobacco cigarettes. From the UK's experience with tobacco cigarettes, advertising, sponsorship, celebrity endorsement and portrayals in film and other media can lead to encouragement of their use, especially among young people. Therefore, if e-cigarettes were to be advertised or promoted in media, it might lead naïve users, who think e-cigarettes and tobacco cigarettes are the same because of similarity in appearance, to take up tobacco smoking. All forms of advertising and promotion of e-cigarettes were therefore restricted in the UK, in line with TPD requirements and domestic regulations on tobacco advertising.

1.8.11 Summary of comparison of e-cigarette regulations in the US and the UK

The differences in regulatory approach to e-cigarettes between the US and the UK were in part due to the type of research evidence considered and the interpretations drawn from the chosen evidence base to influence policy. For example, the FDA drew from *in vivo* animal studies, cited in the 2014 Surgeon General's Report (120), and *in vitro* laboratory studies (138-140) to make conclusions on the toxicity of nicotine in e-cigarettes and the harmful metals produced from e-cigarette use respectively. This led the FDA to view nicotine exposure from e-cigarette use to have adverse consequences for brain development in adolescents and to assert that e-cigarettes contain metals harmful to health. This subsequently influenced some of their regulatory decisions such as raising the age of sale of tobacco products (including e-cigarettes) from 18 to 21 years, to reduce adolescent access to such products (193), and to ban sale of any flavoured, cartridge-based ENDS product (other than a tobacco- or menthol-flavoured ENDS product) which were particularly deemed by FDA to make e-cigarettes attractive to children (194). In the UK, on the other hand, PHE (112) were convinced by observational and epidemiological studies (125, 126) that nicotine delivered by e-cigarettes is extremely unlikely to cause significant short or long-term adverse

events, and by survey evidence (57, 183) that people have completely replaced smoking with electronic cigarettes. This led them to promote the use of e-cigarettes for smoking cessation in their policy recommendations (85).

It appears to me that FDA focused on the absolute risk of e-cigarettes in relation to their components such as nicotine, flavours and the metals found in e-cigarettes, whereas PHE focused on the relative risk of using e-cigarettes compared to smoking tobacco cigarettes and concluded that e-cigarettes are likely to be much less, if at all, harmful to users or bystanders. The FDA responded to PHE's evaluation of the health risk of e-cigarettes by explaining that, in the PHE report (129), the included studies employed an analysis model in which an expert panel quantified the relative health harms of 12 tobacco products using a series of 14 harm criteria. The expert panel determined that, while cigarettes scored 100 percent in their assessment of maximum relative harm, ENDS products were rated to have only 4 percent maximum relative harm. This finding contributed to PHE's assessment that ENDS are around 95 percent safer than smoking combusted cigarettes (129, 195, 196). The FDA further commented that, in their opinion, the cited study had several limitations:

- The study outcomes reported in the PHE report were based on the decision-conferencing process from a group of experts who were selected without any 'formal criterion,' (though the original report indicated that care had been taken to have representatives from many different disciplines a range of geographic locations to ensure a diversity of expertise and perspectives).
- The authors of the PHE report acknowledge that there is a lack of hard evidence related to most of the criteria for the harm of most products (82, 195).
- The authors of the PHE report did not explain what scientific information upon which to base their ratings was available to the experts.
- The authors of the PHE report did not explain the derivation of the quantitative assessment of each harm criterion. It is unclear if the authors of the PHE report carried out or referenced a quantitative risk analysis, a standard practice when assessing relative risk, nor did they indicate that they used mean levels of exposure to Harmful and Potentially Harmful Constituents (HPHCs) in users or other quantitative evidence as an approximation of risk.
- Population effects appear to be largely outside the scope of the analysis in the PHE report since the manuscript did not address the likelihood that the characteristics of the

products would make them more or less likely to appeal to new users, be used in conjunction with other tobacco products or discourage quitting. The authors of the PHE report did not describe an assessment of population effects such as a quantitative assessment of youth use prevalence.

- The FDA did not find the beliefs reported in the prior paper (195) to be sufficiently conclusive or compelling on the relative risks of using different tobacco products (108).

There are some regulatory loopholes in both the US and the UK e-cigarette regulation that were identified in the comparative review of those regulations. These can be viewed as linked to concerning public health occurrences. For example, in the US, the lack of tamper-evident requirements (present in UK regulation) could be argued to have resulted in the practice of 'dripping', whereby vapers manipulate e-cigarettes by directly dripping vape liquids onto the heated coils for inhalation in a bid to produces a thicker cloud of vapour, better flavour taste, a stronger throat hit, or to satisfy curiosity (50, 167). Dripping has the potential to increase the harms from vaping as it involves higher temperatures, leading to higher amounts of nicotine delivered (50), and may expose users to high levels of carbonyl compounds (151). The practice of dripping has not yet been reported in the UK, possibly due to the tamper-evident rules. In the UK, the lack of restriction on giving away free samples of e-cigarettes to young people, despite restricting sale of e-cigarettes to under 18s, is a loophole that could be argued to have led to nicotine initiation amongst children in the UK. Children who become addicted then illegally patronise e-cigarette vendors with adverse consequences manifested in the concerning rise in illegal sale to and use of e-cigarettes among children in the UK (162).

It is also important to note that in both the US and the UK, Public Health authorities had clear stances regarding the impact of e-cigarettes on population health which drove the focus, selection, and interpretation of research evidence within both countries. The US prioritised preventing exposure of youth to nicotine and initiation of smoking (via vaping) in youth and smoking-naïve individuals, whereas UK prioritised helping existing smokers to quit. The US approach was aligned to the health protection end of spectrum described by Campus *et al.* (77), and the UK approach was aligned to the harm reduction end of the spectrum (see section 1.6). As discussed in Section 1.7, US NIH research funding priorities include toxicity, addiction, and health effects of ENDS, but there is no consideration of effectiveness of ENDS in smoking cessation (65). By contrast, in the UK CRUK research

funding foci include role of e-cigarettes in cessation, their use by different populations, etc. (66).

1.9 Summary of each Chapter in the study

Chapter 1: Background

In this chapter I have introduced the context and scope of this research study. I have presented relevant literature about the research area, the rationale, aims and objectives of the research study. I have also presented a comparison of US versus UK e-cigarette regulation, addressing the first objective of my PhD project (see section1.3) which was to 'describe the similarities and differences between e-cigarette regulation and policies in the US and the UK.'

Chapter 2: Methodology

In this chapter I present the various methods used in conducting this research project and discuss the theoretical underpinnings guiding the study. I also reflect on my ethical conduct, biases, and positionality throughout this research.

Chapter 3: Factors influencing e-cigarette regulation and policies in the US and the UK

In this chapter I present and discuss the findings from my first empirical study, which was conducted to explore the factors determining the policies and regulation of e-cigarette in the US and the UK, and to address the second objective of my PhD project (see section1.3). For this study, I carried out qualitative interviews of key UK stakeholders and thematic analysis of interviews. Due to low response to interviews from the UK and no response from the US, a complementary thematic analysis of recorded audio presentations from the relevant organizations with which I was unable to secure an interview was carried out. These presentations were delivered officially by representatives of their organizations at the e-cigarette conference held annually (from November 2013) in parallel in the UK and the US and entitled 'E-cigarette Summit: Science, Regulation and Public Health'.

Chapter 4: The Values and Sentiments of the Public Towards Electronic Cigarettes and its Regulations in the US and the UK

In this chapter I present and discuss the findings from my second empirical study, which was conducted to assess whether the values and sentiments of the public towards e-cigarettes and their regulations were the sort to influence e-cigarette regulatory decisions in the US and the UK, and also contributed to addressing the second objective of my PhD project (see section 1.3). For this study, I carried out thematic and sentiment analysis (using Atlas.Ti) of Twitter™ data representing e-cigarette discussions in the 105-day before and after e-cigarette regulation in the US and the UK (see section 4.3).

Chapter 5: Potential determinant factors of e-cigarette regulation in Nigeria

In this chapter, I present and discuss the findings from my third and final empirical study, which was conducted to identify the potential determinants of e-cigarette regulation in Nigeria and to address the third objective of my PhD project. For this study, I carried out qualitative interviews of key Nigerian e-cigarette regulatory stakeholders and thematic analysis of interviews.

Chapter 6: Discussion

In this chapter, I bring together the findings from all three empirical studies conducted for this PhD project and reported in Chapters 3 to 5, with the comparative analysis of UK and US regulations presented in Chapter 1. I discuss the findings in the context of available literature. I also highlight the strengths and limitations of the project and its component studies. Finally, I make recommendations for policy and future research.

Chapter 2. Methodology

2.1 Research paradigms, ontology, and epistemology

Efforts to improve public health within countries have been linked with calls for evidence-based policy. In other words, public health policy actors see engagement with evidence derived from policy-relevant research into more effective interventions as the way to achieve their overarching policy objectives (197). Therefore, generating research evidence, as this PhD project was designed to accomplish, is vital to improving public health through informing policy. In this PhD project, I aimed to compare US and UK e-cigarette regulations and associated influencing factors, to inform policy approaches in the context of Nigeria. The nature of the enquiry was to find out why e-cigarettes are regulated the way they are in the US and the UK (what factors influenced each country's regulatory approaches?). In what ways are the factors identified as determining the regulatory approach to e-cigarettes in the US and the UK similar to or different from the context of Nigeria? To achieve these research objectives, I have chosen to use an interpretivist research paradigm.

Ontology concerns the nature of social reality, including what and how we can learn about this reality (198). Epistemology in research deals with how we can come to know reality (199). The social reality of this research was a network of factors influencing e-cigarette regulations connected to people (such as regulators and those affected by the regulation), situations (such as those contextual or specific to the regulatory needs of respective countries), events (such as those occurring at the time of e-cigarette regulations) and the processes that connect all of these (200). This reality is a consequence of the interactions in this network. Interpretivist research views 'reality' as a socially constructed activity (201). A qualitative interpretivist approach was deemed the most suitable for this research project because this approach requires understanding the process through which individuals construct the social reality of regulations. Therefore, I adopted an interpretivist paradigm to understand why e-cigarettes are regulated the way they are in the US and the UK, and how the identified factors that determined the regulatory approach to e-cigarettes in the US and the UK are similar to or different from the context of Nigeria.

Survey methods and quantitative data collection were rejected in favour of a multimethod qualitative approach (discussed below in section 2.2), since my focus was on an in-depth understanding of the phenomena of interest and the social context, and this required rich

qualitative data. Methods used for collection and analysis of Twitter™ data were appropriate for achieving the second study objective (see section 4.2). Generally, a multimethod qualitative approach was used because of its methodological appropriateness to my research questions and the practicality of data collection.

2.2 Multimethod qualitative approach

This study used a multimethod qualitative approach. Multimethod research uses multiple forms of qualitative data (e.g., interviews and observations) or multiple forms of quantitative data (e.g., survey data and experimental data) (200). This study involved primary data collection collected through interviews and secondary analysis of audio recordings of presentations by policy makers and other key stakeholders as well as textual material from policy documents and social media (Twitter™). Each of these data forms have their advantages in the context of this project as well as their challenges. These advantages and challenges are highlighted in the discussion section of the various studies that make up this PhD project i.e., Chapter 3 (sections 3.4.5 and 3.4.6), Chapter 4 (sections 4.4.4 and 4.4.5), and Chapter 5 (sections 5.4.2 and 5.4.3).

Qualitative data (both primary and secondary data) were collected from different settings (UK, US and Nigeria) and different sources (field and the internet) using methods appropriate to this type of data (interviews); and qualitative methods of analysis (thematic analysis and sentiment analysis) were deployed. A researcher's choice of research approach is influenced by multiple factors. These typically include: the research question; the researcher's methodological preferences, skills and experience; the intended audience for the research; funding; time (198) and practical considerations. In this PhD project, the main determinant of the chosen approaches was the research question. A secondary determinant was practical considerations. For instance, I ideally wanted to collect primary data through interviewing key stakeholders myself, but because of the lack of response to requests for interviews, I resorted to analysis of secondary data in the form of recorded presentations.

The overall aim of the PhD project was to compare the US and UK e-cigarette regulations and associated influencing factors, to inform policy approaches in the context of Nigeria. Firstly, to compare US and UK e-cigarette regulations, a structured literature review (see section 1.8) enabled me to describe the similarities and differences between e-cigarette

regulation and policies in the US and the UK. To collect data on factors influencing e-cigarette regulations, in-depth interviews with relevant e-cigarette related stakeholders were deemed to be the best method. The factors that influenced their regulatory decisions, and contributions to the regulation, could best be explored in an in-depth interview that provided the platform for them to communicate their opinions openly. Also, with interviews, I controlled what was asked, and of whom such questions were asked, enabling me to find out, from the perspective of key stakeholders involved in the regulatory process, what factors determined the decisions they made regarding regulation of e-cigarettes. However, due to lack of response to requests for interviews, a complementary technique, which involved the analysis of secondary data in the form of recorded presentations (e.g., from conference presentations on e-cigarette regulation) by individuals involved in the regulatory process in the US and the UK, was also used for this element of data collection. Online Twitter™ (now X™) discussions on e-cigarette regulations were collected and analysed to provide contemporary views and opinions being expressed by a wider range of stakeholders before and after implementation of e-cigarette regulations. The specific methods used in the various components of this PhD research project are discussed in more detail below.

2.3 Relevant Theories of Regulation

As this research project centres on e-cigarette regulation, different theories of regulation were used to discuss or validate the findings on factors influencing e-cigarette regulation in the US and the UK, and potential influencing factors of e-cigarette regulation in Nigeria. These theories are discussed briefly below.

2.3.1 Capture Theory

Capture theory suggests a situation whereby government regulatory agencies are gradually 'captured' by the regulated industry, so that, over time, they regulate primarily in the interest of industry, and not in public interest (202). This theory emerged from Marver H. Bernstein (203) who, from his analysis of the American regulatory context, discusses how some regulatory agencies shift away from their mandate of regulating in the public interest to serving the interest of the regulated industry due to being captured by the industry. Regulatory capture is one of the most notable theories that has been applied in understanding and discussing how social and economic interests have influenced regulations

and government decision making. The process is described in the book by Owen and Braeutigam (204), which serves as an 'how to' manual for industry, including techniques that can be used to manipulate government regulatory officials. John Abraham (205) has also discussed another form of regulatory capture known as the 'revolving door', whereby officials begin their career as regulators, but then move on to join the regulated industry, or vice versa. This makes them sympathetic to the regulated industry as they are unduly concerned to maintain 'friendly relations' with industry at the expense of public interest regulation.

My research examined whether Capture Theory had relevance to decisions made regarding e-cigarette regulation in the US and/or UK. Capture theory formed part of the conceptual framework in this PhD, informing framing of some of the questions posed to participants during the interviews in study 1 and study 3. For example, my topic guide included questions along the lines of 'was there any stakeholder engagement during regulation of e-cigarettes?' Capture theory subsequently informed the conceptualisation, refining and discussions of the themes identified from interview transcripts such as 'Role of Industry' (see section 5.3.6) in study 3.

2.3.2 Disease–politics theory/ reputational theory

Sometimes patient or public activism in response to a public health need or a public health crisis can lead to regulatory reforms. This explanation of regulatory reform is known as disease-politics theory (202). Key authors in this area, such as Edgar and Rothman (206), Daemmrich and Krucken (207) and Daemmrich (208), have described how 'disease-based' patient groups have driven regulatory developments and change in the US through patient activism. Steve Epstein (209) and Daniel Carpenter (210) specifically wrote about the AIDS crisis and how drug regulation had become responsive to patient activism. Daniel Carpenter (211) went on to describe a 'soft' version or variant of the disease-politics theory whereby regulators respond to patient activism or media pressure to protect their reputation in the public sphere; they have termed this 'reputational theory' (211).

My research also examined the extent to which disease-politics theory or reputational theory had relevance to decisions regarding e-cigarette regulation in the US and/or UK. Reputational theory, as part of the conceptual framework in this PhD, informed development of Study 2 which aimed to identify the public's sentiments towards e-cigarettes

and their regulations in the US and the UK, to enable an assessment of whether such reactions were of a nature that might have influenced e-cigarette regulatory decisions in those countries or have potential to do so in Nigeria.

2.3.3 Expectation/ marketing theory

Expectation/ Marketing theory supposes that the creation of expectations and promissory science around innovation among networks of medical professionals, research scientists and patients/public puts pressure on regulatory agencies to deregulate those innovations even if they undermine existing regulatory standards (202). Authors such as Arnold Relman (212), Joe Collier (213), and John Abraham (214) have long written about how pharmaceutical companies recruit medical professionals to act as 'opinion leaders' to support the marketing of new products. E-cigarettes are innovative and relatively new products with expectations around their invention and diffusion.

The relevance of Expectation/ Marketing theory was also considered in relation to e-cigarette regulation in the UK. Expectation theory formed part of the conceptual framework in this PhD, informing inquiry during qualitative interview of UK stakeholders on whether the UK's focus on the potential for e-cigarette to be used in a harm reduction approach to reduce harms of tobacco use, as identified in my literature review (see section 1.7), influenced the regulatory measures for e-cigarette in the UK. That is, whether the expectation amongst researchers and public health experts that the innovation of e-cigarettes has a potential as an effective smoking cessation aid, may have influenced how regulators came to regulate e-cigarettes. Expectation theory was therefore also used to inform discussions of one of the themes identified from interview transcripts- 'Public health considerations' (see section 3.3.2.3) in study 1.

2.3.4 Corporate Bias Theory

Even though, ideally, government and international regulatory organisations or agencies should remain autonomous and independent, to sustain public trust, they are often vulnerable to corporate bias, for example as a result of lobbying, in policy making. Individual politicians who receive funding for themselves or their parties from external sources may well have positions, such as non-executive directorships or advisory roles, with commercial

entities, and this may bias their positions when making policies. Corporate bias theory supposes that some organised interests can gain privileged access to executives and legislature, such that they are positioned to set the agenda for regulation, so that it is biased in favour of their interest at the expense of conflicting interest (202). Keith Middlemas (215) was the first author to draw attention to corporate bias when he analysed the influence of the trade union movement on a UK labour government. He wrote on the importance of organised interest in gaining privileged access to the state, so as to ultimately self-regulate through delegation of governing powers to serve the interest groups (215). John Abraham has subsequently developed this theory to understand pharmaceutical regulation in the European Union and the USA (205, 216, 217).

Corporate bias theory may have relevance to decisions regarding e-cigarette regulation in the US and/or UK. Therefore, corporate bias theory, as part of the conceptual framework in this PhD, informed framing of some of the questions posed to interviewees during the interviews in study 1 and study 3. Questions along the lines of 'Were the individuals involved in the development of the regulations in anyway assessed for conflict of interest?' were included in the topic guides. Corporate bias theory was therefore also used to inform discussions of one of the themes identified from interview transcripts- 'Role of Industry' (see section 5.3.6) in study 3.

2.4 Ethics

Ethics in research has to do with how the researcher engages with, informs, and protects participants (198). As the different stages of this research project carried different kinds of risk that can influence the process and outcome of obtaining ethical approval, application for ethical approval was made in a phased manner to cover each stage of the project to be undertaken. Ethical approval was obtained from Faculty of Medical Sciences Research Ethics Committee (FMS-REC) for all component studies of the PhD project (see Appendix B and Appendix C) except for the element that involved obtaining and using publicly available policy documents and social media posts; since these data were in the public domain, no material ethical issues were anticipated. Ethical approval was obtained from the Nigerian National Health Research Ethics Committee (see Appendix D) for the interview of Nigerian stakeholders. A signed Postgraduate Research Confidentiality Agreement was upheld, and all study-related information was stored securely and treated with utmost confidentiality.

Interviewees for this PhD project were given the choice to be anonymous or go on record with their views. Participants were given this choice to mitigate the risk of feeling loss of ownership of the data through concealment of their real identities by use of pseudonyms (218). For interviewees who chose to be anonymous, data collected from them were pseudonymized (by substituting a pseudonym/nickname for their real name). Because data collected from Twitter™ and recorded conference presentations were publicly available and accessible to everyone through the internet, no form of anonymisation was carried out on those data, and no material ethical issues were anticipated. Participants in interviews were also informed that they could leave the study if and whenever they wanted.

I ensured that handling of data was in line with General Data Protection Regulations, and that information provided by participants was only made available to those who needed access to them during the research process (i.e., on a need-to-know basis). Data obtained in the form of audio recordings was stored in a folder on the cloud which could be accessed only by myself. Finally, any piece of work included in the research from another author has been appropriately cited and referenced to avoid plagiarism.

Another ethical consideration is a researcher's value system. Values in research have to do with the usefulness and distribution of the research to the public, including issues of inclusion of underrepresented groups (198). Findings from this PhD project have been summarized and reported in this PhD thesis (which will be generally accessible via Newcastle University's e-theses collection) and may be submitted for publication in an academic or professional journal which will be available to the public. The findings from this project are likely to inform Nigerian regulators of the potential barriers and facilitators to effective e-cigarette regulation when Nigeria moves to regulate e-cigarettes. Effective e-cigarette regulation will have positive impact on tobacco smoking rates, and as a result reduce harms from tobacco use.

2.5 Reflexivity

Reflexivity refers to one's attention to how bias comes to bear during all phases of the research. It has to do with the researcher's attention bias and positionality (198). Throughout the different stages of my PhD, my understanding of the key issues addressed in my research and my opinions of how best to tackle those issues have been evolving. With the evolving understanding and changing positionality, there is likely to have been corresponding unconscious bias infused into how I have addressed my research questions

and how I have interpreted and presented my research findings. These risks are particularly relevant in the context of qualitative research where the researcher is a co-creator of knowledge. It is therefore important to reflect and report here any personal and relational circumstance that could potentially be perceived by my audience to bias the outcome of this research study. This should provide sufficient background or context for any reader of this research project to appreciate the findings of the study.

I am a Registered General Nurse by professional background and have a Master of Science (Public Health and Health Services Research) degree. My education in public health gave me an in-depth understanding of the scale of the problem of tobacco smoking in the world, while my experience as a nurse exposed me to the real-life health challenges of tobacco smoking. A combination of both made me passionate about reducing tobacco smoking and influenced my approaches in this PhD research to mainly focus my discussions of e-cigarettes on its potential to either increase or reduce tobacco smoking within the population. I was born and grew up in Nigeria where the smoking rates for the population are relatively low (4.1%)(35) in comparison to the US (12.5%)(26) and the UK (13.3%)(29). In my personal experience, smokers in Nigeria are perceived as social deviants and my concept of smoking was that it is a moral failing not to abstain from a risky behaviour. Also, because I have never smoked cigarettes, I cannot fully appreciate how hard it is to quit smoking. This meant that, at the start of my PhD, my position was that stopping smoking was something within the willpower of smokers; therefore, enforcing strict tobacco control measures, such as banning cigarettes, would incentivize smokers to stop smoking. When I began to immerse myself in the literature, however, I soon realised that smoking was an addiction not easily stopped by willpower alone. Then I became more receptive to the concept of 'harm reduction' and the potential role e-cigarettes could play in smoking cessation as a harm reduction strategy. At this point, my positionality on the topic had changed from tobacco control through promoting 'restriction of use', to tobacco control through 'harm reduction'. Although review of available literature was the main influence of my positionality, there are other factors that may have passively biased the literature I was exposed to, and how I interpreted the literature. These factors including the positionality of members of my research supervisory team, and interaction with researchers in my research environment.

Two of the three members of my supervisory team – Dr Richard Holliday and Professor Elaine McColl – can be said to have a pro- e-cigarette position or opinion on the role of e-

cigarettes in public Health. They are co-chief investigators for ENHANCE-D – a large NIHR funded trial of the role of e-cigarettes and NRT in smoking cessation in general dental practice and have contributed to a Cochrane Review on interventions for tobacco cessation delivered by dental professionals (219). In their article titled 'Vaping and oral health – an update for the dental team' they conclude that e-cigarettes have a good evidence base to support them as an effective smoking cessation aid for tobacco smokers, and that smokers can expect to see substantial improvements in their oral health if they fully switch to an e-cigarette (220). The other member of my supervisory team, Dr Colin Millard, is a medical anthropologist with expertise in regulation of medicinal products. It is possible that, through interaction with my supervisors and their recommendations on some literature to consider during my research, I may have been biased in my positionality on the role e-cigarettes plays in public health, and the theoretical underpinnings used to address the regulatory issues in my research.

With respect to my research environment, I am based in the Population Health Sciences Institute at Newcastle University, United Kingdom (UK). Because my research environment is the UK, it is likely that most of the researchers I encounter and the public health advice within the country may also have influenced my research positionality. In the UK, most Public Health organisations, including the Office for Health Improvement and Disparities (OHID) and Action for Smoking and Health (ASH), promote the use of e-cigarettes for smoking cessation. At the time of completing my PhD, I was working as a Research Assistant on the ENHANCE-D study referred to above, and I regularly participate in e-cigarette summit conference and e-cigarette research forum meetings organised within the UK. It is possible that the way I analyse and interpret my findings may reflect influence of these events and organisations' guidance on e-cigarettes.

Chapter 3. Factors Influencing E-Cigarette Regulation and Policies in the US and the UK (Study One)

3.1 Introduction

In this chapter I address the second objective of this PhD project, which is to 'Explore the determining factors of the policies and regulation of e-cigarette in the US and the UK'. I begin with elaboration of the purpose of 'Objective 2' (see Section 1.3) of this PhD project and highlight the methods chosen to address the above objective. I then present the findings and discuss the implications of those findings for this PhD project.

Although the US and the UK e-cigarette regulations generally permit the use and sale of e-cigarettes (albeit with caveats and restrictions that vary between the two countries and, in some respects, across states of the US and nations of the UK), there are differences in their overall policy approaches to e-cigarettes and the public health implications thereof. The US largely concerns itself with e-cigarette uptake by young people who would not otherwise smoke, and frames e-cigarettes as posing a risk to non-smoking children and young people (i.e., postulates that they act as a gateway product) (83). By contrast, the UK focuses primarily on existing tobacco smokers and is concerned with reducing smoking prevalence by helping tobacco smokers to reduce consumption or, ideally, to quit smoking through the use of e-cigarettes (82).

As discussed in section 1.7, US's CDC claims that e-cigarettes are harmful especially to adolescents, while UK's PHE claimed that e-cigarettes are safer than tobacco cigarettes. The UK National Institute for Health and Care Excellence (NICE) has also partially updated its guidelines to include the use of e-cigarettes as a tool for smoking cessation in current smokers (221). In this case of two countries (US and UK) with divergent views on the role of e-cigarettes in influencing smoking rates (i.e., the US argues that e-cigarettes are driving smoking rates up by serving as a gateway to smoking, while the UK argues that e-cigarettes are driving smoking rates down by serving as an effective smoking cessation tool), there are likely to be contextual factors that have influenced their respective positions, underpinning the differences in policy approaches.

In my research, I therefore sought to undertake in-depth interviews with key policy makers, health organizations and stakeholders from the US and UK. These included the US Federal Food and Drug Agency (FDA) – Centre for Tobacco Products (CTP), the UK Department of

Health and Social Care (DHSC), the UK Medicines and Healthcare products Regulatory Agency (MHRA), Public Health England (PHE) and NHS Health Scotland, all of whom were involved in e-cigarette regulation and public health policymaking. In this way, I aimed to gain insight into what happened behind the scenes and regarding the rationale for policy decisions, to understand the determinants of their respective policy and regulatory approaches. I present below the methods used for this strand of study.

3.2 Methods used in study one

The second objective of this PhD research project was to 'Explore the determining factors to the policies and regulation of e-cigarette in the US and the UK'. I wanted to gain an in-depth understanding of how regulators and stakeholders went about their decision making and regulation, so I planned a qualitative interview of key stakeholders. A qualitative approach is relevant because it can generate data that is both flexible and sensitive to the social context in which the data is produced. It gives the participants opportunity to express themselves about the topic without restrictions and thereby it provides an in-depth source of information. Because I planned to develop my own framework on the factors influencing e-cigarette regulation in the specific context of the US and the UK, I decided to use a thematic inductive approach in analysis of the data (see section 3.2.1 below). This approach ensured that I was as open as possible to identifying any factor that influenced e-cigarette regulations, as opposed to using preconceived notions or existing frameworks to code data, since that might have limited the scope of the findings.

Ethical approval was granted by Newcastle University FMS REC (Date: 27/8/2021, Ref: 2202/ 14121 /2020) (see Appendix B), and informed verbal consent was sought from participants prior to commencing the interviews. In consultation with my supervisors, I identified prospective interviewees from a range of key e-cigarette policy makers and stakeholders in the UK and the US, using a purposive sampling technique. Purposive sampling was used here because it is appropriate for easy identification of participants based on those best suited to provide the needed information (222).

With regards to UK data collection, different organizations and government agencies were named as competent authorities for different aspects of the TRPR (UK e-cigarette regulation) i.e., MHRA was (and still is) the named competent authority for Part 6 (notification of new e-

cigarette products); DHSC was (and still is) the named competent authority for Part 7 (advertisement of e-cigarettes); and PHE was the named competent authority for Part 8 (cross-border distance sales of e-cigarettes, i.e. sales from a UK producer to consumers outside the UK or from producers outside the UK to UK consumers, but not including sales between the nations of the UK). (With the abolition of PHE, Office for Health Improvement and Disparities (OHID) is now the competent authority for Part 8.) Therefore, I approached MHRA, DHSC and PHE for an interview, but was only able to secure interviews with representatives of DHSC and PHE respectively. A previous qualitative interview study of stakeholders involved in policy introduction and enforcement and implementation of e-cigarette regulation in Wales, Scotland and England through the EU TPD suggested that the devolved nature of some aspects of tobacco control within the UK nations meant that it was theoretically possible that the individual nations took different approaches to tobacco and e-cigarette policy (80). Therefore, I also approached NHS Health Scotland, Public Health Wales, and the Public Health Agency (Northern Ireland) for an interview to find out if and how the devolved administrations contributed towards the TRPR but was only able to secure an interview with a representative of NHS Health Scotland. I also interviewed a Member of the European Parliament (MEP) who was involved in development of the EU TPD, subsequently transposed to the TRPR in the UK.

With respect to US data collection, the department within the FDA that is responsible for tobacco products is the Centre for Tobacco Products (CTP). Therefore, to understand the Influential factors to e-cigarette regulation and policies in the context of the US, I attempted to interview representatives of FDA's CTP. The CTP responded to my email invitation providing links to resources for me to read on the FDA's role in e-cigarette regulation but did not identify nor put me in contact with a member of their staff for me to interview. The linked resources were internet pages related to FDA's official rulemaking process and announcements (for example: https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/fdas-deeming-regulations-e-cigarettes-cigars-and-all-other-tobacco-products#rule and https://www.fda.gov/regulatory-information/fda-rules-and-regulations – (accessed 11/08/2023). The linked resources were reviewed but did not provide any additional information or insight over and above those gained from my review of grey literature as reported in Chapter 1.

Initially, organizations that had been identified were contacted by email with information about the study and a request for assistance to identify participants best suited to provide the needed information from within the organization. In some instances, when response to the initial email was prolonged i.e., more than 4 weeks for feedback, I worked with my supervisors to use professional networks to identify specific named individuals from within those organizations who could be contacted to facilitate a response. After the participants were identified, an invitation was sent via email with information on myself as the researcher, the rationale and the objectives of the study, and duration of the interview. The email also included the topic guide, participant information sheet (see Appendix G) and consent form (see Appendix H), to give the participant sufficient detail of the study to make an informed decision on participation. When participants confirmed their willingness to participate, a suitable place and time was agreed via email correspondence. After agreeing to participate in the study, a calendar invitation was sent to the participants to confirm the interview time. The topic guide was also sent to participants to allow them time to reflect on events during the regulatory period. As interviews took place in 2022, about six years after regulation in 2016, there was a risk that participants might not be able to recall the events quickly or completely. Allowing them time to reflect could help them generate more detailed responses to interview questions. Only one interviewee per organization was recruited for the study due to lack of additional interested participants. A snowballing technique was used to invite some participants from other organizations by re-contacting interviewed participants and asking them to suggest other people who would be potentially rich sources of the type of data I sought for the study. Alternative approaches considered to recruit participants to my study involved making an in-person approach to targeted organisational representatives at conferences or visiting the organisational offices to locate and invite potential interviewees to my study. Such in-person approaches would have had the advantage of providing an opportunity to discuss my study in more depth and to establish rapport; this might have convinced some potential interviewees to participate in my study. However, COVID social distancing constraints at the time of conducting this study, and the potential financial implications of such an approach (i.e., traveling to multiple locations including outside the UK) precluded the use of this approach to recruitment.

I conducted all the interviews virtually using the Zoom facility, as this was convenient for the participants, giving them the opportunity to choose their own space and time to participate.

A topic guide was used to ensure that I did not deviate significantly from the subject, thereby ensuring quality. The topic guide was not identical for all interviews but rather was tailored to the context of the role of the organization in e-cigarette regulation. However, all the questions related to the overarching question of what factors influenced the regulation of e-cigarettes in the US or the UK respectively. The interviews lasted between 30 – 70 minutes. They were audio recorded after consent had been sought. An audio recording was utilized to enable maximum capture of verbal data, thereby ensuring research quality. I also made field notes to record tone of voice. Interviews were conducted between February to November 2022 for the UK participants. I was unable to interview any potential US participant as none of the organisations I contacted agreed to participate in an interview.

As a contingency, due to the difficulty with recruitment of participants to the interview element of the study, I identified and collated secondary data to be analysed in addition to the interviews. The secondary data comprised transcripts of recorded audio presentations from the organizations with which I was unable to secure an interview. These presentations, which were available online in the public domain (See Previous Summit Videos/presentations – The E-Cigarette Summit UK, 2022 (e-cigarette-summit.co.uk – accessed 11/08/2023), were delivered officially by representatives of these organizations at the e-cigarette conference held annually (from November 2013) in parallel in the UK and the US and entitled 'E-cigarette Summit: Science, Regulation and Public Health'. This conference series was selected for two main reasons. Firstly, because it was held in parallel in both the US and the UK, the two countries from which I was collecting data for my research. Secondly, because one of the conference's foci was on regulation of e-cigarettes, a topic central to my PhD study. I screened 327 archived summit videos to identify nine presentations, one Q&A session and one panel discussion that involved the relevant organizations and were related to e-cigarette regulation. The eligibility criterion for selecting the presentations was that the talk was delivered by a representative of one of the organizations of interest i.e., an organization for which I could not obtain an interview but had been determined from the outset as a relevant e-cigarette regulatory stakeholder. From the UK, I selected presentations by: MHRA – the organization responsible for e-cigarette notification scheme across the whole of the UK; Trading Standards – the organization responsible for local enforcement of the TRPR; the Advertising Standards Authority – the body responsible for advertising enforcement in the UK; and the House of Commons Science and Technology

Select Committee, which carried out an independent inquiry on e-cigarettes for the UK government prior to regulation of e-cigarettes. As a substitute to interviewing CTP representatives on regulation of e-cigarettes, the audio component of CTP presentations from the E-cigarette Summit were transcribed and used to identify factors that influenced e-cigarette regulations in the US. One of the selected 11 videos was a panel group discussion, and another was a Question and Answer (Q&A) session in the summit, but both involved at least one representative of one of the US organizations listed above. Only the contributions of such representatives within the panel group or Q&A were extracted for analysis.

3.2.1 Thematic analysis

Thematic analysis is a method for identifying, analysing, organizing, describing, and reporting themes found within a data set (223). Thematic analysis was used in all three component empirical studies of this PhD project. It was carried out using the six-step process both described in 2006 (223) and updated in 2019 (224) by Virginia Braun and Victoria Clarke.

Firstly, I familiarized myself with the data by reading the documents or transcripts several times and correcting auto-transcription errors in transcripts.

Secondly, I coded each document or transcript (applied a paraphrase or label that describes the interpretation) using 'open coding', i.e., coding anything that might be relevant from as many different perspectives as possible. NVivo software was used to carry out this task, because it has the advantage of managing large sets of text. The codes were refined, and a list of latent/interpretative codes were generated. For example, in this study one, responses of UK interviewees that contained 'TPD regulations' were grouped under a code named – 'TPD'. I then refined the code to 'legal obligations' after reading through the sentences in the group and determined that interviewees were suggesting that the UK were legally obliged to transpose the TPD to UK law. An interpretative code was used because this approach examines the underlying ideas and assumptions that are theorized as shaping or informing the semantic content of the data (223).

Thirdly, themes were generated by mapping out codes and finding relationships between codes to establish a commonality. For example, 'legal obligation' as a code was mapped together with 'conventions'- another interpretative code that described the UK's convention

of protecting regulators from industry influence or lobbying when regulating tobacco and related products, in order to uphold the UK's commitment to WHO FCTC. The commonality between the two codes was that both the UK's 'legal obligation' and 'conventions' were external commitments that the UK had when considering e-cigarette regulations. Therefore, the theme generated from mapping out these codes was called 'Nature of e-cigarette regulation.' The theme described the nature of e-cigarette as a tobacco related product that made it subject to the TPD and FCTC.

Fourthly, the themes generated were further reviewed and refined to broaden or narrow their scope depending on the emanating concepts. For example, 'Nature of e-cigarette regulation' as a theme was refined by broadening the scope and renamed it 'Existing regulatory framework.'

Fifthly, themes were defined and named in relation to their importance in answering the research questions. For example, 'Existing regulatory framework' was defined as all the existing regulations and guiding principles that were existing at the time of e-cigarette regulation and were factored into the regulatory process. In other words, 'Existing regulatory framework' was a factor identified as influencing e-cigarette regulations in the UK, thereby answering the question of 'what factors influenced e-cigarette regulations in the US and the UK? Draft themes were discussed with my supervisors who independently examined the data findings by comparing it to selected transcripts to confirm whether the themes were valid and plausible. The themes were then revised and validated by all members of the supervisory team.

Finally, a 'key concepts' analytic framework was used to present the findings. The six step process recommended by Braun and Clarke (223) and described above are summarized in Figure 6 below.

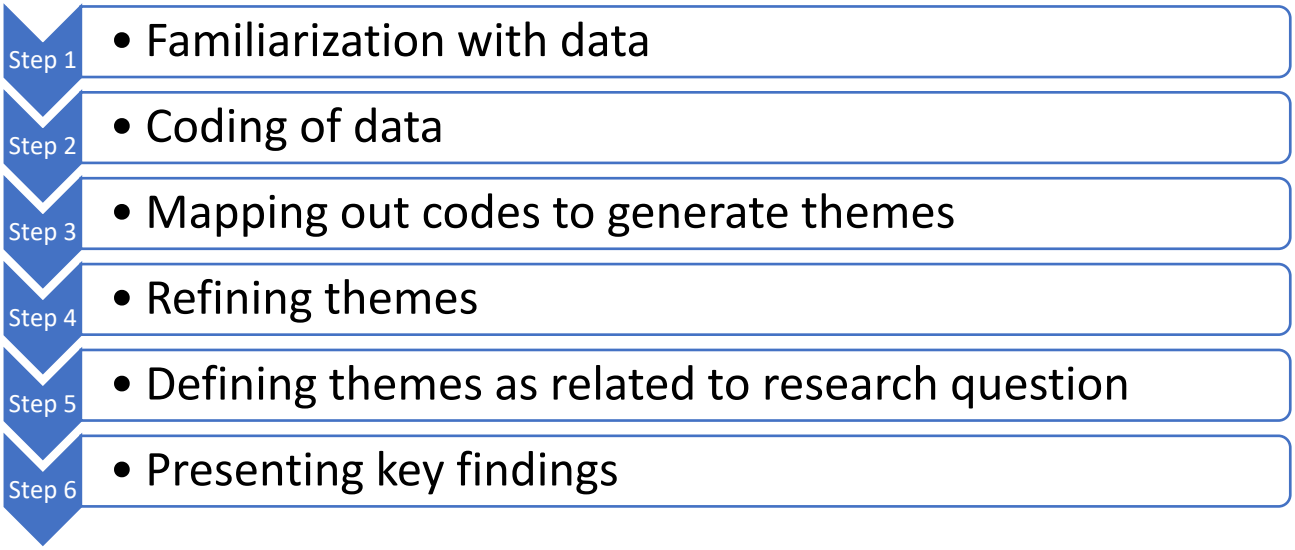


Figure 6: Braun and Clarke's six step process for conducting Thematic Analysis.

A thematic analysis can use either a data-driven, inductive approach where the researcher derives their codes from the data by allowing the narrative or theory to emerge from the raw data itself (225) or a deductive approach where the researcher starts the analysis with some preconceived themes they expect to find reflected there (i.e. an *a priori* template of codes), informed by theory or existing knowledge (226), or indeed a combination of both (abductive thematic analysis)(227). Inductive thematic analysis was used in all the component studies of this PhD project because it allowed me to apply a flexible approach to identify as many themes present in the data.

3.3 Findings from study one

The thematic analysis identified three interrelated factors (see Figure 7) that appear to have influenced e-cigarette regulation in the US and the UK. These factors are discussed below as significant themes. The interviewees who contributed to the data collected and analyzed are listed below in Table 12**.**

Country	Organisation	Code	Data source	Date produced
US	NJOY – Chief Impact Officer	NJOY-R	Summit video	26/5/2021
US	FDA Centre for Tobacco Products (CTP)- Director	CTP-D	Summit video	30/4/2018
US	FDA CTP – Office of Science (Director)	CTP-S	Summit video	26/5/2021
US	FDA CTP – Office of Health Communication and Education (Director)	CTP-HCE	Summit video	25/5/2021
UK	Department of Health and Social Care (DHSC)	DHSC-R	Interview	4/3/2022
UK	Public Health England (PHE)	PHE-R	Interview	23/2/2022
UK	NHS Health Scotland	NHS-SR	Interview	16/3/2022
UK	European Parliament (Member)	MEP-R	Interview	2/11/2022
UK	Medicines and Healthcare Regulatory Agency (MHRA)- E-cigarette Notification Scheme Lead	MHRA-1	Summit video	17/11/2017
UK	MHRA- Vigilance and Risk Management of Medicines (E-cigarette Unit Manager)	MHRA-2	Summit video	7/12/2021
UK	Trading Standards- Co-ordinator for Northwest region and member of DHSC National Tobacco Focus Group	TS-R	Summit video	7/12/2021
UK	House of Commons Science and Technology Select Committee- Chairperson	HCC-R	Summit video	15/11/2018
UK	Advertising Standards Authority (ASA)- Senior Regulatory Policy Executive	ASA-R	Summit video	17/11/2017

Table 12: List of US and UK Interviewees for data collection and analysis

N/B: NJOY is the name of an e-cigarette brand.

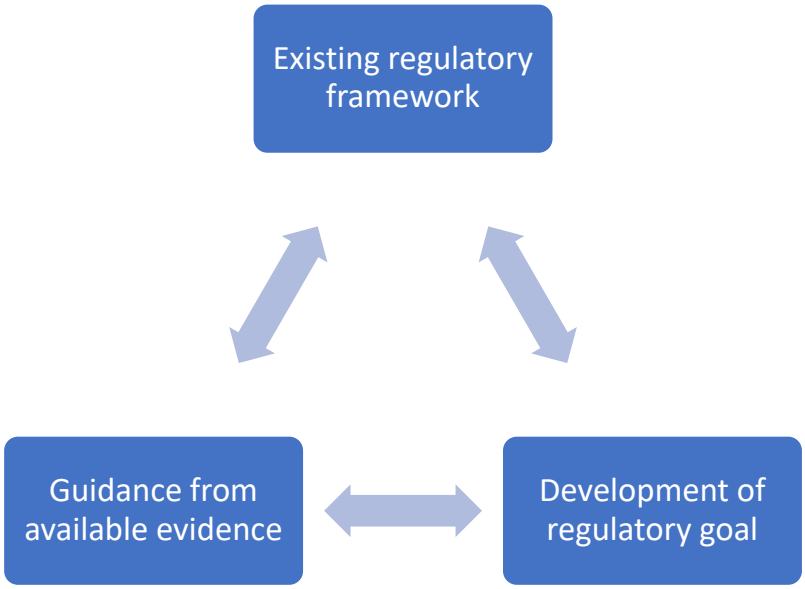


Figure 7: Thematic map of relationship between factors influencing e-cigarette regulations in the US and the UK.

3.3.1 Factors influencing e-cigarette regulations and policies in the UK

From the analysis of UK interview transcripts, three major themes were identified namely: existing regulatory framework, guidance from available evidence, and public health considerations. These themes are presented below with supporting quotes.

3.3.1.1 Existing Regulatory framework

Analysis revealed that the availability of existing regulatory framework in the UK played a role in how e-cigarette regulations were drafted in the UK. In the UK, when e-cigarettes were to be regulated in 2016, the regulation was not developed *ab initio*; rather the majority of the regulation was a direct transposition of an EU directive into UK law. A representative of the DHSC (subsequently referred to herein as DHSC-R) confirmed that:

> *'It was a directive out there and we have to transpose it into UK law, and we did that mainly through the Tobacco Related Products Regulations. Just as the letter of the law we transpose the directives there and we then need to convert that into our interpretation of UK law.'* (DHSC-R, 2022)

Note that the DHSC led the transposition process of TPD to TRPR in the UK. See Appendix A for comparison of the TPD to the transposed TRPR. The DHSC-R also suggested that the TPD

constrained the UK from completely free choice of what it could or could not do with regards e-cigarette regulation. For instance, the DHSC-R stated:

> *'We can't change it because that's what the EU has told us to do. It's set in stone. It's in the directive. So for example, and if we said, we are doing the nicotine concentration limits at 24 milligrams per ml, that's a breach of EU law, so we can't you know, we could have got taken to court or stuff, so we said what the EU said, 20 milligrams per ml and so lots of it was kind of set in stone if you like, so we didn't have much leeway, if you like.'* (DHSC-R, 2022)

Analysis of interview transcripts showed that the transposition of TPD to TRPR had some drawbacks. For instance, the notification scheme requires products to be notified but there is no requirement to verify the notified products. As the MHRA's E-cigarette Notification Scheme Lead (referred to here as MHRA-1) stated:

> *'It's a notification scheme, so we are relying on the declarations of conformity made by the manufacturer, the importer or the re-brander who notifies the products, that their product complies with all the legal requirements. And, once we've done a number of checks then we publish the information on the notification on our website'* (MHRA-1, 2017)

Note that the checks referred to in MHRA-1's statement above do not involve any independent testing by MHRA itself to verify information; rather they take the form of a review by MHRA of information, as reported by the manufacturer or importer, to confirm whether the products meet the requirements of the regulation. MHRA-2 mentioned this process when they said:

> *'We look at the completeness of the information such as dosage for nicotine, toxicology information and ingredients. At the end of that process, we can then go ahead and publish, on our website. Once that product has been published, it is considered a notified product, and that, at that stage can it be legally supplied in Great Britain.'* (MHRA-2, 2021)

PHE-R felt that lack of independent testing was a drawback to regulation of e-cigarettes. PHE-R's statement was that:

> *'It seems to me that we just, you know, accept whatever the manufacturers tell us in the same way that the MHRA don't do independent testing of the E-cigarette products notified to them…. It's meaningless unless you're going to dedicate the resources to scrutinize this stuff.'* (PHE-R, 2022)

A Member of the European Parliament (hereafter referred to as MEP-R) insisted that there was some leeway for European member countries to implement certain aspects of the TPD differently. MEP-R, who was involved with bringing the TPD into European law, alluded to this when they said:

> *'So, the legislation in European level, you see—the way it works is some legislation is directly—you know is direct transposition, there is a law, every country does the same, but this is a directive—an EU directive—which means that it has to be transposed in Governments and there is some leeway sometimes… to interpret certain parts and do different things. So, I'm guessing that in different countries it was implemented differently.* (MEP-R, 2022)

Note also that the UK had voting rights as an EU member state and so were part of original decision-making regarding the TPD. The DHSC represented the UK in the European Council of Ministers who shared responsibility with the Members of European Parliament for decision-making with respect to the TPD. The DHSC-R confirmed that the UK voted for the TPD when they said:

> *'We can do some stuff and I think some people think the EU stops us from doing something, they didn't really, I guess, as a Member State, we were, we voted for the Eus TPD.'* (DHSC-R, 2022)

In the post-BREXIT era, the TPD that governs products in EU member states remained applicable to NI in the UK, and so existing regulatory framework continued to influence e-cigarette regulation in the UK. The DHSC-R alluded to this when they stated that:

> *'It's quite interesting in kind of a new world that the EU still has control of Northern Ireland, because they have to comply with TPD, so if the EU changes the TPD in years to come, which it probably will do, just like we might want to change some stuff, we have to be careful of what we can do or can't do in Northern Ireland.'* (DHSC-R, 2022)

This meant that post-BREXIT, the UK has had to develop mechanisms to ensure that they continue to adhere to the TPD within Northern Ireland. The E-cigarette Unit Manager at MHRA (referred to here as MHRA-2) hinted on this when they said:

> *'During the past few years, we developed a portal to meet the requirements of leaving the EU, whilst maintaining our delivery of the notification process, ensuring we could meet separate reporting functions required under the Northern Ireland protocol.'* (MHRA-2, 2021)

Another existing regulatory framework that played a role in e-cigarette regulation in the UK is the WHO framework Convention on Tobacco Control (FCTC) which demands that member countries take measures to prevent tobacco companies from unduly influencing tobacco related regulations and policies. PHE-R suggested that the UK exercised caution in dealing with industry to prevent influence of commercial vested interests. PHE-R gave insight into this in their statement that:

'It was pretty clear that commercial vested interests were not limited to tobacco industry, and the pharmaceutical industry was lobbying extensively, and I would say aggressively on the e-cigarette issue, trying to seek a maximum, all kind of regulation. Trying to protect the commercial best interests. So, you may know they make a lot of money from over the counter or used to make all their money from over-the-counter nicotine replacement therapy; with the rival e-cigarettes it dropped off really quite dramatically. They wanted that back, they wanted to constrain sales of e-cigarettes as much as possible and so they did some work on that. Including, I think funding academics to do studies that were transparently, I mean, I remember being interviewed by one professor, who said that they received funding from a major pharmaceutical company to you know, to highlight the dangers to society of e-cigarette.' (PHE-R, 2022)

PHE-R's statement shows that there were three competing business interests – the e-cigarette, tobacco, and pharmaceutical industries – all seeking to influence regulations in their favour. MEP-R revealed that, even during the regulatory process of the TPD (which was transposed to UK law in the TRPR), e-cigarette companies were said to have aggressively lobbied for their interest in the outcome of e-cigarette regulation. MEP-R said that:

'The E-Cigarette lobby became very aggressive and very vocal, towards the end of the legislation…. E-cigarette companies were pretty—it's interesting, they created a kind of community of E-Cigarette Users, who became very aggressive in their lobbying tactics. And I mean they made threats to people. My—it was the beginning of social media and I have to say it got very very abusive—I mean, totally misinformed, saying that we were trying to ban E-cigarettes on the market which was never true.' (MEP-R, 2022)

Other existing regulations within the UK that influenced some aspects of e-cigarette regulation includes the Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015, and Classification, Labelling and Packaging of Substances and Mixtures Regulation 2008. DHSC-R and TS-R hinted that existing regulations were adopted in transposing the TPD into the TRPR when they stated respectively that:

'I think TPD allowed if you wish, to bring in age of sales in there, so we implemented age of sale through the nicotine inhaled products, age of sale proxies' sale regulations 2015.' (DHSC-R, 2022)

'The next piece of legislation which applies, are what we call the CLP regulations—Classification, Labelling and Packaging—of substances and mixtures. And like the Tobacco and Related Products regulations, these are derived from EU law, and are now completely transposed into UK law. So, these apply for some products, not all. These insist on having supplier details on the product, and there are various—depending on what it is—hazard warnings and pictograms, I've put a couple in the slide that you may recognize. Tactile warnings, child proof closures. Now the Health and Safety Executive are responsible for enforcement of these regulations, at the manufacturer and

importer, and Trading Standards are responsible at retail. Apart from, for some parts of the CLP regulations—such as tactile warnings—Trading Standards are responsible throughout the supply chain.' (TS-R, 2021)

While the TPD as an existing regulatory framework laid the foundation for the UK's approach to regulation of e-cigarettes and effectively constrained the level of changes that could be made to e-cigarette regulation in the UK, it did not totally limit the UK from bringing in or applying further regulations. Existing regulations and guidance such as the WHO FCTC, Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015, and Classification, Labelling and Packaging of Substances and Mixtures Regulation 2008, were used to introduce further e-cigarette regulations.

3.3.1.2 Guidance from available evidence

Analysis of interview transcripts revealed that at the time of developing e-cigarette regulation in the UK, there was already a perspective among public health organizations and the government that e-cigarettes had a potential to aid smoking cessation. This perspective was informed by research evidence as, arguably, are most regulatory decisions in the UK. The HCC-R hinted this when they stated that:

'Our job also is to scrutinize government, to challenge and to make recommendations for change. And to do this we gather evidence from people such as yourselves, as well as from government, public bodies, academics, professionals, and many others. The work is strictly evidence related.' (HCC-R, 2018)

They elaborated on how research evidence was the basis for their recommendation to the government on e-cigarettes:

'We recently produced our report with clear recommendations to the government, on E-Cigarettes. We wanted to look at E-Cigarettes as we knew that nearly three million people now in the UK are using them and that they were seen, by many as a valuable stop smoking tool. But did their use have an evidence base, that was the question that we asked ourselves.' (HCC-R, 2018)

The DHSC-R also hinted that the DHSC's perspective on e-cigarettes were formed through interpretation of research evidence:

> *'We know it's* (vaping) *helping some smokers quit and they're* (e-cigarettes) *more effective than NRT* (Nicotine Replacement Therapy) *in doing it in some studies.'* (DHSC-R, 2022)

The NHS-SR had a different interpretation of the research evidence on e-cigarettes but also suggested that the research evidence was a factor informing the organization's position on e-cigarettes i.e., not recommending e-cigarettes to the Scottish public. This can be seen in their statement:

> *'The evidence for their* (e-cigarettes) *effectiveness as a smoking cessation tool was really uncertain, so we didn't feel confident that you could say, and should recommend and we still don't recommend e-cigarettes to people.'* (NHS-SR, 2022)

NHS-SR suggested that NHS Health Scotland were not of the same view as PHE with regards e-cigarette's potential for smoking cessation when they said:

> *'So, I think that Public Health England were of the view that e-cigarettes were something which could be used for smoking cessation. Whereas we felt that the evidence for that was [pause] certainly at that point, and I can't speak to it anymore, because I don't know. But the evidence for their effectiveness as a smoking cessation tool was really uncertain, so we didn't feel confident that you could say, and should recommend and we still don't recommend e-cigarettes to people.'* (NHS-SR, 2022)

With this contrast of views, the Scottish Government were more cautious with e-cigarette regulations. For instance, the Senior Regulatory Policy Executive of the Advertising Standards Authority (referred to here as ASA-R) revealed that the Scottish Government had (in 2021) proposed to ban all e-cigarette advertising when they said:

> *'As some of you may know, the year before last, beginning of last year perhaps, Scottish Parliament passed the Health Act, empowers ministers to ban all E-Cigarettes—all E-Cigarette advertising bar point of sale. So that's all the stuff for nicotine and non-nicotine products alike that's not already banned by the TPD. Whether they will go ahead and do this is still an open question. We've had various conversations with the Scottish Government about it. They are thinking I know, about whether that prohibition is required, maybe whether some other kind of content control is required.'* (ASA-R, 2017)

These sort of contrasting views on e-cigarettes had also been present during development of the TPD, resulting in calls for e-cigarettes to be taken out of the TPD. The MEP-R alluded to this when they said:

> *'There was talk at one point of stripping out the E-cigarettes part, but I think that would have jeopardized the whole legislation, so we—that's why we made the compromise. I met top doctors who were public health professionals who were very against E-cigarettes, I met ones who were very in favour of E-*

cigarettes because they help stop people smoking tobacco and tobacco is really bad for you. So, it felt like we didn't have the evidence.' (MEP-R, 2022)

The contrasting views were felt to be related to paucity of evidence for effective regulation at that time. The DHSC-R also spoke about the difficulty of regulating e-cigarettes with the limited availability of information about the product, when they mentioned that:

'*The e-cigarette work, if you like, that was always difficult because it was a new world that no one really knew about, so I think there were lots of regulations, stuff with kind of future proofing a little bit, but without knowing too much about that world, it's probably fair to say that.'* (DHSC-R, 2022)

The variable interpretation of evidence led to varying and sometimes polemic views about e-cigarettes. Stakeholders held strong and contrasting views about e-cigarettes, which affected e-cigarette regulations by influencing the actions of regulators. For instance, the Chair of the House of Commons Science and Technology Select Committee (referred to here as HCC-R), which carried out an inquiry into e-cigarettes to inform policymaking, stated that:

'I would not personally support any proposal which permitted use of E-Cigarettes on public transport. You'd have an enormous public backlash to it, specifically because people find the smell of many vapours unpleasant and intrusive. And I can tell you—from witnessing the extraordinary explosion of anger and angst on social media on the day we published our report—largely because the BBC showed graphics of people vaping on a bus—which carried with it the implication that that's what we were recommending, but it just demonstrated how strong people's views are on this.' (HCC-R, 2018)

NHS-SR, who also shied from involvement with e-cigarette regulations, stated that:

'In general, we had less to do with that. I mean, we had colleagues in PHE who I knew, but we didn't tend to. It was such a sort of polarized debate that I didn't really want to get into big discussions with them about e-cigarettes, because there were people literally falling out who had worked together for decades. So, I didn't want to get into that situation, and I wasn't entirely sure of their views, and I also did that with other people who were very anti e-cigarettes.' (NHS-SR, 2022)

There were general suggestions that the unavailability of sufficient information affected the potential of e-cigarette regulations at the time and might necessitate a review and revision at a later date, in light of newer or more information. These suggestions can be seen in DHSC-R's statements that:

'We could strengthen those areas of regulation; everyone's kind of thinking about that, because lots of things we decided before we knew.' (DHSC-R, 2022)

'I would like to say we will be pushing our post implementation review hopefully very soon.' (DHSC-R, 2022)

3.3.1.3 Public health considerations

Data analysis showed that public health considerations influenced how e-cigarettes were regulated in the UK. In the UK, the perspective that e-cigarettes have a potential for smoking cessation was a dominant narrative when the legislative arm of government (represented in this case by the House of Common Science and Technology Select Committee) sought to look at the evidence base to inform e-cigarette regulations. Indeed, it was so dominant that they were particularly focused on e-cigarettes' potential for smoking cessation. The HCC-R suggested this when they said:

> *'Our job is to look at the evidence on a whole range of issues, including in this case, E-Cigarettes. And looking in particular also at their potential role in helping people to stop smoking given the extraordinary death toll in this country from smoking related diseases.'* (HCC-R, 2018)

It seems likely to me that an evidence-informed belief that e-cigarettes are effective for smoking cessation would encourage regulation in a way that does not hinder adults who are trying to quit smoking from accessing e-cigarettes. Hints of this can be seen from statements from the DHSC-R, HCC-R and MHRA-2 respectively:

> *'We do, promote e-cigarettes, as the UK Government with smokers asked to switch* (to e-cigarettes)*. We know they're not risk free, but they are less risky than smoking,'* (DHSC-R, 20)

> *'If we want to reduce the number of people who smoke conventional cigarettes, we need to have the right regulatory and tax environment in order to achieve that.' (HCC-R, 2018)*

> *'So, we're seeking to encourage licensing of E-Cigarettes for medical use, and for quit smoking.'* (MHRA-2, 2021)

PHE-R further confirmed that the e-cigarette regulators actively regulated e-cigarettes in a way that promotes use of the product as a stop smoking tool. This confirmation can be seen in their statement:

> '*We the British health or the English health system, you know, the DHSC have already come to the view that e-cigarettes were likely helpful for smoking cessation, and we did not want regulations which prevented health groups from recommending that smokers switch.'* (PHE-R, 2022)

Another dominant public health consideration in the UK was how to prevent the appeal of e-cigarettes to youth. The DHSC-R stated that:

> *'We got in there early and regulated to stop where youth use might be appealing, same with the banning in mass media and nicotine strengths.*' (DHSC-R, 2022)

The Advertising Standards Authority (ASA), who seem to have worked collaboratively with the DHSC on reducing the appeal of e-cigarettes, confirmed in their statement that:

> *'In 2014, or 2013/2014 we were hearing huge concerns from people across—from all stakeholders about how E-Cigarettes were being advertised. In 2014 we implemented sector specific rules, focused on the protection of kids. Not targeting non-smokers and non-vapers, and controlling where ads would be placed, to keep them away from young people.'* (ASA-R, 2017)

Concerns such as the appeal of e-cigarettes to youths prompted the governments' commitment to annual reviews of e-cigarettes so that any problem with their use could be identified in a timely manner to inform required regulatory action. The DHSC-R confirmed this when they stated that they made:

> '*A commitment to monitor the evidence of e-cigarettes, to assess if they're effective, any dangers, any problems, and PHE obviously expanding now, but before that was still carrying on, but we did annual reviews to assess that, if you like, and it's very thorough annual reviews.'* (DHSC-R, 2022)

The DHSC were not the only organization committed to monitoring e-cigarettes. The MHRA also has their own mechanism in the form of the Yellow Card Scheme which they use in monitoring the safety of e-cigarette use in respect of adverse effects (the scheme is also used to monitor adverse effects of medicinal products). An MHRA interviewee confirmed this when they stated:

> *'What we have said we did—we would do then and are doing now is concentrating on safety in use. We set up—at the implementation of the scheme—the facility to provide adverse event reporting about E-Cigarettes on our existing yellow card reporting portal that works with medicines and devices.'* (MHRA-1, 2017)

The Yellow Card Scheme was not the only tool adopted by the MHRA to ensure safety of e-cigarettes. The MHRA also committed to efforts to encourage manufacturers to use the medicinal routes to bring e-cigarettes into the market so they could assure the public that such products are safe. The HCC-R highlighted this in their statement:

> *'In the 2017 tobacco control plan for England, the MHRA committed to ensuring, and I quote, 'That the route to medicinal regulation for E-Cigarette products is fit for purpose, so that a range of safe and effective products can potentially be made available for NHS prescription'.* (HCC-R, 2018)

However, it appears that, from the outset, e-cigarette manufacturers have been reluctant to take the medicinal products route to bringing e-cigarettes to the market. The MEP-R alluded to this when they mentioned that-

> *'The Governments of Europe, some of them wanted to go further, and have every E-Cigarette authorized like a pharmaceutical product. And so would have to go through, a supervised—by the MHRA in the UK—that would mean, and they wouldn't be able—they would not be allowed to be placed on the market unless they had gone through this approval path. Whereas the E-cigarette companies, were absolutely against that. They wanted to be on the market as free products. And in the end a kind of compromise was reached.' (MEP-R, 2022)*

The ASA-R also elaborated on how the prohibition of health claims about e-cigarettes were put into regulations as a contingency due to the variability in safety and quality of e-cigarettes at the time, and because no manufacturer or distributor had chosen to go down the medicinal route, which would be essential to making a clinical benefit claim:

> *'Those rules also contain a prohibition on health claim—pardon me, on medicinal claims—reflecting the law. Which means they can't make smoking cessation reduction claims unless they have a medicines license. Those rules also prohibit health claims, which includes claims about products being safer or are healthier than tobacco. That was something that we put in place in 2014, because of very real concerns that we were hearing at that time about the variability, products on the market in terms of their quality and safety. And we didn't think at that time that the ASA was going to be reasonably able to make those kinds of distinctions on an individual product basis. Clearly—for all the reasons that you know, we're talking about today—the sector has moved on. We did some fact-finding work on this last year, and this year we've consulted on a proposal to remove that prohibition.'* (ASA-R, 2017)

The notification requirements of the TRPR also served as a safety net to prevent use of products that have not been assessed by MHRA. Because of the notification requirements, e-cigarette users can verify from the MHRA website that the products have been notified before purchasing them and be reassured by this. MHRA-2 alluded to this when they said:

> *'If it's published it can be supplied legally. Consumers can feel good that it's been assessed, they can buy that product. If it's not on that list, that doesn't mean it won't become compliant at some point in the future, but what it does mean is it shouldn't be available for sale.'* (MHRA-2, 2021)

Some other considerations (such as likely economic impacts of e-cigarette regulation) were weighed up against public health considerations during the regulatory process, as is standard procedure within the UK. DHSC-R hinted on such considerations when they said that:

> *'Sometimes you know you will impact the industry, but there is a trade-off of what you're doing to protect the wider public health.'* (DHSC-R, 2022)

It appears that such economic considerations were a requirement when introducing new regulations as was highlighted in a statement by the DHSC-R:

> '*We start to go through formal procedures if you're introducing any regulations, you need to do an impact assessment, assess why you're doing it, in effect, the impact on business.'* (DHSC-R, 2022)

It can be seen from the analysis above that public health considerations were a major factor that influenced e-cigarette regulations in the UK.

3.3.2 Factors influencing e-cigarette regulations and policies in the US

The inductive thematic analysis carried out on data from sources listed above (Table 12) generated three major themes or factors that influenced e-cigarette regulations in the US. These themes are discussed below and illustrated as a thematic map in Figure 6 above.

3.3.2.1 Existing regulatory framework

Analysis of conference presentations revealed that the FDA had regulatory powers over all tobacco products, including e-cigarettes since they meet the statutory definition of tobacco products as defined in the Food, Drug, and Cosmetic Act (FDCA) as amended by the Family Smoking Prevention and Tobacco Control Act (FSPTCA). The Director of FDA's Centre for Tobacco Products (CTP-D) confirmed this when they said: -

> *'You know that the original grant of authority when Congress put the agency in the business of regulating tobacco products in 2009 was for cigarettes, smokeless tobacco, cigarette and roll your own tobacco. And, through the rule making process and the so-called deeming rule—which was finalized in 2016 and began to go into effect in the summer of 2016—we now have regulatory authority over all products that meet that statutory definition of a tobacco product.'* (CTP-D, 2018)

However, the Director of CTP's Office of Science (CTP-S) acknowledged that, albeit that the existing FSPTCA covers e-cigarette products, e-cigarettes are still only partially regulated in the US. CTP-S said: -

> *'Today I want to talk about the e-cigarette marketplace in the United States. As I think you are all well aware, this marketplace is only partially regulated at this*

> *time… And again, I think as you're all well aware, e-cigarettes are currently being marketed in the United States under enforcement discretion* (CTP-S, 2021)

There was also an indication that application of the FSPTCA in immediate regulation of e-cigarettes afforded the FDA some more time to consider and implement further regulatory mechanisms that covered aspects such as exploding batteries and accidental exposure to e-liquids that are not captured in the FSPTCA. This can be seen from a statement by CTP-D:

> *'The commissioner announced an extension of time for newly deemed products that were on the market… this will give us the time to take advantage of the latest science and get the right rules of the road—or as the commissioner likes to call it—the regulatory gates in place, through regulations, guidance, foundational rules… So, product standard authority could be used to explore issues like, exploding batteries and accidental exposure to E-Liquids—the nicotine in E-Liquids… and we are working on finalizing the guidance for the PMTA pathway for ENDS products.'* (CTP-D, 2018)

The above statement revealed the Premarket Tobacco Product Application (PMTA) to be one of the additional regulatory mechanisms to the FSPTCA. This added approach to regulation of e-cigarettes through PMTAs has meant that the e-cigarette manufacturers have had to adjust their compliance strategies along the regulatory journey, which impacted their business or left them uncertain at times. The Chief Impact Officer of one of the e-cigarette companies, NJOY (NJOY-R), alluded to this when they said: -

> *'During this journey, flexibility was key. But given the very long lead-times of many components for a PMTA, we really had to build the plane as it flies, refining the program along the way.'* (NJOY-R, 2021)

It can be seen from the quotes presented above that the availability of an existing regulatory framework for tobacco products i.e., the FSPTCA, was a factor that influenced how e-cigarettes are regulated in the US. However, the FDA considered further regulations to capture aspects of e-cigarette products not covered by FSPTCA, which meant that regulation of e-cigarettes continued after FDA deemed e-cigarettes as a tobacco product and subjected e-cigarettes to the FSPTCA.

3.3.2.2 Guidance from available evidence

In the regulation of e-cigarettes in the US, research evidence on the potential risk and benefits of e-cigarette use to the public's health was considered. One of the most important pieces of research evidence considered by the FDA was the National Academy of Sciences,

Engineering and Medicine (NASEM) report (228) that CTP-D spoke about when they stated that:

> *'In terms of their growing scientific base when it comes to ENDS, there is more and more reporting in the literature. I want to talk a minute about the so-called NASEM E-Cigarette report, that had been commissioned by FDA at the direction of Congress. This was the report by the National Academy of Sciences, Engineering and Medicine. In the charge that we gave the committee, when they began their work, we asked them to evaluate the available scientific literature, on both the short- and long-term health effects on ENDS. And to identify research gaps and make recommendations for future federally funded research. It's a lengthy report, there's an excellent executive summary at the beginning, and just to highlight a few of the key findings from the report, that are contained in that executive summary, the committee concluded that there is substantial evidence that completely switching from regular cigarettes to e-cigarettes, results in reduced short term adverse health outcomes. The committee concluded that there's conclusive evidence that completely switching reduces an individual's exposure to numerous toxicants and carcinogens, compared to continuing to smoke cigarettes. And the committee concluded that there is substantial evidence to suggest that kids and young adults who use E-Cigarettes are more likely to transition to combustible cigarettes.'* (CTP-D, 2018)

As can be seen from the above quote, CTP-D acknowledged that the NASEM report showed evidence of both benefits and harms of e-cigarette use. It is also evident from the presentations by the selected stakeholders that the FDA continues with research to inform their regulatory decisions as they proceed with e-cigarette regulation through other means such as the PMTA. The Director of CTP's Office of Health Communication and Education (CTP-HCE) showed how research evidence is gathered to inform new e-cigarette policies when they said:

> *'In 2020 FDA conducted qualitative research studies, forty-eight focus groups in total. With current adult smokers as well as former cigarette smokers. And in general, we were trying to understand things like, what is the tobacco landscape? How does it look today? How has it changed? How are emerging products like E-Cigarettes really influenced perceptions of smoking as well as perceptions of quitting? Are there differences among different subgroups? And what unique beliefs, attitudes and perceptions pertain around E-Cigarette users.'* (CTP-HCE, 2021)

In terms of e-cigarette policies, research studies, such as those highlighted in the above statement, were identified as being needed to unravel some complexities. For instance, regarding advertising and labelling, as CTP-S alluded to when they said:

> *'Well, you know, as we do with all products that have unintended consequences, we need to look very careful at how consumers use the information so that we tell them*

in such a way, so that they understand the risk of moving on. Should they move on. And yeah, it's something that we do with products all the time, so a simple statement that doesn't provide them with the information to ensure that they understand that as long as you just use this product, you're fine. But if you move on, you're not fine. You know, it's the reason why FDA has spent so much time on labelling, because we all talk about providing a fact as if it's a simple thing. We all understand that it is very important to understand how consumers perceive and use that information. So, we provide them the fact in the way that it has the intended result. It's not truth versus non-truth, I think it's a more complicated thing. We have mechanisms for doing it, it's totally doable but you have to look at those broader issues.' (CTP-S, 2021)

An additional complexity from the research evidence has to do with regulating e-cigarettes to prevent adolescent initiation to nicotine versus regulating e-cigarettes to encourage adolescent and adult smokers to use e-cigarettes to stop smoking or reduce their risk of harm. CTP-S highlighted the research efforts towards this consideration when they said:

'We've tried to collect data over the years and it's really hard to get that data to tease out, you know, how many of these children are using an E-Cig that might otherwise be using a combusted cigarette, versus, how many would have never picked up a tobacco product altogether but are now picking up an E-Cigarette instead. You know, and so, it's really hard to get that data but I think it's you know, certainly a very important point and something that we, you know, I don't think we're ignoring yet at all, it's just hard to sort of tease that out.' (CTP-S, 2021)

The CTP also sought research evidence to inform their approach to specific areas of e-cigarette regulation, such as with flavours. For example, CTP-D stated that:

'We're seeking comments and data, science and information on the role that flavors are playing in tobacco products. Good or bad. The role that they are playing in getting kids to initiate, on tobacco products and the role that they may be playing in helping addicted adult cigarette smokers successfully switch away from combustible tobacco products. We also are looking for new information on consumer perceptions and the direct health risks, if any, associated with flavors.' (CTP-D, 2018)

It was apparent to me from the quotes presented above that weighing up the overall public health impact of e-cigarette products from available research evidence constituted a complex decision-making process. CTP-D corroborated this when they said:

'When one is trying to use the best available science to assess the net impact at a population level. So, for patterns of use, for smokers who are unable or unwilling to quit, are they completely switching? Or are they becoming permanent dual users? For product toxicity, is the new product less toxic to the user or more toxic to the user? With former smokers, are they relapsing? Or are they remaining

abstinent? And with kids, are they starting to use any of these tobacco products? Or not? And, it gets complicated, because it's not going to be as black and white as all positive population level impacts or all negative population level public health impacts. It's going to be some combination of both.' (CTP-D, 2018)

CTP-D also went on to give an example in another instance of the type of public health impact assessment the FDA carries out when regulating tobacco products. They said:

'Let me give you a real life example—with the PMTA authorization of the Swedish Match snus[7] product—because there, we took some of the most important population level, impact considerations—which goes to the heart of [name of individual] question—and we assured ourselves that we were not concerned that there was a great likelihood that this would divert people who were interested in becoming tobacco free, or get off of cigarettes. We were not concerned that there was a likelihood that kids would be starting the use of the product and on that and a series of other bases we were able to say that the marketing of that smokeless tobacco product was Appropriate for the Protection of the Public Health. The point that I tried to make in the concluding slide is that this can get complicated as we're trying to figure out net impacts.' (CTP-D, 2018)

The Chief Impact Officer of NJOY (one of the largest e-cigarette producers in the US), hinted that the FDA uses scientific evidence to verify that e-cigarette products are compliant with FDA's public health protection criteria before allowing them into the market. NJOY said:

'I believe that with the PMTA process for ENDS, now fully underway in, the United States is on the verge of a transformed ENDS marketplace. One in which the products lawfully on the market are there because FDA has reviewed the scientific evidence and found the availability to be Appropriate for the Protection of Public Health.' (NJOY-R, 2021)

NJOY-R went on to describe the kind of evidence the FDA requires from PMTA applicants mentioning that:

'The comprehensive elements of FDA's ENDS guidance which was then structurally laid out by FDA to include components, ingredients and additives, properties, principles of operation, manufacturing, non-clinical health risk and human health impact information. Including consumer perception, likelihood of an initiation cessation, by both users and non-users, product use patterns, labelling comprehension, self-selection and actual use, human factors, abuse liability. Biomarkers of harm and exposure and health outcomes.' (NJOY-R, 2021)

The FDA has continued to gather research evidence from products already on the market to better understand e-cigarette use within the population. CTP-D alluded to this when asked what the FDA was looking for in their data request to Juul Labs. They replied:

[7] SNUS is a form of heat-treated and pouched smokeless tobacco product which is usually placed under the upper lip for use.

'The data request was very open ended. It's basically, 'Help us better understand what's going on with kids, with your product. And share with us the research that you've done, on any of the health effects'. Section 904b of the Tobacco Control Act, gives us the authority to make these informational demands of companies. We've used the authority in the past, we look forward to getting responsive information from the company and also want to mention that the company had reached out to us in advance and wanted to come in and discuss these issues and that meeting will be taking place shortly.' (CTP-D, 2018)

In general, analysis of conference presentations revealed that the FDA were guided by available evidence when it came to implementing further regulations over and above the existing FSPTCA.

3.3.2.3 Public health considerations

The analysis of audio transcripts showed that a major factor influencing e-cigarette regulation in the US was a public health consideration of how best to impact population's health through the regulatory process. CTP-D indicated this when they said: -

'It's been almost a year since Dr Scott Gottlieb was confirmed by the United States Senate and began his tenure as Commissioner of the Food and Drug Administration. And, literally from the day that Dr Gottlieb assumed the Commissionership, he began a dialogue with the Centre for Tobacco Products to get up to speed on our authorities, our program, um, the center. And as we were having those conversations during the first month or so—that he began as commissioner—we kept on coming back to this question; How can we use the tools of product regulation to have the greatest impact?' (CTP-D)

CTP-S also suggested that public health considerations of tobacco products (which includes e-cigarettes in the US) involves an evaluation that use of such tobacco products is appropriate for protection of public health. CTP-S mentioned this when they said:

'I am going to talk about—throughout the remainder of my talk—an abbreviation of APPH. That stands for Appropriate for Protection of Public Health. This is the statutory standard by which we are required to evaluate products received in PMTAs.' (CTP-S)

There was an indication that evaluation of whether a tobacco product is appropriate for the protection of public health entailed regulatory considerations of the risk: benefit profile of the tobacco product. For example, CTP-S suggested that there may be benefits of regulating

flavours in e-cigarettes in such a way that it does not reduce their effectiveness in smoking cessation. CTP-S said:

> *'The phrases that you know, we started using at the agency a couple years ago is, we want to allow an off ramp for current combusted cigarette smokers, and I think you know, having flavored products out there, may be necessary to do that. And you know, the other thing to be you know, to keep in mind is, you know, E-Liquids are all synthetic so technically all liquids—E-Liquids are flavored. I mean, even tobacco flavored E-Liquids are flavored. They are, you know and so, you know, we do, you know I think from a public health perspective we do I think need flavored products out there to see that shift down that continuum of risk, of combusted cigarette to these less toxic products.'* (CTP-S)

From the statement above, it appears that the CTP aimed to encourage smokers to shift down the continuum of risk from established harmful tobacco products such as combustible cigarettes to less harmful products such as e-cigarettes. CTP-D highlighted that this was central in the FDA's thinking with regards regulation of e-cigarettes when they said:

> *'In a later talk the commissioner* (of FDA) *said that, talking about nicotine while highly addictive, it's delivered through products on a continuum of risk. And the combustible cigarette is where the delivery of nicotine leads to incredible amounts of disease and death. So, the recognition that the continuum of risk exists was a big driver in the agency's thinking, as we came up with the comprehensive plan for tobacco and nicotine.'* (CTP-D)

CTP-D further elaborated on the comprehensive plan for tobacco and nicotine mentioned in the above quote by highlighting the FDA's rationale for focusing on nicotine addiction when it comes to products low on the continuum of risk, such as e-cigarettes. CTP-D stated that:

> *'We look at this as a package of actions with a focus on nicotine and the issue of addiction. And the work that we're doing programmatically is really being guided by a series of principles. We acknowledge that the continuum is out there. Attach nicotine to smoke particles and it is disease and death. Put it into gum, patch or lozenge, and it's so safe and effective you don't need a doctor's prescription. So, the challenge for us as regulators is really to strike the appropriate balance between smart regulation, that encourages innovation of those satisfying and less harmful products for people who need them. All the while being guided by the best possible regulatory and scientific foundation for our actions.'* (CTP-D)

Also, with respect to nicotine use and the continuum of risk, CTP-S expressed the view that the messaging around e-cigarettes could be tailored to encourage smokers to shift down the continuum of risk. Similarly, CTP-D emphasized that the messaging or education of the public is an important aspect of reducing tobacco harm. CTP-S and CTP-D stated respectively that:

'I think when it comes to tobacco products, they've been hearing one message, for decade in the United States, which is these products are all terrible and you shouldn't use them, and you know, I'm not sure I disagree with that message but there's more subtlety to the message right? I mean we've talked about this continuum of risk, and we could say the FDA would like consumers not to use tobacco products because they all have some inherent risk but, if they're going to use them, we want them to shift down the continuum of risk.' (CTP-S)

'Enforcement, alone, is not enough. It's an important prong, but educational efforts when it comes to preventing youth use of tobacco is critically important whether it's education to retailers, or through retailers to the general public. Or our own messaging aimed at vulnerable, at-risk teens and young adults.' (CTP-D)

When it comes to messaging and shaping the public's perception on risks associated with tobacco and nicotine use, CTP-D noted some challenges with the American population. CTP-D indicated that, in the US, there is public misperception of nicotine safety which needs to be corrected through public engagement, messaging and education. CTP-D stated:

'There are some really important and fundamental issues related to nicotine that we all need to engage the public on, and I list them here. The first has to do with the profound misperceptions of nicotine safety that many people in the general public hold. You look at the surveys and when questions are asked about, 'Does nicotine directly cause cancer?' And the correct answer is, 'No, nicotine does not directly cause cancer'. But when you add up the people who answer incorrectly, with the people who say that they don't know, then depending upon the survey you get between sixty to seventy percent of the American public, that can't answer that question correctly. I think that that has implications for everything that we are trying to do, as regulators and all of your day jobs, in whatever sector you are in, because if we are being bold enough to envision a world where cigarettes are no longer capable of creating or sustaining addiction but the alternative products need to be out there for smokers who need them, and so many people are walking around not understanding that nicotine doesn't directly cause cancer, that's a challenge. And that's a problem.' (CTP-D)

In summary, the FDA's agenda to reduce harm from tobacco use by encouraging smokers to shift down the continuum of risk either through messaging and education, or via specific considerations such as flavours in e-cigarettes, influenced the current regulatory state of e-cigarettes in the US.

At the same time, another key public health consideration was the protection of children and adolescents from uptake of nicotine through the use of e-cigarettes. The FDA was concerned with the popularity and increasing use of e-cigarettes amongst adolescents in the US because they contain nicotine which is an addictive substance. CTP-D indicated this when they said:

> *'The concern that you heard the commissioner express last week, was generally about the category of e-cigarettes and specifically about the popularity of products that closely resemble a USB flash drive, that have high levels of nicotine. And that can have emissions that are hard to see. We've all heard the anecdotal reports of kids that are able to use these products literally in class, right in front of their teachers without the teachers knowing. And the concern here is that, um, that these kinds of characteristics can facilitate uptake by kids. Several but not all of these products fall under the Juul brand, but we have seen other products with similar characteristics, whether it's myblu or KandyPens. And kids may be trying these products and liking them, without even knowing that they contain nicotine.'* (CTP-D)

As indicated above, CTP did recognize the potential benefits of e-cigarettes in allowing current smokers to move down the harm continuum by substituting cigarettes with less harmful products such as ENDS. However, this potential benefit was not felt to be relevant in the case of children and adolescents, as shown by CTP-D when they said:

> *'When you factor in the whole kids' issue, really the harm reduction debate is irrelevant, because kids should not be initiating on any nicotine delivering product. Whether combustion is present or not. So that's part of the discussion and the dialogue with the general public that we need to have.'* (CTP-D)

The FDA's concern about nicotine or tobacco initiation in children factored into deliberations on e-cigarette regulation, including with regards to flavours, type of e-cigarette, nicotine type and strength, labelling and advertising, and access to e-cigarettes. The above considerations fed into what appeared to be tensions between the public health consideration of helping existing adult smokers quit while simultaneously stopping children and young people from initiating nicotine use. With respect to flavours in e-cigarettes, CTP-S stated that:

> *'Flavors are a very complicated issue that we certainly are considering in our evaluation. And as I think we all know, flavors can both be appealing to current adult cigarette smokers and help them to switch from combustive cigarettes to e-cigarettes. But on the flip side, they can also be appealing to non-users, particularly youth, and young adults and can entice youth and young adults who are not using tobacco products to begin using e-cigarettes. This will be a major factor—it is a major factor on our evaluation—but is very unlikely there are going to list certain flavors, or category of flavors that are APPH while others are not. Because we have a lot of data on flavors and there are some flavors that are preferred by adult smokers, another set of flavors that are preferred by youth. But there is a lot of overlap, in the flavors. And also, the flavors would change as the marketplace changes and so those preferences by non-users and users could change over time and so this is certainly a factor, that goes into our evaluation.'* (CTP-S)

Note that the statement from CTP-S above highlights the complexities of considerations when it comes to prevention of tobacco initiation to youths and young children versus promoting movement down the continuum of risk for adult smokers.

With respect to the type of e-cigarette (open, closed, reusable or disposable devices) as a consideration in the protection of population health, CTP-S had this to say:

> *'We're looking at these e-cig types as part of our evaluation. But like the flavors I don't think they're going to be certain types of devices that are APPH but other types of devices are not APPH. And very much for the same reasons as flavors, the preferences that non-users, that children or young adults, have for device types, can change with time, in fact we've seen it change with time in recent years. Similarly, the preferences of adult smokers who are switching, from a combusted cigarette to an E-Cigarette can change with time. So, it's very unlikely this is not going to be a static determination, that these preferences will change over time and so, it really is a case-by-case evaluation of the specific product as opposed to some categorical determination of whether a product or marketing product is appropriate for the protection of public health.'* (CTP-S)

With respect to nicotine type (free base nicotine versus nicotine salts) and concentration as a consideration in the protection of population health, CTP-S explained that:

> *'Nicotine type and concentration can lead young adults, and youth, to begin experimenting with and eventually become addicted, to e-cigarettes but on the flip side, we have to have the right nicotine type and concentration to get combusted cigarette smokers to want to switch to an e-cigarette and leave behind the combusted cigarette. So, again I don't believe there's going to be any categorical decisions that certain nicotine types or concentrations are APPH while others are not. I think it's going to be very much a product-by-product assessment of the totality of information in the PMTA that will ultimately lead to either a negative or positive marketing order.'* (CTP-S)

In relation to labelling and advertising as a consideration in the protection of population health, CTP-S mentioned that:

> *'Labelling and advertising can be and has been targeted for certain audiences. So, you know, for product to be able to be APPH, you know, what we'd want to see is the labelling and advertising is directed at adult smokers, and not non-users, particularly not you know, youth and young adults. And that, the placement of that label, that advertising is also targeted.'* (CTP-S)

With regards to access to e-cigarettes as a consideration in the protection of population health, CTP-S pointed out two things:

> *'One, how do consumers get these products? Is there a way to allow to adult smokers, who are—have switched or are interested in switching—get them access to E-Cigarettes. To both the devices and the E-liquids, while limiting access for youth to be able to purchase or obtain these products and so again, this is an area where we want to make sure that the applicant has the intention and the ability to control access, to really limit youth access. Another facet of this is just the technology, you know, with devices being electronic, with E-Cigarette devices being electronic devices, there is the ability to eliminate or reduce access to certain populations and so, very much interested in technology that would not allow kids to be able to activate the E-Cigarette device while allowing legal adult users to be able to activate the device.'* (CTP-S)

Although youth initiation to nicotine was a major consideration in regulating e-cigarettes, the FDA was not oblivious to the fact that there are already adolescent smokers who may benefit from the use of e-cigarettes as an aid to stop smoking. CTP-D noted this when they said:

> *'I do think there's an aspect of FDA's analysis on this that is habitually missing, downplayed or denied. Which is what about the teenage smokers? Okay? Now this—it's pretty clear the more frequent use of e-cigarettes is among adolescent smokers, or people who would otherwise smoke if they weren't vaping. Now that is quite an important insight because, in that model of the world, vaping is a diversion for adolescents, from smoking and possibly a lifetime of smoking. So, we can't really just position it as the interests of adults versus the interests of adolescents. It's the interest of smokers of any age versus non-smokers.' (CTP-D)*

It can be seen from analysis above that public health considerations were a major factor that influenced e-cigarette regulations in the US. The public health considerations were two-folds: the need to promote harm reduction versus the need for harm prevention. This created a tension around how to balance these two public health needs.

3.4 Discussion of Study

This study which aimed to explore the determining factors of the policies and regulation of e-cigarettes in the US and the UK, identified three factors that influenced e-cigarette regulations in the US and the UK. The factors are a) Existing regulatory framework b) Guidance from available evidence, and c) Public health considerations. These findings, which are related to each other, are discussed below.

3.4.1 Existing Regulatory Framework

Results from thematic analysis showed that in both the US and the UK, e-cigarette regulations were not created *ab initio* but were based on and adapted from other existing

regulations binding on the country in question (see section 3.3.1.1 and 3.3.2.1). In my view, the popularity of e-cigarettes after their emergence in the US and European markets potentially put time pressures on regulators to regulate e-cigarettes, leading them to build on existing regulations rather than developing regulations *ab initio*. The UK, as part of the European Union at the time of e-cigarette regulation, were legally obliged to transpose the European regulation of e-cigarettes (TPD) into British law through the TRPR (see section 3.3.1.1). A previous paper (229) has suggested that differences in institutional context and pathways of policy-making and in approaches to legitimize policy decisions through science and the judiciary were factors that help explain why e-cigarette regulation became highly controversial in England, while in Germany this debate has been almost entirely absent. In this study, I found that the UK's regulatory pathway of transposing TPD to TRPR influenced e-cigarette regulations (i.e., restricted regulatory measures in the TRPR) (see section 3.3.1.1), while the US's use of enforcement discretion to legitimize their policy decision influenced their e-cigarette regulations (i.e., subjecting e-cigarettes to existing FSPTCA regulation) (see section 3.3.2.1).

In the US, the approach to regulating e-cigarettes involved placing them under the FSPTCA regulation. This was because e-cigarettes were deemed to meet the statutory definition of tobacco products; even though they do not contain tobacco, they contain nicotine (typically derived from tobacco) and therefore fall within the definition [8]. Note also that Non-Tobacco Nicotine products e.g., e-cigarette products that contain synthetic nicotine as opposed to nicotine derived from the tobacco plant, have more recently (April 2022) been subjected to FSPTCA as a tobacco product [9].

Basing or adapting e-cigarette regulations from other existing regulations binding on the respective countries had implications for the sort of regulatory measures introduced. In the UK for instance, the TPD imposed some restrictions on UK regulation, albeit not prohibiting the UK from bringing in additional (to TPD) regulations for e-cigarettes in the TRPR (see section 3.3.1.1). In other words, the majority of the TRPR was a transposition of the TPD into UK law, but the UK could still introduce aspects such as: smoke-free environments; domestic advertising; domestic sales; age restrictions; nicotine–free cigarettes; and flavourings of e-

[8] Tobacco Product means any product made or derived from tobacco, or containing nicotine from any source, that is intended for human consumption, including any component, part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product).

[9] See Regulation and Enforcement of Non-Tobacco Nicotine (NTN) Products | FDA (accessed 24/08/2023)

cigarettes (111) within the UK, including allowing variation across the four nations of the UK. This allowed the UK to apply existing Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015 (230) and to place restrictions on advertisement of e-cigarettes on TV (see section 3.3.1.1). The Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015 prohibits sale of nicotine inhaling products to persons aged under 18, unless the nicotine inhaling product is a medicinal product or a medical device and is indicated for the treatment of persons of the age of the person to whom the product is sold (230). In addition to the TRPR, Scotland the Health (Tobacco, Nicotine etc. and Care) (Scotland) Act 2016 (100) restricts the sale of single use nicotine-free products (a rule not covered in the TRPR).

In the post-BREXIT era, the TPD continued to influence how e-cigarettes are regulated UK wide because of the Northern Ireland (NI) Protocol, and this may continue with the current Windsor Agreement that replaced the NI protocol. The Northern Ireland Protocol was an agreement between the EU and UK stating that there would be no new checks on goods crossing the border between NI and the Republic of Ireland (which remains part of the EU), meaning that NI in effect remained in the EU's single market for goods. Therefore, e-cigarette regulation in the UK was, and may remain, influenced by its existing regulatory framework. However, with the introduction in February 2023 of the Windsor Framework (81), UK regulators will need to clarify if and to what extent NI should comply with the TPD. The Windsor Framework is an agreement that fundamentally amends the text and provisions of the original NI Protocol to deliver a form of dual regulation that will work for business and consumers in NI, resulting in over 1,700 pages of EU law – with accompanying European Court of Justice (ECJ) jurisdiction – disapplied in NI (81). I was not able to secure any interview with a NI representative and I completed my interviews before the Windsor Framework in February 2023, so could not ask direct questions regarding impact of Windsor Framework on e-cigarette regulations.

Another existing regulatory framework that was identified to have influenced e-cigarette regulations in the UK was the WHO framework Convention on Tobacco Control (6). The UK (unlike the US) is a ratified member of the WHO framework Convention on Tobacco Control (6) which demands that member countries take measures to prevent tobacco companies from unduly influencing tobacco related regulations and policies. As a result, the UK, operating under this convention, were cautious of protecting regulators from industry

influence or lobbying when regulating tobacco and related products (see section 3.3.1.1). This is because the tobacco and pharmaceutical industries have historically influenced regulatory agencies, through the processes of regulatory capture (203) or corporate bias (216, 217, 231), to regulate their products in favour of industry rather than public health interest. Theory related to both these processes was discussed in detail in Section 2.3. Such tactics by tobacco and pharmaceutical industry to influence regulation can be seen as a regulatory capture, which suggests a situation whereby government regulatory agencies are gradually captured by the regulated industry, so that, over time, they regulate primarily in the interest of industry, rather than in the public interest (202). This means that regulators not only had to prevent undue influence from tobacco industry as is required by FCTC. They also had to look out for undue influence from the e-cigarette industry (of which there is some overlap with the tobacco industry) and the pharmaceutical industry, who would have been worried that regulations that promoting use and sales of e-cigarettes might lead to reduction in sales of NRT products. Even during the regulatory process of the TPD (which was transposed to UK law in the TRPR), e-cigarette companies were said to have aggressively lobbied for their interest in the outcome of e-cigarette regulation (see section 3.3.1.1). It is also possible that, had protecting against industry influence not been a convention in the UK, the pharmaceutical industry might have successfully influenced e-cigarette regulation in their vested interest. Conversely, Industry often conducts its own research and has a lot of data on their products which, in my view, could appropriately inform good regulatory decisions if considered with caution (e.g., careful consideration of research findings from industry funded research where there is full disclosure and declaration of conflict of interest by authors). Therefore, if regulators reject all of industry's research, in a bid to resist influence, they potentially risk missing out on useful data.

In the US, the FSPTCA was the existing regulation for tobacco products, albeit focused on cigarettes, smokeless tobacco cigarettes and roll your own tobacco. Basing e-cigarette regulations on this framework meant that they were not tailored specifically for e-cigarettes; rather they were based on those developed more generally for all tobacco products. The FSPTCA was not necessarily responsive to the regulatory needs of novel products such as e-cigarettes that are fundamentally different in design and mode of operation to conventional tobacco products. To provide a more responsive regulatory framework, the FDA has since

brought in the Pre-Market Tobacco Product Application (PMTA) to the FSPTCA in 2021[10] (see section 3.3.2.1), whereby manufacturers are required to apply for their e-cigarette products to be brought into the market (232). This gives the FDA the opportunity to assess that such e-cigarette products are Appropriate for the Protection of Public Health (APPH), over and above the already existing regulatory measures in the FSPTCA. The FDA's general standard for regulating new tobacco products, including e-cigarettes, is that the products must be Appropriate for the Protection of Public Health (see section 3.3.2.3).

3.4.2 Guidance from Available Evidence

Both the US and the UK were guided by (albeit limited) research evidence available to them when they set out to regulate e-cigarettes. In the US, before regulation of e-cigarettes, the FDA (e-cigarette regulators in the US), at the direction of Congress, commissioned the National Academy of Sciences, Engineering and Medicine (NASEM) to conduct research to evaluate the available scientific literature, on both the short- and long-term health effects of e-cigarettes, to identify research gaps and make recommendations for future federally funded research (228). The NASEM report (228) concluded that there was, at the time of publication (2018): substantial evidence that completely switching from regular cigarettes to e-cigarettes results in reduced short term adverse health outcomes; conclusive evidence that completely switching reduces an individual's exposure to numerous toxicants and carcinogens, compared to continuing to smoke cigarettes; substantial evidence to suggest that children and young adults who use e-cigarettes are more likely to transition to combustible cigarettes. The latter finding, albeit based on substantial rather than conclusive evidence, significantly informed the US focus on nicotine addiction and preventing the initiation of children into nicotine use through e-cigarettes (see section 3.3.2.2). Given that there was conclusive evidence from the NASEM report (228) that completely switching from cigarettes to e-cigarette reduces an individual's exposure health harms, it is surprising that the US regulator did not focus on promoting e-cigarette use for smoking cessation (although it was considered). Perhaps it was the increasing popularity and youth uptake of e-cigarettes (179) that put pressure on the FDA to focus on prevention of youth initiation to nicotine (see section 1.8.9.1). The data shows evident tensions between regulation of e-cigarettes in the

[10] See Federal Register :: Premarket Tobacco Product Applications and Recordkeeping Requirements (accessed 24/08/2023)

interests of current adult smokers (especially those attempting to quit) versus the interests/protection of current non-smokers (especially youth) (see section 3.3.2.3). The concept of continuum of risk, and the need for a balanced evidence base on safety or harms of e-cigarettes (including the risk of them leading to current non-smokers, especially children and adolescents, taking up smoking) and on their effectiveness as a smoking cessation aid, makes assembly of the evidence base particularly challenging. So too does the relative novelty of these products and the evolving nature thereof, as time is needed for benefits and harms to become evident. However, research in the US has also continued to focus primarily on prevention of youth initiation to nicotine. The tobacco regulatory research funding priorities of the National Institutes of Health (NIH) include toxicity, addiction, and health effects of ENDS, but there is no consideration of effectiveness of ENDS in smoking cessation (89).

The UK government likewise commissioned a research report on e-cigarettes by Public Health England, which concluded that e-cigarettes only posed about 5% of the risk of tobacco cigarettes and that e-cigarettes were effective for smoking cessation (129). Further UK research findings showed that e-cigarettes were even more effective for smoking cessation than the existing recommended Nicotine Replacement Therapies (NRTs) (22). This research evidence similarly informed the UK focus on harm reduction and the potential for e-cigarettes to be used for smoking cessation interventions (see section 3.3.1.2). Note that the UK also monitored youth use of e-cigarettes but observed that, at the time of their research, this was not increasing at an alarming rate as experienced in the US (see section 1.8.9.3). Therefore, while putting in places measures such as a ban on TV adverts to prevent youth use of e-cigarettes, the UK leveraged the public health benefit of e-cigarettes by also placing measures in UK regulations and policies which directly encourage smokers to switch from combustible cigarettes to e-cigarettes (see section 3.3.1.2). The UK also ensured continued monitoring through surveys and a Post-Implementation Review [PIR](233) of regulations published in March 2022. The PIR utilized commissioned evidence, published peer-reviewed evidence, a public consultation, and a review of key indicator data (233). The report's authors summarized that the TRPR regulations had met their original objectives and expressed the view that those objectives could not be better achieved through alternative regulatory measures; it was concluded therefore that the regulations should remain in force (233). However, it was indicated that the Government would consider further regulatory

reforms, as and when needed. For example, respondents to the public consultation commented that, whilst the advertising restrictions were discouraging use amongst young people, the packaging of e-cigarettes makes them attractive, particularly to young people. Some respondents also suggested that the Government should increase awareness of the health benefits of switching to e-cigarettes (233).

Within the UK, concerns about youth use of e-cigarettes have prompted action at a devolved level rather than UK wide. The Scottish government commissioned a public consultation into tightening rules on advertising and promoting of vaping products (234).[11] The consultation, which ran from 3rd February 2022 to 29th April 2022 on the Scottish Government Citizen Space website, sought views on proposed regulations which aimed to strike a balance between protecting non-smokers and making information available to smokers. A total of 757 validated responses to the consultation were received; the vast majority were from individuals, with only 43 organizational responses. Individual responses to closed questions in the consultation were split equally between individuals who supported the Scottish Government proposals and those who did not support them. In terms of organizational respondents, those who supported the proposals outlined in the consultation document were, in the main, local government and health organizations. Those organizations who were less likely to support the proposals were the vaping sector, tobacco industry, and other organizations with a commercial interest (e.g., those that sell tobacco and vaping related products). The Scottish government plans to use the evidence from this public consultation and their published (May 2023) analysis of data on vaping (235) to inform a refreshed tobacco action plan though this has not been published as at time of writing (April 2024).

A previous study (236) that attempted to understand why Australia and England have such different policies towards ENDS, found that the two countries differ markedly in the priority that they have given to using ENDS to promote smoking cessation or restricting smokers' access to prevent uptake among young people. They attributed the difference to: an influential scientific network that favoured nicotine harm reduction in the United Kingdom and the absence of such a network in Australia; the success of different types of health activism both in England and in Europe in opposing more restrictive policies; and the greater influence on policy in England of the field of illicit drug harm reduction. Therefore, it could

[11] See https://www.gov.scot/publications/tightening-rules-advertising-promoting-vaping-products/pages/4/ (accessed 24/08/2023)

be the activities of an influential scientific network favouring harm reduction that led UK regulators and policymakers to focus on harm reduction as a regulatory approach following the findings of the PHE report. Note also that, in some instances, the same research reports were appraised and interpreted differently in the US and the UK (see section 1.8.11).

3.4.3 Public health considerations

In both the US and the UK, there were public health considerations with the ultimate goal of ensuring public health protection (see section 3.3.1.3 and 3.3.2.3). However, both countries differed in their approach and focus (see section 1.7). I found that during the period of e-cigarette regulation (around 2016), the US emphasis was to make sure e-cigarettes on the market were appropriate for the protection of public health, with a focus on nicotine addiction and particular concerns about non-smokers, especially youth, becoming addicted (see section 3.3.2.3). By contrast, I found that the emphasis in the UK was on reducing the rate of smoking with a focus on harm reduction (see section 3.3.1.3). This latter finding corroborates those from a study (80) that found that there was a broad agreement among stakeholders involved in e-cigarette policy introduction and enforcement in three of the nations of the UK (England, Wales and Scotland), that the overall aim of public health policy in relation to e-cigarettes was reducing access to, and use by, non-smokers, while exploring potential benefits to smokers. Both the US and UK public health representatives acknowledged that nicotine is addictive, is delivered through products on a continuum of risk, and that e-cigarettes are low (relative to burnt tobacco) on that continuum of risk (see section 3.3.1.3 and 3.3.2.3). However, US regulators were concerned that e-cigarettes, while relatively less risky to health than tobacco cigarettes, could potentially lead people (especially non-smokers and children) into smoking and nicotine addiction through a gateway effect (see section 1.7). UK regulators on the other hand, saw e-cigarettes as offering an opportunity to reduce the harms of smoking by encouraging smokers to substitute tobacco cigarettes for e-cigarettes which, as also acknowledged in the US, are relatively less risky to health (see section 1.7). This finding of contrasting priorities and emphasis is in line with a previous study (237) that compared the policy positions of health and medical organizations across Australia, New Zealand and the UK as they relate to sale and supply of nicotine vaping products (NVPs) and evaluated factors that informed the differences in policy recommendations among these countries. The study (237) found that

the majority of health bodies, charities and government agencies in the UK and New Zealand portrayed NVPs (e-cigarettes) as a life-saving harm reduction tool. In contrast, concerns about leading non-smoking youth into addiction to nicotine, a perceived lack of clear and convincing evidence of safety and efficacy and the potential to undermine tobacco control progress continues to define attitudes and recommendations towards NVPs among Australian health and medical organizations. The study (237) also found that the divided views among stakeholders appeared to arise from empirical uncertainties and disagreements over the level and credibility of evidence. They went on to indicate that the source of most of these disagreements can be traced back to fundamental and irreconcilable differences in the framing of the NVP debate, and varied tolerability of risk trade-offs associated with NVPs.

The difference in emphasis and focus – harm reduction versus harm prevention – between the UK and the US does not mean that UK regulators were blind to concerns about the potential risks of e-cigarettes leading to nicotine addiction for previous non-smokers nor that US regulators failed to acknowledge the opportunity of using e-cigarettes to drive down smoking rates. The UK implemented sector-specific rules, focused on the protection of children and youth, including not targeting non-smokers and non-vapers with promotions of e-cigarettes and controlling where adverts could be placed to keep them away from young people (see section 3.3.1.3). The US regulators implemented the PMTA to help bring e-cigarette products safely into the US market (see section 3.3.2.3). PMTAs must provide scientific data that demonstrates that the tobacco product is appropriate for the protection of public health (232). This requirement consolidates FDA's standard for effective regulation of tobacco products which entails evaluation of new tobacco products based on consideration of the risks and benefits of the product to the population as a whole, including users and nonusers (238). Furthermore, FDA's consideration of nicotine initiation in children is supported by the law which requires that, when developing certain regulations, the FDA should apply a public health approach that considers the effect of the regulatory action on the US population as a whole, not just on individual users, with respect to both initiation and cessation of tobacco use (238). This means the FDA should not be concerned solely with current adult smokers, but rather must also consider the population as a whole, including children and current non-smokers, with respect to initiation of smoking or nicotine.

In the UK where the public health consideration resulted in a focus on promoting smoking cessation, the influences on e-cigarette regulation may be seen as being underpinned by the *Expectation / Marketing theory* of regulation which supposes that the creation of expectations and promissory science around innovation among networks of medical professionals, research scientists and patients/public puts pressure on regulatory agencies to regulate such products in a way that does not hinder use of the products (202). In the UK, medical professionals (239) and cohorts of research scientists (59, 65, 91) agree that e-cigarettes are safer alternatives to cigarette smoking, and may be harnessed for smoking cessation efforts. In my view, the UK strategy to reassure consumers of the safety of e-cigarettes was intended to allow manufacturers to bring e-cigarettes to market as a medicinal product as well as a consumer product. However, to license e-cigarettes as medicines, the proposed products should: meet standards of quality, safety and efficacy as defined under medicines regulations; meet the usual quality and safety standards for consumer e-cigarettes that have been developed by national and international standards organizations, where relevant; and comply with the UK medical device regulations, depending on the design of the product (119). To go down this route, manufacturers or importers and distributors would have to pay an application fee of £6,019 and assessment fee of £3,845. A 150-day assessment timeline is offered as the processing time for licensing e-cigarettes (119). Despite MHRA's efforts to establish the medicinal route to bring e-cigarettes into the market, no manufacturer has yet (April 2024) taken that route.

In the US, on the other hand, where the public health consideration resulted in a focus on preventing youth use of e-cigarette, the influences on e-cigarette regulation may be seen as being underpinned by what has been described by Daniel Carpenter as the *reputational theory* of regulation, whereby regulators respond to patient activism or media pressure to protect their reputation in the public sphere (211). In 2019, approximately one in four youths (23.0%) had used a tobacco product during the past 30 days, representing approximately three in ten high school students (31.2%) and one in eight middle school students (12.5%) (179). According to a 2019 survey, since 2014, e-cigarettes had been the most used tobacco product among youths with 27.5% of high school students (4.1 million) and 10.5% of middle school students (1.2 million) reporting use in the past 30 days (179). Public and media concern over these statistics pressured US regulators to cut down the rising use of e-cigarette use among youths, hence focusing on that aspect of the NASEM report.

3.4.4 Implications of Findings from US and UK for the Nigerian context

Some of the factors that were found to have influenced e-cigarette regulations in the US and the UK also have the potential to influence regulatory approaches in Nigeria. For instance, it was found that the UK discouraged industry (pharmaceutical, tobacco, and e-cigarette companies) from influencing its regulation of e-cigarettes (see section 3.3.1.1). The UK (but not the US) is a ratified signatory to the WHO Framework Convention on Tobacco Control (FCTC) (6) which demands that member countries take measures to prevent tobacco companies from unduly influencing tobacco related regulations and policies. Nigeria is also a ratified signatory to the FCTC. Will Nigeria, like the UK, take measures to prevent industry influence when it comes to regulate e-cigarettes? How much influence will such measures exert on potential regulation of e-cigarettes in Nigeria? A study (240) on the analysis of tobacco control policies in Nigeria found that lack of funding and conflict of interest (of protecting the Nigerian populace from harmful effect of tobacco versus the economic gains from the tobacco industry) were the major barriers that slowed Nigeria for a decade (from 2005 when the country became a ratified member of FCTC, to 2015) in developing a comprehensive FCTC compliant policy (240).

In both the US and the UK research evidence influenced e-cigarette regulations, with both countries commissioning research to inform their decisions. Although US and UK drew upon similar sources of evidence to inform their e-cigarette policies, they took different policy approaches to e-cigarettes. The NASEM committee conducted a comprehensive and systematic assessment and review of the literature on the health effects of electronic cigarettes between 1st February 2017 and 31st August 2017 to identify more than 800 peer-reviewed scientific studies in their report (228), while PHE conducted a similar review of the literature and identified 798 articles used to produce their report in August 2015 (241). Both reports were not limited to studies from the respective countries and prioritized human studies for their assessments (228, 241). The evidence drawn upon, including the most influential evidence, contained substantial conflicts of interest (including relationships with e-cigarette and tobacco industries) (242). Nigeria as a country does not invest as much as the US and the UK in research. For instance, in the US, the Office on Smoking and Health monitors tobacco-related topics among youth, adults and specific populations through

surveys[12]; the Office of National Statistics (ONS) does yje same in the UK. But in Nigeria, the first and only comprehensive, evidence-based population level data on tobacco surveillance available to the Federal Ministry of Health is the Global Adult Tobacco Survey (GATS) Nigeria (25) which was conducted about a decade ago (2012). With an apparent lack or up-to-date, country-specific research evidence in the context of Nigeria, what type of evidence will be drawn upon, and to what extent will Nigeria be guided by evidence, including from other countries and settings, in regulating e-cigarettes?

In the US and the UK, consideration of the roles e-cigarettes could play in public health was a major influence on e-cigarette regulation. In both countries, there were three groups of proponents: those who argued that e-cigarettes present a positive potential to aid smokers quit tobacco smoking; those who argued that e-cigarettes pose a negative potential to lead non-smokers (particularly children and adolescents) to tobacco smoking – the so called 'gateway theory'; and those who argued that there was not enough data at the time to determine the potential impact of e-cigarette use to the populations' health (2). In both the UK and the US, the views of the first and second groups were taken into account in regulation, albeit with more weight on the former in the UK and the latter in the US. Will Nigeria prioritise the potential of e-cigarettes in smoking cessation or will their primary concern be preventing initiation of nicotine addiction amongst current non-smokers, especially youth.

A number of context–specific considerations are likely to influence the balance of those two concerns. Firstly, in Nigeria, as of 2020, only 2.7% of people aged 15 years and older currently smoked (tobacco) cigarettes (21). Given this low prevalence, Nigerian regulators may not prioritise the contribution of e-cigarettes to public health through their potential role as a smoking cessation aid. Moreover, e-cigarettes are a relatively expensive option for an average Nigerian. Conventional cigarettes, which are cheaper, still cost the average daily smoker in Nigeria just over 6% of their average annual income (measured by per capita GDP)(35). Due to the (lack of) affordability of e-cigarettes and national cultural barriers to smoking (anecdotal suggestions are that most Nigerians perceive smokers as social deviants), it seems less likely that e-cigarettes would act as a gateway to smoking in Nigeria. On the other hand, the evidence base for the role of e-cigarette in smoking cessation has grown

[12] See- https://www.cdc.gov/tobacco/data_statistics/surveys/index.htm (accessed 25/08/2023)

over recent years, and some evidence that was not available at the time the US and the UK developed their e-cigarette regulations is now available for Nigerian regulators to consider. For example, e-cigarettes have been found to be more effective than Nicotine Replacement Therapy in aiding smoking cessation (22). Nonetheless, with Nigeria having a large population (43%) of children and young people (0 to 14 years) compared to the US (18%) and the UK (17%)(243), the primary consideration in regulation/legislation in that country is likely to be to protect children and youths and to prevent them from taking up vaping.

3.4.5 Strengths of this strand of study

In this element of my PhD research (study one), the strengths of the methods were that the individuals that I interviewed had the opportunity to express themselves without restrictions about the factors that influenced e-cigarette regulations, and those individuals gave me important insights into the process of regulation. Conducting the interviews virtually using the Zoom facility was convenient for the participants and allowed auto-transcription of the recordings, saving time and money. All the interviews were conducted by me which ensured consistency in the data collection process. Organizational names and location were not anonymized because of the risk of losing the identity of the various stakeholders which was important in my analyses to contextualize findings (244). Individual participants were, however, given the choice to remain anonymous or go on record for their views. Participants were given this choice to mitigate the risk of feeling loss of ownership of the data if their real identities were concealed by use of pseudonyms (218). The topic of e-cigarettes has some very outspoken personalities, and it was felt that some might prefer to go on record with their views. However, in practice all the participants preferred not to be named.

3.4.6 *Limitations of this strand of study*

In terms of limitations of the methods used in this study, it is likely that some participants knew one another, since purposive sampling and snowballing techniques were used in recruitment of interviewees and participants were employed by organisations that work closely with one another and therefore, internal confidentiality could not be guaranteed; it is possible that participants may be able to identify one another in the report of interview findings (245). However, external confidentiality was assured for all the participants who

chose to be anonymised in the study. Similarly, in respect of the secondary data analysed, the names of speakers are freely available on The E-Cigarette Summit – Director (vimeo.com) (accessed 11/08/2023).

Another limitation to the study is that of recall and hindsight biases. Participants were asked about events that had happened more than five years ago (before or in the year 2016), so there is the possibility that they may have forgotten some of the events, may have recalled them incorrectly or may have reconstructed the past in the light of subsequent events. However, the topic guide was given to the participants some days before the interview to allow them time to reflect on the events they would be questioned on.

Note that recall and hindsight biases and *post hoc* rationalisation are likely to exist to a lesser degree in the video presentations I analysed because the presentations were recorded closer to the time of regulation (2016). However, this form of data collection has its own weakness. It is likely that under interview conditions and prompted by my questions, a representative of an organisation might have expressed different or additional views compared to those expressed in a structured presentation. This has implications for the findings of my study; some factors that are found to have influenced e-cigarette regulations in the UK (where primary data was obtained through interviews), were less apparent in the US data, which were less rich owing to the fact that direct questions could not be posed by me to probe the influence of particular factors in the US. Also, the selection of only one conference series may confer its own bias i.e., the conference organisers may be promoting a particular agenda, influencing the profile of speakers invited to the conference.

A further limitation is that some of the organisations that were to be interviewed had temporary officials who may have been involved in the e-cigarette regulatory process at the time (2016) but were no longer in office at the time of this study. For example, when I contacted the House of Commons Science and Technology Select Committee for recruitment of participants into my study, their reply indicated that it was the previous Science and Technology committee who ran the inquiry on e-cigarettes, and the members of staff who supported them during the inquiry no longer worked for the House of Commons. This resulted in a potential loss of a rich source of information for my study. As a substitute, secondary data (recorded video presentations) from the House of Commons on their enquiry into e-cigarettes have been analysed.

In consultation with my supervisors, I decided against conducting interviews with industry representatives to avoid a negative perception of my study as being associated with or influenced by the tobacco or vaping industry. The available conference presentations did include one presentation from industry in the US, which I selected and analysed, but there were none from the UK. This may be because the UK is a signatory of WHO FCTC which prohibits industry interference in tobacco control. The US is not a signed party to WHO FCTC and is therefore without similar obligation. I decided to include the secondary data from the US industry representative because, with the relatively small amount of data available from the US, that presentation shed light on the impact of US regulatory process on industry.

3.5 Conclusion

Findings from this study shows that both the US and the UK had an overarching public health approach to regulating e-cigarettes in a way that both protects non-smokers and takes advantage of the potential public health benefits of e-cigarettes. However, my interpretation of the findings is that the US focused on protecting non-smokers (with emphasis on children and youths) from nicotine initiation and used the PMTA to apply discretionary measures in taking advantage of the potential public health benefits of e-cigarettes. By contrast, the UK focused on maximising the potential public health benefits of e-cigarettes by permitting e-cigarettes to come into the market as either consumer or medicinal products, but placing measures such as advertising and age of sale restrictions to protects non-smokers.

This link between e-cigarettes and smoking was informed by influential research evidence in the US from NASEM (228)that suggested that children and young people who use e-cigarettes are more likely to transition to combustible cigarettes. On the other hand, the Public Health England report (241) suggested that many people in the UK are successfully using e-cigarettes (which poses lesser harm than tobacco cigarettes) to quit smoking. However, all the regulatory measures brought on by the FDA and MHRA were in addition to already existing FSPTCA and TPD requirements. Therefore, public health considerations, available research evidence and the existing regulatory framework are interrelated factors that worked together to determine e-cigarette regulation in the US and the UK.

It is likely that Nigerian e-cigarette regulations would be influenced by similar factors to the US and the UK for three main reasons. These comprise: the existing regulatory frameworks in

Nigeria, particularly the WHO FCTC; the public health obligation of protecting young non-smokers from initiation of and addiction to nicotine, since the Nigerian population is a youthful one; and greater availability of research evidence on e-cigarettes in comparison to when the US and the UK first implemented e-cigarette regulations. In Chapter 5, I explore further the regulatory approach that Nigeria may take in respect of e-cigarettes, considering available evidence from around the world on the role of e-cigarettes in public health.

Chapter 4. The Values and Sentiments of the Public Towards Electronic Cigarettes and its Regulations in the US and the UK (Study Two)

4.1 Background

In this chapter I continue to address the second objective of this PhD project, which is to 'Explore the determining factors of the policies and regulation of e-cigarette in the US and the UK'. I begin by setting out the relevance of this element of my research (study two) in achieving 'Objective 2' (see Section 1.3), using methods discussed in Section 4.2. I then present the findings of study two and discuss their implications for this PhD project.

My literature review suggested that regulators can sometimes respond to patient activism or media pressure to protect their reputation in the public sphere; this is referred to as 'reputational theory'(211) (see Section 2.3.2). I was interested in how members of the public and relevant stakeholder organisations contributed to/reacted to actions of regulators in the UK and the US. A previous study (246) carried out a content analysis of Twitter™ data to identify key conversation trends and patterns over time, and discern the core voices, message frames, and sentiment surrounding e-cigarette discussions on Twitter™. The study (246) found that positive sentiment (3754/4432, 84.70%) dominated the discourse surrounding e-cigarettes, and some of the most common themes presented in tweets were advertising or promoting e-cigarette products (2040/4432, 46.03%), promoting e-cigarette use or intent to use (970/4432, 21.89%), and discussing the potential of e-cigarettes to be used as a smoking cessation aid or tobacco alternative (716/4432, 16.16%), as well as the perceived health and safety benefits and consequences of e-cigarette use (681/4432, 15.37%). I carried out an observational study of Twitter™ data to understand the values and sentiments of the public towards e-cigarettes and its regulations in the US and the UK. Both my study and the previous one (246) aimed to identify key themes and sentiment surrounding e-cigarette discussions on Twitter™, but the previous study (246) used content analysis, while I chose to carry out a thematic and sentiment analysis.

Social media is currently a popular means of dissemination of health information and, sometimes, disinformation. It comprises a group of Internet-based platforms whereby contents, which are publicly available and created by end-users, are continuously modified by all users in a participatory and collaborative fashion (247). Applications such as Twitter™ enable users (individuals, groups and organisations) to connect with one another by creating

personal information profiles, inviting others to have access to those profiles and posting and responding to instant messages (247). The popularity of social networking sites for communication makes them a valuable medium for understanding the values and sentiments of the public towards a particular subject.

Twitter™ (as of August 2023 rebranded as X™) is one such social networking site; others include Facebook, MySpace, etc. It has been shown to be a useful health communication tool; governmental and similar organisations use it to carry out public engagement (248, 249) by providing updates on relevant information, organisational actions, and recommendations. They also receive feedback in the form of comments to tweets posted. This form of interaction facilitates studying patterns of tweets from organisations on a particular topic, to identify the organisation's interest or any embedded agenda. It also provides a means of identifying issues that are of interest to the public and the sentiments of responders who comment on tweets regarding such issues.

Twitter™ is the preferred social network for news consumption and as of January 2023, around seven in ten (69%) US Twitter™ users said they use the network to get their news (250). Twitter™ provides a unique 'big data' source for public health researchers because of the real-time nature of the content, and the ease in accessing and searching publicly available information, making it a valuable asset among social media networks (251). In addition, the reach and volume of data accessible via Twitter™ are also significant; as of March 2023, there were 237.8 million monetizable daily active users on Twitter™ worldwide, 500 million tweets were being sent per day, and roughly 55% of Twitter™ users were on the platform daily (250). As of January 2023, the US had 95.4 million Twitter™ user while the UK had 23.15 million Twitter™ users (250).

Members of the US Congress have been encouraged to use Twitter™ to encourage government transparency, communication, and engagement with the public (252). But it is not only governmental and quasi-governmental organisations who are using Twitter™ to engage with the public on certain topics, including health-related topics such as e-cigarettes and public health. Individual members of the public and other stakeholders, including news outlets, research organisations and advocacy groups, also initiate and contribute to online discussions on aspects of the topic that they value. When governmental organisations or regulatory and health protection agencies, such as the FDA and MHRA, announce their intentions to regulate a product, it is likely to stimulate discussions on Twitter™ about the

proposed regulation and the aspects of the regulated product that are important to such stakeholders and individuals. These discussions can remain live and topical for an unspecified period, during which time a lot of data on the subject is generated.

As this strand of research is concerned with the 'values' of the public and organised groups with regards e-cigarettes and its regulations, it is important to describe 'values' in the context of this study. There are different definitions of values, largely from sociology and political economy. In the context of this study, I draw on the description of values in sociology by the American anthropologist Clyde Kluckhohn (253)(pg. 388) who defines a value as '*A conception, explicit or implicit, distinctive of an individual or characteristic of a group, of the desirable which influences the selection from available modes, means, and ends of action*.' This means that values are the specific notions and ideologies we hold, and which guide our choices. Since values influence the selection from available modes, means, and ends of action, it is likely that the way individuals and organisations engaged in e-cigarette discussions on Twitter™, i.e., their choice of what aspects of e-cigarettes and their regulation to discuss, was guided by their values.

To get an even richer understanding of organisations and individuals' values with regards e-cigarettes, it is useful to analyse not only <u>which</u> aspects of e-cigarettes they discussed, but also in <u>what manner</u> they discussed it, i.e., did their discussion show any underlying sentiments? This is important because the underlying sentiments would give an inkling as to why people valued certain aspects of e-cigarettes and discussed them on Twitter™ at that time. Sentiment analysis is an active area of study in the field of natural language processing that analyses people's opinions, sentiments, evaluations, attitudes, and emotions via the computational treatment of subjectivity in text (254). As Scheibe (255) notes, value judgements refers to '*what is wanted, what is best, what is desirable or preferable, what ought to be done'* (pg. 41-42). Sentiment analysis can show, through positive or negative subjectivity in their tweets, whether people want e-cigarettes to be regulated, what they think is the best way to regulate e-cigarettes, if they desire to use e-cigarettes or if they prefer e-cigarettes to other nicotine containing products, and what they think the government and regulators ought to do with e-cigarettes. Sentiment analysis of Twitter™ data has been used in the past to link peoples' Twitter™ sentiments to their opinions or perceptions. For example O'Connor *et al.* (256) linked Twitter™ sentiment with public opinion polls to analyse several surveys on consumer confidence and political opinion over

the 2008 to 2009 period, and Lu *et al.* (257) studied user perceptions of different electronic cigarette flavours on social media.

In previous studies, text classifiers (258)[13] and thematic analysis (259) have been used to identify and describe nicotine-related topics and pro- e-cigarette policy arguments on Twitter™ respectively. I chose to use thematic analysis to enable me to organise and analyse Twitter™ discussions in a meaningful way that identified and described aspects of e-cigarettes and their regulation that are of value to individual people and groups. Thematic analysis allowed me to familiarize myself with the data, through transcription, coding, establishing commonalities between codes, and defining emanating key concepts, following the six step processes described by Braun and Clarke (223) (see Section 3.2.1). I believe that this process led to a better understanding of the data-driven concepts and hence the values of people and groups regarding e-cigarettes and their regulation.

Sentiment analysis was also carried out to determine the views or opinions that are held or expressed in comments posted by individuals or organised groups in response to e-cigarette related discussions during the regulatory period. This helped identify the public's sentiments towards e-cigarettes and their regulations in the US and the UK. As the findings of this study described the public's reaction to e-cigarette regulations, it also enabled an assessment of whether such reactions were of a nature that might influence e-cigarette regulatory decisions, in a *Reputational theoretical* fashion (see Section 2.3.2).

Thematic and sentiment analysis have been used in several studies to understand how content related to substances such as e-cigarettes are portrayed on various social media platforms. For instance, a recent systematic review (260), that included original qualitative studies published post-2004, found 73 studies that used thematic and sentiment analyses to analyse social media (Twitter™, YouTube, Instagram, Pinterest, TikTok and Weibo) content on tobacco, alcohol, psychostimulants, e-cigarettes, cannabis, opiates, stimulants/amphetamines, inhalant and novel psychoactive substances. One previous study (261) analysed Twitter™ conversations regarding FDA's authorization of IQOS as a Modified Risk Tobacco Product (MRTP) to determine the reactions of the public on social media to the policy decision. The study (261) found that nearly 42% of tweets showed a 'bot' score, indicative of a possibility of automation, and suggested that this may have been as a result of

[13] Text classification is a machine learning technique that assigns a set of predefined categories to open-ended text

industry's attempts to create a climate of false consensus and circulate misinformation regarding MRTP on social media. This calls for caution when researchers are interpreting findings of social media contents.

My study focused on analysing Twitter™ content on e-cigarettes for the reasons already explained above and to understand whether the contents of Twitter™ discussions are such that could influence e-cigarette regulations in the US and the UK.

Analysis of Twitter™ data for the period immediately before and after regulation of e-cigarettes was felt likely to provide insight into what was of value to organised groups (groups of people united by a common goal such as smoking cessation or e-cigarette advocacy e.g., ASH, Tobacco Free Kids, Fight to Vape) and the public with regards to e-cigarettes and the proposed or enacted regulation. Analysis could also allow exploration of whether these values changed between the periods before and after implementation of e-cigarette regulations.

4.2 Methods used in study two

Twitter™ (now X™) was searched for published posts related to e-cigarettes and their regulation. Four datasets, relating to specific periods, were collected from Twitter™. The periods for collection of data were selected by me in consultation with my supervisors; they were based on a fixed number of days after proposal of e-cigarette regulation and after implementation of the regulation. The first period selected was from 25th April 2014 (when the FDA published a Notice of Proposed Rulemaking [NRPM] for the Final Rule [regulation of e-cigarettes]) to 8th August 2014 (when the NRPM was closed for public comments). A NPRM is a notice in the US Federal Register that announces the intent of an agency to promulgate a particular rule, thereby giving the public an opportunity for public comment; this is often the first time the public becomes aware of an agency's proposed rule (109). This 105-day period was immediately prior to regulation of e-cigarettes in the US, and likely to be a time when there were ongoing discussions about e-cigarettes in social media, provoked by initial tweets from FDA on the topic. For comparative purposes, further 105-day periods were used in analysing tweets for the 'after' period in the US and for 'before' and 'after' periods in the UK. Thus, the second selected time interval was a 105-day period from 10th May 2016 (the date e-cigarette regulation came into force in the US) to the 23rd of August 2016, i.e. the period

immediately after e-cigarette regulations were enacted in the US. For the UK, two time intervals were also selected. The first was a 105-day period from 2nd January 2016 to 17th April 2016 (i.e., the period prior to 18th April 2016 when e-cigarette regulation was initially proposed). [The UK did not have a process similar to the US NPRM, but, post-regulation, expert witnesses were invited to give evidence, between January to May 2018, in a House of Commons Science and Technology Select Committee inquiry on the health impacts and on e-cigarettes' role as a smoking cessation tool.[14]] The second was a 105-day period from 20th May 2016 (when the e-cigarette regulation came into force) to 2nd September 2016.

After selection of dates for data collection, I and my supervisors agreed on a search strategy to target tweets relevant to e-cigarette and its regulation. Table 13 below presents the keywords or terms used in the search strategy.

[14] See https://publications.parliament.uk/pa/cm201719/cmselect/cmsctech/505/50504.htm#_idTextAnchor002 (accessed 11/08/2023)

Hash tagged Electronic Cigarette related keywords (Y)		
#e-cigarette #e-cig #e-cigs #ecig #ecigs #electroniccigarette #ecigarette #ecigarettes #vape #vapers #vaping #vapes #e-liquid #ejuice #eliquid #e-juice #vapercon #vapeon #vapefam #vapenation #juul		
US Twitter™ Account Addresses (X)	**UK Twitter™ Account Addresses (X)**	
@Surgeon_General	@MHRApress	@SwitchFinder
@FDATobacco	@MHRAdevices	@TheBHF
@US_FDA	@MHRAgovuk	@lunguk
@CDCTobaccofree	@PHE_UK	@NICEComms
@CDCgov	@P_H_S_Official	@NCSCT
@HHSGov	@PublicHealthW	@GlobalStateTHR
@NIH	@Publichealthni	
@ACSHorg	@ASH_LDN	
@theNASEM	@ASHScotland	
@ScottGottliebMD	@ASHWalesCymru	
@American_Heart	@UKCTAS	
@LungAssociation	@SMC_London	
@GlobalStateTHR	@CochraneTAG	
Example: To form a search phrase combine an item from '**X**' with an item from '**Y**' **i.e. X+Y** = @Surgeon_General #e-cigarette		

Table 13: List of items for formation of search phrases

The search strategy involved combining the address of a Twitter™ account with a hash-tagged e-cigarette term to form a search phrase. The selected Twitter™ accounts were those of organisations (or their representatives) which are related to e-cigarettes in a regulatory or health protection manner (see Table 14 below). The e-cigarette hash-tagged terms were validated e-cigarette-related keywords that have been used in other studies (257, 262, 263). All the possible combination of Twitter™ accounts plus e-cigarette terms were used as search phrases to collect data for analysis, even though some of the search phrases did not return any results.

All Twitter™ accounts present in the collected data were classified into agent-type; in other words, they were placed into groups according to similarities in features such as function of

the organisation, and under group names assigned by me to describe the distinctive characteristics of the group. For example, all organisations whose primary goal is to advocate for reduction in smoking in the society were classed as one type of agent and assigned the group name 'smoking cessation advocacy'. To enable classification of the Twitter™ accounts into various agents, I viewed the profile of each account and read their 'biography' to determine whether the account was a personal account or for an organised group. It is important to note, however, that although some people using a personal account tweet as individuals and state that 'views are all their own', they may have links to particular organisations that influence their views. For example, Prof. Simon Capewell was President of the Faculty of Public Health at the time of the study, while Prof. Kevin Fenton was PHE's National Director for Health and Wellbeing. Where the account was for an organised group, I also ascertained the function of the group. For organisational accounts where the profile did not have enough information to determine its classification into an agent, a Google search of the name of the account was conducted to read further from the organisation's website. For individual accounts that explicitly had the title of a political office on their biography, such accounts were classified as 'Politicians'. Note, however, that there was a degree of arbitrariness in assigning Twitter™ users to category of agents in this study. The agent type is shown in Tables 14 and 15 to provide transparency.

US Twitter™ Accounts (Type of agent)	Rationale for inclusion
@Surgeon_General (Health protection)	This is official X™ account of the US surgeon general. The surgeon general of the United States is the operational head and leading spokesperson on matters of public health in the federal government of the US. The surgeon general has been producing reports on tobacco smoking since the 1960s, and in 2016's report focused on E-cigarette use among youth and young adults.
@FDATobacco (Regulatory agency)	This is the official X™ account used to share news and updates from of the FDA Center for Tobacco Products (CTP). FDA CTP oversees the implementation of the Family Smoking Prevention and Tobacco Control Act. E-cigarettes are subjected to the FSPTCA as tobacco products and regulated by the FDA.
@US_FDA (Regulatory agency)	This is the official X™ account of the US FDA. The FDA is a US federal agency responsible for protecting and promoting public health including through the control and supervision of tobacco products (which includes e-cigarettes). FDA public health activities are funded annually by Congress, user fees paid by industries that make and market FDA-regulated products, and user fees paid by certain other entities. E-cigarettes are regulated by the FDA.
@CDCTobaccofree (Health protection)	This is the official X™ account used to share news and updates from the US Centre for Disease Control and Prevention (CDC) about smoking and tobacco use. Described on X™ biography as – Protecting health by working toward a world free from commercial tobacco-related death & disease. E-cigarettes are regulated as tobacco products and their use was framed as a public health emergency in the US.
@CDCgov (Health protection)	This is official X™ account of the CDC, and official source for daily credible health & safety updates from CDC. The CDC is the national public health agency of the US. E-cigarette use was framed as a public health emergency in the US.

US Twitter™ Accounts (Type of agent)	Rationale for inclusion
@HHSGov (Health protection)	This is the official X™ account used to share news and updates from the US Department of Health & Human Services (HHS). The HHS is a federal government department functioning to enhance the health and well-being of all Americans, by providing for effective health and human services and by fostering sound, sustained advances in the sciences underlying medicine, public health, and social services. HHS published and oversaw the Notice of Proposed Rule Making (NPRM) for e-cigarettes.
@NIH (Health research and education)	This is the official X™ account of the National Institutes of Health (NIH). The NIH is the US national medical research agency and part of the HHS. NIH is the largest public funder of biomedical research in the world, and funds research including on e-cigarettes.
@ACSHorg (Health research and education)	This is the official X™ account of the American Council on Science and Health (ACSH). The ACSH is a pro-science, research and education organization operating under Section 501I(3) of the Internal Revenue Code. The Council was founded in 1978 by a group of scientists with a singular focus: to publicly support and utilize evidence-based science and medicine and to educate the public by debunking junk science and exaggerated health scares. ACSH is funded by public (freewill) donations. The controversial nature of e-cigarette research findings poses a potential to be used for scaremongering.

US Twitter™ Accounts (Type of agent)	Rationale for inclusion
@theNASEM (Health research and education)	This is the official X™ account of the National Academies of Sciences, Engineering, and Medicine (NASEM). The NASEM is a US national institution that provide independent, trustworthy advice and facilitate solutions to complex challenges by mobilizing expertise, practice, and knowledge in science, engineering, and medicine. The US congress commissioned NASEM to conduct research to evaluate the available scientific literature, on both the short- and long-term health effects of e-cigarettes, to identify research gaps and make recommendations for future federally funded research.
@ScottGottliebMD (Individual)	This is the official X™ account of the 23rd Commissioner of the FDA. Scott Gottlieb was FDA commissioner from May 2017 until April 2019 (post e-cigarette regulatory period) and regarded in the literature as one of the most vocal commissioners on e-cigarette related matters.
@American_Heart (Health research and education)	This is official X™ account of the American Heart Association (AHA). The AHA is a voluntary charitable organization registered as a non-profit corporation dedicated to fighting heart disease and stroke. AHA also funds cardiovascular and cerebrovascular disease research. AHA has been vocal in their opinion about e-cigarette use within the population.
@LungAssociation (Health research and education)	This is official X™ account of the American Lung Association (ALA). The ALA is the leading Non-Governmental & Non-profit Organization working to save lives by improving lung health and preventing lung disease through education, advocacy, and research. E-cigarette use involves inhalation of an aerosol into the lungs. Therefore, e-cigarette use is an area that ALA are likely to educate the public on.

US Twitter™ Accounts (Type of agent)	Rationale for inclusion
@GlobalStateTHR (Smoking cessation advocacy)	This is official X™ account of the Global State of Tobacco Harm Reduction (GSTHR). The GSTHR is an advocacy organisation advocating the use of safer nicotine products (including e-cigarettes), regulatory responses to them, and the public health potential of tobacco harm reduction. GSTHR is funded by the tobacco industry.

Table 14: US Twitter™ accounts used in search strategy and rationale for inclusion.

UK Twitter™ Accounts (Type of agent)	Rationale for inclusion
@MHRApress (Regulatory agency)	This is the official X™ account used to share news and updates from the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA is an executive agency that regulates medicines, medical devices, and blood components for transfusion in the UK. MHRA is also the competent authority for the registration/notification of e-cigarettes in the UK. This account
@MHRAdevices (Regulatory agency)	This is the official X™ account used to share the latest health and safety information from MHRA. Since e-cigarettes can be regulated as medical devices and reported through the Yellow card scheme in the UK, information about their safety can be shared through this account.

@MHRAgovuk (Regulatory agency)	This is the official X™ account of the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA is an executive agency that regulates medicines, medical devices, and blood components for transfusion in the UK. MHRA is also the competent authority for the registration/notification of e-cigarettes in the UK.
@PHE_UK (Health protection)	This is the official X™ account of Public Health England (PHE). The PHE was an executive agency of the Department of Health and Social Care (DHSC) in England between 1 April 2013 to 1 October 2021 functioning to protect and improve health and wellbeing and reduce health inequalities. PHE was commissioned by the UK government to conduct research on the potential benefits and risk of e-cigarettes. They were also the competent authority for regulation of cross border sales of e-cigarettes.
@P_H_S_Official (Health protection)	This is the official X™ account of Public Health Scotland (PHS). PHS is the national agency for improving and protecting the health and wellbeing of the people of Scotland. PHS performed similar e-cigarette responsibilities to PHE within the Scottish jurisdiction.
@PublicHealthW (Health protection)	This is the official X™ account of Public Health Wales (PHW). PHW is the national public health agency in Wales. PHW performed similar e-cigarette responsibilities to PHE within the Welsh jurisdiction.
@Publichealthni (Health protection)	This is the official X™ account of Public Health Agency (PHA). PHA is the regional organisation in Northern Ireland for health improvement and health protection. PHA performed similar e-cigarette responsibilities to PHE within the jurisdiction of Northern Ireland.
@ASH_LDN (Smoking cessation advocacy)	This is the official X™ account used to share latest tobacco and smoking news from Action on Smoking and Health (ASH). ASH is an advocacy organisation advocating for policy measures to reduce the burden of disease and premature death caused by tobacco. ASH produces reports that covers patterns of use of e-cigarettes.

@ASHScotland (Smoking cessation advocacy)	This is the official X™ account of Action on Smoking and Health (Scotland). ASH Scotland is an independent Scottish charity taking action to reduce the harm caused by tobacco. ASH Scotland produces reports that covers patterns of use of e-cigarettes.
@ASHWalesCymru (Smoking cessation advocacy)	This is the official X™ account of Action on Smoking and Health (Wales). ASH Wales is the leading organisation working for a smokefree Wales. ASH Wales produces reports that covers patterns of use of e-cigarettes.
@UKCTAS (Health research and education)	This is the official X™ account of the UK Centre for Tobacco and Alcohol Studies (UKTAS). UKTAS is a consortium of 13 University teams conducting research on tobacco and alcohol use and addiction. UKTAS research activities include research on e-cigarettes.
@SMC_London (Health research and education)	This is the official X™ account of the Science Media Centre UK (SMC). SMC is an independent press office helping to ensure that the public have access to the best scientific evidence and expertise through the news media. SMC have published various scientific media responses to e-cigarette reports and policies around the world.
@CochraneTAG (Health research and education)	This is the official X™ account of the Cochrane Tobacco Addiction Group. The Cochrane Tobacco Addiction Group is based in the Nuffield Department of Primary Care Health Sciences. The group promotes evidence-based prevention and treatment, including use of e-cigarettes in smoking cessation.
@SwitchFinder (Individual)	This is the X™ account of Martin Dockrell. Martin was the Tobacco Control Programme Lead for Public Health England at the time of regulation of e-cigarettes.
@TheBHF (Health research and education)	This is the official X™ account of the British Heart Foundation (BHF). BHF is an independent charity that funds vital research into heart diseases, stroke and vascular dementia, and their risk factors like diabetes. Some of the research evaluating the potential risk of e-cigarettes involves risk of use of e-cigarettes to the heart.

@lunguk (Health research and education)	This is the official X™ account of the British Lung Foundation (BLF). BLF is the UK's lung charity fighting for right to breathe. BLF funds lung research and advocate for clean air and access to lung treatments. Some of the research evaluating the potential risk of e-cigarettes involves risk of use of e-cigarettes to the lungs.
@NICEComms (Health protection)	This is the official X™ account of the National Institute for Health and Care Excellence (NICE). NICE is the national experts that produces evidence-based health and social care guidance to help practitioners and commissioners get the best care to patients, fast, while ensuring value for the taxpayer. E-cigarettes have been included in NICE guidelines as a tool for smoking cessation.
@NCSCT (Smoking cessation advocacy)	This is official X™ account of the National Centre for Smoking Cessation and Training (NCSCT). NCSCT is a social enterprise committed to supporting the delivery of effective evidence-based tobacco control programmes and smoking cessation interventions provided by local stop smoking services and colleagues in the NHS. NCSCT is funded by Public Health England to train and support professionals so they can be effective in helping people stop smoking. E-cigarettes are a recommended smoking cessation tool in the UK.

Table 15: UK Twitter™ accounts used in search strategy and rationale for inclusion.

The collected data were put into Atlas.Ti, a software package for qualitative analysis. The data were read through by me, and key themes were identified and coded, with the coded data grouped according to the themes (see Appendix E). My supervisors carried out sense-checks by reading through coded data and comparing to identified themes. Sentiment analysis was then carried on tweets that generated either up to ten comments or the highest number of comments among tweets under each theme. The sentiment analysis carried out by the Atlas.Ti software automatically classified comments into positive, neutral, and negative sentences through interpretation of the emotions within the text data (see Appendix F). This means that Atlas.Ti classified comments as positive if they contained a majority of positive words such as 'easier', 'better'; as negative if they contained majority of negative words such as 'bad', 'kill'; and neutral if they contained words that were neither positive nor negative. During manual sense checking, if necessary, I reclassified comments that were in support of the initial post as positive, comments that disagreed with the initial post as negative, and comments that merely contributed to the initial post but were neither agreeing nor disagreeing with the initial post as neutral. The themes generated from the data are presented in Section 4.3 to understand the interest of organised groups and individuals related to e-cigarettes during the period of e-cigarette regulations. The findings of the sentiment analysis are also presented in Section 4.3 to understand public sentiments towards e-cigarettes and its regulation during the period of e-cigarette regulations.

Other methods considered for analysing the data in this study comprise Content Analysis – which seeks to determine the frequencies of aspects of language to understand a body of data (264) – and Discourse Analysis which looks strictly at what is said or written and how things are said to produce an understanding of the data within a social context (265). However, I was not interested in why people 'tweeted' about e-cigarettes in a particular way or the language they used in doing so (requiring discourse analysis) or how often people tweeted about e-cigarettes during the regulatory periods (requiring content analysis). Rather, I was interested in what people tweeted about e-cigarette regulation (requiring thematic analysis), and in their sentiments or emotions about e-cigarette and its regulations (requiring sentiment analysis).

Newcastle University Ethics approval was not required to carry out this study as all the data used were publicly available online and so no ethical issues were anticipated. However, all

analyses adhered to the terms of service, privacy policy, and rules and policies of Twitter™ (266).

4.3 Findings from study two

The search on Twitter™ across four periods produced a total of 454 tweets from different types of Twitter™ accounts that could be classified into 12 agents within different social fields. These agents comprised: Individuals; Regulatory agencies; Health protection agencies; Smoking cessation advocacy groups; Audit and public accountability institutions; Health research and educational organisation; News outlets and magazines; Vape companies, sellers and suppliers; Vape advocates; Politicians; Professional Health associations; and Unclassified organisations. The results from analysis of the data are presented in four sections, corresponding to the four time periods for which data were collected. Tweets which generated either up to ten comments or the highest number of comments among tweets under each theme were included in the sentiment analysis. Table 16 below shows the agents and total number of tweets analysed in each regulatory period.

Data collection period	**Type of tweet posters/ Agents**	**Number of agents**	**Number of tweets analysed**
US E-cigarette Pre- regulatory period (25/04/2014 – 08/08/2014)	Audit and public accountability institutions	1	1
	Health professional associations	3	3
	Health research and educational organisations	7	7
	Individuals	19	25
	News outlets and magazines	4	4
	Regulatory agency	1	3
	Smoking cessation advocates	6	12
	Vape advocates	4	8
	Vape companies	4	5
	Politicians	2	2

	Unclassified	3	5
	Total	**54**	**75**
US E-cigarette Post- regulatory period (10/05/2016 to 23/08/2016)	Audit and public accountability institutions	2	3
	Health professional associations	5	9
	Health protection organisation	5	11
	Health research and educational organisations	3	4
	Individuals	45	67
	News outlets and magazines	4	5
	Regulatory agency	1	13
	Smoking cessation advocates	5	15
	Vape advocates	13	31
	Vape companies	5	11
	Politicians	1	1
	Unclassified	2	2
	Total	**91**	**172**
UK E-cigarette Pre- regulatory period (2-1-2016 to 17-4-2016)	Health professional associations	2	3
	Health protection organisations	3	4
	Health research and educational organisations	6	9
	Individuals	31	47
	News outlets and magazines	7	10
	Regulatory agency	1	1
	Smoking cessation advocates	5	9
	Vape advocates	2	4
	Vape companies	7	13
	Unclassified	2	3
	Total	**66**	**103**

UK E-cigarette Post- regulatory period (20-5-2016 to 2-9-2016)	Health professional associations	3	5
	Health protection organisations	3	4
	Health research institutions	5	8
	Individuals	38	49
	News outlets and magazines	6	9
	Smoking cessation advocates	4	11
	Vape advocates	3	3
	Vape companies	6	12
	Unclassified	2	3
	Total	**70**	**104**
	Overall Total	**281**	**454**

Table 16: Sample description of analysed Twitter™ posts

As can be seen in Table 16 above, study two analysed 454 tweets from 281 Twitter™ accounts. Similar agents were involved in e-cigarette related discussions pre- and – post e-cigarette regulation in the US and the UK, with four exceptions. Audit and public accountability institutions, and politicians featured only in the US but not the UK pre- and – post regulatory period. Health protection organisations feature in three of the four time periods, the exception being the US pre- regulatory period. Regulatory agencies feature in three of the four time periods, the exception being the UK post- regulatory period

4.3.1 US E-cigarette Pre- regulatory period (25/04/2014 – 08/08/2014)

Data collected from Twitter™ to cover the e-cigarette pre-regulatory period in the US, as represented in this study by dates ranging from 25th April 2014 to 8th August 2014 (referred to hereafter as Data Set 1), produced a total of 75 initial tweets with their associated comments. The highest number of tweets (7 tweets) was from a smoking cessation advocacy agent, CDC Tobacco Free, and one of their tweets (*'Are you a former smoker? Share your story & inspire others to quit')* also generated the highest number of responses (72 comments) in this e-cigarette pre-regulatory dataset. Note that CDC (the Centre for Disease

Control and Prevention) is a US government health security agency. The tweet with the second highest number of responses (42 comments) was from the American Heart Association (@American_Heart), a Professional Health Association, and read *'STUDY: E-cigs may not help you #kickthehabit after all. #stopsmoking #smoking #ecigs.'*

Four themes were identified in Data Set 1: Updates or Clarification on e-cigarette regulation; E-cigarettes as a smoking cessation aid; E-cigarettes as a public health concern; and Growing use and popularity of e-cigarettes. These themes are discussed below. Figure 8 below shows the themes in the Data Set 1.

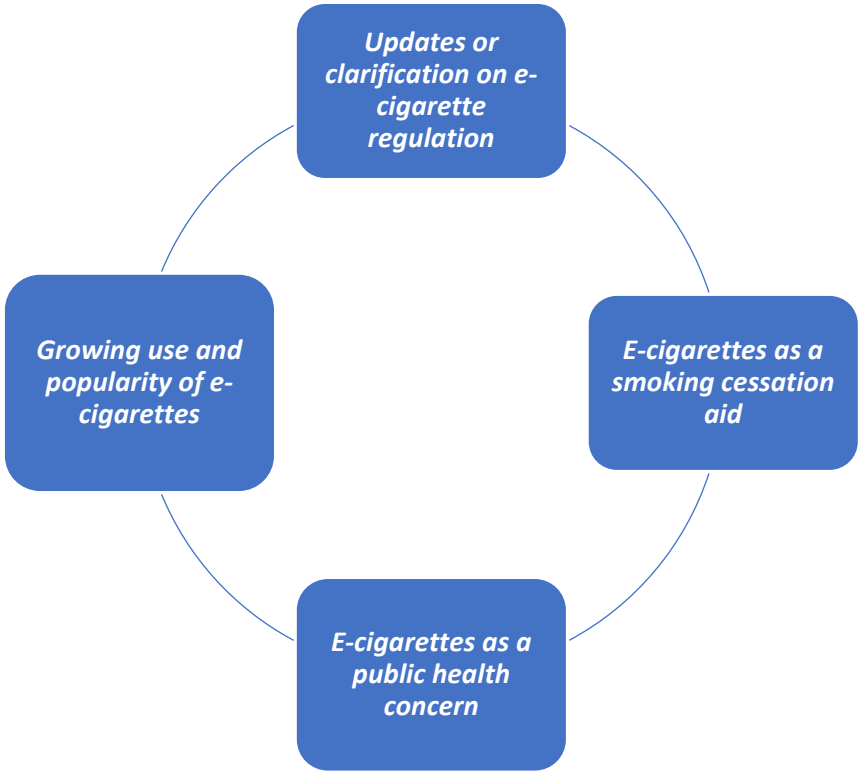


Figure 8: Themes identified from US pre-regulatory Twitter™ discussions.

4.3.1.1 Updates (or clarification) on e-cigarette regulation

In Data Set 1, a total of 12 tweets appeared as an update on the proposed e-cigarette regulations in the US. These tweets were from seven different agents: Regulatory agencies (FDATobacco); Smoking cessation advocacy groups (SCLC_UCSF, tobaccofreemass); Audit and public accountability institutions (USGAO); Health research and educational organisation (science2_0); News outlets and magazines (JRCarrollNews); Vape advocates (FightToVape, sfataorg); Individuals (DyNama, unclejohnCC). Some of these tweets were general in nature

and informed the public of the FDA's intention to regulate e-cigarettes. For example, one tweet from the US Government Accountability Office (@USGAO) read *'@FDATobacco proposes to regulate cigars, pipe tobacco, #ecigarettes. We've reported on differences in federal reg.'* Others reflected expectations of e-cigarette regulations; for example, one tweet from a smoking cessation advocacy group (@tobaccofreemass) read *'indoor air policies must include all tobacco products and electronic nicotine delivery systems/#ecigs.'* Some other tweets suggested some of the possible reasons for the proposed e-cigarette regulation. For example, @FDATobacco – the regulatory body regulating e-cigarettes – tweeted that *'FDA oversight of additional tobacco products can help limit youth exposure to products like #ecigs & #cigars #tobaccocontrol'*.

A sentiment analysis of the ten comments following the latter tweet showed that eight of the responses were negative and in disagreement with the FDA tweet. For example, one read *'aside from age restrictions on purchase, nothing you have ever done or ever will do will make any difference to curious kids.'* The only comment identified by Atlas.Ti software as positive was sarcastically negative on closer inspection and read *'you bet. Because it worked so well so far. Almost 20 years of #tobaccocontrol and hardly a change.'*

Overall, this theme was represented by organised groups and individuals updating their audience on the proposed e-cigarette regulations, either by directly creating awareness of the proposed regulation, putting forward opinions on some rules they expected from the proposed regulation of e-cigarettes, or informing their audience of the perceived benefits of regulating e-cigarettes.

4.3.1.2 E-cigarettes as a public health concern

During the US e-cigarette pre-regulatory period, some Twitter™ users posted tweets (21 tweets) that were related to health concerns with the use of e-cigarettes. Apart from individuals, the class of agent most likely to tweet about public health concerns was Health research and educational organisations (4 Twitter™ accounts: UR_Med, AmericanLungDE, SDCollab, URMCSHORE). Some of the tweets revealed the poster's negative sentiments towards e-cigarettes. For example, one Twitter™ user (an individual) posted sarcastically *'If I were a kid, I'd much rather have beer and firecrackers than an #ecig but thanks for keeping*

me safe. #vaping #WHO #FDA #CDCTobaccoFree.' However, seven of the tweets that addressed health concerns related to e-cigarettes were in respect of a study that had found third hand nicotine from e-cigarette exposure (i.e., nicotine affecting non-users of e-cigarettes when they have not been exposed to e-cigarette use). An example of such a tweet is one from an individual (@1eaguilera) that read *'Study of third hand nicotine from e-cigarette exposure wins top NIH Addiction Science Award #ecig.'* No link was provided to the cited research.

Fourteen tweets suggested that some Twitter™ users perceived some of the tobacco or e-cigarette related organisations posting e-cigarette health concerns as having an anti-vaping agenda or a biased position regarding e-cigarettes. The organisation that appeared to come under the most attack was @CDCTobaccoFree (the Twitter™ handle for the US Centre for Disease Control and Prevention's Office on Smoking and Health: https://www.cdc.gov/tobacco/). @CDCTobaccoFree were the subject of five out of the nine tweets representing this theme. One such tweet, calling out the organisation, was from a vaping advocacy group (@FightToVape) and read *'@CDCTobaccoFree Will the Anti-Tobacco #HarmReduction Lobby finally recognize their Anti-#Ecig Campaigns as Harmful?'* Another tweet was from an individual (@JeffaStier) who wrote *'Thanks to @CDCTobaccoFree & other anti- #Ecig activists, many are going back to cigarette smoking.'* It was not only smoking cessation advocacy groups such as @CDCTobaccoFree that came under public scrutiny. Thematic analysis showed that professional health organisations were evaluated on their positions with regards e-cigarettes. For example, the American Heart Association was accused of being biased in their position on e-cigarettes in one tweet from an individual (@Dave_in_Ok) that read *'@American_Heart How many smokers will continue to smoke because of your shameful biased position on #ecigs? #Improof.'*

Not all of the tweets associated with this theme related to risks associated with e-cigarettes. There were also tweets that seemed to allay people's concerns regarding e-cigarettes. Notably, two tweets that reported studies with positive outcome for e-cigarettes came from the same individual (@DyNama), who did provide links to the cited research. One of the tweets read *'New study finds no health concerns in #ecig vapor http://acsh.org/2013/08/new-study-finds-no-health-concerns-in-e-cig-vapor/ @acshorg,'*

while the other read *'new study confirms heart effects from smoking not present in #vaping* *http://acsh.org/2014/06/new-study-e-cig-expert-confirms-heart-effects-vaping/* *@acshorg.'*

Another tweet classified under this theme of e-cigarettes as a public health concern and producing over ten responses was from a public health physician (@DonnaWillisMD) and read '*Ref #Nicotine = HEROIN @CDCgov @NIH @UMNews #ecigs*.' All the responses (15 comments) to this tweet were either questioning the premise of the tweet or explicitly disagreeing with it, such as one comment that read *'hmm saying Nicotine is as addictive as heroin does not equate to NICOTINE = HEROIN. Or am I missing something here?'*

Generally, with regards public health concerns, during the US e-cigarette pre-regulatory period, individuals tended to tweet their concerns directly, or tweet news and studies that resonated with their concerns or reassurances about e-cigarettes. The public, especially vape activists, were aware of and in opposition to what they perceived as a biased and anti-vaping agenda from various organistions.

4.3.1.3 E-cigarettes as a smoking cessation aid

A total of 23 tweets in Data Set 1 were related to the effectiveness of e-cigarettes as a smoking cessation aid, indicating that the role of e-cigarettes in this aspect of public health was a major talking point during the e-cigarette pre-regulatory period. One tweet that generated a lot of responses (42 comments) was from the American Heart Association (@American_Heart) who posted *'STUDY: E-cigs may not help you #kickthehabit after all. #stopsmoking #smoking #ecigs.'* All 42 responses to this tweet were either a testimony to the opposite or a disagreement with the tweet. For example, one individual (@_joker_mike) tweeted – *'After all I can tell you, me and my fellow vaping friends did quit smoking, upps. Maybe a wrong study #ecigs.'* Also, the original tweet by @American_Heart neither cited the study referred to, nor provided a link to it, prompting comments such as: *'I quit smoking a year ago with e-cigs. Cite research or stop lying.'* No commenter, however, cited a research study that contradicted @American_Heart's assertion and showed that e-cigarettes may help people stop smoking; responses were about anecdotal evidence of individual experience.

A sentiment analysis showed that 30 out of the 42 comments to @American_Heart's tweet represented a negative sentiment towards the primary tweet, which translates to disagreement with the tweet. On close inspection, the remaining 11 positive and one neutral comment were also testimonials of the effectiveness of e-cigarette as a smoking aid. For example, one comment read *'4 Years #smokefree thanks to #ecigs!! Look at the real studies and evidence!!,'* and another stated *'I quit. Wife quit. Sister quit. 5 friends I helped to start e-cigs quit. My personal experience begs to differ. #Improof.'*

In addition to the initial tweets that directly made reference to e-cigarettes and smoking cessation, some other tweets from regulatory agencies such as the FDA, smoking cessation advocacy agents such as CDC Tobacco Free and professional health associations such as the Lung Association, simply called on people to quit smoking and to share their quit smoking stories to inspire others. The responses to these set of tweets also ended up being in the main testimonials to the effectiveness of e-cigarettea as a quit smoking aid. For example, the tweet from CDC Tobacco Free that read '*Are you a former smoker? Share your story & inspire others to quit,'* had the highest (72 comments) number of responses in Data Set 1. Amongst these responses, the only smoking cessation aid mentioned to be effective in the stories shared was the e-cigarette. For example, one comment read *'I tried everything.The only thing that worked was ecigs. Over a year tobacco free and never felt better,'* and another read '*ex-smoker 31yrs quit the day I started ecigs 1yr 6mo ago. Tried the pill, patch, and gum all failed but ecigs. Feel better.'*

Generally, during the US e-cigarette pre- regulatory period, several organisations campaigned for people to quit smoking, and the most popular means indicated by respondents as being effective for smoking cessation attempts were e-cigarettes. Any tweet that suggested that e-cigarettes were ineffective for smoking cessation was largely met with opposition and negative sentiments.

4.3.1.4 Growing use and popularity of e-cigarettes

The US e-cigarette pre-regulatory period had five tweets about the growing use and popularity of e-cigarettes. Two of the tweets came from news outlets - @PrairieBiz and @ThePortlandTrib who tweeted *'As #e-cigarette use rises, #doctors split on advice to*

patients @mnmed @TCMSMN @CDCgov #Pbiz' and *'Cigarette giant to release its own e-cig in Portland: In another sign of the emergence of electronic cigarette'* respectively. However, tweets within this theme were not only about information on the rise in production and use of e-cigarettes, but also on promotion of use and vaping knowledge. For instance, one individual (@ECRJohn) tweeted that *'American Heart Association and Others Praise Missouri Governor for Allowing #Ecig Sales to Teens via @ecigadvanced,'* while a vaping advocacy group (@VapeRights) tweeted that *'@ACSHorg is on a roll today. Give them a follow for some solid wisdom. #vaping.'* Therefore, during the US e-cigarette pre regulatory period, online activities on Twitter™ included e-cigarette promotional activities and suggestions of an increase in the use of e-cigarettes. However, discussion of this theme is limited by the low numbers of tweets and lack of comments to any of the tweets in Data Set 1, precluding the conduct of sentiment analysis.

4.3.2 US E-cigarette Post- regulatory period (10/05/2016 to 23/08/2016)

Data collected from Twitter™ to cover the e-cigarette post-regulatory period in the US, as represented in this study by dates ranging from 10th May 2016 to 23rd August 2016 (hereafter referred to as Data Set 2), produced a total of 172 initial tweets with their associated comments. However, only 129 posts could be grouped into themes, as the remaining 43 post and associated comments did not have enough information to allow classification. For example, one tweet from an individual (@Anisyaaaaaaaaaa) read *'Here for you #vape #vapelife #vapecommunity #vapeon #vaper #vapegram #vapegirls'*; there was no comment to this post.

Data Set 2 had tweets from a range of different agents as shown in Table 15 above. The highest contributor to Data Set 2 was a Regulatory agency, @FDATobacco, with 13 posts. The second highest contributor was a Smoking cessation advocate, @CDCTobaccoFree (10 posts), who also had the highest number of comments (36 comments) in response to one of their posts which read *'Tobacco and tobacco smoke are a toxic mix of more than 7,000 chemicals, including tar. What's in your lungs?'*.

Five themes were identified from analysis of Data Set 2: Updates or clarifications on e-cigarette regulation; Research on e-cigarettes; Opposition to e-cigarette regulations and

policies; E-cigarettes as a smoking cessation aid; and E-cigarette as a public health concern. These themes are discussed below. Figure 9 below shows the themes in the Data Set 2.

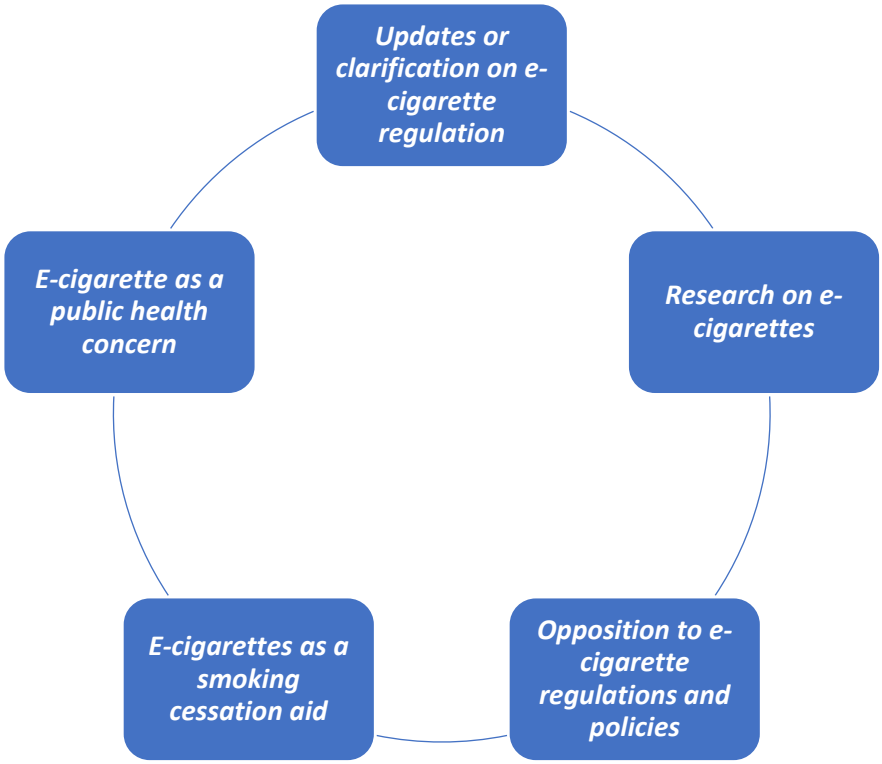


Figure 9: Themes identified from US post-regulatory Twitter™ discussions.

4.3.2.1 Updates (or clarification) on e-cigarette regulation

In Data Set 2, 42 posts appeared as an update or clarification on e-cigarettes and their regulation. The highest contributor to Data Set 2 was a Regulatory agency (@FDATobacco); for 'tobacco products.' @FDATobacco posted 12 tweets which either updated the Twitter™ community on e-cigarette regulations or clarified parts of the e-cigarette regulations. For example, one of their update tweets read *'REMINDER: The comment period for our draft guidance on pre-market tobacco applications for ENDS closes at 11:59 PM (ET) tonight,'* and another read *'CTP updates its Safety Reporting Portal with more ways for submitting suspected problems with tobacco products: http://1.usa.gov/1YbhSXq.'* One of their tweets clarifying e-cigarette regulations read *'#Ecig regulations aren't a ban; they allow manufacturers to apply to have #ecigs brought to, or stay on, the market,'* and another read '*To protect public health, all #tobacco products are being regulated to ensure they are in compliance with safety standards.'* @VitalStrat (whose Twitter™ profile declares them to be

a non-governmental and non-profit organisation '*reimagining public health, working for a world where everyone, everywhere is protected by equitable and effective public health systems')* posted an update that read *'The @FDATobacco Director Mitch Zeller discusses the new regulations on #ecigarettes tobacco products in the US.'* @HHSGov (which provides '*News and information from the U.S. Department of Health & Human Services'*) posted that *'FDA regulation of new tobacco products is a crucial step in reducing tobacco-related disease & death'.* @mihotep (Individual) challenged this post with the comment: *'prove it! Show evidence #FDA regulation has made any #tobacco product safer. They've had 7 years. Where's the safe #smoking?'*

Research organisations and news outlets also provided updates on the state of e-cigarette regulations as in a tweet from @PHMC_Research that read *'New @FDATobacco regs on #ecigarettes and #cigars go into effect Monday! What can your state do? http://bit.ly/2areB1f,'* and one from @NJSpotlightNews that read *'New @US_FDA Rules Limit the Sale of E-Cigarettes @HillNJTV reports @FDATobacco #ecigarettes http://bit.ly/2b6mLkF.'* Posts from Individuals in Data Set 2 tended to be mostly questions seeking clarifications from the FDA on e-cigarette regulations and policies. For example, one post from @ThaumaturgeRN asked *'If I assemble random parts into an #ecig for personal use, do I need a PMTA? #AskCTP @FDAtobacco'* and another from @CrazedChemist1 enquired *'@FDATobacco So you're saying my e-liquid that is made using synthesized nicotine is NOT a tobacco product?'* The post that generated the highest response (28 comments) was a tweet from @FDATobacco that read *'If they contain nicotine derived from tobacco, #ecigs meet the definition of a 'tobacco product' and are regulated accordingly.'* The information in this post was the most common clarification by @FDATobacco in response to query from other Twitter™ users, as they posted five other similar tweets; the comments in response to these further posts were quite similar in content and sentiments.

A sentiment analysis of the comments to the above tweet showed that the majority (20 out of 28 comments) of commenters expressed a negative sentiment to the initial post. i.e., disagreed with FDA's argument on why e-cigarettes were being regulated as tobacco products. For example, one of the negative sentiments was from @K_d_a7 (Individual), and it read '*Basically it's because @FDATobacco says they are. We all know #ecigs are not really tobacco*.' Another from @Vapingit (Vape advocate) read *'What are you babbling about,*

@FDATobacco? Milk isn't beef. Syrup isn't wood. Nicotine isn't tobacco. Government isn't honest.' The four comments classified by Atlas.Ti as exhibiting neutral sentiments were also identified by me as negative comments in the context of e-cigarette regulations. For example one of the comment from @stuartf100 (Individual) read *'@FDATobacco This is how it's affecting the most vulnerable in society. Hope you're proud https://m.facebook.com/story.php?story_fbid=1743170175950526&id=1606220196312192'* Likewise, the four comments classified by Atlas.Ti as illustrating positive sentiments were identified by me as sarcastically negative comments in the context of e-cigarette regulations. For example, one of the comments from @MattDidius77 (Individual) read *'because Prohibition worked so well, almost as well as the 'war on drugs'. You guys reach a fuckwit scale of 10/10,'* and another comment from @dwthompson891 (Individual) read *'You mean how quickly you will shut down the #ecig industry?'*

Overall, during the US e-cigarette post-regulatory period, four different types of agents, comprising Regulatory agencies, Health protection agencies, Research organisations and News outlets, provided updates on the state of e-cigarette regulations. Individuals also asked the FDA questions about their e-cigarette regulations, and @FDATobacco provided clarifications in response to such queries and regarding other aspects of e-cigarette regulation and policies. Clarifications from FDA that had to do with why e-cigarettes were being classified as tobacco products were mostly responded to negatively.

4.3.2.2 E-cigarettes as a public health concern

Analysis of Data Set 2 showed that 20 Twitter™ posts related to public health concerns associated with the use of e-cigarettes. The tweet under this theme with the most responses (15 comments) was from a health protection agency (@CDCDirector), and read *'Emerging tobacco product use (hookahs & e-cigarettes) highest among 18-24 year olds. @CDCMMWR http://bit.ly/29GzMqK.'*

It appeared that there were concerns about the increasing use of e-cigarettes among high schoolers as represented by one tweet from a health research institution (@CDHSDelaware) which read *'CDC Press Release: #Cigarette use among high schoolers at all time low, but #E-cigarette use a concern http://cdc.gov/media/releases/2016/p0609-yrbs.html via @CDCgov,'*

while another from a health professional association (@ASAMorg) read *'By @CDCgov's Nat'l Youth #Tobacco Survey: there has been a 10-fold incrs. In current #ecig use among H.S. students.'* The main concern about an increase in use e-cigarettes by high schoolers was that e-cigarettes may serve as a gateway to smoking cigarettes. For example, one smoking cessation advocate (@FACTmovement) posted *'Teens who try e-cigs are 6 times more likely to try reg cigarettes within 2 years than those who never used them.'* However, one vape company (@blackhatcigs) opposed such claims of e-cigarettes as a gateway to smoking in their post which read *'We called the @CDCgov out on their claim vaping is a gateway to cigs. http://bit.ly/1Q3JnQZ #vapenews #vape #ecig.'* Also, one individual (@Amelia_RH), a Sociology PhD candidate researching on vaping tech/politics/panic, appeared to have started a trend suggesting that the CDC had misplaced priorities and there were more important things that the CDC should be concerned about rather than e-cigarettes. For example, @Amelia_RH posted four tweets as follows: *'17.7% of students seriously considered attempting suicide in past 12mo but #ecigarette use a concern #YRBS http://cdc.gov/media/releases/2016/p0609-yrbs.html @CDCgov'*; *'25.6% of students hadn't been to the dentist in 12 months, but #ecigarette use is a concern #YRBS http://cdc.gov/media/releases/2016/p0609-yrbs.html @CDCgov'*; *'41.7% of students play more than 3 hours of video games per day, but #ecigarette use is a concern #YRBS http://cdc.gov/media/releases/2016/p0609-yrbs.html @CDCgov'*; and *'39.0% of students did not eat any vegetables in 7 days before survey but #ecigarette use is a concern #YRBS http://cdc.gov/media/releases/2016/p0609-yrbs.html @CDCgov.'*

Another concern with the use of e-cigarettes that appeared in Data Set 2 came from a health professional association (@LungAssociation) who tweeted *'Even though we know that diacetyl causes popcorn lung, this chemical is found in many e-cigarette flavors http://bit.ly/29pLUa8.'*

Five tweets from five different individuals also suggested that some of the public health concerns presented by *@FDATobacco and @LungAssociation* were a dishonest representation of e-cigarettes. @BrisyCoe (Individual) posted a tweet that read *'@FDATobacco When people seek the Truth they will find it in abundance, it's alive and well in all #Vapers #Vapeon.'* This tweet appeared to suggest that the FDA, as the regulatory agency for e-cigarettes in the US was dishonest in their communication about e-cigarettes.

This perception of FDA dishonesty can also be seen in another tweet from @imarocker14 (Individual) which read *'@FDATobacco @POTUS #nomorecasualties #nomorelies #VapingSavesLives #iamproof #notblowingsmoke #truthiscoming #vapeon.'* The @LungAssociation was also called out as dishonest in their communications about e-cigarettes. For example, @scottie_freeman (Individual) posted *'@LungAssociation you have misled the people about e cigs for funding. I have forgiven Hitler and will forgive you but ask to please stop,'* @VocalEK (Individual) wrote *'@LungAssociation Your mission is 'save lives by improving lung health and preventing lung disease', why #ecig lies?'* and @whycherrywhy (Individual) tweeted *'Want donations from millions of vapers, @AmericanCancer @LungAssociation? Quit lying to smokers about the risk of switching to e-cigs.'*

A sentiment analysis of the comments to the tweet above from @CDCDirector regarding increased use of hookahs and e-cigarettes among 18-24 year olds showed that the majority (11 out of 17 comments) of the responses to the initial tweet exhibited negative sentiments i.e., disagreed with how the statistics were presented. For example, one of the negative comments read *'They often comingle combustible tobacco & ecigs. Easier to demonize that way.*' Indeed, both positive and neutral comments also appeared to address how the initial tweet was presented. For example, one of the neutral comments from @markse68 (Individual) read '*where's the tobacco in ecigs?How long will you keep lying?? Shouldn't your job description include caring for health?'*

Overall, during the US e-cigarette post-regulatory period, some Twitter™ users had concerns that e-cigarettes had the potential to lead people to smoking, and about increasing use among teenagers. Other Twitter™ users opposed the assertions that e-cigarettes act as a gateway to smoking, and thought there were more important things than e-cigarettes for the government agencies such as CDC to concern themselves with. Some Twitter™ users were uncomfortable with the classification of e-cigarettes as tobacco products, and some accused a regulatory agency (FDA) and a health professional association (American Lung Association) of being dishonest in their communications about the risk of switching from smoking to e-cigarette use.

4.3.2.3 E-cigarettes as a smoking cessation aid

Data Set 2 had 34 posts about e-cigarettes and smoking cessation. Some posts, mainly from health protection agencies (@CDCChronic and @CDCDirector) and smoking cessation advocates (@swimdaily, @SmokefreeUs, @TobaccoFreeKids, and @CDCTobaccoFree) basically advocated for people to quit smoking. The responses from vape advocates and individuals indicated that they considered e-cigarettes as the most effective quit smoking aid but CDC made no such explicit recommendation. For example, @CDCChronic posted that '*Cravings are a difficult thing about quitting #smoking, but they disappear about 3 weeks after you quit. http://1.usa.gov/1OmsECo*.' The post attracted comments such as from @mihotep (vape advocate) – *'No they don't. That's why 97% of quitters relapse to #smoking w/in 1yr. Except #vapers, those stay #quit,'* and also from @VaporAnecdote (vape advocate) – *'Says the nonsmoker. Longest quit on 'approved' methods = 7 months, craved them the WHOLE time. Only e-cigs kept me smoke free.'* The individuals who contributed to the posts in Data Set 2 also seemed to be surprised that the FDA did not yet recognise e-cigarettes as a smoking cessation aid. For example, @Animated_NC posted that *'So @FDATobacco doesn't see #vaping as a smoking cessation alternative, yet I've been smoke-free for 17 months now. #vape #vapingsaveslives,'* while @foxymiraj also posted *'Hey @FDATobacco – even the UK can acknowledge that more people use #vaping to #QuitSmoking – http://bit.ly/29tPwWy #ecig #vape #savemylife.'* Furthermore, a vaping advocate's (@Vapingit) tweet called for an explanation of why the FDA does not recognise e-cigarettes as a smoking cessation aid, in a post which read *'@HHSGov @FDATobacco @US_FDA Explain denial of #ecigs as a way of curbing tobacco deaths. https://dropbox.com/s/qyr1nq0mais08qk/Nicotine%20without%20smoke_2016_WEB.PDF?dl=0*'. One tweet from an individual (@JeffaStier) suggested that CDC sees e-cigarettes as the reason people are not quitting smoking. The post from @JeffaStier read *'Got it... thanks. Interesting stuff. @CDCgov blames #ecigs for people not quitting tobacco use.'*

There were 12 tweets that suggested e-cigarettes are a safer alternative to smoking and that the relative safety of e-cigarettes compared to tobacco cigarettes was the reason people preferred e-cigarettes to smoking or using them as a quit aid. Some individuals posted tweets in this regard as in these examples: @foxymiraj wrote *'Hey @FDATobacco – You say you don't have evidence that #vaping is safer? Here it is:*

http://bizjournals.com/buffalo/news/2016/08/18/roswell-park-study-finds-e-cigarettes-safer-less.html?ana=twtms #ecig #vapingsavedmylife; @PxDIZZLE wrote *'The American Heart Association Says #Vaping Is Safer Than Smoking http://motherboard.vice.com/read/the-american-heart-association-says-vaping-is-safer-than-smoking @motherboard #VapingSavesLives #Vape #IvapeIvote;* @pandaflop1 posted *'@FDATobacco given the fact e cigs are 95% healthier than traditional cigarettes – I'd prefer to stay on ecigs rather than smoke again.'* A vape advocate (@BRAVEmediaMO) also posted *'Want to quit smoking? Switch to a much safer product! #ecigs do that and more! Guess who can't silence me? @FDATobacco @CDCTobaccoFree.'* Other vape advocates also emphasized in their tweets that e-cigarettes are relatively safer than tobacco cigarettes. For example, @Vapingit posted *'@FDATobacco #Ecigs 'We don't know what's in them' LESS HARM~That's what's in them. @jbcoleman13 Keep ON #Vaping ON,'* and @mihotep posted *'@VapinGreek @BfloBizFirst @FDATobacco amazing! If outdated #vape gizmos w/no safety features are #harmless & effective imagine today's tech.'*

In Data Set 2, the tweet with the most responses (36 comments) was from a smoking cessation advocacy organisation (@CDCTobaccoFree) who posted *'Tobacco and tobacco smoke are a toxic mix of more than 7,000 chemicals, including tar. What's in your lungs?'* This post did not directly refer to e-cigarettes but many of the responses were about e-cigarettes. A sentiment analysis of the comments to this post showed some negative and neutral sentiments related to e-cigarettes. An example of a negative comment related to e-cigarettes is from @ABL_Fanpage (Individual) - *'Since I had the opportunity to vape – I have clean lungs! But I only till @FDATobacco laws kills me and other vapers.'* One example of a neutral comment is from @VapeEducation (Vape advocate) – *'I worked in the tar industry; trust me this isn't in cigarettes. U smoke u die right away. Lol. More govt lies.'*

Another tweet with 11 comments under this theme was from an individual (@Clive_Bates) and read *'So @FDATobacco says: 'we don't want the public to perceive [ecigs] as a safer alternative to cigarettes' http://parallax.news/should-vaping-be-regulated/ #Lawyers.'* A sentiment analysis of the comments to the initial tweet from @Clive_Bates shows that eight of the comments had negative sentiments, two had positive sentiments, and one had a neutral sentiment. An example of a negative sentiment is from @Cloudy_Judgemnt (Individual) who said '*why would they do that? The way I see it, the $$ they stand to make*

from PMTA, they would be pushing #ecigs.' One of the positive comments from @CarmAndria (Individual) read 'Which means '*We prefer to lie to the public than tell them the truth about e-cigs. And this is our GOV'T!*' The only neutral comment from @nigelrudd (Individual) read *'Used to be called deception. Used to be unlawful.'* Although the three comments above have been classed by ATLAS.Ti as'negative, positive and neutral respectively, they all seem to me to disagree with @FDATobacco's statement in @Clive_Bates post.

Overall, Data Set 2 showed that, during the US e-cigarette post-regulatory period, health protection agencies and smoking cessation advocates were concerned about bringing down smoking rates but were reluctant to acknowledge that e-cigarettes, a popular quit smoking aid among ex-smoker Twitter™ users and vaping advocates, were an effective smoking cessation tool.

4.3.2.4 Opposition to e-cigarette regulations and policies

In Data Set 2, there were 23 posts opposing e-cigarette regulations and policies. Aside from posts from Individuals (13 posts), Vape companies and Vape advocates were the groups of agents most opposed to e-cigarette regulations, with nine posts in Data Set 2. Only one post came from outside the above-mentioned agents and was from a News outlet (@Nature) which tweeted *'Scientists should unite over electronic-cigarette regulation, or big tobacco will step in. http://bit.ly/24O5sdk.'* Some of the individuals who were in opposition to e-cigarette regulations appeared to be concerned about a perceived negative implication of e-cigarette regulation, i.e., that the regulations could get in the way of the use of e-cigarettes to aid smoking cessation attempts. For example, one individual (@wilpertheone) tweeted *'@US_FDA @FDATobacco @BarackObama #supportHR258 Quit helping Big Tobacco kill billions! 5 years tobac free with E cigs,'* while another (@VCPHX_MARK) tweeted *'Knowing you cannot be helpful to those in need because of @FDATobacco regulations. #vapenation #ALLLIVESMATTER.'* One of the tweets from a Vape advocacy organisation (@BRAVEmediaMO) showed similar concerns, saying *'@FDATobacco #ecig regs will push people back to smoking http://motherboard.vice.com/read/how-e-cigarette-regulations-might-push-vapers-back-to-smoking-e-cigarettes-fda #vaping.'*

Vape sellers and advocates also updated the Twitter™ community on their efforts to fight against the e-cigarette regulations. For example, @blackhatcigs (vape seller) tweeted that *'The @FDATobacco had to know #vapers weren't going down without a fight! #vapeshop #vapetruth #vapefam #vapenation https://vapes.com/blogs/news/historical-lawsuit-slams-fda-e-cig-regulations-with-8-violations';* @sfataorg (vape advocate) posted *'#Vapor industry prevented @FDAtobacco #ecig flavor ban with our collective efforts & OMB meetings. #Advocacymatters https://regulations.gov/#!documentDetail;D=FDA-2014-N-0189-83193';* and a post from @JeffaStier (individual) read *'@HHSGov denied our request for expedited processing of my @FDATobacco #ecig #FOIA request. I argued it was life or death. HHS disagrees.'*

During the US e-cigarette post-regulatory period, some tweets (5 posts) suggested that @SenRonJohnson (Republican senator, representing Wisconsin) was a vocal advocate against the e-cigarette regulations. For example, one individual (@Fieryredvaper) posted *'@SenRonJohnson Thank you so very much for standing up to @FDATobacco and standing up for #ecigs #eliquid and #VapingSavesLives #SaveVaping,'* while a vape advocate (@freshvaper_com) also tweeted that *'We want to thank @SenRonJohnson for investigating the poor choices of @FDATobacco Thank You! #vape #VapeCommunity.'*

Finally, one post from a vape advocate (@GregTHR) seemed to suggest that the CDC were not in favour of e-cigarettes. The post, which had more than 11 comments in response, read *'CDC loves low nicotine cigarettes, hates vapor products regardless of nicotine content http://businesswire.com/news/home/20160616005829/en/22nd-Century%E2%80%99s-Proprietary-SPECTRUM%C2%AE-Cigarettes-Identified-Crucial #ecigs #vaping.'* Atlas.ti's sentiment analysis of responses to the post from @GregTHR revealed that the majority (six comments) of the commenters had negative sentiments towards the post i.e., they were not pleased with the idea that the CDC loves low nicotine cigarettes but hates vapour products, regardless of nicotine content. For example, one of the negative comments from @IamBroony (Individual) read *'It befuddles me Regardless of nic content smoking is still smoking & #vaping isn't but @CDCgov supports smoking but not #ecigs,'* and another from @ZVSLO (vape advocate) read *'Lower NIC = More smoke = More Harm = More disease = More deaths. I wonder if they know from where harm comes from when smoking.'* Note that, although the above two comments are classed as negative comments, when put in the

context of @GregTHR's post, they are in support of what @GregTHR had said. The positive comments, as analysed by Atlas.Ti, appeared to also be in support of the initial post. For example, one of the positive comments from @NovaScotiaLive (Individual) read *'I swear to god we have been sucked into an extended episode of The Twilight Zone. There's no other explanation!'* and a response from @IamBroony (Individual) read *'No twilight zone, Just Government GREED And CORRUPTION. We are ALL slaves to the 1%. The Land of the Free = MYTH.'*

Overall, during the US e-cigarette post-regulatory period, some individuals and vape advocates expressed their concerns about how e-cigarettes were being regulated and updated the Twitter™ community on what they were doing to oppose the e-cigarette regulations. Some of them appeared to identify @SenRonJohnson as a vocal e-cigarette advocate who represented their interest within government.

4.3.2.5 Research on e-cigarettes

In Data Set 2, 11 posts were research-related, representing either an update on e-cigarette related studies, a call for research on e-cigarettes and their components, or questioning of the e-cigarette related research that was being carried out. An example of one of the updates on e-cigarette related studies is the post from a news outlet (@Reuters_Health) that read *'Vaping teens more apt to move on to regular cigarettes: U.S. study http://reut.rs/24KHZEo,'* and another from a health professional association (@spirometershop) that read *'Ohio State studying effects of e-cigarettes on lungs http://ow.ly/aNjX503LhI9 #ecigarettes #NIH #clinicaltrial.'*

With regards to a call for research on e-cigarettes and its components, there were three relevant posts, two of which were from @FDATobacco which read *'HHS supports & encourages research into cessation tools, including the potential role of e-cigarettes,'* and *'New regulations incentivize manufacturers to conduct research & submit data to establish the public health benefit of #ecigs.'* The other post was from an individual (@Hello_Alex) who expressed concern for animal experimentation on vaping liquids when they tweeted *'@FDATobacco will be requiring [#ratTorture] studies for each #eliquid product.'*

With regards to questioning the e-cigarette related research that had been or was being carried out, one individual (@jeski66) posted *'@FDATobacco why do we need more research if components are already approved & used for consumption, i.e. glycol, glycerol, food flavoring?'* while a vaping advocacy group (@VapinXsmoker) also posted *'NIH Wastes More Tax Dollars on Misguided Smokeless Tobacco Research http://bit.ly/1R9vL0k #ecigs #vaping.'*

Overall, during the US e-cigarette post-regulatory period, different types of agents updated the Twitter™ community on e-cigarette related studies and issued calls for more research. Some Twitter™ users questioned the type of e-cigarette related studies that were being promoted. No posts had sufficient responses for sentiment analysis.

4.3.3 UK E-cigarette Pre- regulatory period (2-1-2016 to 17-4-2016)

Twitter™ data, collected to cover the e-cigarette pre-regulatory period (2nd January 2016 to 17th April 2016) in the UK (Data Set 3), produced a total of 103 initial tweets with their associated comments. However, only 35 posts could be grouped into themes, as the remaining 68 post and associated comments did not have enough information for classification.

Data Set 3 comprised posts from a range of agents including the Regulatory agency (MHRA), News outlets, Vaping advocates, and Individuals. In Data Set 3, the Twitter™ user with the most posts (6 posts) was an individual, @SimonCapewell99 who is a Professor of Public Health Policy at University of Liverpool. The post with the most responses (19 comments) was from another individual (@grannylouisa) who was a Stop Smoking Service Lead at Leicester who were the first Stop Smoking Service to go e-cigarette-friendly, Interim Chair for New Nicotine Alliance, freelancer for @NCSCT, and Business Development Manager for Smoke Free app. @grannylouisa tweeted *'I lost the debate, seems full screen pic of explosion damage to face top-trumps PHE & @NCSCT guidance #ecigs Plus he said all made by BAT.'*

Four themes were identified from Data Set 3: Updates or clarification on e-cigarette regulation; E-cigarettes as a smoking cessation aid; E-cigarettes as a public health concern; and Research on e-cigarettes. Figure 10 below shows the themes in the Data Set 3 and their relationships. The identified themes in Data Set 3 are presented below.

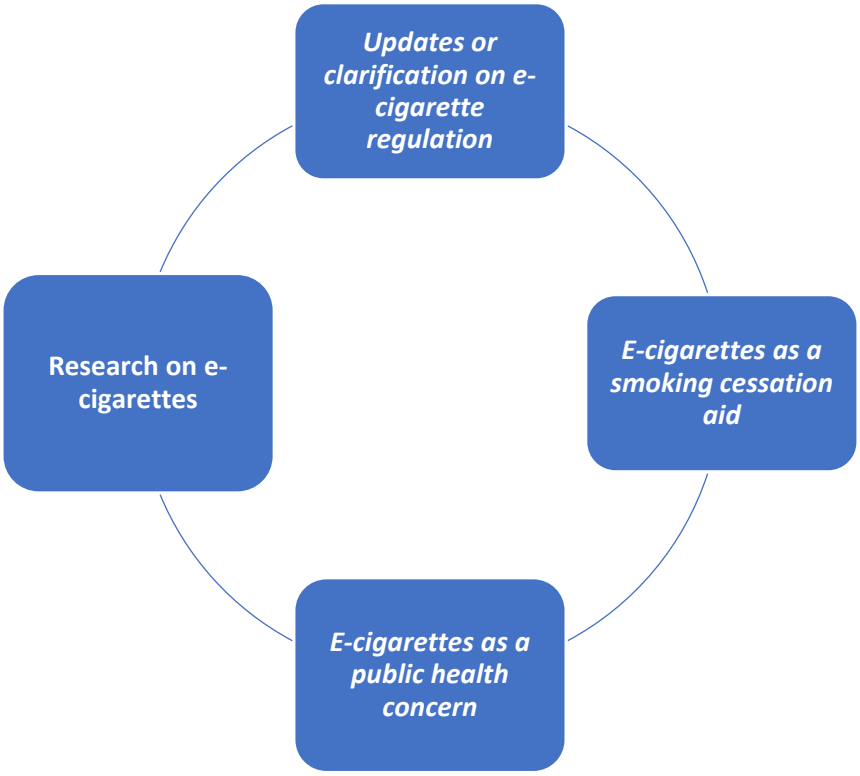


Figure 10: Themes identified from UK pre-regulatory Twitter™ discussions

4.3.3.1 Updates (or clarification) on e-cigarette regulation

In Data Set 3, some Twitter™ users posted updates on issues related to e-cigarette regulation. A total of 27 posts were identified under this theme and are discussed here. Some of the posts in Data Set 3 were directional information pointing readers to resources relating to new regulatory guidance on e-cigarettes. For example, the press office team of the regulatory agency (@MHRApress) posted *'Want to know how TPD #eCigarette notifications affect you & your business? Take a look at our latest guidance http://ow.ly/YvyxX,'* while a smoking cessation advocate (@NCSCT) posted *'Brand new e-cigarette briefing for stop smoking services launched today: http://bit.ly/1SUcCWS.'* Some other posts updated Twitter™ users on the latest developments with e-cigarettes and their regulation. For example, a smoking cessation advocate (@SCLC_UCSF) posted *'@MHRAgovuk approved #ecigarette for clinical use for first time http://tinyurl.com/qn5fpa7,'* while a health protection organisation (@calderdaleccg) also

posted *'Recently @PHE_uk published an evidence review about e-cigarettes. Read more here http://bit.ly/1bHw4AE #NHS #ecigarette.'*

Overall, in Data Set 3, some Twitter™ users updated the Twitter™ community on e-cigarette regulatory activities, often with signposting to further materials for more information. No post had sufficient responses to allow for sentiment analysis.

4.3.3.2 E-cigarette as a public health concern

In Data Set 3, 10 posts suggested some public health concerns related to e-cigarettes. Some posts highlighted ways in which e-cigarette use may have negative impacts on the public, while others contradicted some of the popular concerns around e-cigarette use. For example, indicative of negative opinions of e-cigarettes, one Individual (@citzgirl) posted *'Some people who would not smoke may consider e cigs safer. Tobacco companies buying into them.'* In contradiction to the popular negative opinion that e-cigarettes may lead non-smokers into smoking, one News outlet (@PGVGmagazine_en) posted *'Vaping to tobacco: No gateway effect on French teenagers http://ow.ly/Xp2td @ASH_LDN @Clive_Bates #ecig #vaping.'*

There were also posts suggesting that proposed e-cigarette regulations might adversely affect the public's health. For example, an individual (@PaulJBelcher) tweeted that *'Draft EU plan to tax #ecigarettes is 'detrimental to #publichealth' say health campaigners @ASH_LDN http://dailym.ai/1Y0R6Pn'.* (Note that, in actual fact, there was nothing in the finalised TPD on taxation of e-cigarettes).

However, the posts that received the most responses (19 comments) was from an individual (@grannylouisa), and read *'I lost the debate, seems full screen pic of explosion damage to face top-trumps PHE & @NCSCT guidance #ecigs Plus he said all made by BAT.'* A sentiment analysis of the comments to this post was carried out using Atlas.ti and further reviewed by me for sense-checking. The sentiment analysis revealed that most (12) of the comments exhibited negative sentiments, five comments showed positive sentiments, while two comments were neutral. Two examples of positive comments are *'No one wants to let facts get in the way of a good story, sadly,'* and *'That's appaling, what sink to such misinformation? What org was he with? I think we should do something about this.'* Two

examples of comments with negative sentiments include,- *'well, they loved him. Lots of nodding, gasps, murmuring of agreement, esp when he showed explosion slide,'* and *'Indeed,including children over dosing on NRT gum given to them by school nurse!'* The two comments with neutral sentiments read '*Next presentation include pics of laptop, mobile & smoking fires*,' and '*Love it!'*

Overall, during the UK pre-regulatory period, some Twitter™ posts suggested that e-cigarette use may have negative impacts on the public's health, while others suggested the opposite. It was also suggested that some aspects of e-cigarette regulations, such as taxation, could be detrimental to public health.

4.3.3.3 E-cigarette as a smoking cessation aid

A total of 25 posts and associated comments related to e-cigarettes and the role in smoking cessation were identified in Data Set 3. Not all the initial posts referred explicitly to the use of e-cigarettes for quit smoking attempts, but responses to these posts suggested how e-cigarettes could be used for smoking cessation. For example, a health professional organisation based outside the UK (@cancersociety – the Canadian Cancer Society) posted *'Our researchers are discovering more and more about how to help people #quitsmoking: http://bit.ly/1P2T0Pb #NNSW'* but the only response to the post was from an individual (@OhCanadaLady) and read *'@cancersociety Again we ask you, when will you consider @PHE_uk report and start supporting #Vapers?'* Similarly, another Canadian health protection agency (@TOPublicHealth) posted *'It's normal not to succeed on your first attempt to #QuitSmoking. Don't give up. http://youtube.com/watch?v=QLF3sttOdO0 #NNSW,'* and one of the responses to that post from @OhCanadaLady read *'#VapersLivesMatter too! Should never be about $$$. #Vapingworks, ask the #Millions in the UK and USA.'*

There were a number of posts that directly asserted that e-cigarettes were effective for smoking cessation. For example, a UK-based smoking cessation advocacy group (@ASHWalesCymru) posted *'Poll shows 'two thirds' of e-cig users quit smoking in Wales http://itv.com/news/wales/2016-03-09/poll-shows-two-thirds-of-e-cig-users-quit-smoking-in-wales/ @itvwales'.* A vape company (@FontemVentures) also posted *'@NCSCT says*

#ecigs can help smokers quit & evidence does not support the view of ecigs as gateway.' However, there were also posts that suggested otherwise, i.e that e-cigarettes are not effective for smoking cessation. For example, an individual (@SimonCapewell99) posted that *'#eCigs are NOT helping #smokers #quit – Specific responses by @ProfGlantz to @SMC_London 'expert' criticism http://tobacco.ucsf.edu/our-new-meta-analysis-entire-relevant-literature-shows-e-cigarettes-used-are-associated-less-not-more-quit#comment-17171 #vape?'*

Some posts updated the Twitter™ community with regards to the state of affairs on the use of e-cigarettes for smoking cessation. For example, a News outlet (@newshourbd) posted that *'@MHRAgovuk gives licence to @BATPress #ecigarette as quit smoking medicine @mehrabmasayeedh http://newshour.com.bd/2016/01/04/uk-drug-regulators-gives-licence-to-bat-electronic-cigarette-as-quit-smoking-medicine/,'* and a smoking cessation advocate (@ASHScotland) posted *'ASH Scotland manifesto calls: '5: Focus #ecigarettes debates on the goal of reducing tobacco use' http://bit.ly/1Rptrbq #SP16 #ecig.'*

Overall, during the UK pre-regulatory period, some Twitter™ posts suggested that e-cigarettes were effective for smoking cessation and pointed to ongoing efforts in the UK to harness their potential in quit attempts. Other posts argued the opposite i.e., e-cigarettes are not effective for smoking cessation. No post had sufficient responses to allow for sentiment analysis.

4.3.3.4 Research on e-cigarettes

In Data Set 3, 12 posts updated Twitter™ users on e-cigarette related research activities. For example, one health research organisation (@QMBCI) tweeted that *'@CR_UK has set up the UK Electronic Cigarette Research Forum with @PHE_uk & @UKCTAS- follow for updates on #ecigs #stopsmoking findings!'* and another (@UKCTAS) posted *'Check out all our posts on #ecigarette research over the past year: https://ukctas.wordpress.com/category/e-cigarettes-2/ #Vaping.'* Some Twitter™ users seem to have responded to news headlines that read *'E-cigarettes can cause cancer'* and *'Vaping 'no better' than smoking'* For example, a health research organisation (@UKCTAS) posted *'Public Health Experts respond to recent #ecig research from the U.S! https://ukctas.wordpress.com/2016/01/05/public-health-experts-respond-to-recent-ecig-research,'* while an individual (@jsummers71) tweeted *'New research claiming ecig risk nothing new or worrying*

https://ukctas.wordpress.com/2016/01/05/public-health-experts-respond-to-recent-ecig-research/ *#vapingtruth #100k.'* An individual Twitter™ user (@vancopd) also called for research to monitor potential harms of e-cigarette as they posted *'@lunguk I hope BLF/NHS will record and monitor #COPD mortality in Vapers as well as continuing smokers, ex smokers etc over future years.'*

Overall, in Data Set 3, some Twitter™ users updated the Twitter™ community on e-cigarette related research. No post had sufficient responses to allow for sentiment analysis.

4.3.4 UK E-cigarette Post- regulatory period (20-5-2016 to 2-9-2016)

Data were collected from Twitter™ during the e-cigarette post-regulatory period (20th May 2016 to 2nd September 2016) in the UK; these data are hereafter referred to as Data Set 4. Data Set 4 contains a total of 104 Twitter™ posts with associated comments from a range of agents as seen in Table 15 above. A smoking cessation advocacy group (@ASHWalesCymru) has the highest number of posts (5 posts) in Data Set 4, but the post with the highest number of responses (19 comments) came from a News outlet (@TheSun) who tweeted *'Tomorrow's front page: Boozy Lily Allen collapses at Notting Hill Carnival.'* This caption had nothing to do with e-cigarettes; however, a picture of the front page of the paper was posted together with the tweet. The front page also had two other headlines that read '*E-cigs seriously damage heart*' and '*Vaping as bad as fags*'. These elicited e-cigarette related responses; indeed all the comments to the original post were about e-cigarettes.

Five themes were identified within Data Set 4: Updates or clarifications on e-cigarette regulation; Research on e-cigarettes; Opposition to e-cigarette regulations and policies; E-cigarettes as a smoking cessation aid; and E-cigarette as a public health concern. Figure 11 below shows the themes in the Data Set 4.

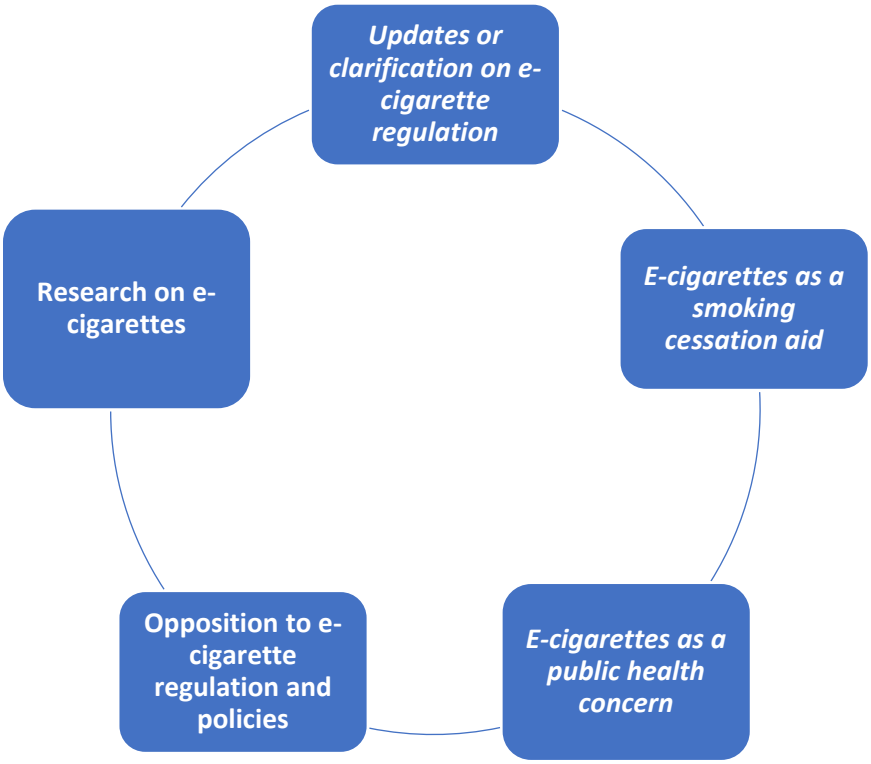


Figure 11:Themes identified from UK post-regulatory Twitter™ discussions

4.3.4.1 Updates (or clarification) on e-cigarette regulation

In Data Set 4, a substantial number of posts (29) provided updates and clarification of issues related to e-cigarettes and their regulation. Some of the posts simply updated Twitter™ users on the latest developments with e-cigarette regulations and provided links to further reading. For example, a health research institution (@MedicineGov) posted *'#Tobacco Products Directive is here! Read & share @MHRApress latest #ecig guidance http://ow.ly/YvyxX #NHS #SharedLearning,'* and a regulatory agency (@MHRApress) also posted *'The #TPD comes into effect today – are you prepared? Please share our guidance on #ecigs & #vape regulation http://ow.ly/YvyxX.'* Some posts posed questions, seeking clarification of aspects of e-cigarettes and their regulation. For example, an individual (@vaper_the) tweeted *'@NNAlliance Whatever happened to the BAT/@MHRAgovuk approved #eCig? Did they crawl back under their rocks after getting the sound-bytes out?'* while a vape advocate (@v_a_p_e) also posted *'So @ASH_LDN, my friend needs high strength #eliquid to stay smoke free, when I give it to him does that make me a criminal or a lifesaver?'*

Some tweets from Individuals informed the Twitter™ community of ongoing e-cigarette related events. For example, @ProfKevinFenton posted *'Great start to the @PHE_uk @CR_UK #Ecig Symposium with Alison Cox and @LindaBauld discussing the future research agenda & ongoing studies,'* and @grannylouisa also tweeted '*Exhilarating to be with vaper advocates, researchers, @NCSCT, commissioners, practitioners & so many more @PHE_uk #ecig event. New horizons.'* Other posts provided the Twitter™ community with updates on e-cigarette guidance relating to specific places and specific groups of people such as pregnant women or youth. For example, a Health protection organisation (@ukphnetwork) tweeted *'Updated consensus statement & new guidance from @PHE_uk on #ecigs and #vaping in public places https://gov.uk/government/news/vaping-in-public-places-advice-for-employers-and-organisations,'* and a Vape advocate (@IVVA_IE) posted *'New g/line from @PHE_uk on use of #ecigs in pregnancy out today – https://vivbennett.blog.gov.uk/2016/05/26/achieving-a-smokefree-pregnancy-can-e-cigarettes-help-jo-locker/ & http://smokefreeaction.org.uk/SIP/files/eCigsIP.pdf.'* Likewise, a Health research institution (@KingsAddictions) posted *'@ASHScotland: Advice for youth organisations on how to respond to electronic cigarettes https://tobaccounpacked.wordpress.com/2016/07/14/advice-for-youth-organisations-on-how-to-respond-to-electronic-cigarettes/ #ecigs #vaping #vape.'*

Overall, during the UK post-regulatory period, Twitter™ users updated the Twitter™ community on the latest e-cigarette developments as regards regulations, policies, and events.

4.3.4.2 E-cigarettes as a public health concern

In Data Set 4, 14 posts expressed or refuted potential harms of e-cigarettes. Some posts focused on absolute harms of e-cigarette use, particularly the risk of encouraging young people to take up smoking. Examples of such posts include one from an Individual (@gwelfor57) that read *'http://tinyurl.com/qrtqcvq Study #ecigs vaping encouraging children to try tobacco @The_CIEH @WHoEHG precaution needed @PHE_uk @PublicHealthW,'* and one from another individual (@SimonCapewell99) that read '*#vape? #eCig ads luring #ex-smokers: Quit Vic #ProtectOurKids #Nomarketing @ASH_LDN @ASHscotland.'*

By contrast, others focused on the lower risk of vaping compared to smoking. For example, one individual (@KalliSnae) tweeted *'The BATman to the #ecig rescue! Sure, who else? @PHE_uk @RCPLondon Vaping is risky but tobacco is much worse, http://ln.is/www.thetimes.co.uk/a/tFhbQ'*. A vape company (@FontemVentures) said *'@PHE_uk: '#Vaping carries fraction of the risk of smoking yet many smokers are still not aware' #publichealth #ecig'.*

Other tweets in Data Set 4 opposed two commonly perceived harms of e-cigarettes, namely that they act as a gateway to smoking especially among young people, and the potential risks of second-hand e-cigarette vapour to bystanders. For example, one vape company (@TmaxJuices) tweeted *'there is currently no evidence of harm from secondhand e-cigarette vapour.. (@PHE_uk, 2016) – https://gov.uk/government/news/vaping-in-public-places-advice-for-employers-and-organisations #vapeon #vapefam,'* and a smoking cessation advocacy agency (@ASHWalesCymru) posted *'Press release | Research by @ashwalescymru shows e-cigarettes are not a gateway for young people to takeup smoking | http://ashwales.org.uk/en/whats-new/new-research-shows-e-cigarettes-are-not-a-gateway-for-young-people-to-take-up-smoking.'* This latter post had the highest number of responses (12 comments) under this theme, and so a sentiment analysis of the comments were carried out using Atlas.ti software.

The sentiment analysis showed that ten of the comments had negative sentiments, i.e. expressed disagreement with @ASHWalesCymru's assertions. One example of such response is from @carlvphillips (who describes themselves as Epidemiology and economics consultant/researcher in their profile) who posted *'Too bad @ASHWalesCymru seems to have no idea what this means, and that their data tell us nothing on the point.'* Another example response was from an individual (@Rathmacan) who posted *'It's bad because it has no definition for 'gateway' and no evidence it is or isn't happening ½.'* The other two comments that were coded by Atlas.ti as neutral were from @carlvphillips: *'The info itself? None. @ASHWalesCymru is a political org and this is a political document, so it might reflect intent,'* and an individual (@BrisyCoe): *'Your 9% will one day be the 91% - it's a transitional period, I.e I started at 24 mg – now 4 mg 3 years on.'*

There were also calls on the responsible stakeholders to act to either prevent perceived harms of e-cigarette use or correct negative perceptions of e-cigarettes and their

constituents. For example, a Health professional association (@PCRSUK) posted *'BMA calls for ban on ecigarettes in public places to avoid passive vaping http://bit.ly/28THhmd @noelbaxter @ARNS_UK @lunguk #ecigs,'* while an Individual (@nickwa76) tweeted that *'50% in UK STILL think nicotine CAUSES cancer!!! @PHE_uk @CR_UK @NCSCT @LindaBauld #ecigs #PH we need to do better!'*

Overall, during the UK post-regulatory period, there was a lack of consensus amongst Twitter™ users regarding absolute and relative risks (vis-à-vis smoking) of e-cigarette use.

4.3.4.3 E-cigarettes as a smoking cessation aid

In Data Set 4, seven posts and associated comments identified e-cigarettes as a smoking cessation aid. Some expressed support for e-cigarettes in smoking cessation attempts, as in one tweet from a Smoking cessation advocacy group (@SfreeHampshire) that read *'Worried about recent news stories about #vaping flavours? This is a very useful post from @lunguk. We support switching to #vaping and #ecigs as a means to #QuitSmoking. Your Quit4Life adviser can help you make the right decision for YOU.'* Other posts also suggested that e-cigarettes could potentially reduce smoking rates and smoking associated harms when used for smoking cessation. For example, a News outlet (@theGHS) tweeted that *'Impact of e-cigarette uptake is highlighted in annual smoking statistics @hscic @MHRAgovuk #ecig http://thegoodhealthsuite.co.uk/Pharmacist/pharmacy-practice/1178-impact-of-e-cigarette-uptake-is-highlighted-in-annual-smoking-statistics.'* A Vape company (@FontemVentures) posted *'We recognise the potential of #ecigs to reduce harm associated with smoking, says Ashley Gould from @PublicHealthW.'*

Overall, during the UK post-regulatory period, some Twitter™ users indicated their support for the use of e-cigarettes in smoking cessation and highlighted their potential to drive down smoking rates and associated harms of tobacco smoking. No post had sufficient responses to allow for sentiment analysis.

4.3.4.4 Opposition to e-cigarette regulations and policies

Data Set 4 contains 11 posts and associated comments that show that, during the UK post-regulatory period, some Twitter™ users were opposed to e-cigarette regulations and

policies. The e-cigarette regulation tweeted about was the Tobacco Product Directive (TPD), while the e-cigarette policies included e-cigarette bans in public or indoor places and vape breaks at work. With regards opposition to the TPD, one Individual (@Lucy Foxen) posted *'Stop the TPD. Save vaping. Save lives #RIPvape #vapelove #vape @ASH_LDN,'* and another (@Thribbulous) tweeted *'Well done @ASH_LDN, TPD will keep you all in work for a few more years. Screw the vapers, eh? Keep smoking folks! #slowclap #vapefam.*' It is unclear what aspect of the regulations the above Twitter™ users thought would deter people from vaping, because the TPD from its inception to date (April 2024) has always permitted the use and sale of e-cigarettes to adults.

With regards to opposition to e-cigarette bans in both public places and outdoors, a medical publication from a News outlet (@pulsetoday) posted *'#Gpnews: Banning e-cigarettes in public places 'could be damaging' warns @PHE_uk http://bit.ly/28QdmJY #ecig #NHS,'* while an Individual (@Dick_Puddlecote) posted *'There @ASHWalesCymru go again, happily endorsing outdoor bans which include #ecigs http://bbc.co.uk/news/uk-wales-36504482.'* Another Individual (@SimonCapewell99) called for indoor bans of e-cigarettes in their post which read *'#Vapers SUPPORT Non-vapers' autonomy #ProtectOurKids #Indoor bans@robertjwest @martinmckee @ASH_LDN @ASHScotland http://onlinelibrary.wiley.com/doi/10.1111/add.13322/abstract?platform=hootsuite.*' Some Individuals also expressed their opinion that the activities of @ASH_LDN (a smoking cessation advocacy group) were opposing the use of e-cigarettes. For example, @_Mr_Obsidian tweeted *'@ASH_LDN proud of yourselves for your work on Article 20 to crush vapers? #allaboutthefunding #shameful #vape #vapingsaveslives #TPD,'* while @dougrmurphy posted *'@ASH_LDN works to eliminate the harm of tobacco, yet throw 2.8mill #vapers under a bus. Tell me where the tobacco is in vaping?'*

Overall, in Data Set 4, some posts opposed e-cigarette regulation (TPD), though sometimes their objections suggested a misunderstanding of the provisions of the TPD. Others objected to the suggestion by an individual doctor to ban outdoor and public use of e-cigarettes, and to the activities of smoking cessation organisations (e.g., @ASH_LDN), despite these working to advance e-cigarette regulations and policies. No post had sufficient responses to allow for sentiment analysis.

4.3.4.5 Research on e-cigarettes

In Data Set 4, 11 posts updated the Twitter™ community on e-cigarette research, reviews, and reports. For example, a Health research institution (@UKCTAS) posted *'Check out our round up of the @RCPLondon e-cigarette report released on 28/04/2016 #vape #ecigarette #NRT http://ukctas.net/rcp.html,'* while an Individual (@DrNLindson) also posted *'@CochraneTAG #e-cig review: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010216.pub2/full. Used as eg. Of good dissemination @EvidenceLive #EvidenceLive.'*

Overall, during the UK post-regulatory period, Twitter™ users updated the Twitter™ community on the latest e-cigarette research, reviews, and reports. No post had sufficient responses to allow for sentiment analysis.

4.4 Discussion of Study

4.4.1 Stakeholders contributing to Twitter™ discussions.

The findings of this study showed how interested individuals, groups and organisations shared views of e-cigarettes and their regulation on social media in the time periods running up to and immediately after regulations were put in place in the US and the UK. In the US, similar types of agents were involved in e-cigarette related discussions on Twitter™ both pre and post US e-cigarette regulation, except for one agent (see Table 15). Health protection organisations were involved in e-cigarette related discussions post- e-cigarette regulation, but not pre-regulation in the US. Likewise, in the UK, similar types of agents were involved in e-cigarette related discussions on Twitter™ both pre and post UK e-cigarette regulation (see Table 15). These showed that a similar profile of Twitter™ users were interested and actively contributing to e-cigarette related discussions on Twitter™ both pre and post e-cigarette regulation in the US and the UK. This observation is consistent with the literature that Twitter™ is a social media platform through which governmental and similar organisations carry out public engagement by providing updates on relevant information, organisational actions, and recommendations, and via which they receive feedback in the form of comments to tweets posted (248, 249). Also, other stakeholders (than regulators) of tobacco

control policy, including the tobacco industry, tobacco control advocacy groups, news outlets, and researchers use social media platforms, such as Twitter™ for disseminating information, promoting public awareness on the tobacco control agenda, and influencing policies (267, 268). Note that in both the US and the UK, interested parties from other countries contributed to Twitter™ discussion, even though the regulations being discussed were not of direct relevance/impact to them. For example, @Clive_Bates, who is a British national and described in his Twitter™ profile as having worked for a British organisation and government (i.e., ASH, Cabinet Office, Welsh Government), contributed to US e-cigarette discussions as can be seen in section 4.3.2.3.

The findings of this study also showed that audit and public accountability institutions, and politicians were agents that featured only in the US datasets but not in the UK in either the pre- and – post regulatory periods. The US regulatory agency (@FDATobacco) particularly tended to communicate e-cigarette regulatory plans on Twitter™. This may be because the US particularly encourages public service organisations and personnel such as Members of the US Congress, to use Twitter™ to encourage government transparency, communication, and engagement with the public (252).

4.4.2 Discussion of key themes identified in Twitter™ discussions.

This study conducted to identify the values and sentiments of the public towards e-cigarette regulations in the US and the UK, found six themes reflecting the e-cigarette discussion points that were of value to the public and associated sentiments pre-and- post e-cigarette regulation in the US and the UK. The six themes were: Updates (or clarification) on e-cigarette regulations; E-cigarettes as a public health concern; E-cigarettes as a smoking cessation aid; Opposition to e-cigarette regulations and policies; Growing use and popularity of e-cigarettes; and Research on e-cigarettes.

These themes identified in this study was consistent with the findings of previous studies. For example, a recent systematic review (260) that included 73 studies that aimed to summarize how content related to substances is portrayed on various social media platforms found that most studies identified themes relating to Health, Safety and Harms (65.0% of studies) of substance use; and themes relating to Promotions/Advertisements (63.3%), Informative content (55.0%) and Use behaviours (43.3%) were also frequently identified. The

theme of 'Updates (or clarification) on e-cigarette regulations' found in this study is related to 'informative content'; 'E-cigarettes as a public health concern' is related to 'Health, Safety and Harms'; 'E-cigarettes as a smoking cessation aid' is related to 'Use behaviours' in the systematic review (260).

In the US and the UK, there were some similarities in the foci of e-cigarette discussions on Twitter™ before and after e-cigarette regulations, albeit sometimes within different contexts. For instance, pre-regulation of e-cigarettes, there were updates on the proposed regulations and rationale for regulaton, whereas post-regulation, the updates were about implemented e-cigarette policies and regulation, and clarifications on aspects of that regulation. These updates and clarifications before and after e-cigarette regulations, mainly came from the regulators themselves.

E-cigarettes as a public health concern was identified as a theme in the pre- and- post e-cigarette regulatory period in both the US and the UK. In both the US and UK e-cigarette pre-regulatory period, Twitter™ users posted their public health related concerns around e-cigarettes, but some Twitter™ users also posted reassurances regarding these e-cigarette concerns. The key concerns were that e-cigarettes had the potential to lead people to smoking, and that e-cigarette use was increasing among teenagers. During the US pre-regulatory period, health organisations (such as the US Centre for Disease Control and Prevention's Office on Smoking and Health) communicating these concerns were perceived by other stakeholders as biased and having an anti-vaping agenda. In my view, this may be because when stakeholders are commenting via informal routes such as social media, there seems to be little expectation to abide by conventional procedures for supporting claims with evidence. For example, @American_Heart (a Professional Health Association) posted a tweet that generated a lot of responses (42 comments). The tweet – *'STUDY: E-cigs may not help you #kickthehabit after all. #stopsmoking #smoking #ecigs,'* was posted without sharing a link, citation, or any critical comment (see Section 4.3.1.2). Such uncited posts, coming from known health organisations, can lead observers to perceive those organisations as biased or having a hidden agenda. The concerns listed above continued in the post-regulatory period. In addidtion, in the US post-regulatory period, Twitter™ users expressed dissatisfaction with the classification of e-cigarettes as tobacco products, and some called out the US regulatory agency (FDA) and a health professional association (American Lung

Association) as being dishonest in their communications about the risk of switching from smoking to e-cigarette use. In the UK post-regulatory period, on the other hand, there was a lack of consensus amongst Twitter™ users regarding absolute and relative risks (vis-à-vis smoking) of e-cigarette use. A previous UK study (269) carried out a quantitative and qualitative content analyses of 104 articles about e-cigarette regulation published in eight UK and three Scottish national newspapers between 1 January 2013 and 31 December 2014. The aim of that study (269) was to establish how frequently different types of stakeholders were cited in the UK media debate about e-cigarette regulation, their stances towards different forms of e-cigarette regulation, and what rationales they employed in justifying those stances. The study (269) found that, although all commentators supported e-cigarette regulation, those who emphasized the harms of vapour and concerns about renormalizing smoking disagreed with others, who emphasized the role of e-cigarettes as a smoking cessation aid, about whether e-cigarette use should be allowed in enclosed public spaces.

Another theme identified in the pre- and- post e-cigarette regulatory period in both the US and the UK was E-cigarettes as a smoking cessation aid. In all time periods in this study, many Twitter™ users generally suggested that e-cigarettes are a safer alternative to tobacco smoking and that they are effective for smoking cessation. This corresponds with a Cochrane living review (22) which found e-cigarettes to be more effective than NRT for smoking cessation, and did not detect evidence of serious harm from nicotine-containing e-cigarettes over a follow-up period of up to two years. Other posts argued the opposite i.e., e-cigarettes are not effective for smoking cessation, but such tweets were largely met with opposition and negative sentiments. A meta-analysis (270) involving 64 studies that aimed to determine the association between e-cigarette use and smoking cessation concluded that, in observational studies, e-cigarettes were not associated with increased smoking cessation in the adult population, but in randomized control trials, e-cigarettes as a therapeutic intervention was associated with increased smoking cessation. The different findings on the association between e-cigarettes and smoking cessation may be fueling the differences in public perception about e-cigarette use in smoking cessation.

Growing use and popularity of e-cigarettes was a theme identified only in the US pre-regulatory period. This theme was not found in the UK. This may be because the discussion around growing use of e-cigarette in the US was focused on use among children and

teenagers which was increasing in the US (178) (see section 1.8.9.1). Use of e-cigarettes amongst under 18s was low in the UK at the time (129), creating less of a discussion point than in the US.

Opposition to e-cigarette regulations and policies was a theme identified in both US and UK post regulatory periods, but not in US and UK pre-regulatory periods. This is because regulations were not in place during e-cigarette pre-regulatory period; Twitter™ users could not be opposed to what does not exist. During the US e-cigarette post-regulatory period, there appeared to be organised activities carried out to oppose e-cigarette regulations, seemingly championed by Senator Ron Johnson who was mentioned by Twitter™ users as representing their interest within government. By contrast, in the UK e-cigarette post-regulatory period, there seemed to be some misunderstanding that the regulations aimed to restrict use of e-cigarettes, resulting in misplaced opposition to the TPD and to the activities of smoking cessation organisations (e.g., @ASH_LDN), despite these working to advance e-cigarette regulations and policies.

My study corroborates a previous study (271) on a sample of US adults that found that beliefs about protecting people from second-hand use of e-cigarette and preventing youth from trying e-cigarettes significantly predicted stronger support for e-cigarette restricting policies, whereas concern about government intrusion into individual choices was associated with reduced support or opposition.

During UK pre-and-post e-cigarette regulation and US post regulation, Research on e-cigarettes was identified as a theme. Different types of agents updated the Twitter™ community on e-cigarette related studies and issued calls for more research. Some Twitter™ users questioned the type of e-cigarette related studies that were being promoted. A relatively recent (2022) narrative review (272) carried out a critical appraisal of 24 popular e-cigarette studies published in medical journals that purported to evaluate the association of e-cigarette and smoking cessation, smoking initiation or health outcomes. The authors of the study (272) suggested that the body of literature on the “gateway” theory for the initiation of smoking was particularly unreliable, and overall, the results and discussion of the included studies contained numerous unreliable assertions due to poor methods, including data collection that lacked relevance, and assertions that were unfounded. This may be the

reason for Twitter™ users questioning the type of e-cigarette studies being promoted on social media.

4.4.3 Applicability of reputational theory to findings in this strand of study

This study had sought to explore whether e-cigarette Twitter™ discussions in the US and the UK had the potential to influence regulators when making regulatory decisions. This was based on the framework of reputational theory (211), a situation whereby regulators respond to media pressure to protect their reputation in the public sphere (see section 2.3.2). Health organisations are now increasingly using Twitter™ to promote health literacy and for public engagement (248, 249), while journalists and reporters regularly use it as a source of material to generate further stories which may reach the wider public. For these reasons, regulators who use Twitter™ to engage the public on their regulatory activities may be looking at what issues with regards e-cigarette regulation are valued by the public, with the potential to influence their regulatory decisions. This study found that the Twitter™ discussions and associated sentiments of Twitter™ users in the US and the UK were indeed of a nature that had the potential to influence regulators' regulatory decisions.

In all four time periods, Twitter™ users discussed public health concerns regarding e-cigarette use. In my view, these concerns had the potential to put pressure on both the FDA and MHRA to strictly regulate e-cigarettes to protect their reputation in the public sphere. For example, in my study one, an interviewee who was a government representative informed me that, to avoid an 'enormous' public backlash (see quote in section 3.2.2.2), they would personally not support any proposal which permitted use of e-cigarettes on public transport. Here in study two, Twitter™ discussions in 2016 suggested that UK Twitter™ users were opposed to proposals to ban use of e-cigarettes in public places (see section 4.3.4.4). Also in 2016, PHE published a new policy on the 'Use of e-cigarettes in public places and workplaces' (273) which they stated to be deliberately non-prescriptive but was intended to set out some key principles for organisations to develop their own policies. In doing so, it acknowledged that there were both benefits and risks associated with the use of e-cigarettes, and that no one-size-fits-all answer exists to the issue of e-cigarette use in public places and workplaces. This study cannot confirm that UK regulators were influenced by

Twitter™ discussions, but it shows that the Twitter™ discussion before and after regulations were in line with regulatory considerations and actions.

In all four time periods, Twitter™ users discussed the use of e-cigarettes for smoking cessation. In my view, FDA and MHRA may have observed the several campaigns and testimonies of people using e-cigarettes to effectively quit smoking, while tweets that suggested that e-cigarettes were ineffective for smoking cessation was largely met with opposition and negative sentiments. This again had the potential to put pressure on the FDA and MHRA to deregulate e-cigarettes to protect their reputation in the public sphere.

4.4.4 Strengths of this strand of study

A key methodological strength of this study was the collection of data for specified and equivalent time periods, focusing particularly on periods of time before and after regulatory landmark dates. This focus ensured that the information retrieved would be sensitive to the scope of the study. Using the same number of days across all data collection periods enabled fair comparison of different periods.

The search strategy adopted, i.e., combining e-cigarette search terms with specific relevant Twitter™ accounts, ensured that only data relevant to e-cigarettes and these focused accounts were extracted for analysis. This brought about compliance with the scope of the study and reduction of irrelevant data.

Combining sentiment analysis and thematic analysis also strengthened the quality of the analysis and provided richer understanding of the e-cigarette related discussions on Twitter™. Using a qualitative analysis software (Atlas.Ti) for the thematic and sentiment analysis in combination with my manual analysis enabled thorough examination of the data and adequate sense checking of the automated output from Atlas.Ti.

4.4.5 Limitations of this strand of study

A methodological limitation was that thematic analysis relies on the researcher's interpretation of the data in theme identification (see section 3.2.1). This results in some subjectivity in the analysis of data (274). Review by and discussion of themes with supervisors, along with ongoing reflexivity on my behalf, was used to mitigate this risk.

The choice of Twitter™ accounts used for the search strategy was to some extent arbitrary, albeit with the criterion that the organisations/individuals had to be associated with e-cigarette regulation or health protection. Therefore, there is a possibility that some relevant stakeholders were omitted. For example, Cancer Research UK which is an independent charity in the UK that funds research into tobacco and related products such as e-cigarettes, was omitted in the list of Twitter™ accounts for the search strategy. However, there was some element of iteration in searching for tweets where posts that had comments from key organisations were added for analysis. Also, people tweet as individuals but may have links to particular organisations that influence their views, e.g., Prof. Simon Capewell was President of the Faculty of Public Health at the time of this study, while Prof. Kevin Fenton was PHE's National Director for Health and Wellbeing

A further limitation is that sentiment analysis was carried out only for tweets that either had up to ten responses and or had the highest number of responses amongst other tweets within a thematic group. It is possible that some relevant and interesting tweets were not sentiment analysed because of the low number of responses. This means that some meaningful findings may have been missed. Also, Atlas.Ti did not always capture, for example, the ironic tone of some tweets which was often conveyed by use of emojis, and therefore misclassified some sentiments. However, manual sense checking of Atlas.Ti classifications was used to mitigate this risk.

An acknowledged limitation in using Twitter™ messages to gauge public opinion is that this (or any) social media platform is not representative of the underlying population. For example, 80% of Twitter™ users are affluent millennials (250) and this category of people represent only a fraction of a population's demographics. Despite these limitations, the scale of use of Twitter™ in the US and the UK, and regulators' use of Twitter™ in disseminating e-cigarette regulatory activities, suggest that it was and remains an influential public medium for online discussions about e-cigarette regulations in both countries. Also, since this strand of study did not conduct any bot analysis to exclude tweets from bots, there is risk of bias. Previous studies (246, 261, 275) show that a high number of tobacco-related tweets are from bots in attempts to interfere in tobacco control.

4.5 Conclusion

Public consultations are traditionally the formal means of gathering public comments regarding proposed or implemented regulations. However, social media platforms such as Twitter™ can be an informal and initial means of identifying public concerns in response to regulations. These public concerns and response can have a potential to influence regulatory and policy decisions, especially when regulators are cautious of protecting their reputation in the public sphere. Therefore, Nigerian regulators should be mindful when engaging with the public through social media platforms. They should also be aware that social media opinions may not always be representative of the general public both because of the demographic profile of users, and because the universal accessibility of these platforms transcends borders and makes it difficult to limit contributors of regulatory discussions to nationals of the regulated country. In Chapter 5 of this PhD thesis, I present my final primary study conducted to explore the potential determinant factors of e-cigarette regulations in Nigeria.

Chapter 5. Potential Determinant Factors of Electronic Cigarette Regulation in Nigeria (Study Three)

5.1 Background

Nigeria has historically attempted to legislate against tobacco, starting in 1990 with the establishment of the Tobacco Smoking (Control) Decree 20, 1990 which was converted to the Tobacco (Control) Act 1990 (see Appendix N) under democratic governance. The Tobacco (Control) Act 1990 prohibited smoking in specific places, such as schools and sports stadia, and required warning messages to be placed on all tobacco and sponsorship advertisements. The warning 'The Federal Ministry of Health warns that smokers are liable to die young,' resulted from the enforcement of the Act, but the ban on smoking in the specified public places was not enforced and was ineffective. In 2002, the Advertising Practitioners' Promotion Council of Nigeria (APCON) placed a total ban on tobacco advertising which has been enforced. In 2004, Nigeria signed the World Health Organisation's Framework Convention for Tobacco Control (WHO- FCTC) and ratified it on 20th October 2005 (25). However, it was only in 2015 that Nigeria developed a comprehensive Framework Convention for Tobacco Control (FCTC) compliant policy.

The comprehensive FCTC compliant policy is enshrined in the National Tobacco Control Regulations, 2019 (NTCR) (276). For example, prior to the NTCR, the warning on cigarette packs as required by the Tobacco (Control) Act 1990 (see Appendix N) was 'The Federal Ministry of Health warns that tobacco smoking is dangerous to health' and 'Smokers are liable to die young'. However, the NTCR now requires tobacco products to have health warning graphics that rotate every 24 months between: 'Smoking causes lung cancer'; 'Smoking causes mouth cancer'; and 'Smoking causes throat cancer'. The health warning graphics comply with Article 11 of the FCTC, which recommends that health warnings for tobacco products refer to specific illnesses caused by tobacco and use graphic images demonstrating the harm of tobacco use.

Since Nigeria has now established its regulatory and policy mechanisms to control the use and trade of tobacco products within the country, it may be time to also consider other emerging novel products coming into the Nigerian market. A 2021 cross-sectional survey (15) showed an e-cigarette ever-use prevalence of 7.9% among the 949 respondents aged 15-35

years that were surveyed. This comes after the Managing Director of British America Tobacco (BAT) Nigeria, Chris McAllister, stated in 2018 that the company planned to launch their world leading range of e-cigarettes in Nigeria 'in the near future' (16). However, BAT has not yet (April 2024) launched their range of e-cigarettes in Nigeria.

For all new products manufactured within or imported to Nigeria, SON (Standards Organisation of Nigeria) is obligated to develop a 'Standard'. A Nigerian Standard as defined on the SON website as *'…a document established by consensus and approved by the Standards Organization of Nigeria, that provides, for common and repeated use, rules, guidelines or characteristics for products and services and related processes or production methods, aimed at the achievement of the optimum degree of order in a given context*'(277)(p.3). SON is the standardization body in Nigeria; it is legally mandated to prepare standards relating to products, measurements, materials, processes, and services amongst others (see https://son.gov.ng/about-son/). Therefore, regulation of e-cigarettes in Nigeria may begin with SON.

It is likely that Nigeria will now look to regulate e-cigarettes and may look at what other countries have done with respect to in this respect. In this final element (study three) of my research project, I aimed to identify the potential determinants of e-cigarette regulation in Nigeria, in pursuance of the third objective of my PhD.

5.2 Methods used in study three

The third objective of this PhD research project was to 'Understand the similarities and differences between contextual factors in Nigeria versus factors identified as having determined the regulatory and policy approach to e-cigarettes in the US and the UK'. To achieve this objective, I planned to carry out qualitative interviews with e-cigarette stakeholders in Nigeria. Qualitative in-depth interviews and thematic analysis were chosen and used as the methods of data collection and analysis in this element of my research for the same reasons as in collection and analysis of data from UK and US stakeholders (see section 3.2.1).

In preparation for these interviews, the factors that were found to have been taken into account in e-cigarette regulations in the US and the UK were presented to key Nigerian

policymakers and stakeholders to aid them in reflecting whether and how they might come into play in the context of Nigeria during its e-cigarette regulatory journey. These factors were presented as PowerPoint slides at the beginning of the interview to serve as a vignette. Vignettes are a written description of events which relate to the central topic of study, and are sometimes incorporated in qualitative interviews to gain access to rich and detailed accounts more rapidly and more effectively (278). Interviews were then conducted with these regulatory stakeholders to discuss factors that might potentially influence or determine e-cigarette regulations and policies in the context of Nigeria, including, but not limited to, those influencing regulation in the UK and US.

Four interviewees were selected and interviewed in this study (study three), using purposive sampling. The first interviewee is a consultant cardiologist and clinical lecturer at the University of Nigeria Teaching Hospital (UNTH). This interviewee was selected to represent physicians in Nigeria. The interviewee's experience as a consultant and clinical lecturer in one of Nigeria's leading hospitals has provided them with the right level of exposure to research and clinical practice to provide a medically informed view on the topic. The views of a physician were sought in this study because considerations for regulation of e-cigarettes in the US and the UK involved assessing the health risks and harm profile of the product. The other three interviewees interviewed were members of the Nigerian National Tobacco Control Committee (NATOCC). I interviewed members of NATOCC based on the assumption that the NATOCC will be involved in the regulation of e-cigarette in Nigeria. NATOCC is a committee established by Nigerian law under the National Tobacco Control Act, 2015, and is responsible for making recommendations for tobacco control policies to the Nigerian Minister of Health (279). Therefore, it is highly likely that when Nigeria moves to regulate e-cigarette, it is the NATOCC that will make or contribute significantly towards e-cigarette regulations.

To identify and contact NATOCC members, I sent a letter to the MOH containing information about the study, seeking permission to interview NATOCC members, and requesting support in identifying appropriate members for interview. The Federal Ministry of Health (FMOH) then put me in contact with three members of NATOCC for the proposed interviews. These three participants were rich sources of data as they were strategic members of NATOCC and therefore represented potential e-cigarette regulatory bodies. These were also the only

participants that the FMOH were able to put me in contact with within the timeframe of my research data collection period (November 2022 to April 2023).

Prior to commencement of this element of my study, ethical approval was granted by Newcastle University FMS REC (Date: 09/08/2022, Ref: 24590/2022) (see Appendix C) and National Health Research Ethical Committee of Nigeria (Date: 23/01/2023, Approval Number NHREC/01/01/2007-23/01/2023) (see Appendix D). Informed verbal consent was sought from participants prior to commencing the interviews.

5.3 Findings from study three

From thematic analysis (see section 3.2.1) of the four interviews conducted with Nigerian e-cigarette stakeholders, I identified six factors which may influence e-cigarette regulations in Nigeria. The themes are discussed below. The interviewees who contributed to the data collected and analyzed are listed below in Table 17.

Organisation	Representative code	Data source	Date produced
Federal Ministry of Health, Nigeria/ National Tobacco Control Committee	RFMOH	Interview	17/02/23
Standards Organisation of Nigeria/ National Tobacco Control Committee	RSON	Interview	16/02/23
Federal Competition and Consumer Protection Commission/ National Tobacco Control Committee	RFCCPC	Interview	17/02/23
University of Nigeria Teaching Hospital	RUNTH	Interview	14/11/22

Table 17: List of Nigerian Interviewees for data collection and analysis

5.3.1 Existing regulatory framework

I found from analysis of interviews that regulation of e-cigarettes would start from development of an e-cigarette Standard which would, in turn, determine the classification of e-cigarettes either as a tobacco product (as seems the more likely option) or a non-tobacco

product. The choice of classification would influence the kind of existing regulations and policies that would be applied to e-cigarettes, and by implication the potential regulators and the regulatory mechanisms that would be used.

A representative of the Standards Organisation of Nigeria (SON), hereafter referred to as RSON, confirmed that classification of e-cigarettes will be done when developing a standard for e-cigarettes and described the process of developing such a Standard. RSON stated that:

> *'It* (classification of e-cigarettes) *is going to be determined by the technical committee… under consensus by all stakeholders involved… It* (draft Standard) *will be sent for a wider enquiry. Different bodies, different stakeholders that we need their comment, let them review and then give us their comment… Those comment that has been collated, during the technical meeting, they will be deliberated… If there is justification, and it's accepted by the technical committee... at the end of the day all this now comes into form the standard to which the Council will approve.'* (RSON)

RSON also identified the type of people who will form the technical committee for developing e-cigarette Standard:

> *'As far as the technical committee is concerned, they are technical expert. And these expert cuts, cut across all the relevant MDAs* (Ministries, Departments, Agencies) *that have something to do with that product… somebody will be selected from there to represent the committee, from Ministry of Health. From Federal Ministry of Trade, and Investment also, we have, from Federal Competition, Consumer Protection Council… Independent Public Analyst of Nigeria, IPAN… the manufacturers associations… research institutes—particularly the universities… all relevant MDAs and bodies, and agencies that have expertise in contributing to that are brought together to sit and form that technical committee.'* (RSON)

RSON further highlighted the options available for development of an e-cigarette Standard when they stated:

> *'Standard elaborations involve either, you start the product fresh, or by looking for available literatures, positive and validated literatures…. But if there is a standard already existing internationally, either through Codex, or ISO standard*[15]*, so what it simply means is that you can either do modify adoption, or you do, identical adoption. Identical adoption means that you don't change anything, you only just change the foreword… But if you are doing modify adoption, then it means that along the body, there are some areas that those condition might not be favourable to the condition we have here (*in Nigeria*) … So, all these things are*

[15] There are currently five published standards by ISO/TC 126/SC 3 (Vape and vapour products) from France (275)

things that will be put together by the technical committee, to discuss and then agree.' (RSON)

A representative of the Federal Competition and Consumer Protection Commission (FCCPC), and referred to hereafter as RFCCPC, felt that e-cigarettes should be regulated as a tobacco product in Nigeria, based upon the interpretation of the National Tobacco Control Regulations. RFCCPC expressed this opinion when they stated:

'For us here, I think it (e-cigarette) *… have to be regulated as tobacco product because, the position of the law, which is the legal provision in this sense now, is to the extent that it covers any product whether it is tobacco or tobacco related.'* (RFCCPC)

A representative of the Federal Ministry of Health (FMOH), hereafter referred to as RFMOH, and RSON shared similar opinions to RFCCPC about how e-cigarettes are likely to be classified in Nigeria, when they respectively stated:

'The global direction is to regulate this product (e-cigarettes) *as tobacco products. And when you regulate them as tobacco products, other as—every aspect of tobacco regulation would come into play.'* (RFMOH)

'Looking at the definition (of e-cigarettes) *… our standard calls them tobacco and tobacco products… by the time you write tobacco and tobacco product, you now write what particular product you are referring to. It will now be an E-cigarette.'* (RSON)

RFCCPC, RFMOH and RSON all believe that e-cigarettes are likely to be considered as a tobacco product in Nigeria. The above three interviewees are representatives of organisations that form, alongside others, the National Tobacco Control Committee (NATOCC), the body responsible for tobacco product regulations in Nigeria. RFCCPC elaborates on the composition and function of NATOCC when they stated that:

'The National Tobacco Control Committee is actually an interagency, and interdisciplinary committee. So, you have a number of agencies that are represented on that body. I represent my commission like I said, you have like the National agencies. You have like the Federal Ministry of Health. You have others that are also members of the committee. And they all—even the Federal Minister of Justice, NAFDAC (National Food and Drug Agency) *and a host of other agencies are part of it. Including the non-governmental organisations. The police is there. The NDLEA* (National Drug Law Enforcement Agency) *is there, the Nigeria Customs Service is there, and those who—Federal Minister of Education is also represented on that committee. So, you have an interdisciplinary committee that would sit and in one fell swoop and would be able to look at issues holistically.'* (RFCCPC)

RSON indicated that SON had a regulatory role to play through development of the e-cigarette Standard. This role would pertain to aspects of quality, safety, and trade of e-cigarettes. RSON conveyed their thinking when they said:

> *'…. Writing standard to ensure, the aspect of quality, the aspect of safety, and also any area related to trading.'* (RSON)

RSON and RFCCPC also believed the FCCPC had a part to play in the regulation of e-cigarettes. Both representatives conveyed this belief when they respectively said:

> *'There are some agencies that also may likely have their own part of the regulation, but clearly the FCCPC, the Federal Competition and Consumer Protection Council. The issues that are relating to market entry and consumer access.'* (RSON)

> *'It's just that there has to be a standard, then we have to have like, my organisation* (FCCPC) *release regulation.'* (RFCCPC)

With respect to what interviewees believed should be introduced in e-cigarette regulations, RFCCPC and RUNTH mentioned a few potential regulatory measures when they stated respectively that:

> *'Well, some of the things we would be doing in that respect are the limitations we would place. For instance, you would still not be allowed to advertise it (e-cigarettes), we still want you to label it appropriately. That would include having the health warning. We want to discourage for instance, exposure, maybe during hours… where the young people would still be watching TV. We would be discouraging a form of marketing that places that product directly in front of young people... consumer access and all of that. And then market entry and everything. So that's the area that our regulations will capture essentially.'* (RFCCPC)

> *We need to make it, you know, limited to youths… who are old enough otherwise their kids can abuse it... I would prefer they make it a bit more expensive so that it would discourage people… who can't afford it… you can rarely see, you know, showing tobacco use in Nigeria… So, that material should equally, continue in that direction… as much as we want people to switch from tobacco use —via e-cigarette to quit the entire process. But we should be careful—so that people don't you know, eventually end up in nicotine use, via e-cigarettes.'* (RUNTH)

RUNTH above suggested that existing NTCR, particularly with respect to TV advertising for tobacco cigarettes, should apply to e-cigarettes. RFMOH highlighted the FCTC as another piece of existing guidance that is relevant to potential e-cigarette regulations when they stated that:

> *'You know we are guided by the FCTC... And if the FCTC, which we are party to, is still cautious about these products* (e-cigarettes) … *the best way now is to go with the WHO FCTC.'* (RFMOH)

In summary, as per the existing framework for developing regulation of new products in Nigeria, it was explicitly stated that e-cigarette regulation would begin from development of a Standard that would classify e-cigarettes as either a non-tobacco product or a tobacco product (as is more likely). The classification of e-cigarettes as a tobacco product would likely mean that they would be subjected to the existing NTCR and WHO FCTC guidance; therefore, measures for regulation of tobacco cigarettes may apply to and influence e-cigarette regulations in Nigeria.

5.3.2 Research evidence

As presented in section 5.3.1 above, e-cigarette regulations will start from the development of an e-cigarette Standard by a SON technical committee. RSON indicated that the technical committee would rely on research evidence from the available literature to inform its deliberations and decision making:

> *'We must also dwell into other established literature, by way of looking at what is already happening in all part of the world, with regard to the information that's available for the e-product, e-cigarette… there are some department or unit that I think have that responsibility of conducting research. In addition to liaising with reputable institutions in the country. Universities that have a capacity to conduct this research… we will be able to pick out something… to put, in our own standard to say okay fine, this will guide us in the—in elaborating a standard in relation to quality.'* (RSON)

RSON also suggested that there would be a kind of team appraisal of the research evidence:

> *'There are some department or unit that I think have that responsibility of conducting research… those institutions and will also help us in bringing out those literatures and then from there, there are submissions, because they will make presentation (about) how they go about it, and then those things are things we will take together… when we are also reviewing or sitting down for consideration during standard elaborations.'* (RSON)

Other potential stakeholders in the regulation of e-cigarettes, such as the FCCPC, will also be reliant on research literature to inform their regulatory considerations and decisions. For example, when speaking about potential e-cigarette regulations with respect to the role of flavours in attracting people to use e-cigarettes, RFCCPC stated:

'We would be looking at research that would have been done in this respect to be able to corroborate such claims and if for any reason there are verifiable claims, we want to go with them.' (RFCCPC)

Therefore, research evidence is highly likely to influence e-cigarette regulations. It seemed from interviews that the direction of the influence will be dependent upon: how the evidence is interpreted by the regulators in the context of Nigeria; how the evidence weighs up against competing interests within Nigeria; and if the evidence can be validated. For example, with respect to how research evidence is interpreted in the context of Nigeria, a consultant cardiologist and clinical lecturer at the University of Nigeria Teaching Hospital (UNTH), hereafter referred to as RUNTH, responded to research claims that e-cigarettes have been shown to be effective for smoking cessation, by stating:

'Even the nicotine has side effects, but the open tobacco that comes with it has lots of you know, agents harmful to the body that cause a lot of effect on the cardiovascular system and the pulmonary environment- it's not good. So, E-cigarettes would be a better option. But like I said, those who are going to use E-Cigarette, how many are they? Can they afford it?' (RUNTH)

RUNTH acknowledged e-cigarettes as a less risky alternative to tobacco but expressed concerns about their affordability to people in Nigeria.

With respect to how research evidence weighs up against competing interests within Nigeria, interviewees suggested that potential e-cigarette regulations and policies will be developed in an interdisciplinary team, such as the SON technical committee and NATOCC. Such committees have representatives of different interests such as public health, economic considerations, consumer protection etc. It appeared likely that if there is competing research evidence – for example of an economic benefit of trade in e-cigarettes versus evidence from a public health perspective to support limitations of or a ban on e-cigarette sales – the way in which such a committee resolves such competing interest will determine how e-cigarettes eventually becomes regulated in Nigeria. The RFCCPC raised the possibility of this type of conflict of interest in the Nigerian context:

'My organisation is under the Federal Ministry of Industry, Commerce and—sorry and Trade and Investment. So, for us, certainly our parent ministry is interested in industrial development… So, you will find a situation where they go to WTO, which is the World Trade Organisation, they have obligations to fulfil there. The Federal Ministry of Health goes to WHO, and they also have obligations that's almost at crossed purposes but the whole idea is to bring everybody under one

roof, to be able to look at assessing considerations like I said earlier, so, when we hold meetings, at least everybody has an input to make.' (RFCCPC)

RSON also suggested that, when the SON technical committee sets out to develop an e-cigarette Standard, there are some aspects of e-cigarettes presented in the research literature that will need to be scientifically validated before it can be adopted into the Nigerian Standard. RSON referred to such evidence validation when they said:

'You can also take that sample, and then find a way to test it in the lab and confirm that those parameters or those requirement as stated there, when you get the—a result from the lab, you can compare those result with what the literature you have gotten.' (RSON)

This means that any laboratory testing in Nigeria must yield a similar result to that presented in the literature; otherwise, the existing research evidence will be disregarded and will not influence e-cigarette regulation in Nigeria.

In summary, it seems to me that research evidence that is judged to be relevant to the Nigerian context, that weighs highly in the regulatory needs of Nigeria (i.e., deemed more beneficial than other competing evidence), and that can be validated or verified by Nigerian regulators is likely to be most influential on e-cigarette regulation in Nigeria.

5.3.3 Public Health Considerations

Interviewees suggested that potential Nigerian e-cigarette regulators are highly likely to be influenced by public health considerations in their decision making, and that these considerations are likely to be prioritised above others (such as economic imperatives). In terms of public health considerations, ensuring the safety of Nigerians, especially the vulnerable in Nigerian society (children and women), is of importance to potential e-cigarette regulators. RFMOH elaborated on this when they cited the US as an example of a country that has experienced negative public health outcomes from use of e-cigarettes. RFMOH stated:

'I think the concern for the safety of Nigeria is surely the younger population because with the experience in America for e-cigarette to be causing that kind of harm and leading to other addiction because there are several studies that have shown that this product, in itself, it's a gateway product to other more dangerous products. So, for us, I think that should take precedent.' (RFMOH)

'There had been this—the report of E-Cigarette and it—and its use among teens, among adolescents in US, how it had been a product that had led to addiction and to the use of other products. So, yes, EVALI was one of the issues that globally drew concerns with the use of E-Cigarette. But that's not the only issue US have had to deal with. They've had to deal with addiction caused by these products, especially with the use of deceptive flavourings, that are attractive to kids, and the younger population. You would know that these products were targeted at these people.' (RFMOH)

RFCCPC, who also shared similar safety concerns, was particularly interested in the public health protection of women and children. They were similarly cautious that e-cigarettes may serve as a gateway to smoking or use of other harmful products by appealing to non-smokers. RFCCPC stated:

'One of the things too that guides whatever we do, is the fact that we want to try as much as possible to discourage underage smoking. As well as smoking by… a group like the womenfolk… Underage smoking would be a very crucial one for us. If it looks like it's something that would glamourise smoking—we would be very—quite wary of it.' (RFCCPC)

It was not only the RFCCPC that associated 'glamour' with the use of e-cigarettes in Nigeria. The RFMOH similarly perceived e-cigarettes as a product that Nigerians would see as glamourous, with the consequent outcome of attracting non-smokers to e-cigarettes and potentially future use of more harmful products. The RFMOH stated:

'Nigerians, they love new thing. Especially things that would attract class, glamour, they love it… And if not for the expensiveness of these product, it only takes those people to promote it and the youth would take to that culture and before you know, even people who are not looking for alternative, people who just want to be like their stars (celebrities)*, would take to these products. And you know these guys also use hard drugs* (Dangerous drugs)*. It would just be from one shift to the other. So, I think Nigerian situation will really take after what the findings from US.'* (RFMOH)

'Globally, public health controls tobacco regulation because it's an aspect that is topmost in terms of tobacco, public health… In any debate, with regards E-Cigarette in the world, the number one consideration is public health.' (RFMOH)

RSON also confirmed that, for SON, the evaluation of the safety of e-cigarettes will be an integral part of the bases of their regulatory decision making. RSON stated:

'We look at the level of whether it's (e-cigarettes) *going to be harmful indeed, or it's not going to be harmful, whether it's going to be just as stated in the literature, established and validated literature, that it has a reduced harm compared to tobacco. So, all these things are part of things I'm saying, by the*

time we put them together, it will guide whatever position we need to take.' (RSON)

Although the interviewees suggested that the regulatory process is likely to involve an assessment of the harm profile of e-cigarettes compared to tobacco cigarettes, none of the interviewees indicated a perception that e-cigarettes might be actively encouraged for smoking cessation in Nigeria. On the contrary, RFMOH seemed not to approve of e-cigarettes for smoking cessation, saying:

'The fact that somebody stops using cigarette and is using e-cigarette only... you are still exposing him to harm. And that's why we are calling it harm reduction… but, in the medical setting, you're not exposing the person to harm. You're just ensuring that you wean the person out of the addiction and in fact, for cessation service… the nicotine replacement therapy is the last phase. It's for people who you cannot counsel out of this habit. But where does the e-cigarette come in? (RFMOH)

In summary, public health considerations regarding the risks of e-cigarettes and their potential to serve as a gateway to smoking or use of dangerous drugs are likely to be a key influence on and to be prioritised in e-cigarette regulations in Nigeria. There are no suggestions that Nigeria may promote the use of e-cigarettes for smoking cessation.

5.3.4 Economic considerations

Interviewees mentioned economic considerations with potential to influence e-cigarette regulatory decisions. These include Nigeria's economic obligations and the potential economic benefits of e-cigarette commerce in Nigeria.

With respect to Nigeria's economic obligations, RSON stated:

'Because we cannot impede trade as we are members of the WTO. Therefore, it becomes very important that we do not cause technical barrier to trade.' (RSON)

It appeared that regulations in Nigeria are likely to be developed in a way that does not unnecessarily impede international trade in e-cigarettes. RFCCPC suggested that, within Nigeria, there is an obligation to protect consumers' right of access to products they want and traders' rights to establish commerce in such products; preventing or reducing barriers to trade in e-cigarettes are therefore likely to influence e-cigarette regulation. The RFCCPC highlighted this when they said:

> *'So, for us, even outside of consumer rights, maybe right to choose and right to have access to a product that they desire to have, we also have an obligation to be responsible to the industry group. We say, okay look… there won't be an artificial barrier to entry… we're keen on harm reduction. We want a situation where—particularly when claims are made, with respect to harm reduction. We want a situation where these claims can be empirically verified. And can be corroborated and when those happen, we are happy because, reason is that our concern like I say is the consumer. We want a situation where they can get a product that they desire.'* (RFCCPC)

E-cigarette regulators are also likely to consider how trade in e-cigarettes may affect the economy of the country. For example, RSON said:

> *'If we allow—because of our open borders, porous borders, these things* (e-cigarettes) *will continue to find their way into the country, and therefore as long as there is no regulations and no policy that will determine how these things—economically we are going to be losing.'* (RSON)

The RSON was suggesting in the above statement that having an e-cigarette regulation in place provides guidance for trading legally in e-cigarettes. If there are no guidelines, consumer demands for e-cigarettes can lead to illegal entry and illicit trade in e-cigarettes. Since such illicit trade does not follow the right channels, imported products do not get taxed and revenues are not generated which has economic implications. RSON was clearly concerned that poor border control in Nigeria increases the potential for illegal entry of e-cigarettes, and unregulated sales i.e., sales on the black-market. The RSON went further to elaborate that potential e-cigarette regulations will focus not only on entry of e-cigarettes manufactured elsewhere through the borders but also that some products will be manufactured in Nigeria, to maximize economic benefits of trade in e-cigarettes. The RSON suggested this when they said:

> *'The essence of the whole regulation is to give a clear level ground for both product that have manufactured, locally and those that are imported. Because if you don't do that then you'll be impeding trade, and therefore whoever is producing in the country it would be in the best interest of the country because it will add to the GDP of the country.'* (RSON)

The RFCCPC also described how e-cigarette regulations could be utilised to promote industrialisation and boost economic growth:

> *'If at all, those sciences (*that e-cigarettes are safer alternatives that are effective for smoking cessation*) are verified and then corroborated, we want a situation where we have additional, or rather we have advantages from people consuming them as there should also be something like production. So, we would be looking*

at tying, even licencing to production facilities that you have within the country… we are looking at how to promote industrialisation, how to create job opportunities for Nigerians and all of that.' (RFCCPC)

Despite these potential economic benefits, discussions suggested that RFMOH, RSON and RFCCPC were agreed that any form of economic consideration will come secondary to public health considerations. This opinion is encapsulated in the statement by RFMOH that:

'The health component far outweighs any gain, any gain from any economic benefit that we could get… because all over, there have been several cases to that effect that have ruled, in favour of public health. That, public health supersedes any economic benefits a country can make.' (RFMOH)

In conclusion, there are likely to be economic considerations of: fulfilling the country's economic obligations internationally and internally; protecting the rights of consumers and manufacturers; and promoting economic growth in Nigeria. However, public health considerations will take priority over economic considerations in Nigeria.

5.3.5 Infrastructural insufficiency

Interviewees spoke of how the availability (or lack thereof) of certain infrastructure in Nigeria will influence how e-cigarettes become regulated and implemented. Relevant areas of infrastructure include health, manpower and equipment. Interviewees expressed concerns that Nigeria lacks sufficient health infrastructure to tackle any possible public health challenge that e-cigarettes may pose if they prove to be more harmful than beneficial. For instance, the RFMOH and RFCCPC stated:

'For E-Cigarette, we don't know what is to come. It could be the next pandemic. It could be, something that Africa cannot withstand.' (RFMOH)

'So, that public health concern is one of the things that informs why we must regulate that product. More so that we also know that we have a situation where health services may not be as top notch. We are advancing bit by bit, but we don't want a situation where something comes and it's like an epidemic.' (RFCCPC)

With respect to manpower and equipment, RFMOH suggested that these may be insufficient to successfully implement and enforce regulations in the desired manner:

'For instance, a major issue in Africa is manpower shortage. Acute shortage of personnel and the equipment to be able to regulate because in regulation, you need—you need your labs to be able to test these products, you need personnel, you need toll free lines. You need all these things to be in place. And these are

issues that we are still struggling with in Africa… The labs, the communication, the hotlines and all the rest. The reporting system. How do we report a product that contravenes guidelines?' (RFMOH)

In summary, it is possible that the deficiencies in the health services, personnel shortage and lack of appropriate equipment might place constraints on how Nigerian regulators regulate e-cigarettes.

5.3.6 Role of Industry

Analysis showed how the e-cigarette industry could potentially influence the e-cigarette regulatory process in Nigeria. Roles and activities might include stimulating the introduction of e-cigarette regulation and influencing the direction of regulatory change. RSON suggested that vested interests of e-cigarette companies in investing in the Nigerian market might stimulate the development of e-cigarette regulations. They perceived that the availability of an e-cigarette regulatory framework would provide an appropriate legal framework and reassurance to enter and invest in the Nigerian e-cigarette market. RSON stated:

'Already we know that there are some companies who really wanted to start a business in Nigeria. And the only fear they have is that the issue of policy or regulation that, possibly have not been developed. But I'm—as I'm speaking, I have heard, that the responsible ministries have gone far, in ensuring that those policies are developed. Because no investors will want to come and invest in your country when there's no policy framework and regulatory framework. This is one area that will scare all investors. So, for that reason, this I am very aware that something has started in that area.' (RSON)

Companies were also seen as likely to influence the process of regulatory change as it concerns e-cigarettes. For instance, the RFCCPC, when talking about the likelihood of e-cigarettes being regulated as a tobacco product through the already existing tobacco and tobacco product regulations (i.e., the NTCA), said:

'The industry can on their own, trigger an amendment. Like I say, even for instance if you—maybe the provisions that are there in the regulations for cigarette will not favour whatever they would do for the licencing of e-cigarette, it could raise some issues. And say okay look, we don't think this is sufficient for you to use for the regulations of e-cigarette… to say okay look, this can't happen like this and then certainly, we might have to have a consideration to say okay look, let us take these things back to the National Assembly.' (RFCCPC)

From the RFCCPC's perspective, the e-cigarette industry appears to be a major stakeholder in potential e-cigarette regulations in Nigeria. [Note that the RFCCPC represents the FCCPC who have a responsibility to advocate for the fair treatment of consumers and industry groups when regulations are negotiated.] RFCCPC further elaborated on a potential ways e-cigarette regulation might not favour e-cigarette companies. They used the time it would take to bring on e-cigarette regulations as an example when they said:

> *'if for instance the industry tells you that look, you would need to have an amendment, or maybe a new infusion into this regulation* (NTCA)*, that is specifically for E-Cigarette, that would have to go to the National Assembly for approval. But I think the industry might not even want to go to that route, because from my understanding, they are doing everything possible for the regulation to commence as fast as we can. So, they wouldn't want anything that takes that matter back to the Assembly because it would take the next four, five years and the regulation is not amended.'* (RFCCPC)

RFCCPC suggested that the e-cigarette industry would have the ability to challenge or negotiate proposed amendments or inclusions in e-cigarette regulations when they said:

> *'If for instance you look at something like the—having a production facility, as a condition for allowing or licencing your E-Cigarette, definitely you know that is capital intensive. The industry might kick, and say, well, we think this is quite onerous for us and it's not something that is in your present, existing regulation. So, we would want these things to happen, without you tying our hands to that extent. And the Honourable Minister might feel well, since it's not in the regulation and the industry has raised it, let me take it to FEC. So FEC can transmit this to the National Assembly to regulate.'* (RFCCPC)

The RFCCPC even highlighted an example of how, in the past, the tobacco industry influenced tobacco regulations to constrain the kind of amendments that can be made to the existing NTCR. They said:

> *'The National Tobacco Control regulations is the only subsidiary legislation in Nigeria that would say have to go back to the National Assembly for approval if there has to be any amendment to it… the reason was that the industry was able to get something into the Act, that says all the regulations made pursuant to the Act, must—be approved by the National Assembly.'* (RFCCPC)

In summary, it is evident that the e-cigarette industry has the potential to influence e-cigarette regulation in Nigeria, either by affecting the pace of e-cigarette regulatory process, or by impacting the regulatory decisions that would be made through lobbying and advocacy.

5.4 Discussion of Study

5.4.1 Discussion of Key Findings

In this study, I found that six broad factors were likely to influence e-cigarette regulations in Nigeria: existing regulatory framework; research evidence: public health considerations; economic considerations; infrastructural insufficiency; and role of industry. One of the objectives of this study was to identify the factors that influenced e-cigarette regulations in the US or the UK and may potentially determine e-cigarette regulations in the context of Nigeria. Three factors (existing regulatory framework, research evidence, and public health considerations) found in this study to be likely to influence Nigerian e-cigarette regulation similarly influenced e-cigarette regulations in the US or the UK. By contrast, infrastructural insufficiency, and role of industry which were found in this study to have the potential to influence e-cigarette regulations in Nigeria were not apparent in the US and the UK. This does not necessarily mean that these three factors did not influence e-cigarette regulations in the US and the UK; rather it simply means that these factors were not found in my study. The absence of evidence of these influences in the US and the UK may be due to how data was collected (conference audio recordings) in the US (see discussion of this limitation in section 3.4.5), and the active prevention of Industry influence (as discussed in section 3.4.1) in the UK, due to the UK's commitment to WHO FCTC. There were some economic considerations in both the US and the UK with respect to e-cigarette regulations. However, I did not find in my study that these economic considerations had influenced e-cigarette regulations in the US and the UK. But economic considerations are likely to influence e-cigarette regulations in Nigeria.

E-cigarette regulation in Nigeria is likely to start from an E-cigarette Standard which would be developed by SON and would contain the classification of e-cigarette products. Figure 12 below summarises the potential regulatory pathway for e-cigarette regulation in Nigeria. This regulatory process of SON setting a standard for e-cigarettes is different from the approach the US and the UK took in their regulation. Standards were not used for developing e-cigarette regulations in either the US or the UK. When e-cigarettes came into the US market, the FDA published the 'Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and

Required Warning Statements for Tobacco Products' (108). This legislature clarified that e-cigarettes were to be subjected to the existing tobacco products regulation, i.e., FSPTCA. Therefore, a new regulation for e-cigarettes was not needed as e-cigarettes were, in legal terms, considered to be a tobacco product. In the UK, e-cigarette regulation (TRPR) was a transposition of the EU e-cigarette regulation (TPD) into British law. The TPD itself began from the European Commission drafting e-cigarette regulations; European Members of Parliament and Council of Ministers agreed by majority vote for it to become law. The TPD then had to be transposed into national law in each EU member state.

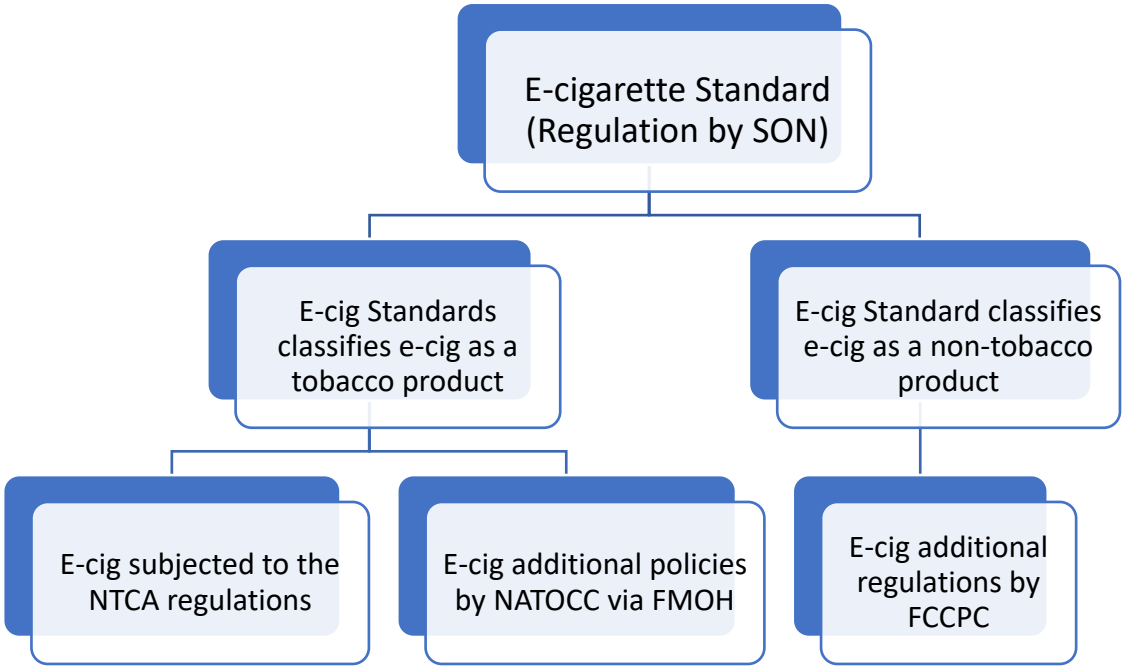


Figure 12: Potential regulatory pathway for e-cigarette regulation in Nigeria

Abbreviations: SON- Standards Organisation of Nigeria |NTCA- National Tobacco Control Act |NATOCC- National Tobacco Control Committee |FMOH- Federal Ministry of Health |FCCPC- Federal Competition and Consumer Protection Commission

If, as seems likely, e-cigarettes were to be classified as a tobacco product in Nigeria, it appears to me that: aspects of e-cigarettes would be regulated by SON through an e-cigarette Standard; NTCR regulations (276) would apply to e-cigarettes; and the NATOCC, through the FMOH, could set out additional e-cigarette policies. In this likely scenario, it appears that SON and FMOH would be the regulators of e-cigarettes in Nigeria. Conversely, if e-cigarettes were to be classified as non-tobacco products, my findings suggest that SON

and FCCPC would be the likely regulators, with SON regulating the safety and quality aspects of e-cigarettes and FCCPC regulating aspects of trade and consumer protection. I surmise that, in the latter circumstances, there might be other potential additional regulators, depending on the actual specific classification of e-cigarettes e.g., consumer product, pharmaceutical product, etc. Analysis of the interview transcripts suggests, however, that it is more likely that e-cigarettes would be regulated as a tobacco product. In these circumstances, any entity manufacturing or importing e-cigarettes in Nigeria will be required by law to obtain a license for trading of the product from the Ministry of Health (MOH) before commencement of trade as required by the NTCR (276). Note that a requirement of the application to the MOH is to have product certification from SON (which certifies that the product meets the Nigerian e-cigarette Standard) (276). Therefore, an e-cigarette Standard will need to be in place to be able to enforce the NTCR in Nigeria. Note also that the regulatory measures that may follow if e-cigarettes are classified as a tobacco product are not only those in the NTCR but, by extension, also include guidance from the World Health Organisation (WHO) Framework Convention for Tobacco Control (FCTC) on e-cigarettes[16] (see Appendix O). Nigeria is a party to the FCTC (6) and the NTCA (279) has as one of its main objectives to undertake activities recommended in the FCTC.

As seems likely to occur in Nigeria, in the US e-cigarettes are classified as tobacco products and subjected to the FSPTCA which regulates tobacco and tobacco products in that country (116). E-cigarettes are also classified and regulated as tobacco products in 62 countries worldwide (78). This means that Nigeria would mirror the US approach and would be in line with the global (WHO) direction.

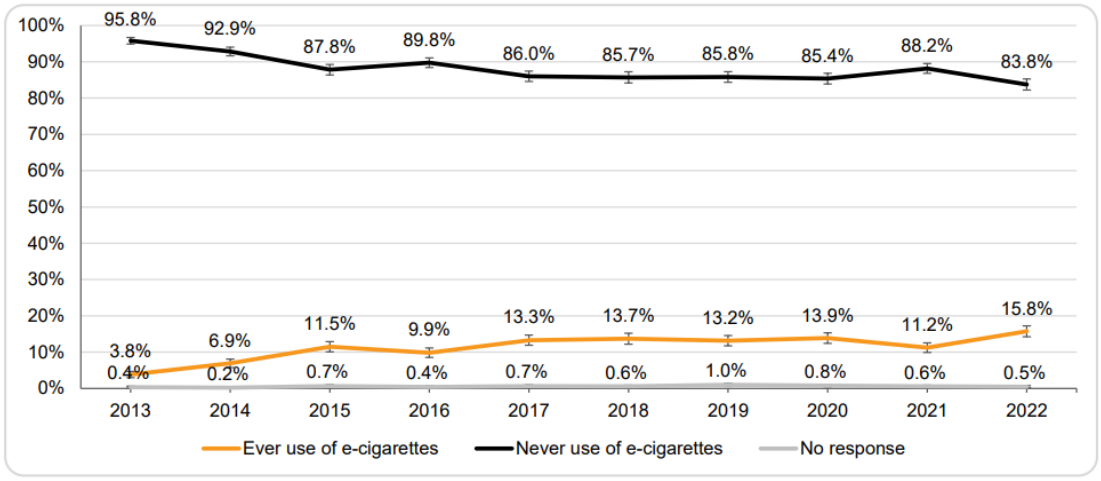
As shown in Chapter 3, both the US and the UK e-cigarette regulations were hugely influenced by the evidence on the potential public health benefits and risks of e-cigarette use. For instance, in the US, where research evidence (179) suggested increase in uptake of e-cigarette use by children, the Tobacco 21 Act (193) was introduced, increasing the minimum age of sale of tobacco products, including e-cigarettes, from 18 to 21 years. By contrast, in the UK, where research evidence has suggested that e-cigarettes are effective for smoking cessation (280), these products have now been added into national guidelines for smoking cessation (85). Nigerian interviewees indicated that the outcome of reviewing

[16] See FCTC_COP6_10Rev1-en.pdf (who.int) (accessed 24/08/2023)

the evidence and of testing it for validation processes would also inform the regulatory measures that would be applied to e-cigarettes in Nigeria. They went on to suggest that review of evidence entails consideration of all the available published standards for e-cigarettes worldwide. There are currently five published standards by ISO/TC 126/SC 3 (Vape and vapour products) from France (281) that are therefore likely to be reviewed by Nigerian regulators. With regards to potentially testing e-cigarette products for validation processes, as proposed by Nigerian interviewees, this is a measure that neither the US nor the UK regulatory bodies carried out. The FDA and the MHRA only require manufacturers to submit comprehensive reports on the constituents of the e-cigarette product and evidence of laboratory testing, but they do not themselves carry out independent testing (108, 158).

As found in study one of this PhD, in both the US and the UK, public health considerations influenced several aspects of regulatory and policy decisions. Both countries wished to protect youth. In the US, public health authorities were concerned that the flavours in e-cigarettes were attractive to children who did not smoke to use e-cigarettes, and a ban on flavoured e-cigarettes was subsequently imposed (157). In UK e-cigarette regulations (158), no restrictions were placed on the production and sale of flavoured products, but regulations included restrictions on product advertisement which interviewees from study one (see section 3.2.2.3) suggested was to prevent or reduce children from being attracted to e-cigarettes. Increasing use of disposable vapes by children has also led to their proposed ban in England, Wales and Scotland with effect from April 2025 (164). Similarly, study three found that, in Nigeria, public health considerations are likely to be the top priority when developing e-cigarette regulations. The dominant public health consideration in Nigeria has to do with protection of non-smokers, especially children and women. While the US, UK, and Nigeria are all concerned with protecting children, evidence from study one (see section 3.3.3) suggested that the UK has focused more on the harms to existing smokers of burnt tobacco and the potential for e-cigarettes to aid in smoking cessation. This difference in emphasis in the UK has perhaps been due to the relatively low prevalence, albeit with a marked increase over time, there of underage (11-17-year-olds) 'ever' use of e-cigarettes which was 3.8% in 2013, rising to 15.8% in 2022 (see Figure 13 below) (282). In the US, e-cigarettes have been the most commonly used 'tobacco product' among youth since 2014 (e.g., see Figure 14 below for use of tobacco product among high school students in 2018)

(20), and therefore as evidenced from study one (see section 3.3.3), US regulators have focused on the risk of attracting non-smokers, particularly youth, to vaping, and therefore to nicotine addiction and the possibility of e-cigarettes being a gateway to tobacco smoking.



ASH Smokefree GB Youth Surveys, 2013-2022. Unweighted base: All 11-17 year olds (2013 = 1,895, 2014 = 1,817, 2015 = 1,834, 2016 = 1,735, ,2017 = 2,151, 2018 = 1,807, 2019 = 1,982, 2020 = 2,029, 2021 = 2,109, 2022 = 2,111).

Figure 13: Use of e-cigarettes by youths (11-17years) in the UK between 2013-2022.
Source: Adopted from ASH (282).

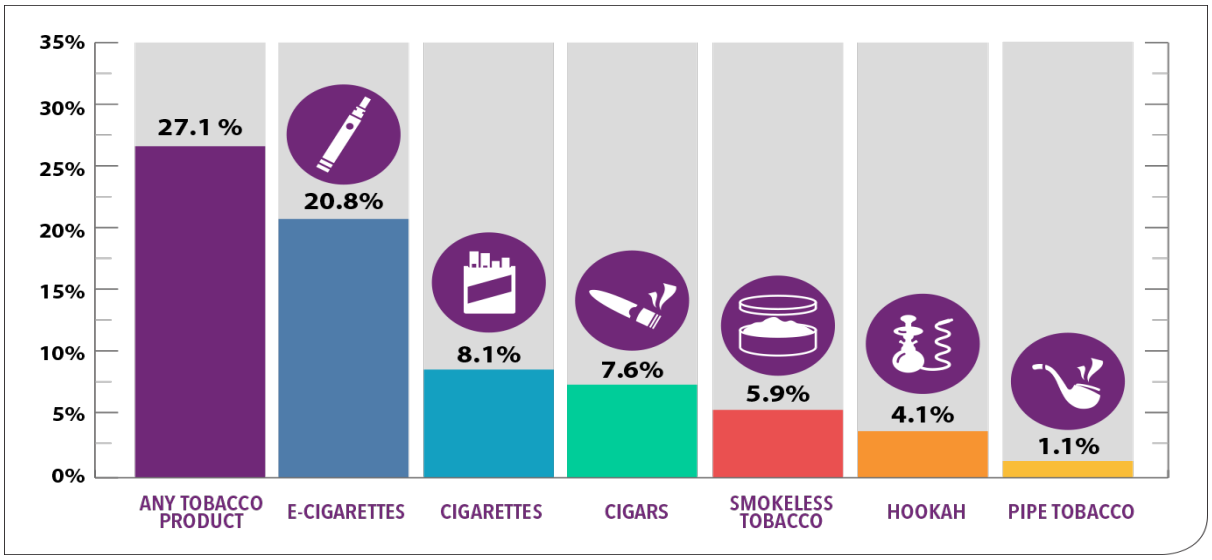


Figure 14: Tobacco product use among high school students in 2018
Source: Adopted from CDC (20).

The demographic profile of Nigeria's population (in 2021, about 43.29 percent of Nigeria's total population were children aged 0 to 14 years)(5) could be the reason why potential regulators there are so concerned with protection of children. By contrast, Nigeria has a

relatively low prevalence of smoking amongst adults (latest estimate 2.7%)(21) compared to the US (26) and the UK(29)(11.5% and 12.9% respectively), so the use of e-cigarettes for smoking cessation may be seen as a lower priority.

There were some economic considerations in both the US and the UK with respect to e-cigarette regulations. In the US there was an economic impact assessment of proposed e-cigarette regulations.[17] From my interviews with e-cigarette regulatory stakeholders in the UK, I also found that as part of the standard procedures, an impact assessment on businesses was done during regulation of e-cigarettes (see section 3.2.2.1). Similarly, in interviews with Nigerian stakeholders I found that economic considerations are likely to influence e-cigarettes regulations in that country (see section 5.3.4). There was no indication from the interviews with Nigerian stakeholders that the economic consideration would comprise a formal impact assessment as seen in the US and the UK. Rather, there was an impression that the economic considerations would be orally presented by economic stakeholders (such as representatives of the Federal Ministry of Trade and Investment, and the Federal Competition, Consumer Protection Council) in the SON technical committee and to NATOCC during their deliberations of the pros and cons of potential e-cigarette regulatory measures (see section 5.3.4). Key economic considerations mentioned were taxation and potential requirements for manufacturers to produce locally to benefit the economy. It seemed to me that the type of economic measures Nigerian regulators may introduce is likely to be dependent on their public health assessment of e-cigarettes. I believe that economic measures could be used not only to produce economic gain but also to promote public health goals. For instance, the taxation of tobacco cigarettes in the UK is aimed at discouraging people from smoking tobacco cigarettes (283).

In Nigeria, there are already suggestions of independent testing of e-cigarette products. Findings from study one (see section 3.2.2.1) showed that independent testing would have been ideal in the UK, but the existing regulatory framework precluded this from happening as the TRPR required only notification of e-cigarette products. In Nigeria where potential regulators appear to be in favour of independent testing, would funding for procurement of equipment for independent testing be provided to regulators? A 2018 study (240) on the analysis of tobacco control policies in Nigeria found that lack of funding slowed the policy

[17] See https://www.fda.gov/media/97875/download (accessed 25/08/2023)

implementation process (240). It remains to be seen whether lack of appropriate equipment in Nigeria may have an influence on e-cigarette independent testing or regulatory process.

The role of the e-cigarette industry, identified in this study as a factor with potential to influence e-cigarette regulation in Nigeria, was not found to influence e-cigarette regulations in the US and the UK, although they attempted to influence regulations in the UK (see section 3.3.1.1). Note that, as already discussed above, the absence of evidence in my study to suggest that Industry influenced regulatory decisions in the US and the UK, does not necessarily mean that Industry did not influence regulations (or at least seek to do so) in both countries. Regulatory capture is not new, especially to the US. Marver H. Bernstein (203) in his writings about the American context, has discussed how some regulatory agencies shift away from their mandate of regulating in public interest to serving the interest of the regulated industry due to a capture by the industry. Capture theory suggests a situation whereby government regulatory agencies are gradually 'captured' by the regulated industry, so that, over time, they regulate primarily in the interest of industry, and not in public interest (202). I found from my interviews with e-cigarette regulatory stakeholders in the UK that the e-cigarette industry attempted to influence e-cigarette regulations through extensive lobbying to suit their interest in the regulations, but such attempts were blocked by regulators (see section 3.3.1.1). As I was unable to interview any e-cigarette regulatory stakeholders from the US, I did not have the opportunity to pose any direct questions regarding influence of e-cigarette or tobacco industry in e-cigarette regulation. Unlike the US, the UK is a party to the WHO framework Convention for Tobacco Control (FCTC), and Article 5.3 of the FCTC mandates member countries to '*protect public health policies with respect to tobacco control from commercial and other vested interests of the tobacco industry*'(284). This is presumably why the UK were cautious and resisted influence of tobacco industry. In my study, it was found that the e-cigarette industry has the potential to influence e-cigarette regulation in Nigeria (see section 5.3.6). However, Nigeria is also a party to the FCTC; the FMOH, who are potential Nigerian e-cigarette regulators, have indicated commitment (see section 5.3.1) to the FCTC which mandates member countries to resist industry influence in tobacco control, which may include e-cigarettes in the Nigerian context. And with a comprehensive FCTC compliant policy now in place in Nigeria since 2015

(240), it is likely that Nigeria will attempt to resist industry influence when e-cigarette regulations are made.

The six factors identified in this study findings above, was in achievement of the third objective of this PhD project – to understand the similarities and differences between contextual factors in Nigeria versus factors identified as determining the regulatory and policy approaches to e-cigarettes in the US and the UK.

Other specific contextual Influences that may determine e-cigarette regulatory approach or activities in Nigeria were identified. With the emphasis of Nigerian interviewees on protecting vulnerable groups in Nigeria (i.e., women and young people (under 15 years) who represent the largest (43%) age group of Nigeria's total population (5)), demographic composition is a key contextual factor relevant to Nigerian regulators. The lower prevalence of adult smoking for Nigeria (3.7%) compared to the US and the UK (11.5% and 13.3% respectively), is a further contextual factor likely to be considered by Nigerian regulators. These findings fulfilled the third objective of this study which was to understand the similarities and differences between contextual factors in Nigeria versus factors identified as determining the regulatory and policy approach to e-cigarette in the US and the UK.

5.4.2 Strengths of this strand of study

The choice of methods used in this study had its strengths and weaknesses, similar to those for study one above. I used qualitative interviews of potential e-cigarette regulators which gave the participants opportunity to express themselves about the potential factors that may influence e-cigarette regulations without restrictions, with the aim of providing in-depth information. The interview topic guide was not identical for all interviews but rather it was tailored to the context of the professional role of each interviewee. However, all the topics covered were aligned to answering the overarching question of what factors will potentially influence the regulation of e-cigarettes in Nigeria. Secondly, purposive sampling was used to identify participants based on those best suited to provide the needed information. All the interviews were conducted virtually using the Zoom facility, as this was convenient for all the participants, giving them the opportunity to choose their own space and time to attend the interview; this method also allowed auto-transcription of the recordings, saving time and

money. All the interviews were conducted by me which ensured consistency in the data collection process. Lastly, in the study, organizational names and location were not anonymized because of the risk of losing the meanings of names which is important in my analyses, to contextualize findings (244). Individual participants were, however, given the choice to either remain anonymous or go on record for their views. The use of vignettes, i.e., presenting interviewees with the factors that were found to have been considered in e-cigarette regulations in the US and the UK, stimulated discussion and provided a frame of reference for interviewees to use.

5.4.3 Limitations of this strand of the study

In this strand of study, some participants were members of the same committee (NATOCC) in the Ministry of Health and were officially shortlisted as representatives by the Ministry of Health to be interviewed for this study. This means that they worked closely with one another, and so may be known to each other. Therefore, participants may know other interviewees. Therefore, internal confidentiality, which involves the ability of participants in a research project to identify each other in the final publication of the research findings could not be guaranteed. However, external confidentiality was assured for all the participants who chose to be anonymized in the study. Also, presenting interviewees with the factors that were found to have been taken into account in e-cigarette regulations in the US and the UK may have biased or limited the interviewees' information on the potential influencing factors for Nigerian e-cigarette regulation because there is a possibility for interviewees to look at questions posed through the lens of events presented to have taken place in the US and or the UK. However, participants were directly asked about factors that may influence e-cigarette regulations in Nigeria but was not found to have influenced regulations in the US and or the UK.

5.5 Conclusion

The young population of Nigeria and WHO recommendations on regulation of e-cigarettes provides stimulus for Nigerian regulators to impose some form of regulation of e-cigarettes in Nigeria. Adhering to Nigerian regulatory framework requires compliance to already

existing policies, and multiple stakeholder consultation. The involvement of multiple stakeholders can be beneficial for inclusivity but may introduce three competing interests (i.e., public health, economic, and industry interest) which may conflict and unduly influence e-cigarette regulations in Nigeria. With the potential insufficiencies in the infrastructure to ensure adequate implementation and policing of regulations in Nigeria, regulators should be prioritising regulatory measures that serve the most essential needs of the population. Evaluating available research evidence and assessing other country approaches (such as in the US and UK) against outcomes (such as, smoking cessation rates, rate of teenage use of e-cigarettes, smoking rates, etc.) provides a legitimate basis for regulatory choices. In Chapter 6 of this PhD thesis, I bring together all the findings from my literature review and three primary studies to discuss how the US and UK e-cigarette regulatory policies and public health initiatives and policies may inform policy approaches in the context of Nigeria. I also make recommendations for Nigerian regulators and for further research. The overall strengths and limitations of this PhD project is discussed in Chapter 6.

Chapter 6. Discussion and Conclusion

6.1 Summary and Discussion of Findings

In this PhD project, I sought to compare the US and UK e-cigarette regulatory and public health policies, to inform policy approaches in the context of Nigeria. To understand the similarities and differences between e-cigarette regulation and policies in the US and the UK (Objective 1), I carried out a literature review and found out that there were nine areas where the US and the UK were similar or differed in their regulatory measures. These were: Classification, Registration/ Notification, Health warning labelling, Ingredients / flavours, Nicotine volume / concentration, General safety, Child safety packaging, Minimum age of sale, and Advertising / Promotion / Sponsorship. Of the nine areas, the US and the UK had similar regulatory measures in three areas. These were Registration / Notification, Health warning labelling, and Child safety packaging. They had different regulatory measures in the remaining six areas discussed below. In the discussions below, I link my findings from all the studies conducted towards answering the overall questions in this PhD project: What factors determined e-cigarette regulations in the US and the UK and may similarly determine e-cigarette regulations in Nigeria? I also discuss my findings in the context of the broader literature on regulations and policy regarding e-cigarettes and tobacco smoking.

6.1.1 Classification of e-cigarettes

Classification of e-cigarettes is one of the six areas where e-cigarette regulatory measures differed between the US and the UK. The US has classified e-cigarettes as a tobacco product while in the UK they are classified as consumer products but regulated under a tobacco and related products regulation (i.e., TRPR); there is also the option of a manufacturer seeking labelling as a medicinal product if licensed as a medicine. I found that the main reported reasons for the US classifying e-cigarettes as a tobacco product was because the nicotine in e-cigarettes is derived from tobacco; thus, they meet the country's legal definition of a tobacco product. By contrast, the UK classified e-cigarettes as a consumer or medicinal product in line with the TPD, and in favour of helping adult smokers quit smoking; classification as a consumer or medicinal product would allow adult smokers to try them in

their smoking cessation attempts. In Nigeria, interviewees suggested that e-cigarettes are likely to be classified as tobacco products in line with WHO recommendations. Figure 15 below shows the link between the key findings in this study relating to classification of e-cigarettes in the US, UK, and Nigeria.

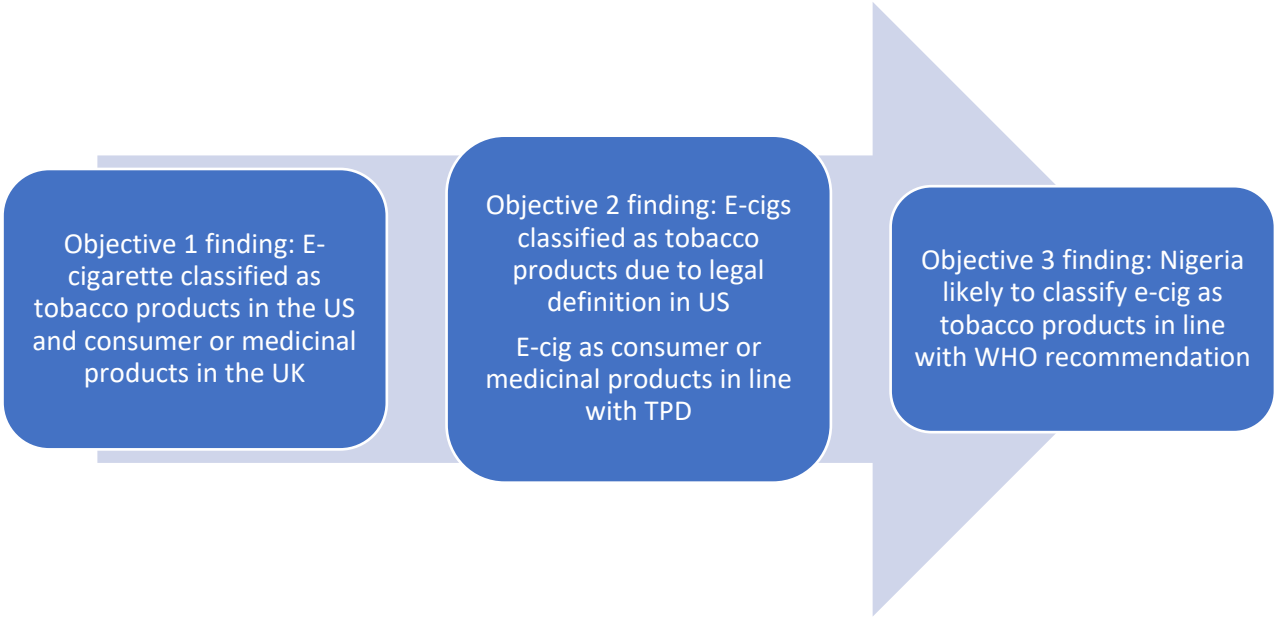


Figure 15: Classification of e-cigarette and determinant factors

A Nigerian interviewee referred to the WHO recommendation to classify e-cigarettes as a tobacco product as 'the global direction'. Nonetheless, it is important to clarify that the WHO FCTC guidance on e-cigarettes is not necessarily a universally agreed approach to regulation of e-cigarettes. An ethnographic account of how e-cigarettes were tackled at the 6th Conference of the Parties to the WHO FCTC revealed that uncertainties about e-cigarettes and differences of opinion meant that a consensus on specific regulatory approaches or universally applicable regulatory measures could not be reached. Hence 'agreeing to disagree' as a consensus position and 'strategic use of time' were the principles that ensured completion of the conference events (285). Campus *et* al. (77), comparing regulation of e-cigarettes across 97 countries in 2021, reported five different ways in which e-cigarettes are classified worldwide: medicinal products, poisons, tobacco products, consumer products, and/or unique products. There are currently (April 2024) 187 countries with a classification of e-cigarettes. As seen in Figure 16 below, of the 187 countries/jurisdictions, 33% classify e-cigarettes as tobacco or related products (tobacco

imitation, tobacco derivatives, or tobacco surrogates); 13% as consumer products, devices, or combination products; 13% as medicines/drugs/medical devices; 40% as ENDS/e-cigarettes or vaping products (equivalent to classification as 'unique products' by Campus *et* al. (77)); and 1% as poisons or hazardous substances (78). Therefore, a 'global direction' to classification of e-cigarette could be taken to mean classification as ENDS or vaping products which the majority (40%) of countries use, rather than as tobacco or related products (33%).

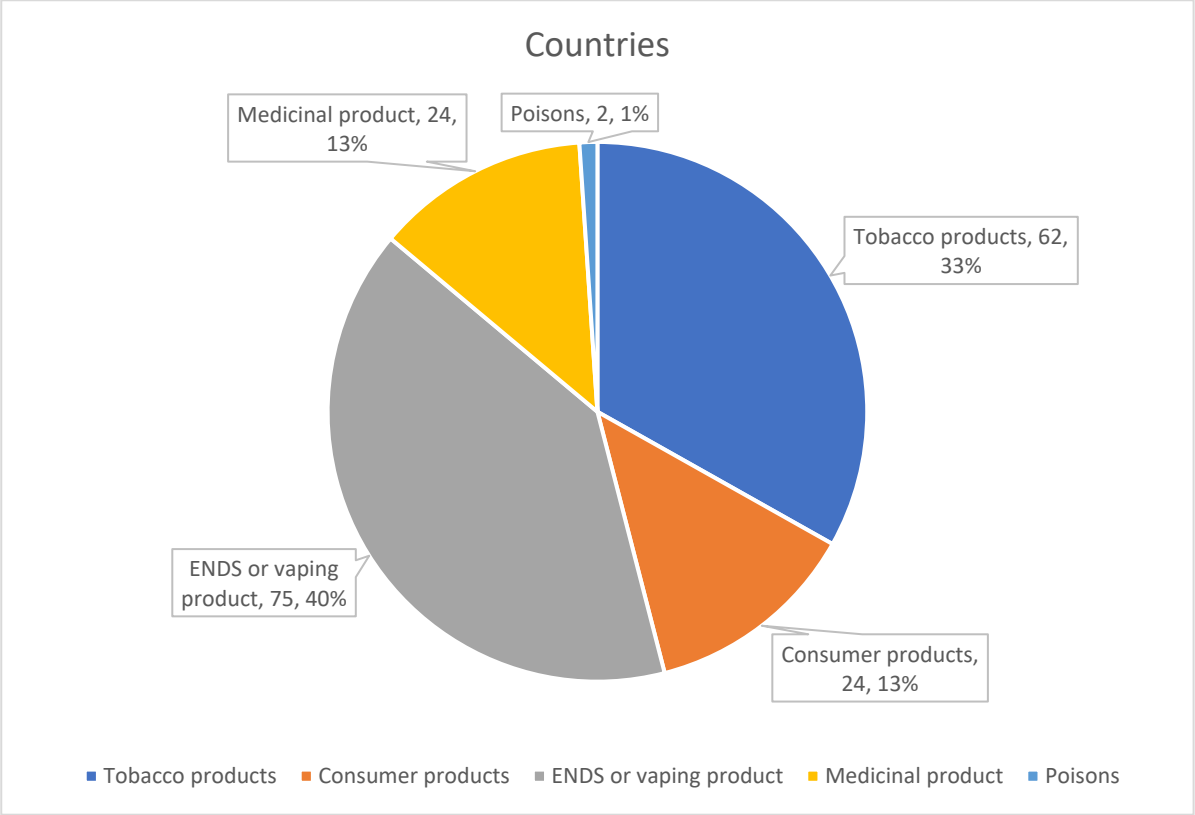


Figure 16: Classification of e-cigarettes worldwide according to the Global Tobacco Scanner

From my findings in this study, there was no indication that the US factored WHO guidance into their regulation of e-cigarettes (US is not a signatory of WHO FCTC). Although the UK is a ratified party to WHO FCTC, there was also no indication that FCTC was the main consideration for classifying e-cigarettes. Rather e-cigarettes were classified as consumer/medicinal products in line with the TPD and to allow adult smokers to try them in their smoking cessation attempts. This action can be said to have been underpinned by Expectation/ Marketing theory (202), i.e., the expectations among public health

professionals and researchers in the UK that e-cigarettes can potentially reduce smoking rates as a cessation aid may have put pressure on regulators to deregulate e-cigarettes by classifying them as consumer or medicinal products rather than tobacco products (i.e. as other tobacco products in the TRPR are classified) (see Section 2.3.3). NRTs, which have been recommended by WHO and in many countries for smoking cessation, are similarly licensed as medicines in such countries. In the US, NRTs are regulated as a medicine with some products (nicotine patches, gums and lozenges) sold over-the-counter, while sale of others (nicotine spray and inhalers) requires a prescription (286). In the UK, NRTs (which includes nicotine gums, inhalators, lozenges, nasal spray, oral spray, sublingual tablets, and transdermal patches) are classified as medicines and can be purchased over-the-counter from pharmacies and other shops, or obtained on prescription from a doctor or NHS Stop smoking service (287). In Nigeria, NRTs are sold in pharmacies but do not require a prescription for purchase (288).

If e-cigarettes are classified and treated as a tobacco product, this may signal that Nigerian regulators do not view them as a prospect for harm reduction in Nigeria. South Africa is the only African country (out of nine that currently regulate e-cigarettes) that allows the sale (albeit with prescription required) of nicotine-containing e-cigarettes at pharmacies, and the only one that regulates e-cigarettes as medicines. Other African countries regulate e-cigarettes as tobacco products, imitation tobacco products, ENDS, and derivative products (78).

Nigerian interviewees suggested that the e-cigarette industry has the potential to influence e-cigarette regulation in Nigeria, either by affecting the pace of the e-cigarette regulatory process, or by impacting the regulatory decisions that would be made, through lobbying and advocacy (see Section 5.3.6). Therefore, of all the regulatory theories discussed in Section 2.3, regulatory capture (202) is the most likely to influence Nigerian e-cigarette regulation. E-cigarette companies may seek to influence some regulatory decisions, such as the classification of e-cigarettes, in their interest. This is a particularly important aspect of regulation due to its implications in determining potential regulators and regulatory measures to apply to e-cigarettes. One of the Nigerian interviewees was keen to point out that, if e-cigarettes are classified as tobacco products, e-cigarette companies may argue that existing tobacco regulations are not appropriate for their regulation (see Section 5.3.6).

However, as party to the FCTC, Nigerian regulators would be expected to prevent industry influence or regulatory capture (202). My study showed that attempts were made by industry to influence e-cigarette regulation in UK (see Section 3.3.1.1), but as a ratified party to the FCTC, the UK sought to prevent industry influence throughout the regulatory process. In terms of Article 5 of FCTC (General obligations including reducing industry interference), a Global Tobacco Control Progress Hub[18] (a live platform for monitoring countries' progress on adherence to FCTC) scores (7 out of 8) and ranks (32nd out of 180 countries) the UK and Nigeria equally and highly on progress made with reducing tobacco industry interference in regulations and policies.

6.1.2 Registration/ Notification of E-cigarettes

Both the US and the UK required e-cigarette manufacturers to notify regulators about new products before bringing them into market or continuing to sell products already on the market. The existing regulatory framework was an influential factor in both the US and the UK respectively. Neither country developed e-cigarette regulations *ab initio*; rather they added them on to existing regulations, in the case of the US, or transposed existing EU regulations into UK law, in the case of the UK. Thus, both countries ended up with e-cigarette regulatory measures combined, albeit in different ways, with tobacco product regulations. The US classified e-cigarettes as a tobacco product and treated them like every other tobacco product in the FSPTCA. By contrast the UK classified e-cigarettes as a consumer product and treated them as a tobacco related product with a dedicated section of regulatory measures in the TRPR, rather than dealing with them identically to all other tobacco products. Despite these differences between the US and the UK, the incorporation of e-cigarette regulations within tobacco and related product regulations in both the US and the UK is a likely reason behind the requirement for manufacturers to notify regulators of new or existing e-cigarettes on the market, mirroring the requirement for notification of new and existing tobacco products. My interviews with Nigerian stakeholders suggested that e-cigarettes are also likely to be regulated as a tobacco product in Nigeria. In Nigeria, manufacturers of tobacco products or companies are required to notify and acquire a license

[18] See https://public.tableau.com/app/profile/globalprogresshub/viz/WHO-FCTC-Dashboard-June-28/CountryLandingPage (acessed 22/08/2023)

from the Minister of Health for their products before they can be sold in the Nigerian market. Figure 17 below shows the link between the key findings in this study relating to notification of e-cigarettes in the US, UK, and Nigeria.

Figure 17: Notification requirement and determinant factors

Registration or notification of tobacco products are common practice in countries that regulate tobacco products, and 43 countries currently (April 2024) require manufacturers/retailers to notify the competent authority prior to introducing e-cigarettes to the market (78). However, not many countries additionally require manufacturers or retailers to obtain a license for sale of tobacco products as is the case in Nigeria. In the UK, as with many European countries, retailers do not require a licence to sell tobacco products (289). In the US, albeit in the absence of a country-wide requirement to license tobacco product retailers, seven states and three territories require retailers to have a license to sell tobacco products over the counter, while 33 states and four territories require retailers to have a license to sell either non-cigarette tobacco products or e-cigarettes over the counter (290). It has been suggested in the literature, and is recommended by WHO, that licensing retailers is effective in helping reduce tobacco use (289, 291, 292). In a special communication that recommended tobacco retail licencing systems in Europe (289), the authors concluded that tobacco retailer licencing would bring about effective monitoring of the retail environment and denormalization of smoking through better enforcement of policies against selling tobacco products to youth and reduction in the number of tobacco

retailers. Nigerian regulators cannot be certain of the public health or economic impact of e-cigarette licensing prior to placing that regulatory measure. Nonetheless, an assessment of the public health impact of e-cigarette retail licensing in those US states that do require licences for the sale of e-cigarettes might provide lessons to inform Nigerian e-cigarette regulation.

6.1.3 Health Warning Labelling of E-cigarettes

With respect to health warning labelling, both the US and the UK regulations stipulate similar health warning labels along the lines of 'This product contains nicotine which is a highly addictive substance'. It appeared likely that both countries simply carried over health warning labelling requirements for tobacco products to e-cigarettes, communicating the internationally acceptable fact that nicotine is an addictive substance. However, it is also possible that they acted on their public health concerns to adopt a cautious approach to e-cigarette labelling and regulation. Findings from interviews with Nigerian stakeholders also indicated that there are nicotine addiction related public health concerns that may be addressed in e-cigarette regulations in Nigeria. Figure 18 below shows the link between the key findings in this study relating to health warning labels on e-cigarettes in the US, UK, and Nigeria.

Figure 18: Warning label requirement and determinant factors

There are currently (April 2024) 51 countries/jurisdictions that mandate the placement of health warnings on e-cigarette packaging (78). In Nigeria, the National Tobacco Control Regulations, 2019 (NTCR) (276) requires tobacco products to have health warning graphics that rotate every 24 months between the three pictures merged in Figure 19 below. The graphics carry health warnings that smoking causes lung cancer, mouth cancer and throat cancer. E-cigarettes do not contain tobacco, which is what carries the carcinogenic potential of smoking, and to date (April 2024) available evidence does not suggest that e-cigarettes cause any form of cancer. This means that in terms of correct messaging, it would be misleading for Nigeria to use the same health warning message for e-cigarettes as it does for cigarettes or other tobacco products.

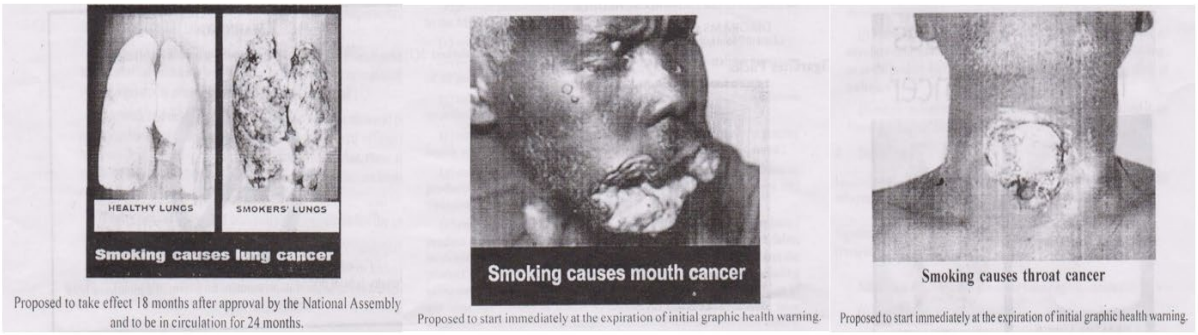


Figure 19: Required NTCR health warning graphics for tobacco products in Nigeria.

The NTCR health warning graphics complies with Article 11 of the FCTC, which recommends that health warning for tobacco products carry specific illnesses caused by tobacco and use graphic images demonstrating the harm of tobacco use. WHO currently states that 'evidence reveals that these (e-cigarette) products are harmful to health and are not safe. However, it is too early to provide a clear answer on the long-term impact of using them or being exposed to them'(293)(p.1).[19] A Cochrane review of e-cigarettes (22) did not detect evidence of serious harm from nicotine containing e-cigarettes over a follow-up period of up to two years. However, the number of studies (8 studies) in the review was small and the follow-up period relatively short.

In the absence of evidence to support any specific illness caused by e-cigarette use, Nigerian e-cigarette regulation may be silent on health warnings for e-cigarette products or may require one that focuses its warning message on the nicotine present in e-cigarettes as is the

[19] See https://www.who.int/news-room/fact-sheets/detail/tobacco (accessed 24/08/2023)

case in the US and the UK. WHO currently states that 'consumption of nicotine in children and adolescents has deleterious impacts on brain development, leading to long-term consequences for brain development and potentially leading to learning and anxiety disorders'(293)(p.1). The FDA currently shares WHO's position on consumption of nicotine in children and adolescents, yet the e-cigarette regulation in the US only requires a health warning message that 'This product contains nicotine which is a highly addictive substance'. How Nigerian regulators move to regulate the health warning aspect of e-cigarettes remains to be seen.

6.1.4 Ingredients/ Flavours in E-cigarettes

Regulatory measures for Ingredients/ Flavours are an area where I found the US and the UK to have diverged in their e-cigarette regulations. The US did not have any specific measures to control the ingredients in e-cigarettes but has regulated flavours in e-cigarettes since 2020. In January 2020, the FDA issued a policy directive instructing companies to cease manufacture, distribution, and sale of any flavoured (other than a tobacco- or menthol-flavour, similar to those found in tobacco cigarettes) cartridge-based ENDS product (194). The FDA stated that the action was taken to combat an 'epidemic' of youth use of e-cigarettes by reducing access to the e-cigarette flavours appealing to children (194). The FDA referred to and tackled youth use of e-cigarettes in the US as an 'epidemic' because the 2019 National Youth Tobacco Survey (NYTS) results showed that more than 5 million US middle and high school students were current e-cigarette users i.e., had used e-cigarettes within the last 30 days, with a majority reporting cartridge-based products as their usual brand (294). However, as the ban only affected cartridge-based products there was a policy loophole as flavours continued to be available in products via disposable vape products such as Puff bars, and these products were promoted through social media discussions (295). FDA's ban of flavoured cartridge-based ENDS products can be said to have been underpinned by disease-politics theory (202) where patient or public activism in the aftermath of a crisis can lead to regulatory reforms (see Section 2.3.2). I found from my study (see Section 3.3.2.3) that the FDA were concerned with prevention of uptake of e-cigarettes by children and took preventive actions, including the flavour ban. On the other hand, the UK TRPR has

restrictions on ingredient in e-cigarettes such as vitamins, additives, and ingredients (see Table 6). The recently proposed Tobacco and Vapes Bill 2024 also provides powers to ministers to regulate the flavours and contents of vaping products in the UK (164). I found that potential Nigerian regulators did not suggest any specific regulatory measures for the ingredients and flavours in e-cigarettes but were particularly cautious of preventing appeal and uptake of e-cigarettes by children (see Section 5.3.3).

Figure 20 below shows the link between the key findings in this study relating to Ingredients / Flavours of e-cigarettes in the US, UK, and Nigeria.

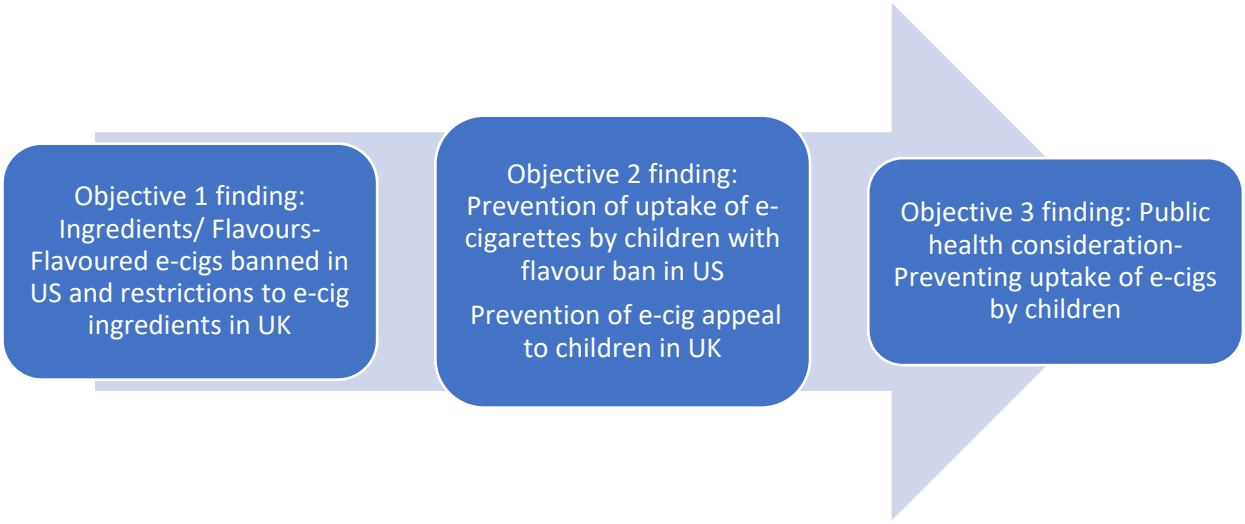


Figure 20: Regulation of ingredients/ flavours in e-cigarettes and determinant factors

Thirty-nine countries/jurisdictions, including the UK but not the US, currently (April 2024) either do not permit the use of ingredients (other than nicotine) that pose a risk to human health in heated or unheated form in nicotine-containing e-liquid or regulate flavours in e-liquid (or do both) (78). Also, 34 countries/jurisdictions, including the UK but not the US, regulate the quality of nicotine and other ingredients used to manufacture e-liquids (78). The Nigerian interviewees suggested that preventing appeal and uptake of e-cigarettes by children involved restricting anything that makes e-cigarettes and smoking 'attractive' or 'glamorous.' Flavour of e-liquids has been suggested in the literature to have the potential to initiate children and young people to vaping and smoking. Although among adult current and former smokers the availability of a variety of flavours in e-cigarettes is associated with

higher abuse potential and appeal of e-cigarettes, it might also facilitate complete substitution for cigarettes, making it an important aspect of smoking cessation success (296). In countries such as the US where there are e-cigarette flavour restrictions, the regulatory goal of that measure is to prevent youth uptake of e-cigarettes through limiting flavours that are deemed attractive to children. A systematic review of the use of e-cigarette flavours by young people, while recognising the low-quality of evidence, concluded that flavours may be an important motivator for e-cigarette uptake, but the role of flavours in tobacco smoking uptake or cessation is unclear (297). Note that, unlike the US that brought in flavour restrictions in response to an 'epidemic' of youth use of e-cigarettes, the UK has had relatively low e-cigarette use among children until relatively recently (January 2023) when Trading Standards raised concerns about vaping increasing among children in the UK as shops are illicitly selling vaping products, often disposable vapes, to under 18s (162). The proposed Tobacco and Vapes Bill which, if passed into law, will take effect from April 2025, prohibits the sale of non-nicotine vaping products to under 18s in England, Wales and Northern Ireland (Scotland already has this in place)(164). Nigerian regulators are likely to be determined to prevent vaping or smoking from being attractive to children, given that about 43 percent of Nigeria's population are children aged 0 to 14 years (5). When Nigerian regulators come to decide whether to adopt flavour restriction to control use of e-cigarettes, they will need to bear in mind that evidence suggest that flavours may be an important motivator for e-cigarette uptake but are also relevant for attracting smokers to switch from tobacco cigarettes to e-cigarettes (which are a relatively safer alternative to smoking).

6.1.5 Nicotine volume/ concentration in E-cigarettes

Nicotine volume/ concentration in e-cigarettes is not currently regulated in the US. By contrast, the UK's TRPR specifies a maximum nicotine concentration of 20 milligrams per millilitre (mg/ml) in an e-cigarette or refill container. Also, the e-cigarette cartridges should contain no more than 2 millilitres of nicotine-containing liquid, while refill containers should contain no more than 10 millilitres of nicotine-containing liquid (see Table 8). Findings from my study showed that both the US (see Section 3.3.2.3) and the UK (see Section 3.3.1.3) regulators had concerns about the addictiveness of nicotine in e-cigarettes. However,

because the US has focused on nicotine uptake by children, their regulatory interventions have been to ban flavours appealing to children and to increase the age of sale of e-cigarettes from 18 to 21 years old. The UK, on the other hand, has focused on helping existing adult smokers quit cigarettes; therefore, in regulation, it simply imposed limits on nicotine volume and concentration, in common with those applicable across the EU and in line with the TPD. Addictiveness of nicotine in e-cigarettes was an area also concerning to potential e-cigarette regulators in Nigeria (see Section 5.3.3), and these regulators are likely to review available evidence on the addictiveness of nicotine in e-cigarettes before adopting any regulatory measures involving nicotine volume and concentration (see Section 5.3.2). Figure 21 below shows the link between the key findings in this study relating to nicotine volume and concentration in e-cigarettes in the US, UK, and Nigeria.

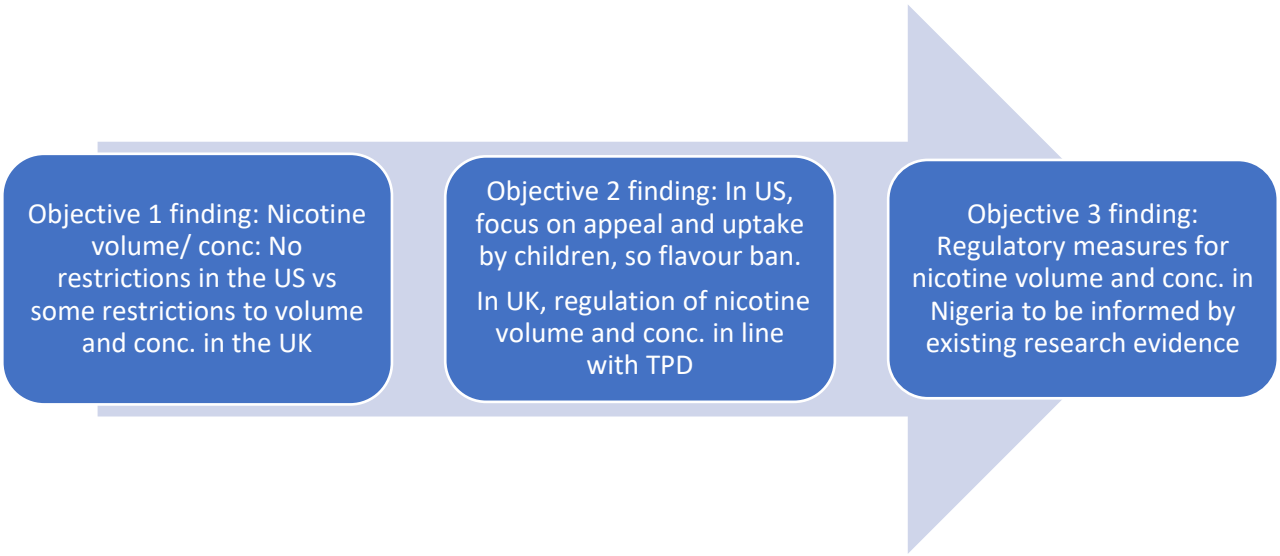


Figure 21: Nicotine volume/ concentration and determinant factors

There are currently (April 2024) 39 countries/jurisdictions that regulate the amount (concentration/volume) of nicotine in e-liquids (78). In situations where people use e-cigarettes to quit smoking, addictiveness of nicotine in the e-cigarette should not be a major concern because smokers are already exposed and probably addicted to nicotine through smoking cigarettes. For these individuals, the use of e-cigarettes satisfies their urge for

nicotine while reducing their health risk from smoking and therefore it makes sense that the permitted concentration should be similar or lower to that available in tobacco cigarettes.

However, not everyone uses e-cigarettes for smoking cessation attempts. There is a risk for initiation to nicotine uptake through e-cigarettes among never smokers and young people who may experiment. A 2015 US nationally representative survey showed that 8th, 10th, and 12th Graders in the US used e-cigarettes for experimentation (53.0%), taste (37.2%), boredom (23.5%), having a good time (22.4%), and relaxation (21.6%) (298). With the increasing popularity of e-cigarettes, researchers have sought to find out whether e-cigarettes are more addictive than tobacco cigarettes. Early (between 2014 to 2017) findings from studies (299-302) assessing nicotine dependence in e-cigarette users versus smokers, using blood tests and the Fagerström test for nicotine dependence (FTND), showed that e-cigarette users were less dependent on e-cigarettes than smokers were on tobacco cigarettes. However, a 2019 study (303) conducted in Poland, showed that the nicotine dependence levels measured with FTND were over two times higher among e-cigarette users compared to tobacco smokers. The authors of the latter study alluded to a potential reason for the deviation of their finding from previous study findings; more than half of their participants were using technically advanced e-cigarettes with a high-capacity battery or accumulator, characterized by the production of a larger volume of aerosol and delivery of significantly higher doses of nicotine compared to older models (first or second generation) of e-cigarettes. Another factor that could lead to increased uptake and dependence on nicotine from e-cigarettes is the concentration and volume accessible to users through e-cigarettes. In the UK and most European countries (mainly due to TPD), e-cigarettes concentration in e-liquid is limited to 20mg/ml. In the US, where there is no limitation to nicotine concentration in e-cigarettes, JUUL e-cigarettes have as high as 59mg/ml nicotine concentration in its e-liquid (160).

Whilst there is an argument that limiting nicotine concentration in e-liquids can help limit nicotine addiction from use of e-cigarettes, there is an opposing argument that people who attempt to quit smoking through the use of e-cigarettes may return to smoking because they do not get enough nicotine ‘hit’ as they were previously obtaining from smoking tobacco cigarettes; in other words, their nicotine cravings are not satisfied. A systematic review of the evidence suggest that higher nicotine concentrations are associated with higher abuse

potential and appeal of e-cigarettes but may help facilitate complete switching from cigarettes to e-cigarettes (296). The authors of the review (296) implied that regulations of nicotine concentration, aimed at decreasing naïve uptake, may inadvertently decrease uptake and complete switching among smokers, reducing the harm reduction potential of e-cigarettes. Whether or not Nigerian regulators decide to introduce measures to control nicotine volume and concentration in e-cigarettes may be dependent on whether they view e-cigarettes as a potential smoking cessation aid, and whether they view nicotine in itself as a harmful substance, amongst other factors.

6.1.6 General Safety

There is no specific safety guidance that pertains to the peculiar specifications of e-cigarettes, over and above the generic measures for all tobacco products in the FSPTCA. However, I found that the FDA's concerns over the safety of e-cigarettes led to the enactment of the PMTA (see Section 3.3.2.3). Since 2019 (three years after the FDA deemed e-cigarettes to be a tobacco product and subjected it to the FSPTCA in 2016), the FDA considers the safety of each e-cigarette product through a Pre-Market Tobacco Application (PMTA), to verify that the product is Appropriate for the Protection of Public Health (APPH), before it is brought to the market (232). Unlike the US, the UK's TRPR has regulations that specify safety measures relevant to the unique nature of e-cigarettes; these include the requirements for e-cigarettes to be tamper-evident and protected against breakage and leakage, etc. (see Table 8). I found that, at the time (2016) of legislating the TRPR, the UK health agencies and regulators had concluded that using e-cigarettes is relatively safer than smoking (see Section 3.3.1.3). The safety measures they incorporated into e-cigarette regulations, such as ensuring e-cigarettes are tamper-evident and protected against breakage and leakage, ensured that e-cigarettes do not expose users (and others, such as small children who may get their hands on the devices) to unexpected harm and that they are used in the way it was intended. I also found that, in Nigeria, testing of product constituents is likely to be used as a regulatory safety measure to determine that e-cigarette products meet specified requirements (see Section 5.3.2). The set requirements are likely to be informed by comparative reviews of other countries' policies and comparison to other

international standards. Figure 22 below shows the link between the key findings in this study relating to general safety of e-cigarettes in the US, UK, and Nigeria.

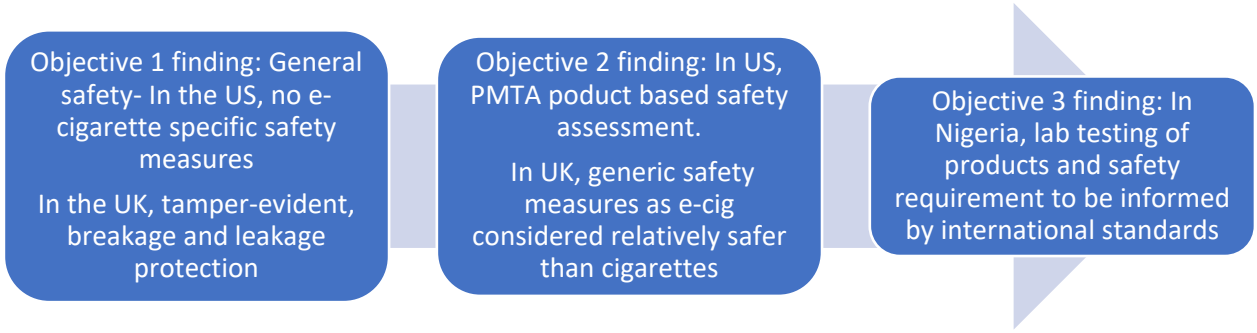


Figure 22: General safety and determinant factors

There are currently (April 2024) 34 countries/jurisdictions that require products to pass safety and quality evaluation, or have instituted other safety-related regulations for e-cigarettes (78). Nigerian e-cigarette regulators might have the desire in principle to include testing of all e-cigarette products, but they might be wary of the financial and infrastructural demands of such a regulatory measure. A UK interviewee in my study suggested that lack of dedicated resources for testing of e-cigarette products was preventing independent testing of such products (see Section 3.3.1.2). Another study (80) further identified budgetary and staffing limitations as affecting capacity to communicate new TPD measures and enforce change. Lack of funding has previously been shown in a 2018 study (240) to have slowed the tobacco control policy implementation process in Nigeria, and Nigerian interviewees in this study pointed out that personnel shortage and lack of appropriate equipment might place constraints on how Nigerian regulators regulate e-cigarettes (see Section 5.3.5). Therefore, Nigerian regulators may only impose regulatory measures within the limitations of enforcement capacity within the country.

Other factors that might determine general safety measures in e-cigarette regulation in Nigeria are how e-cigarettes are classified there and, consequently, what federal agency would lead regulation of e-cigarettes. If, as is likely, e-cigarettes are classified as tobacco products in Nigeria, the Ministry of Health may consider setting additional safety standards for e-cigarettes, as currently there are no tamper-evident or breakage and leakage

protection requirements in the NTCR. If cigarettes can come into the Nigerian market as medicinal products (as is possible in South Africa and the UK), the safety requirements or testing would be determined by the National Agency for Food and Drug Administration and Control (NAFDAC) who already have standards and regulations for medicines (304). If e-cigarettes can come into the Nigerian market as consumer products (the main route in the UK), then the responsibility for safety of e-cigarettes would fall within the remit of the Standards Organisation of Nigeria (SON). In all three scenarios, there is likely to be interagency collaboration to ensure the safety of e-cigarettes marketed and sold in Nigeria. The safety measures that will be applicable to e-cigarettes in Nigerian regulation are likely to be decided from research evidence and after wider interagency consultation. However, in tobacco control in sub-Saharan Africa, the challenge of limited capacity to generate local research evidence exists (305). Will Nigerian regulators be willing and able to invest in generating research evidence, or will they rely on evidence emanating from other countries? Will the evidence from other countries hold similar implications to the Nigerian context as to the countries from where they have been generated and used to inform policy?

6.1.7 Child safety packaging

Although the FSPTCA does not set out its own regulatory measure for child safety packaging in the US, it points to adherence to the Child Nicotine Poisoning Prevention Act of 2015 in its regulation. The Child Nicotine Poisoning Prevention Act of 2015 requires child-resistant packaging for nicotine-containing e-liquid containers. The UK's TRPR similarly specifies that an e-cigarette or refill container must be child resistant. Child safety packaging regulations are usually for prevention of unintended use or exposure of children to harmful contents of products. I found that potential Nigerian regulators were concerned with protecting children. However, the measures suggested were to do with preventing uptake of nicotine or smoking in children by means such as: minimum age of sale restriction, flavour restrictions, restrictions to e-cigarette advertising on TV before 10pm and marketing directly in front of young people (see Sections 5.3.3); but not child safety packaging for e-cigarettes. A study (306) that analysed themes from written answers to open-ended questions placed to 55 UK-based e-cigarette users, found a slightly different suggestion to the approach for

protecting children in regulation. It suggested that protecting children should be achieved through childproofing (i.e., child resistant packaging), age limits, no advertising aimed at children and health warnings about addictiveness of nicotine, but not the restriction of flavours (306). Figure 23 below shows the link between the key findings in this study relating to child safety packaging of e-cigarettes in the US, UK, and Nigeria.

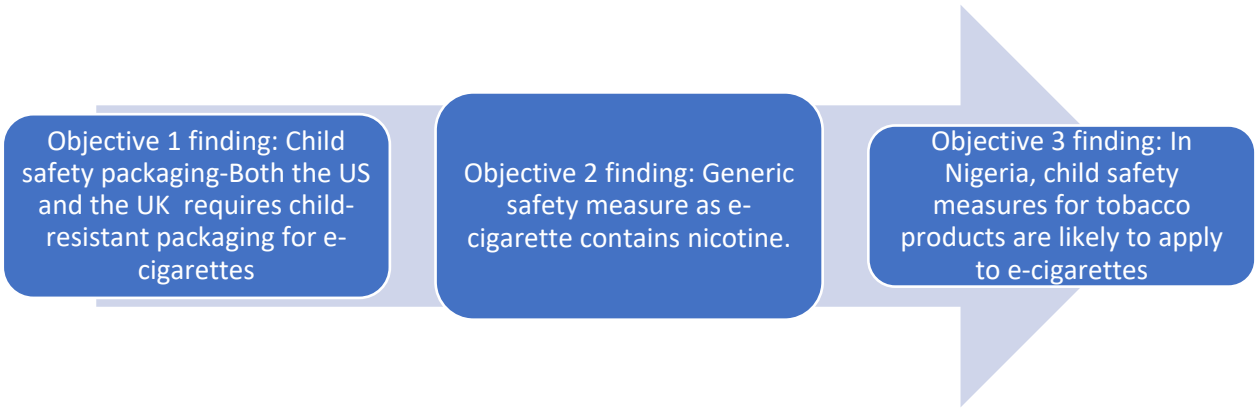


Figure 23: Child safety packaging and determinant factors

There are currently (April 2024) 38 countries/jurisdictions that have regulations on child safety packaging (78). The NTCR does not contain child-resistant packaging requirement for tobacco products. Therefore, if e-cigarettes are regulated as tobacco products as suggested by Nigerian interviewees in this study, there would be no requirement for child resistant packaging of e-cigarettes sold in Nigeria. It is unclear what impact lack of child resistant packaging may have in Nigeria because, in 2015, both the CDC (168) and PHE (129) reported increased calls for e-liquid exposure to the poison control centres in the US and the UK respectively, despite the UK having child resistant packaging requirement in regulation whereas the US did not. Nonetheless, PHE has noted that child-resistant packaging is likely to be an acceptable practice within the e-cigarette industry, as all e-liquids they had seen in the UK and globally up to the time (2015) of reporting were sold in child-resistant packaging (129). However, it may be of benefit to Nigerian regulators, in terms of enforcement, to include requirements for child-resistant packaging. Nicotine poisoning to children can have

fatal consequences. For example, in the US in 2014, a 1-year-old was reported to have died due to ingestion of liquid nicotine from a glass bottle containing liquid nicotine that did not have a childproof cap (307). Nicotine exposure is not present in all tobacco products as they are in e-liquids for e-cigarettes. For example, tobacco cigarettes do not utilise extracted liquid nicotine but rather contain nicotine in its unextracted form in tobacco. Therefore, if the NTCR is used to regulate e-cigarettes, and Nigerian regulators decide to include requirement for child-resistant packaging, they will need to add such requirements in a way that is relevant to other tobacco products or to use a different regulatory instrument to implement child-resistant packaging requirements.

6.1.8 Minimum age of sale

In the US, the Tobacco 21 Act prohibits sales of all tobacco products (including e-cigarettes) to people under the age of 21 years. Prior to the Tobacco 21 Act, which was enacted and took effect on 20th of December 2019, the US, like the UK, restricted sale of e-cigarettes and other tobacco products to people over the age of 18 years. In the UK, the TRPR prohibits sales of e-cigarettes to people under the age of 18 years (equivalent to the age of sale restriction for tobacco cigarettes); this has been the case since the enactment of the regulations in 2016. However, a regulatory loophole in the TRPR is that, although supply of e-cigarette to under 18s is prohibited, giving out vapes for free to under 18s is not prohibited, creating room for e-cigarette companies to exploit in their marketing strategies. However, the Tobacco and Vapes Bill 2024, currently (April 2024) going through the UK parliament, the provisions of which would take effect from April 2025, prohibits free distribution of vaping products to under 18s in England and Wales, and provides Northern Ireland with a power to also introduce a ban. Scotland already has these powers (164). I found that potential Nigerian regulators were concerned about uptake of e-cigarettes by young people (see Section 5.3.3), and that measures used in tobacco control are likely to be used for e-cigarettes (see Section 5.3.1). In Nigeria, sales of tobacco products are prohibited for people under the age of 18 years. Figure 24 below shows the link between the key findings in this study relating to minimum age of sale of e-cigarettes in the US, UK, and Nigeria.

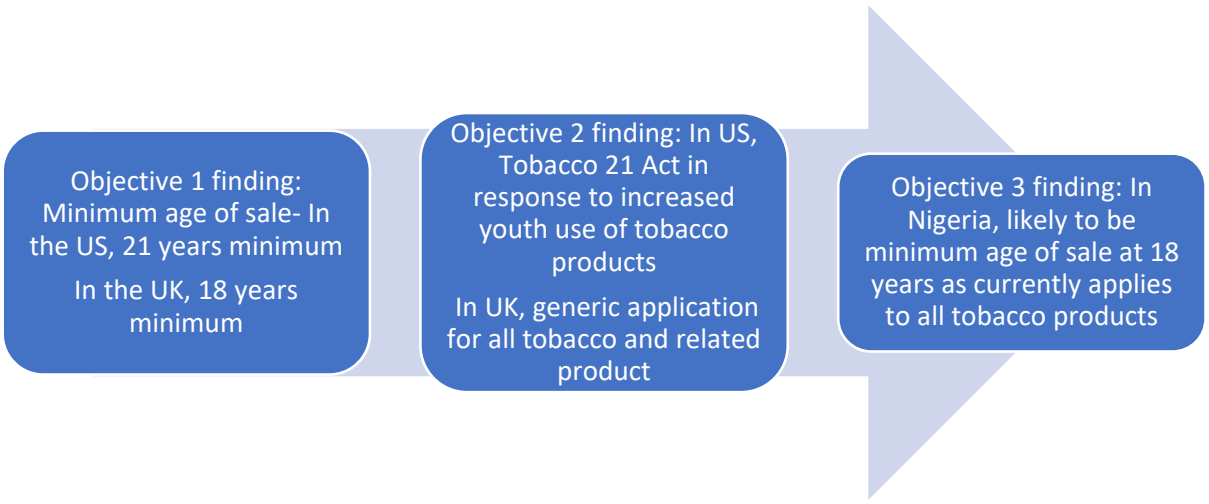


Figure 24: Minimum age of sale and determinant factor

In 56 countries/jurisdictions, a minimum age restriction exists for the purchase and/or use of e-cigarettes. Among the 56 countries, the minimum age of purchase is 18 years in 46 countries; 19 years in three countries (Jordan, Republic of Korea, and Turkey); and 21 years in seven countries/jurisdictions (Guam, Honduras, Kuwait, Niue, Palau, Philippines, and the US)(78). In Nigeria, the NTCA (279) requires anyone selling or trading in tobacco product to verify the age of the purchaser (who should be at least 18 years old) by checking any form of official identification prescribed by law. The NTCA also prohibits sale or distribution of tobacco products through mainstream media (i.e., TV, radio, newspapers, and magazines), internet, or other online outlets where age verification can be challenging. Since potential Nigerian e-cigarette regulators were particularly interested in preventing uptake of e-cigarettes and smoking by young people, they may consider raising the minimum age of sale of e-cigarettes alone or of all tobacco products. The US raised minimum age of sale from 18 to 21 years because there was a growing rise in youth use of tobacco products in the US immediately prior to 2019, and because evidence (181, 182) suggested that an increase in minimum age of sale of tobacco products from 18 years to 21 years can be an effective means of reducing youth smoking initiation. This move was part of an overall aim to reduce youth access to e-cigarettes due to concerns about their potential to harm youths and lead to smoking or nicotine initiation (see Section 3.3.2.3). This action can be said to have been

underpinned by disease-politics theory (202) where patient or public activism in the aftermath of a crisis can lead to regulatory reforms (see Section 2.3.2). Nigeria has not experienced a similar rise in e-cigarette use and regulators have not yet aligned themselves to any position with regards potential for e-cigarettes to be promoted for smoking cessation. The position of Nigerian regulators on the use of e-cigarettes for smoking cessation in Nigeria might have policy implications with regards to minimum age of sale of tobacco products. For example, despite the Khan review (308) that recommended increasing the age of sale of tobacco cigarettes from 18 by one year every year until no-one (of any age) can buy a tobacco product in the UK, the government had in April 2023, ruled out plans to raise age of sale of tobacco cigarettes from 18 years; their rationale for this decision was because they deemed it would represent a departure from their current policy which focuses on helping people quit smoking rather than imposing bans on adults (309). However, with the rise in use of e-cigarettes among children in the UK, the government has now put forward plans to raise the age of sale of tobacco products by one year each year (164); if enacted, this would mean that those currently (April 2024) aged fifteen or younger would never be able to purchase cigarettes legally. However, there is no indication that this age limit will include e-cigarettes, presumably because e-cigarettes are classified as consumer rather than tobacco products.

Another factor that may affect minimum age of sale is the classification of e-cigarettes in regulation. For instance, in the UK where e-cigarettes are classified as either consumer or medicinal products, although the minimum age of sale of tobacco products is 18 years, e-cigarettes that are licensed as medicines can be sold to people under 18 years in certain circumstances. The Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015 provide exceptions to the minimum age requirement for the sale of nicotine inhaling products, including e-cigarettes as well as NRT inhalators; in other words e-cigarettes can be sold to under 18s if the e-cigarette is a prescription only medicine (none are yet – as of April 2024 – on the market) or indicated for the treatment of persons of the age of the person to whom the product is sold (230). Nigerian regulators are likely to consider all these factors when they come to regulate e-cigarettes.

6.1.9 Advertising/ Promotion/ Sponsorship

In the US, e-cigarettes can be advertised if the advertisement bears the required warning statement. In the UK, e-cigarette adverts are prohibited in newspapers, periodicals, magazines, billboards, TV, radio, and cinemas. Both the US and the UK were concerned that advertising e-cigarettes can make them appealing to children (and others) who do not smoke, but each country has taken different approaches to deal with their concerns. While the UK prohibited advertising in regulations from the outset, the US has dealt with such issues on a product-specific basis through the PMTA i.e., any product deemed to be advertised, promoted, or marketed in a way that is not appropriate for the protection of public health is denied permission to be sold in the US. For example, in June 2022, the FDA issued marketing denial orders (MDOs) to JUUL Labs Inc. for all their products currently marketed in the US because they did not meet public health standards (310). I found that, in Nigeria, potential e-cigarette regulators had public health concerns related to initiation of children and youth to nicotine and smoking and suggested they may adopt measures similar to those currently in place for tobacco products. Figure 25 below shows the link between the key findings in this study relating to Advertisement of e-cigarettes in the US, UK, and Nigeria.

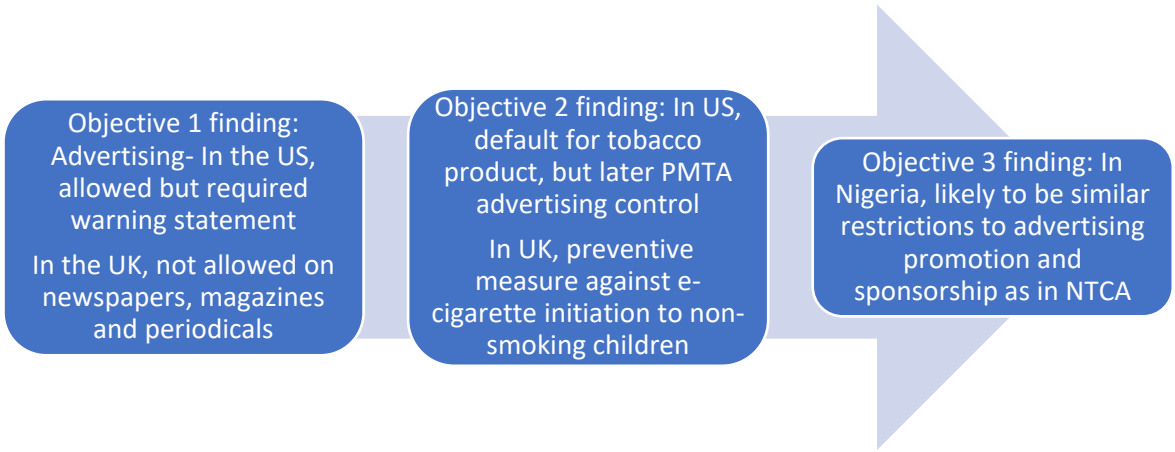


Figure 25: Advertising and determinant factors

There are 78 countries/jurisdictions which currently (April 2024) prohibit or regulate advertising, promotion, or sponsorship of e-cigarettes; of which six of those countries (Canada, Costa Rica, Ecuador, Japan, Mexico, Montenegro) apply the advertising restrictions only to e-cigarettes that contain nicotine or that are regulated as medicines (78). Nigerian

interviewees highlighted the sort of advertising restrictions that might be considered as: restrictions to advertising on TV before 10pm; and restrictions to marketing e-cigarettes products directly in front of young people (see Section 5.3.3). However, the NTCA currently completely prohibits advertising, promotion and sponsorship of tobacco products in any form (279). Nigerian interviewees also suggested that e-cigarettes are likely to be regulated in line with WHO recommendations on e-cigarettes. In relation to advertising, promotion and sponsorship of e-cigarettes, WHO recommended in their Q&A response on 25th May 2022, to the question 'What are the policy options for regulating ENDS?', the prevention of initiation of ENDS use by non-smokers and children, through measures such as preventing or restricting advertising, promotion and sponsorship and preventing unproven health claims (293)(p.1).[20] The argument for restriction of e-cigarette advertising has been that e-cigarettes carry a potential to lead to the renormalisation of smoking by making smoking attractive (311-313). Nigerian interviewees also expressed a caution towards e-cigarettes, in that they might 'glamourise' smoking and result in increasing numbers of smokers in Nigeria. However, since the evidence (22) shows that e-cigarettes are effective for smoking cessation, restrictions to e-cigarette advertising could be potentially costly to public health. It is in the interest of smokers to access information regarding smoking cessation products, and this should be taken into account in regulatory decisions about advertising restrictions on e-cigarettes (314). One challenge that a study (305) identified in relation to tobacco control in sub-Saharan Africa was the limited support from mainstream media to back policy and advocacy efforts. Therefore, Nigerian regulators would need to work collaboratively with media outlets to deliver marketing-related policy effectively.

6.1.10 Taxation of E-cigarettes

Taxation of e-cigarettes was not identified as a regulatory domain covered by the US and or the UK regulations in study one and three. However, taxation of e-cigarettes is a regulatory measure that was suggested by Nigerian interviewees and has been used for regulation of other tobacco products worldwide. There are 35 countries/jurisdictions that currently (April 2024) tax e-cigarettes; this is mostly through taxation of e-liquid and is based on its volume

[20] See Tobacco: E-cigarettes (who.int) (accessed 22/08/2023)

or price, but some countries tax the e-cigarette device and accessories as well. In 19 countries/jurisdictions specific excise tax based on volume is applied to e-liquids, while in 15 countries/jurisdictions an *ad valorem* (based on value / price) tax is used to tax e-cigarettes (78).

Nigerian interviewees suggested that the e-cigarette regulatory process is likely to involve economic considerations to promote economic growth in Nigeria. The suggested economic measures include: requiring companies licensed to sell e-cigarettes to manufacture their e-cigarette products locally; and taxation of e-cigarettes.

Taxation of tobacco products is primarily to deter people from smoking, but it also raises revenue for the government. Governments argue that revenue generated from taxing tobacco products can be used to fund programs to buffer the health and economic impacts of smoking. This concept is referred to in the literature as 'Hypothecation' and means explicit earmarking of revenues from a particular tax so that they are only used for the advertised purpose (315). A popular example is the 'Sin Tax' reform law initiated in the Philippines in 2012 which taxes alcohol and tobacco products with revenues earmarked and used to finance the Universal Health Care programme of the government (316). In the UK, although tobacco products are subject to both excise duty and value-added tax (VAT), and e-cigarettes are subject to VAT, the revenue from both products were not ringfenced to pay for health care until the Spring Budget 2024 (317) was recently (April 2024) announced. The Spring Budget 2024 introduced a new duty on vaping, commencing October 2026, to discourage non-smokers from taking up vaping, and to raise £445 million in 2028-29 to help fund public services like the NHS (317). The Spring Budget 2024 will also raise further £170 million in 2028-29 by increasing the tobacco duty from October 2026 to maintain the current financial incentive to choose vaping over smoking (317). Nigerian interviewees appeared to see taxation of e-cigarettes as an opportunity to generate revenue but are likely to trade-off economic gains for public health protection as they also suggested that economic considerations would be trumped by public health considerations. Therefore, public health considerations, such as preventing youth initiation to nicotine and smoking, reducing health harms from smoking and/or aiding smoking cessation through use of e-cigarettes, are more likely to determine whether and how taxation is used as a measure in e-cigarette regulation in Nigeria.

Taxation of tobacco products is a measure that WHO has suggested for countries to implement to control tobacco smoking (6). In many countries, including the US and the UK, conventional cigarettes are heavily taxed, primarily to discourage people from smoking. The aim is that high taxes drive prices up, making the products less affordable and as a result less accessible. Increase in tobacco tax and price has been found to decrease smoking in Africa (318). However, with the role of e-cigarettes as a less risky alternative to smoking or as a smoking cessation aid, taxation of e-cigarettes becomes more complex than taxation of conventional cigarettes. Whilst taxation of e-cigarettes can similarly (to taxation of cigarettes) lead to reduction of e-cigarette use (319), it can have a negative effect of increasing smoking if the tax raises the price of e-cigarettes considerably higher than that of conventional cigarettes. For example, a study (320) that looked at the effects of conventional cigarette and e-cigarette taxes on use of these products among adults in the United States, found that higher e-cigarette tax rates increase conventional cigarette use and reduce e-cigarette use. In the context of the US, the study found that a proposed national e-cigarette tax of $1.65 per millilitre of e-liquid would lead to an extra 2.5 million adult daily smokers compared to the counterfactual of not having the tax (320). In both the US and the UK, e-cigarettes are not taxed as highly as other tobacco products. In the UK for instance, e-cigarettes that enter the market as consumer products are subject to a 20% Value Added Tax (VAT), while e-cigarettes regulated as Medicines are levied 5% VAT. Additionally, UK government has recently (March 2024) announced a tax on e-cigarette liquid (321). By contrast, in addition to the standard rate VAT (*ad valorem)* at 20% on tobacco products, conventional cigarettes have a tobacco duty of 16.5% of the retail price plus £5.89 on a packet of 20.[21] In the US, there is no federal law (i.e. US-wide) taxing e-cigarettes, but as of May 2023, 30 states, the District of Columbia, Puerto Rico and the U.S. Virgin Islands have passed legislation that requires a tax on e-cigarettes with variable tax rates across these jurisdictions.[22]

If Nigerian regulators focus on reducing health harms from smoking and or aiding smoking cessation through use of e-cigarettes, the obvious regulatory approach would be to tax e-cigarettes at a lower rate than it currently taxes cigarettes. If Nigerian regulators focus instead on preventing youth initiation to nicotine and smoking, there is an argument for

[21] See https://www.gov.uk/tax-on-shopping/alcohol-tobacco (accessed 22/08/2023)
[22] See https://www.cdc.gov/statesystem/factsheets/ecigarette/ECigarette.html (accessed 22/08/2023)

setting and equalizing the tax rate for both conventional cigarettes and e-cigarettes at a high rate to deter people from use of both products. However, at the current time (April 2024), although e-cigarettes are not specifically taxed in Nigeria, the prices of e-cigarettes are already (pre-tax) relative higher than conventional cigarettes. Therefore, applying tax to e-cigarettes and equalizing the tax rate with that for conventional cigarettes would drive the prices of both products even higher, with economic and public health consequences to smokers who are already the poorest in society. Moreover, it has been argued by Warner *et al.*(322), that equalizing the tax burden, and hence raising the relative cost of e-cigarettes, risks causing net harm to public health. For example, when Minnesota (US state) increased e-cigarette taxes to levels comparable to cigarette taxes, smoking cessation decreased and smoking increased among adults (323). In their proposed policy agenda for e-cigarettes in the US, Warner *et al.*(322) suggested that the federal government should levy large excise taxes on cigarettes and other combustible tobacco products and a more modest excise tax on e-cigarettes, with an expectation that this policy would decrease youth use of tobacco and nicotine products and increase adult use of e-cigarettes to quit smoking.

A 2017 study (23) showed that in 2014, prices for smoking products in Nigeria were: combustible cigarettes (pack of 20 cigarettes) $1.29; disposable e-cigarettes $12.78; e-liquid $5.45; rechargeables $63.89. E-cigarettes are more expensive than combustible cigarettes in Nigeria. Nigerian interviewees described e-cigarettes as unaffordable for most of the population. Nigerian regulators should factor the current price of e-cigarettes (relative to tobacco cigarettes) into their policy decisions and consider the implications for public health.

6.1.11 Influence of commercial actors on e-cigarette policy development

In study one, a UK interviewee (PHE-R) suggested that the tobacco and pharmaceutical industry were commercial actors seeking to influence e-cigarette regulations in the UK in their interest. PHE-R explained that pharmaceutical companies, for instance, used to make all their money from over-the-counter nicotine replacement therapy which dropped off dramatically due to rival e-cigarettes. Therefore, these companies wanted to constrain sales of e-cigarettes as much as possible to regain their market sales (see section 3.3.1.1). Another UK interviewee (MEP-R) also suggested that e-cigarette companies were another

commercial actor that sought to influence regulations during European TPD (see section 3.3.1.1). Perhaps due to the nature of US data collection in study one (conference audio recordings as opposed to interviews), I did not identify the role of commercial actors in e-cigarette regulations in the US. However, the influence of commercial actors in regulations is not new to the US. Marver H. Bernstein's (203) analysis of the American regulatory context has shown that some regulatory agencies shift away from their mandate of regulating in the public interest to serving the interest of the regulated industry due to being captured by the industry. In study three, I identified the e-cigarette and tobacco industries as having the potential to influence e-cigarette regulatory decisions in Nigeria (see section 5.3.6).

Industries or commercial actors have historically influenced regulatory agencies, through the processes of regulatory capture (203) or corporate bias (216, 217, 231), to regulate their products in favour of industry rather than public health interest. This is why the WHO Framework Convention on Tobacco Control (6) demands that member countries take measures to prevent tobacco companies from unduly influencing tobacco related regulations and policies. A recent (January 2024) study (324) aimed to investigate the impact of tobacco industry interference on the implementation and management of tobacco control and the tobacco epidemic using the Tobacco Industry Interference Index (TIII), MPOWER, and adult daily smoking prevalence in 30 countries. The study (324) found that: TIII was inversely correlated with a country's package of tobacco control measures ($\beta = -0.088$, $P = 0.035$); TIII was correlated with weaker warnings about the dangers of tobacco ($\beta = -0.016$, $P = 0.078$) and lack of enforcement of bans on tobacco advertising promotion and sponsorship ($\beta = -0.023$, $P = 0.026$); the higher the TIII, the higher the age-standardized prevalence of adult daily tobacco smokers for both sexes ($\beta = 0.170$, $P = 0.036$); and that adult daily smoking prevalence in males ($\beta = 0.417$, $P = 0.004$) was higher in countries where the tobacco industry received incentives that benefited its business.

In study one, PHE-R suggested that the UK were cautious in preventing industry interference during the UK e-cigarette regulatory period in 2016. Perhaps this was because the UK are a ratified member of WHO FCTC. However, the latest data (325) ranking 90 countries on their implementation and compliance with measures designed to prevent the tobacco industry interference with policymaking, showed that the UK which was ranked 1st in 2019, and third in 2021, is now ranked 24th globally. Nigeria which is also a ratified member of WHO FCTC,

ranked 50th, while the US which is not a ratified member of WHO FCTC ranked 83rd in the survey (325).

The tobacco industry has historically used different tactics to influence regulation of tobacco and related products. These tactics include: legal threats and actions, intimidation, lobbying and influencing policy, claiming a public health role, support through allies, controversial marketing, corporate social responsibility, involvement in illicit tobacco, influencing science, and undermining national or international laws (326). Nigerian regulators should be aware of these tactics and put measures in place to prevent undue influence of industry in e-cigarette regulations.

6.2 Recommendations

6.2.1 Recommendations for Nigerian Regulators

1. Nigeria has a young population (43.29% are under-15s) (5), and relatively low smoking rate (2.7% in 15years or over) (21). Nigerian regulators should prioritise regulatory measures that discourage youths from use of e-cigarettes over measures that promote use of e-cigarette in smoking cessation. A range of regulatory measures are identified and discussed above in this study (see Section 6.1).
2. Social media platforms such as Twitter™ are a useful health communication tool that governmental and similar organisations use to carry out public engagement (248, 249). Nigerian regulators should utilise social media platforms to engage with the public on regulatory actions, providing a rationale and reference to the evidence base for their e-cigarette regulatory decisions. This would promote transparency in the regulatory process. Social media engagement can also be an informal and initial means of identifying public concerns in response to regulations. Findings from study two may provide a guide to likely concerns of stakeholders and could be used by Nigerian regulators to inform their messages and to pre-empt likely responses.
3. This study identified a potential for the tobacco, e-cigarette and pharmaceutical industries to influence regulation. Nigerian e-cigarette regulators should ensure conflicts of interest (COI) assessments are rigorous and transparent for people involved in making

recommendations for e-cigarette policies. This would limit the undue influence of industry in e-cigarette regulations.

4. Regulatory measures for single tobacco products often have off-target (and possibly undesirable) effects for multiple other tobacco products (327). For instance, as discussed in Section 6.1.10, increased taxation of e-cigarettes increases their price to consumers with potential consequences in terms of switching to tobacco cigarettes and an increased number of smokers. Therefore, Nigerian e-cigarette regulators should assess the effect of potential e-cigarette regulatory measures on use of other tobacco products and public health, when making regulatory decisions.
5. Nigeria has the advantage of learning from the experience of countries (such as the US, UK, Australia, etc.) who have had years of experience regulating e-cigarettes. Nigerian regulators should ensure their regulation of e-cigarettes captures already identified loopholes in other countries' regulations. For example, if Nigeria decides to ban flavoured e-cigarettes, such a ban should include both cartridge-based, disposable and any other form of e-cigarette. Likewise, if Nigerian regulators decide to prohibit sale of e-cigarettes to people under the age of 18 years, such policy should also prohibit giving away free e-cigarettes to children. By noting weaknesses in different regulations, and implications of regulatory decisions in other countries, Nigeria could avoid similar loopholes and ineffective regulatory policies.
6. As e-cigarettes are a novel product, Nigerian e-cigarette regulators would benefit from having an agile and responsive regulation (328), i.e., to be able and ready to quickly amend regulation when required. Regulatory amendments should typically be triggered by findings from periodic monitoring of the impact of regulation through a Post-Implementation Review (PIR) or surveillance. For example, the US raised age of sale of tobacco products in response to increased use of e-cigarettes among children (193). More recently (March 2024), the Environmental Protection (Single-use Vapes) (England) Regulations 2024, was proposed to ban the sale of disposable vapes in England with a effect from 1st April 2025 (96). This draft regulation was developed to tackle the observed rising use (between 2021 to 2023) of disposable vapes, particularly among children and young adults, and the adverse environmental impact of disposable vapes (96). The Tobacco and Vapes Bill 2024 (164) is also proposed to tackle use of e-cigarettes among young people and children.

6.2.2 Recommendations for Further Research

1. Further research (especially longitudinal and clinical studies) is needed to establish the absolute risk of use of e-cigarettes. Current relative risk arguments (i.e., vaping relatively safer than smoking) have not been sufficient to get the majority of public health stakeholders and healthcare professionals (63) worldwide behind the use of e-cigarettes (rather than NRTs) in a harm reduction strategy for smoking cessation, despite research showing that e-cigarettes are more effective for smoking cessation than NRTs (280).
2. Further research is needed to examine the impact of the regulatory environment for e-cigarettes on their real-world effectiveness for smoking cessation. Yong *et al's* (329) study showed that, in a less restrictive e-cigarette regulatory environment, use of e-cigarettes during a quit attempt facilitates, but in a more restrictive environment, it inhibits short-term sustained abstinence. That study compared Australian and Canadian (as restrictive) regulatory environments versus US and the UK (as less restrictive) regulatory environments. More studies are needed to compare countries with substantially different policies to examine the impact of their regulatory environment on e-cigarettes' effectiveness for smoking cessation. More studies are also needed to develop and apply a regulatory scale with wider scope than Shah *et al.'s* (330) study which measured and compared e-cigarette regulations within the European Union. The result of multiple comparisons would be the availability of broader evidence that e-cigarette regulators can draw on when considering regulations and policies. Such evidence could inform regulatory approaches towards maximizing benefits in countries aiming to promote e-cigarettes for smoking cessation.
3. Nigerian e-cigarette regulators should consider commissioning independent research and impact assessments (as the US and the UK did) to inform their deliberations and the contextual considerations for Nigeria. This would help Nigerian e-cigarette regulators develop transparent policies with the least adverse economic and public health consequences.
4. Nigerian regulators should consider conducting an impact assessment of the public health impact of e-cigarette retail licensing before enforcing regulations that require e-cigarette retailers to be licensed. The NTCR requires tobacco retailers to be licensed by

the MOH. If e-cigarettes are subject to the NTCR, it is likely that similar requirements would apply to e-cigarettes.

6.3 Strengths and Limitations of this PhD project

6.3.1 Strengths of this PhD project

1. The use of multiple qualitative date types (primary and secondary data), and methods for data collection (interview, audio recording, social media), and analysis (thematic and sentiment analysis) ensured the study was flexible, robust and sensitive to multiple contexts.
2. The use of regulatory theories and reference to the Global Tobacco Control policy dimensions ensured the findings of the study were comparable to existing literature and provided context for discussions of the finding in relation to relevant and current public health considerations.
3. This study, which compared the US and the UK e-cigarette regulations and associated influencing factors, provides valuable insights and understanding of factors that led these two countries with differing e-cigarette regulatory and public health priorities to develop their policies.
4. The US and the UK have had at least a decade of experience with e-cigarettes being regulated by the FDA and MHRA; these are long-standing regulatory agencies that can provide capital institutional knowledge, beneficial in terms of policy development to countries like Nigeria looking to regulate e-cigarettes.

6.3.2 Limitations of this PhD project

1. Although the US and the UK have several benefits for comparison of both countries' e-cigarette policies and regulations in terms of relevance of findings to Nigerian e-cigarette regulators, the demographic, cultural and legislative context of both countries are different from Nigeria. This may make translation of some findings from the US and the UK to the Nigerian context challenging. The demographic context is particularly relevant. The US and UK have an older population than Nigeria's youthful population. In 2021, only 18.2 percent of the US population and 17.7 percent of UK population were below the age

of 15 years, compared to Nigeria's 43.3 percent under the age of 15; in other words, Nigeria has more of their population in the at-risk age-group (5, 331, 332) for uptake of vaping and smoking. The US and the UK are part of the western world and have different cultural values to Nigeria. For example, a study that explored the socio-cultural risk influences for cigarette smoking among Southern Nigerian youth found that, while it is regarded as a thing of pride for older men and women to use tobacco in the form of snuff or to smoke its dried leaves in pipes, tobacco use in the form of cigarette smoking by the youth has always been frowned upon by older adults because It is perceived as an irresponsible behaviour and a sign of deviancy (333). The legislative difference is that the US and the UK have more enforcement capabilities than Nigeria. For example, the Nigeria Police Force (NPT) is the primary law enforcement agency in Nigeria, along with other federal organizations. However, the NPT has low enforcement capacity and most Nigerians do not perceive the NPF as an effective law enforcement body (334-336). Also, by comparing only US and UK approach to e-cigarette regulation, I may have missed out on other different regulatory approaches (e.g., Australian regulation) that may be beneficial to Nigeria's context.

2. This PhD project relied to some extent on secondary data for analysis; for study one, only four of thirteen data sources were primary interviews; study two made use entirely of secondary social media data; study three made use of entirely primary interviews, but only four participants were interviewed. In terms of sample selection, study one made use of audio recordings from only one conference series; study two made use of Twitter™ data collected using a search strategy that involved only a selected number of Twitter™ accounts; study three involved interview of participants selected as representatives by the Nigerian Ministry of Health. Therefore, in this PhD project, I had little control over the volume and quality of some analysed data in terms of bias and accuracy.
3. In this PhD project, both the primary and secondary data were collected at specific points in time. Note that e-cigarette usage patterns and the evidence base regarding the risk-benefit relationship is an ever-moving target. For example, at the time (2016) of regulating e-cigarettes in the UK (implementation of TRPR), the emphasis was on adult smokers who could potentially use e-cigarettes as a tool to quit smoking. However, recent (2023) statistics shows an increasing use of e-cigarettes by children (163).

Therefore, recommendations from this study with respect to e-cigarette regulations need to be considered alongside best available current evidence, and regularly reviewed to determine if any changes or updates to regulations are needed.

4. The strands of studies reported in Chapters 3 to 5 made use of secondary data. Therefore, I have had to draw inferences from the data sources available to me about the factors that influenced e-cigarette regulators' decisions. In the absence of direct questioning about whether a particular factor was influential, I cannot be certain that it was, but the balance of evidence is suggestive that it played a part.

6.4 Conclusion

As the role of e-cigarettes in public health remains a contentious topic amongst public health stakeholders, they have been regulated differently in various countries across the world. The US and the UK have both had more than a decade's experience with e-cigarette use but have adopted different regulatory approaches, albeit, in both countries, generally in the interests of public health. The US has utilised a precautionary approach (to public health concerns) in regulating e-cigarettes by deeming e-cigarette products as tobacco products, enacting flavour bans, Tobacco 21 Act and PMTA for assessment of e-cigarette products (see section 1.8). By contrast, the UK has utilised a risk-benefit optimization approach by putting in regulatory measures (such as restrictions on advertising, nicotine volume and concentration, tamper, and child resistant measures, etc.) that reduces the risk of harm while promoting, through regulations and policies, the use of e-cigarettes for smoking cessation (see section 1.8). Note that an arguably more effective approach to risk-benefit optimization would be licensing of e-cigarettes as a medicinal product so that the public can be confident of the safety of e-cigarettes and to encourage smokers make the switch from tobacco cigarettes to e-cigarettes (see section 1.8.2.2). NRTs are regulated as medicines in the UK and so widely used for quitting smoking attempts. The MHRA currently offers a route for e-cigarette companies to apply to license their e-cigarettes but, to date (April 2024), no e-cigarette brand or company has taken that route.

Similar to this study, a previous study (237) has compared the policy positions of health and medical organisations across Australia, New Zealand, and the UK as they relate to sale and

supply of e-cigarettes and evaluated factors that informed the differences in policy recommendations among these countries. The study (237) found that the source of the divided views on policies is fundamentally within the framing of e-cigarette debate (i.e., e-cigarette as a life changing harm reduction tool versus e-cigarette as a tobacco policy undermining tool for renormalisation of smoking), and varied tolerability of risk trade-offs associated with e-cigarettes. Another study (229) also compared UK and Germany to examine how two EU countries differed in transposition of TPD into national law. Nigerian e-cigarette regulators would need to be clear where it stands in relation to this debate, so that they can effectively create an e-cigarette regulatory environment that optimizes their public health risk trade-offs. Evidence (329) from comparison of countries with restrictive policies towards e-cigarettes (Canada and Australia) versus countries with less restrictive policies (US and UK) suggests that the benefits of e-cigarette for smoking cessation are likely to be highly dependent on the regulatory environment.

Nigeria, who are now starting their journey with e-cigarettes, has the advantage of learning from the experience of different countries, including, but not exclusively, the US and the UK. Nigeria remains committed to tobacco regulation and now has a WHO FCTC compliant policy for tobacco control. The US is aligned with the WHO (despite not having formally ratified the WHO FCTC) on their stance regarding the safety of e-cigarettes and has suggested regulatory measures in line with WHO recommendations. The UK, who are formally signed up to the WHO-FCTC, have remained compliant with the FCTC but have promoted different views (to WHO) on the safety of e-cigarettes. Nigerian regulators can learn from both the US and the UK, by considering aspects of their regulatory measures that are most beneficial to Nigeria's context and public health needs while remaining compliant to the WHO FCTC.

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Appendices

Appendix A: Comparison of European Tobacco Product Directive to British Tobacco and Related Product Regulations

TPD	TRPR
1. Manufacturers and importers of electronic cigarettes and refill containers shall submit a notification to the competent authorities of the Member States of any such products which they intend to place on the market. The notification shall be submitted in electronic form six months before the intended placing on the market. For electronic cigarettes and refill containers already placed on the market on 20 May 2016, the notification shall be submitted within six months of that date. A new notification shall be submitted for each substantial modification of the product.	A producer who supplies or intends to supply electronic cigarettes or refill containers must notify the Secretary of State in accordance with this regulation *(TRPR)*. Information must be submitted to the Secretary of State— a) in electronic form; b) by means of the entry gate for data submission referred to in Article 2.2 of Commission Implementing Decision (EU) 2015/2183 of 24 November 2015 establishing a common format for the notification of electronic cigarettes and refill containers (1); c) in accordance with the administrative requirements set out in that Decision; and d) in the format specified in the Annex to that Decision. A person submitting information under regulation 31 must specify any

	information which that person considers to constitute a trade secret. Where an electronic cigarette or refill container is substantially modified ('a modified product') a producer must comply with paragraph (1) *(as above)* in respect of the modified product.
2. The notification shall be submitted in electronic form six months before the intended placing on the market. For electronic cigarettes and refill containers already placed on the market on 20 May 2016, the notification shall be submitted within six months of that date.	Notification must be submitted in respect of a product— a) at least one day before the day the producer first supplies the product, where— i. a producer intends to first supply a product which is not a modified product during the period beginning with 20th May 2016 and ending with 19th November 2016 ('a new transitional product'), or ii. a producer intends to first supply a modified new transitional product during the period beginning with 20th May 2016 and ending with 19th November 2016; b) on or before 19th November 2016, where— i. a producer first supplied a product before 20th May 2016 ('an existing product') and intends to continue to supply that product on or after 20th November 2016, or

	ii. a producer intends to first supply a modified existing product during the period beginning with 20th May 2016 and ending with 19th May 2017; or iii. in any other case, at least six months before the date on which the producer intends to first supply a product or a modified product.
3. The notification shall, depending on whether the product is an electronic cigarette or a refill container, contain the following information: a) the name and contact details of the manufacturer, a responsible legal or natural person within the Union, and, if applicable, the importer into the Union; b) a list of all ingredients contained in, and emissions resulting from the use of, the product, by brand name and type, including quantities thereof; c) toxicological data regarding the product's ingredients and emissions, including when heated, referring in particular to their effects on the health of consumers when inhaled and taking into account, inter alia, any addictive effect; d) information on the nicotine doses and uptake when consumed	A notification must contain the following information (so far as relevant to the product concerned)— a) the name and contact details of the person who manufactures the product, the importer (if applicable) and, if neither is based in a member State, a responsible person within a member State; b) a list of all ingredients contained in, and emissions resulting from the use of, the product by brand and variant name, including quantities; c) toxicological data regarding the product's ingredients (including in heated form) and emissions, referring in particular to their effects on the health of consumers when inhaled and taking into account, amongst other things, any addictive effect; d) information on the nicotine dose and uptake when consumed

under normal or reasonably foreseeable conditions; e) a description of the components of the product; including, where applicable, the opening and refill mechanism of the electronic cigarette or refill containers; f) a description of the production process, including whether it involves series production, and a declaration that the production process ensures conformity with the requirements of this Article; g) a declaration that the manufacturer and importer bear full responsibility for the quality and safety of the product, when placed on the market and used under normal or reasonably foreseeable conditions. Where Member States consider that the information submitted is incomplete, they shall be entitled to request the completion of the information concerned. Member States may charge manufacturers and importers proportionate fees for receiving, storing, handling and analysing the information submitted to them.	under normal or reasonably foreseeable conditions; e) a description of the components of the product including, where applicable, the opening and refill mechanism of the electronic cigarette or refill container; f) a description of the production process and a declaration that the production process ensures conformity with the requirements of this Part; and g) a declaration that the producer bears full responsibility for the quality and safety of the product when supplied and used under normal or reasonably foreseeable conditions.
4. Member States shall ensure that:	Nicotine-containing liquid which is presented for retail sale must be

a) nicotine-containing liquid is only placed on the market in dedicated refill containers not exceeding a volume of 10 ml, in disposable electronic cigarettes or in single use cartridges and that the cartridges or tanks do not exceed a volume of 2 ml; b) the nicotine-containing liquid does not contain nicotine in excess of 20 mg/ml; c) the nicotine-containing liquid does not contain additives listed in Article 7(6); d) only ingredients of high purity are used in the manufacture of the nicotine-containing liquid. Substances other than the ingredients referred to in point (b) of the second subparagraph of paragraph 2 of this Article are only present in the nicotine-containing liquid in trace levels, if such traces are technically unavoidable during manufacture; e) except for nicotine, only ingredients are used in the nicotine-containing liquid that do not pose a risk to human health in heated or unheated form; f) electronic cigarettes deliver the nicotine doses at consistent levels under normal conditions of use; g) electronic cigarettes and refill containers are child- and tamper-	in— a) a dedicated refill container in a volume not exceeding 10 millilitres; or b) a disposable electronic cigarette, a single use cartridge, or a tank, in a volume not exceeding 2 millilitres. The capacity of the tank of a refillable electronic cigarette must not exceed 2 millilitres. Nicotine-containing liquid which is presented for retail sale in an electronic cigarette or refill container must not contain nicotine in excess of 20 milligrams per millilitre. Nicotine-containing liquid in an electronic cigarette or refill container— a) must not contain any additive referred to in regulation 16 (no vitamins, colourings or prohibited additives in tobacco products);

proof, are protected against breakage and leakage and have a mechanism that ensures refilling without leakage.	b) must be manufactured using only ingredients of high purity; c) must not contain substances other than the ingredients notified under regulation 31, unless present in trace levels, where such trace levels are technically unavoidable during manufacture; and d) must not include ingredients (except for nicotine) which pose a risk to human health in heated or unheated form. An electronic cigarette must be able to deliver a dose of nicotine at consistent levels under normal conditions of use. An electronic cigarette or refill container must be— a) child-resistant and tamper-evident; and b) protected against breakage and leakage. An electronic cigarette or refill container must have a mechanism for ensuring re-filling without leakage (unless it is a disposable electronic cigarette).

	A product is tamper-evident if it has one or more indicators or barriers to entry which, if breached or missing, can reasonably be expected to provide visible evidence that the product (or its packaging) has been opened. A product has a mechanism for ensuring re-filling without leakage if the mechanism— a) entails— i. the use of a refill container possessing a securely attached nozzle at least 9 millimetres long which is narrower than, and slots comfortably into, the opening of the tank of the electronic cigarette, and ii. in the case of refill containers, a flow control mechanism that emits no more than 20 drops of refill liquid per minute when placed vertically and subjected only to atmospheric pressure at a temperature between 15 and 25 degrees Celsius; or b) operates by means of a docking system which only releases refill liquids into the tank of an electronic cigarette when the electronic cigarette and refill container are connected.

5. Member States shall ensure that: a) unit packets of electronic cigarettes and refill containers include a leaflet with information on: i. instructions for use and storage of the product, including a reference that the product is not recommended for use by young people and non-smokers; ii. contra-indications; iii. warnings for specific risk groups; iv. possible adverse effects; v. addictiveness and toxicity; and vi. contact details of the manufacturer or importer and a legal or natural contact person within the Union; b) unit packets and any outside packaging of electronic cigarettes and refill containers: i. include a list of all ingredients contained in the product in descending order of the weight, and an indication of the nicotine content of the product and the delivery per dose, the batch number and a recommendation to keep the product out of reach of children; ii. without prejudice to point (i) of this point, do not include	No person may produce or supply an electronic cigarette or refill container unless it complies with the below Each unit packet of the electronic cigarette or refill container must include a leaflet with information on— a) instructions for use and storage of the product, including a reference that the product is not recommended for use by young people and non-smokers; b) contra-indications; c) warnings for specific risk groups; d) possible adverse effects; e) addictiveness and toxicity; f) contact details of the producer; and g) if the producer is not based in a member State, a contact person within a member State. Each unit packet and any container pack must include— a) a list of all ingredients contained in the product set out in descending order by weight;

elements or features referred to in Article 13, with the exception of Article 13(1)(a) and (c) concerning information on the nicotine content and on flavourings; and iii. carry one of the following health warnings: 'This product contains nicotine which is a highly addictive substance. It is not recommended for use by nonsmokers'. or 'This product contains nicotine which is a highly addictive substance.' Member States shall determine which of these health warnings is to be used; c) health warnings comply with the requirements specified in Article 12(2).	b) an indication of the nicotine content of the product and the delivery per dose; c) the batch number; and d) a recommendation to keep the product out of reach of children. Each unit packet and any container pack must carry a health warning consisting of the text: 'This product contains nicotine which is a highly addictive substance'. The health warning must— a) appear on both the front and back surfaces of the unit packet and any container pack; b) cover 30% of the area of each of those surfaces, calculated in relation to the area of the surface concerned when the pack is closed; c) be in black Helvetica bold type on a white background; d) be in a font size which ensures that the text occupies the greatest possible proportion of the surface area reserved for it; and

	e) appear at the centre of that area. The health warning must be parallel to the main text on the surface concerned. The instructions for use must— a) include appropriate instructions for refilling, including diagrams; and b) does not apply to instructions for use that relate to disposable electronic cigarettes. c) comply with the below. Instructions for use comply with this paragraph where— a) if the refill mechanism is as described in regulation 36(10)(a), the instructions for use indicate the width of the nozzle or the width of the opening of the tank (as appropriate) in a manner that enables consumers to identify the compatibility of refill containers and electronic cigarettes; or b) if the refill mechanism is as described in regulation 36(10)(b), the instructions for use specify the type or types of docking system

	with which the electronic cigarette or refill container is compatible.
6. Member States shall ensure that: commercial communications in Information Society services, in the press and other printed publications, with the aim or direct or indirect effect of promoting electronic cigarettes and refill containers are prohibited, except for publications that are intended exclusively for professionals in the trade of electronic cigarettes or refill containers and for publications which are printed and published in third countries, where those publications are not principally intended for the Union market; commercial communications on the radio, with the aim or direct or indirect effect of promoting electronic cigarettes and refill containers, are prohibited; any form of public or private contribution to radio programmes with the aim or direct or indirect effect of promoting electronic cigarettes and refill containers is prohibited; any form of public or private contribution to any event, activity or individual person with the aim or direct or indirect effect of promoting electronic cigarettes and refill containers and involving or	No person may in the course of a business publish, or procure the publication of, an electronic cigarette advertisement in a newspaper, periodical or magazine. No person may in the course of a business sell, offer for sale or otherwise make available to the public a newspaper, periodical or magazine containing an electronic cigarette advertisement. The above two paragraphs do not apply— a) to a newspaper, periodical or magazine which is intended exclusively for professionals in the trade of electronic cigarettes or refill containers; or b) to a newspaper, periodical or magazine which is printed and published in a third country and is not principally intended for the Union market. No person may in the course of a business include, or procure the

taking place in several Member States or otherwise having cross-border effects is prohibited; audio-visual commercial communications to which Directive 2010/13/EU of the European Parliament and of the Council (1) applies, are prohibited for electronic cigarettes and refill containers.	inclusion of, an electronic cigarette advertisement in an information society service provided to a recipient in the United Kingdom. No service provider established in the United Kingdom may in the course of a business include an electronic cigarette advertisement in an information society service provided to a recipient in an EEA State other than the United Kingdom ('a non-UK-EEA-State'). No proceedings for an offence for breach of paragraph (1)(4) may be instituted against a service provider who is established in a non-UK-EEA-State, unless the derogation condition mentioned in paragraph 4 is satisfied. The derogation condition is satisfied where the institution of proceedings— a) is necessary for the purposes of public policy, the protection of public health or the protection of consumers ('the objective'); b) relates to an information society service that prejudices the objective or presents a serious and grave risk of prejudice to the

	objective; and c) is proportionate to the objective. Paragraphs (1) and (2) do not apply— a) to an information society service which is intended exclusively for professionals in the trade of electronic cigarettes or refill containers; or b) to an electronic cigarette advertisement which is not principally intended for the Union market. Schedule 1 (liability of intermediary information society service providers) has effect. No person may in the course of a business provide electronic cigarette sponsorship to— a) an event or activity which takes place in or has an effect in two or more member States ('a cross-border event or activity'); or b) an individual taking part in a cross-border event or activity. In this regulation 'electronic cigarette sponsorship' means any form of

	public or private contribution to any event, activity or individual, with the aim or direct or indirect effect of promoting an electronic cigarette or refill container.
7. Member States shall require manufacturers and importers of electronic cigarettes and refill containers to submit, annually, to the competent authorities: a) comprehensive data on sales volumes, by brand name and type of the product; b) information on the preferences of various consumer groups, including young people, non-smokers and the main types of current users; c) the mode of sale of the products; and d) executive summaries of any market surveys carried out in respect of the above, including an English translation thereof. Member States shall monitor the market developments concerning electronic cigarettes and refill containers, including any evidence that their use is a gateway to nicotine addiction and ultimately traditional tobacco consumption among young people and non-smokers.	A producer of electronic cigarettes or refill containers must submit the following information to the Secretary of State— a) comprehensive data on the producer's sales volumes in the United Kingdom, by brand and variant name; b) any information available to the producer, whether published or not, on the preferences of consumer groups in the United Kingdom, including young people, non-smokers and the main types of current users; c) the mode of sale of the producer's products in the United Kingdom; and d) executive summaries of any market surveys carried out by the producer in respect of paragraphs (a) to (c). The information listed in paragraph (a) to (d) *above* must be submitted annually on or before 20th May each year and must relate to the preceding calendar year.

Member States shall ensure that the information received pursuant to paragraph 2 is made publicly available on a website. The Member States shall take the need to protect trade secrets duly into account when making that information publicly available. Member States shall, upon request, make all information received pursuant to this Article available to the Commission and other Member States. The Member States and the Commission shall ensure that trade secrets and other confidential information are treated in a confidential manner. Member States shall require manufacturers, importers and distributers of electronic cigarettes and refill containers to establish and maintain a system for collecting information about all of the suspected adverse effects on human health of these products. Should any of these economic operators consider or have reason to believe that electronic cigarettes or refill containers, which are in their possession and are intended to be placed on the market or are placed on the market, are not safe or are not of good quality or are otherwise not in conformity with this Directive, that economic operator shall immediately take the corrective action necessary to bring the product concerned	The first submission under paragraph (2) is to be made on or before 20th May 2018 in respect of the calendar year 2017. The information listed in paragraph (a) to (d) *above* relating to the period beginning with 20th May 2016 and ending with 31st December 2016 must be submitted on or before 20th May 2017. The Secretary of State must monitor the market developments concerning electronic cigarettes and refill containers, including any evidence that their use is a gateway to nicotine addiction and ultimately traditional tobacco consumption amongst young people and non-smokers. The Secretary of State must— a) ensure that information submitted under regulation 31 is made publicly available on a website, taking the need to protect trade secrets duly into account; b) provide the European Commission and the competent authorities of other member States with access to information

into conformity with this Directive, to withdraw or to recall it, as appropriate. In such cases the economic operator shall also be required to immediately inform the market surveillance authorities of the Member States in which the product is made available or is intended to be made available, giving details, in particular, of the risk to human health and safety and of any corrective action taken, and of the results of such corrective action. Member States may also request additional information from the economic operators, for example on the safety and quality aspects or any adverse effects of electronic cigarettes or refill containers. The Commission shall submit a report to the European Parliament and the Council on the potential risks to public health associated with the use of refillable electronic cigarettes by 20 May 2016 and whenever appropriate thereafter. In the case of electronic cigarettes and refill containers that comply with the requirements of this Article, where a competent authority ascertains or has reasonable grounds to believe that specific	submitted in accordance with any provision of this Part on request, ensuring that trade secrets are treated in a confidential manner.

electronic cigarettes or refill containers, or a type of electronic cigarette or refill container, could present a serious risk to human health, it may take appropriate provisional measures. It shall immediately inform the Commission and the competent authorities of other Member States of the measures taken and shall communicate any supporting data. The Commission shall determine, as soon as possible after having received that information, whether the provisional measure is justified. The Commission shall inform the Member State concerned of its conclusions to enable the Member State to take appropriate follow-up measures. Where, in application of the first subparagraph of this paragraph, the placing on the market of specific electronic cigarettes or refill containers, or a type of electronic cigarette or refill container has been prohibited on duly justified grounds in at least three Member States, the Commission shall be empowered to adopt delegated acts in accordance with Article 27 to extend such a prohibition to all Member States, if such an extension is justified and proportionate. The Commission shall be empowered to adopt delegated acts in accordance with Article 27 to adapt the wording of the health warning	

in paragraph 4(b) of this Article. When adapting that health warning, the Commission shall ensure that it is factual. The Commission shall, by means of an implementing act, lay down a common format for the notification provided for in paragraph 2 and technical standards for the refill mechanism provided for in paragraph 3(g). These implementing acts shall be adopted in accordance with the examination procedure referred to in Article 25(2).	
Member States may prohibit cross-border distance sales of tobacco products to consumers. Member States shall cooperate to prevent such sales. Retail outlets engaging in cross-border distance sales of tobacco products may not supply such products to consumers in Member States where such sales have been prohibited. Member States which do not prohibit such sales shall require retail outlets intending to engage in cross-border distance sales to consumers located in the Union to register with the competent authorities in the Member State, where	The following persons must register with the Secretary of State— a) a retailer established in the United Kingdom who engages or intends to engage in a cross-border distance sale of a relevant product with a consumer located in any other member State; and b) a retailer who is established elsewhere than in the United Kingdom who engages or intends to engage in a cross-border distance sale of a relevant product with a consumer located in the United Kingdom.

the retail outlet is established, and in the Member State, where the actual or potential consumers are located. Retail outlets established outside the Union shall be required to register with the competent authorities in the Member State where the actual or potential consumers are located. All retail outlets intending to engage in cross-border distance sales shall submit at least the following information to the competent authorities when registering: a) name or corporate name and permanent address of the place of activity from where the tobacco products will be supplied; b) the starting date of the activity of offering tobacco products for cross-border distance sales to consumers by means of Information Society services, as defined in point 2 of Article 1 of Directive 98/34/EC; c) the address of the website or websites used for that purpose and all relevant information necessary to identify the website. The competent authorities of the Member States shall ensure that consumers have access to the list of all retail outlets registered with	A person seeking registration must submit to the Secretary of State— a) the information specified in paragraph (3) ('the retailer information'); b) in the case of a retailer who falls within paragraph (1)(a), the information specified in paragraph (4) ('the additional information'); and c) such other information as the Secretary of State may reasonably require. The retailer information is— a) the retailer's name; b) the retailer's trading name, if different; c) the address of each place of business used by the retailer for the supply of a relevant product; d) the date on which the retailer first supplied or, if the retailer has not yet so supplied, intends to supply a relevant product via a cross border distance sale; e) the address of any website on which the retailer offers or intends to offer to supply a product, together with any other

them. When making that list available, Member States shall ensure that the rules and safeguards laid down in Directive 95/46/EC are complied with. Retail outlets may only start placing tobacco products on the market via cross-border distance sales when they have received confirmation of their registration with the relevant competent authority. The Member States of destination of tobacco products sold via cross-border distance sales may require that the supplying retail outlet nominates a natural person to be responsible for verifying — before the tobacco products reach the consumer — that they comply with the national provisions adopted pursuant to this Directive in the Member State of destination, if such verification is necessary in order to ensure compliance and facilitate enforcement. Retail outlets engaged in cross-border distance sales shall operate an age verification system, which verifies, at the time of sale, that the purchasing consumer complies with minimum age requirements provided for under the national law of the Member State of	information required to identify the website; and f) a description of the details and functioning of the retailer's age verification system (see paragraph (6)(b)). The additional information is— a) confirmation of any registration provided by the competent authority of any member State in which the retailer is registered to supply products via a cross-border distance sale to a consumer located in that member State; and b) the name of any other member State to which the retailer has applied, or is intending to apply, for registration. The Secretary of State must— a) provide confirmation of registration to a retailer who complies with paragraph (2); b) publish a list of retailers registered with the Secretary of State. A retailer must not supply a relevant product to a consumer via a cross-border distance sale unless— a) the retailer has received confirmation of registration from the

destination. The retail outlet or natural person nominated pursuant to paragraph 3 shall provide to the competent authorities of that Member State a description of the details and functioning of the age verification system. Retail outlets shall only process personal data of the consumer in accordance with Directive 95/46/EC and those data shall not be disclosed to the manufacturer of tobacco products or companies forming part of the same group of companies or to other third parties. Personal data shall not be used or transferred for purposes other than the actual purchase. This also applies if the retail outlet forms part of a manufacturer of tobacco products.	Secretary of State and from the competent authority of any member State in which the consumer is located or in which the retailer is established; b) the retailer operates an age verification system; and c) prior to, or at the time of sale, the retailer's age verification system confirms that the consumer's age is not lower than the minimum age applicable for the purchase of the product in the member State in which the consumer is located. d) A retailer must not supply a relevant product via a cross-border distance sale to a consumer located in a member State in which cross border distances sales are prohibited in accordance with Article 18(1) of the Tobacco Products Directive. In this regulation— 'age verification system' means a computing system that confirms the consumer's age electronically; and 'confirmation of registration' means written confirmation provided by the competent authority of any member State in accordance with the requirements in that member State which implement Article 18 of the Tobacco Products

	Directive; and ‘relevant product’ means a tobacco product, an electronic cigarette or a refill container.

Appendix B: Ethical approval for study of the factors influencing e-cigarette regulations and policies in the US and the UK

Date: 08/12/2021

Anthony Weke

PHSI

Faculty of Medical Sciences
Newcastle University
Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Anthony

Title: Factors influencing e-cigarette regulation and policies in the US and the UK
Application No: 2202/ 14121 /2020
Start date to end date: 01/09/2021 to 31/12/2021

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: 2202/ 14121 /2020. If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project, you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation. *

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee. *

Best wishes,

Yours sincerely

Carol Fereday
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Mrs Kay Howes, Research Manager

*Please refer to the latest guidance available on the internal Newcastle website.

Appendix C: Ethical approval from FMS REC for study on the potential determinant factors of e-cigarette regulations in Nigeria

Ethics Form Completed for Project: Potential determinant factors of electronic cigarette regulation in Nig...

Reply | Reply All | Forward

P

Policy & Information Team, Newcastle University <noreply@limesurve

To Anthony Weke (PGR)

Tue 09/08/2022 23:34

You forwarded this message on 10/08/2022 09:04.

Ref: 24590/2022

Thank you for submitting the ethical approval form for the project 'Potential determinant factors of electronic cigarette regulation in Nigeria' (Lead Investigator: Anthony Weke). Expected to run from 29/08/2022 to 30/12/2022.

Based on your answers, the University Ethics Committee grants its approval for you to start working on your project. Please be aware that if you make any significant changes to your proposal then you should complete this form again, as further review may be required. This confirmation may be used within a research portfolio as evidence of ethical approval. Please note: this confirmation will be the only correspondence you should expect to receive as evidence of ethical approval. There will be no other confirmation provided. You may now proceed with research. If you have any queries, please review the internal and external ethics FAQ pages before contacting res.policy@ncl.ac.uk**.**

In order to limit the spread of COVID-19, any research projects which include direct contact with human participants must adhere to local physical distancing guidelines and the restrictions imposed by the government of the country in which the research is being undertaken.

Best wishes

Research Policy Intelligence and Ethics Team,

Research Strategy & Development

res.policy@ncl.ac.uk

Appendix D: Ethical approval from NHREC for the study of the potential determinants of e-cigarette regulations in Nigeria

National Health Research Ethics Committee of Nigeria (NHREC)

Promoting Highest Ethical and Scientific Standards for Health Research in Nigeria

Federal Ministry of Health

NHREC Protocol Number NHREC/01/01/2007- 15/01/2023
NHREC Approval Number NHREC/01/01/2007-23/01/2023
Date: 23 January, 2023

Re: Potential determinant factors of electronic cigarette regulation in Nigeria

Health Research Committee assigned number: NHREC/01/01/2007

Name of Student Investigator: Mr. Anthony Weke
Address of Student Investigator: Newcastle University Population Health Sciences Institute
Faculty of Medical Sciences Newcastle University
The Medical School Framlington Place Newcastle upon Tyne
NE2 4HH, United Kingdom
Email: a.c.weke2@newcastle.ac.uk
Tel: +447852823811

Date of receipt of valid application: 15/01/2023

Date when final determination of research was made: 23-01-2023

Notice of Expedited Committee Review and Approval

This is to inform you that the research described in the submitted protocol, consent form, advertisement and other participant information materials have been reviewed and *given expedited committee approval by the National Health Research Ethics Committee.*

This approval dates from 23/01/2023 to 22/01/2024. If there is delay in starting the research, please inform the HREC so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the HREC assigned number and duration of HREC approval of the study.* In multiyear research, endeavour to submit your annual report to the HREC early in order to obtain renewal of your approval and avoid disruption of your research.

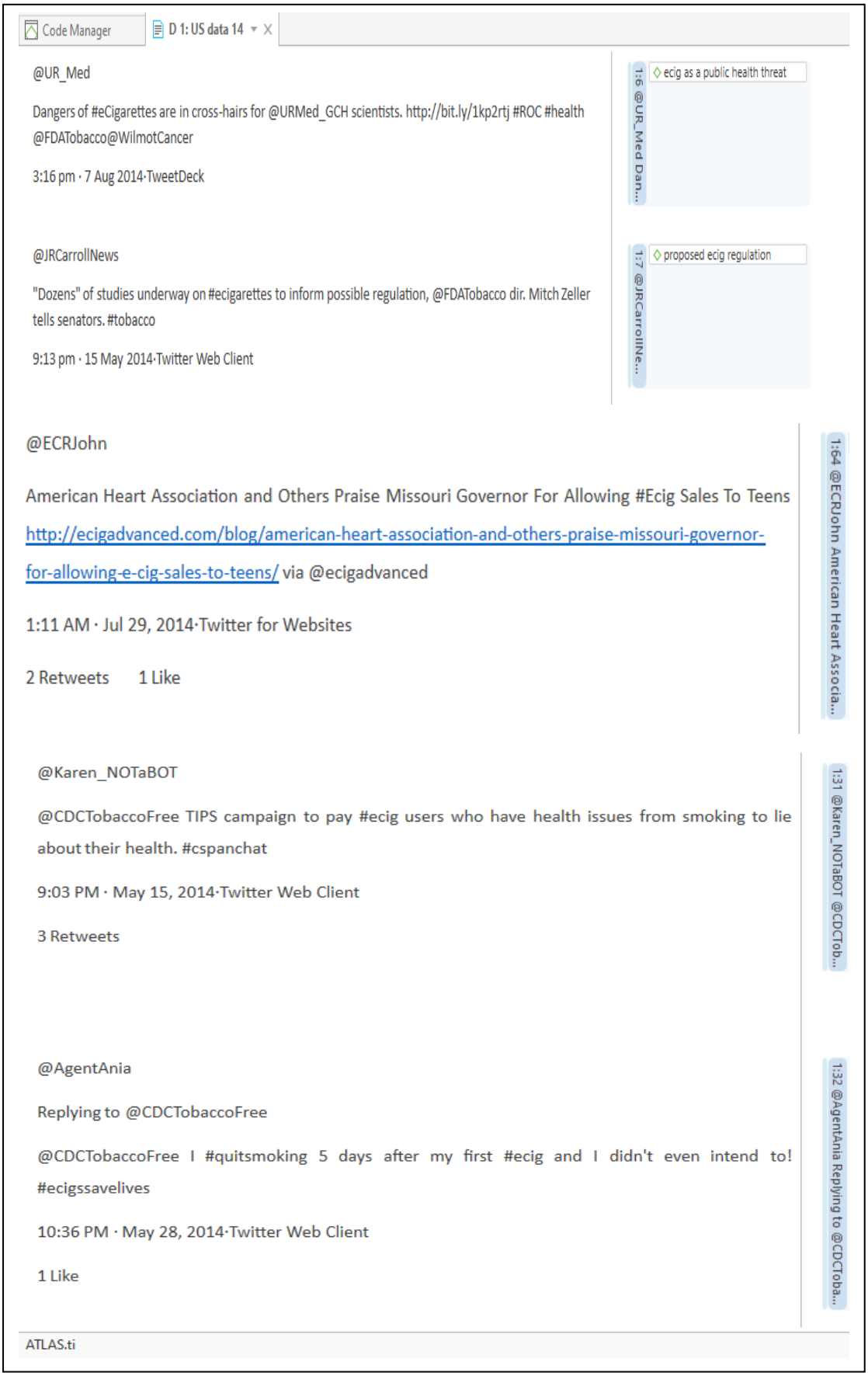
The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the HREC. No changes are permitted in the research without prior approval by the HREC except in circumstances outlined in the Code.

The HREC reserves the right to conduct compliance visit to your research site without previous notification.

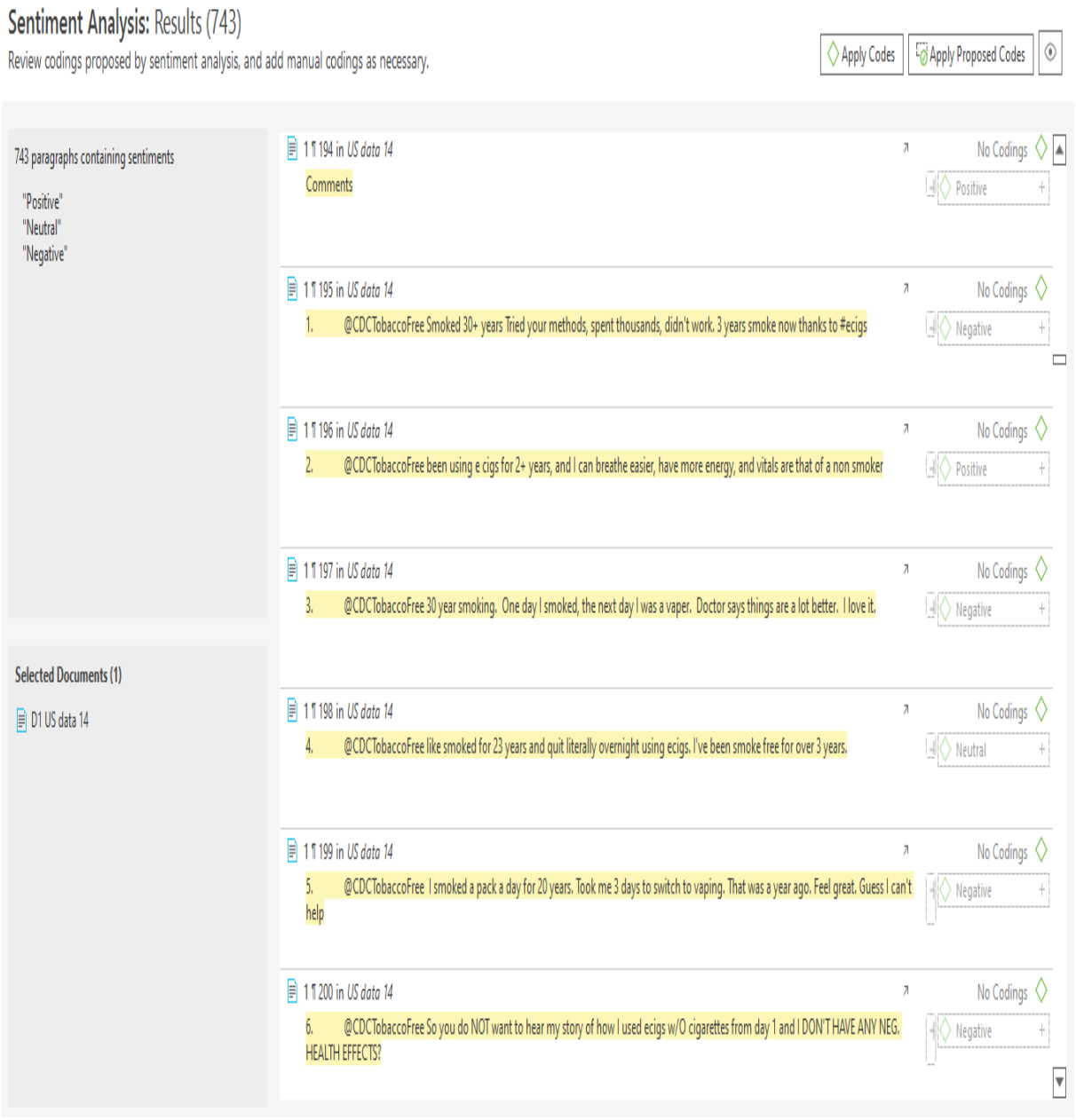
Signed

Professor Zubairu Iliyasu MBBS (UniMaid), MPH (Glasg.), PhD (Shef.), FWACP, FMCPH, FFPH(UK)
Chairman, National Health Research Ethics Committee of Nigeria (NHREC)

Appendix E: Coding of themes on Atlas.Ti



Appendix F: Example of sentiments in Twitter™ comments



Appendix G: Participant Information Sheet (PIS) for interview of US and UK e-cigarette stakeholders

Study Title: Factors influencing e-cigarette regulation and policies in the US and the UK

Invitation

You are invited to take part in a research study. Before you decide whether you wish to take part it is important that you understand why the research is being done and what it will involve. Please read this information carefully and discuss it with others if you wish. Take time to decide whether you wish to take part. If you decide to take part, you will be asked to give recorded verbal consent before the start of the interview. However, you are free to withdraw at any time, without giving any reason and without any penalty.

Why have I been invited?

You are being invited because you are either a former/current policymaker, researcher or stakeholder related to e-cigarette regulation and policies.

What is the purpose of the study?

The US and the UK are known world leaders in terms of public health and have long standing regulatory agencies (FDA and MHRA respectively) with huge capital institutional knowledge beneficial in terms of policy development. Therefore, many countries look to learn from them for policy development. This PhD project aims to understand the contextual factors that influenced the public health approaches to e-cigarette regulation and policymaking in both countries, as this would be beneficial for other nations looking to develop their own e-cigarette policies. This is because comparing cross-country experiences is a useful way of developing policy instruments for problem-solving in a particular country as it provides guidance on what to do and what not to do.

What does it involve taking part?

You will be interviewed once. In the interview, we would like to discuss the topic 'Factors influencing e-cigarette regulation and policies in the US/UK' in more depth and try to explore

what you think are the factors that influenced the public health, regulatory and policy approaches to e-cigarette in your country. The discussion will last no more than an hour.

Anonymization

The interview will be audio recorded and transcribed to a written form which would be anonymized (by substituting a pseudonym for your real name) unless you prefer for your views to be on public record. If you choose not to conceal your identity, you would be required to confirm this during consent before the start of the interview. Please note that when your interview is anonymized and incorporated into themes, it might not be possible to be withdrawn, though every attempt can and will be made to extract your data up to the point of publication if requested by you.

What information will be collected and who will have access to the information collected?

The researcher will be using information from you to undertake this research study and will act as the data controller for this study. This means that he is responsible for looking after your information and using it properly. When researchers use personally identifiable information from people who have agreed to take part in research, they ensure that it is in the public interest. Your rights to access, change or move your information are limited, as the researcher needs to manage your information in specific ways for the research to be reliable and accurate. If you withdraw from the study, the researcher will keep the information about you that has already been obtained. To safeguard your rights, minimum personally identifiable information will be used. The researcher will generally manage your data in line with Newcastle University guidance. You can find out more about this at http://www.ncl.ac.uk/data.protection/PrivacyNotice and/or by contacting Newcastle University's Data Protection Officer (Maureen Wilkinson, rec-man@ncl.ac.uk).

The researcher will use your name and contact details [telephone number and/or email address] to contact you about the research study. The researcher may need to contact you to check any information provided and to share a copy of the findings. The only individuals at Newcastle University who will have access to information that identifies you, will be the researcher and his PhD supervisors who need to contact you to arrange the interview or

representatives of Newcastle University (the study sponsor) who may need to audit the data collection process. Your contact details are expected to be deleted no later than 5th January 2024 (Theses submission deadline) and will be password protected and stored securely on the University's server and separately from the research data before deletion.

What will happen to the results?

The information from your interview will be pooled with other participants' responses. The results will be summarized and reported in a PhD thesis and may be submitted for publication in an academic or professional journal. It will be ensured that you cannot be identified in any of the reports unless you choose to go on record. You can request a summary of the study from the researchers once it is completed.

Are there any risks?

There are no risks anticipated with participating in this study. However, if you experience any distress following participation you are encouraged to inform the principal investigator.

Are there any benefits to taking part?

Although you may find participating interesting, there are no direct benefits in taking part.

Who has reviewed the project?

This study has been reviewed and approved by Newcastle University's Research Ethics Committee (prior to recruitment of any participants).

Who is funding this research?

This study is part of the researcher's PhD project and is not externally funded. The researcher's PhD studies is partially funded by a Newcastle University Overseas Research Scholarship.

Who should I contact for further information relating to the research?

If you have any questions about the study, please contact the principal investigator:

Mr. Anthony Weke

Email: a.c.weke2@newcastle.ac.uk

Who should I contact to file a complaint?

If you wish to make a complaint or raise concerns about any aspect of this study and do not want to speak to the researcher, you can contact the principal project supervisor:

Professor Elaine McColl

Email: elaine.mccoll@newcastle.ac.uk

If you wish to raise a complaint on how your personal data is handled, you can contact the Newcastle University's Data Protection Officer (Maureen Wilkinson, rec-man@ncl.ac.uk) who will investigate the matter.

Appendix H: Consent Form for US and UK interviewees

Participant ID: ……

Study Title: Influential factors to e-cigarette regulation and policies in the US and the UK

We are asking if you would like to take part in a research project. Before you consent to participating in the study, I will read out to you the consent form and ask that you confirm verbally if you agree. If you have any questions or queries before verbal confirmation of consent, please ask me. Your verbal confirmation of consent will be audio recorded and a copy of the written transcription saved till the end of the study.

Delete as appropriate from box after verbal confirmation of consent		
1.	I confirm that I have read the participant information sheet (version 1.0; dated: 19/08/2021) for the above study and fully understand what is expected of me within this study.	YES/NO
2.	I confirm that I have had the opportunity to consider the information, ask any questions and to have them answered satisfactorily.	YES/NO
3.	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, or my legal rights being affected.	YES/NO
4.	I understand that my interview will be audio recorded and then made into a written transcript.	YES/NO
5.	I understand that I can choose to have my written transcript anonymised or not if I prefer to go on record with my views.	YES/NO
6.	I understand that audio recordings will be kept until the research project has been completed and that the recordings are stored securely on cloud and used for research purposes only.	YES/NO
7.	I consent to the retention of my personal information such as my name, email address and telephone number until the research project has been completed, for the purpose of being re-contacted.	YES/NO
8.	I understand that once my data have been anonymised and incorporated into themes it might not be possible for it to be withdrawn, though every attempt will be made to extract my data, up to the point of publication.	YES/NO
9.	I understand that the information from my interview will be pooled with other participants' responses, anonymised if preferred, and may be published.	YES/NO
10.	I consent to information and quotations from my interview being used in reports, conferences, and training events.	YES/NO
11.	I agree to take part in this research	YES/NO
12.	I prefer for my interview responses to be anonymized, i.e., my identity concealed	YES/NO

Name of Participant: _____

Date: _____

Name of Researcher: _____

Date: _____

Appendix I: Interview guide for Interview of DHSC representative

1. What was the role of the Department of Health and Social care (DHSC) in e-cigarette regulation in the UK?

a. In what way was the DHSC involved in transposing the TPD to TRPR?
b. What aspects of the TRPR did the DHSC contribute towards?
c. Was their involvement in the form of a consultation? Whose views were sought? How did these views influence the transposition process?
d. At what stage of the regulatory process was the DHSC involved? Why?
e. What team or individuals within the DHSC were involved in the process? Why? Were they assigned by default or how were they selected? Were they in anyway assessed for conflict of interest?

2. To what extent does the DHSC regulate e-cigarettes?

a. Other than the provisions of part 7 of TRPR (advertisement of e-cigarette), is the DHSC responsible for implementing other parts of the TRPR?
b. Other than the TRPR, is the DHSC responsible for implementing any other e-cigarette or related regulation or policy? If yes, which regulation or and policy?
c. At what stage of the regulatory process was the DHSC made the competent authority for advertisement of e-cigarette? Why?
d. Did the TPD in anyway influence how the DHSC were to regulate any aspects of the TRPR? If yes, how?
e. Did any other regulation influence how the DHSC were to regulate any aspects of the TRPR? If yes, which regulation? How?

3. How did the DHSC decide on their methods for implementing provisions of Part 7 of the TRPR?

a. How did the DHSC decide on how advertisement of e-cigarette were to take place?
b. Was there any consultation on decisions made? If yes, who was consulted? Why? At what stage did the consultation take place? Was all the feedback considered? If no, why not?

c. Was there any stakeholder (i.e., e-cigarette manufacturers and retailers) engagement on advertisement of e-cigarette? If yes, what stakeholders were involved? Why? Who made the first approach (DHSC or the stakeholders)? Was all their recommendation considered? If no, why not?
d. How did the House of Commons Select Committee contribute to DHSC input to e-cigarette regulations?

4. To what extent did the DHSC contribute to regulation of aspects of e-cigarette regulation other than the provisions of part 7 of the TRPR?
   a. Why and how was it decided to give the responsibility of regulation of some aspects of e-cigarette to other government agencies? What are the practical implications for having different agencies regulate different aspects of e-cigarette?
   b. Did the DHSC contribute towards the part 8 of TRPR (cross-border sales of e-cigarettes)? if yes, what was their contribution? Does the DHSC support PHE in implementing provisions of part 8 of the TRPR?
   c. Did the DHSC contribute towards the part 6 of TRPR (Notification scheme of e-cigarettes)? if yes, what was their contribution? Does the DHSC support the MHRA in implementing provisions of part 6 of the TRPR?

Appendix J: Interview guide for interview of Public Health England (PHE) representative

1. What was the role of PHE in e-cigarette regulation in the UK?

a. In what way was PHE involved in transposing the TPD to TRPR?

b. What aspects of the TRPR did PHE contribute towards?

c. Was their involvement in the form of a consultation? Whose views were sought? How did these views influence the transposition process?

d. At what stage of the regulatory process was PHE involved? Why?

e. What team or individuals within PHE were involved in the process? Why? Were they assigned by default or how were they selected? Were they in anyway assessed for conflict of interest?

2. To what extent if any, does OHID currently regulate e-cigarettes?

a. Other than the provisions of part 8 of TRPR (Cross-border distance sales of e-cigarettes), is OHID responsible for implementing other parts of the TRPR?

N/B: Cross-border here refers to importation or sales of e-cigarettes across the British borders

b. Other than the TRPR, is OHID responsible for implementing any other e-cigarette or related regulation or policy? If yes, which regulation or and policy?

c. At what stage of the regulatory process was PHE made the competent authority for Cross-border distance sales of e-cigarettes? Why?

d. Did the TPD in anyway influence how PHE were to regulate any aspects of the TRPR? If yes, how?

e. Did any other regulation influence how PHE were to regulate any aspects of the TRPR? If yes, which regulation? How?

3. How did PHE decide on their methods for implementing provisions of Part 8 of the TRPR?

a. How did PHE decide on how cross-border distance sales of e-cigarettes were to take place?

b. Was there any consultation on decisions made? If yes, who was consulted? Why? At what stage did the consultation take place? Was all the feedback considered? If no, why not?
c. Was there any stakeholder (i.e., e-cigarette manufacturers and retailers) engagement on cross-border distance sales of e-cigarettes? If yes, what stakeholders were involved? Why? Who made the first approach (PHE or the stakeholders)? Was all their recommendation considered? If no, why not?

4. To what extent did PHE contribute to e-cigarette regulation other than the provisions of part 8 of the TRPR?
   a. Why was it decided to give the responsibility of regulation of some aspects of e-cigarette to other government agencies? What are the practical implications for having different agencies regulate different aspects of e-cigarette?
   b. Did PHE contribute towards the part 7 of TRPR (advertisement of e-cigarette)? if yes, what was their contribution? Does PHE support the Department of Health and Social care in implementing provisions of part 7 of the TRPR?
   c. Did PHE contribute towards the part 6 of TRPR (Notification scheme of e-cigarettes)? if yes, what was their contribution? Does PHE support the MHRA in implementing provisions of part 6 of the TRPR?

Appendix K: Interview guide for Interview of MEP representative

1. How did the European Commission go about formulating e-cigarette regulation or policies?

a. Were there existing guidelines for such a task?

b. To what extent did the team/individuals have freedom to apply their own methods to achieve the task?

c. What methods/ strategies were applied? Why?

d. Did any other existing regulation or policies inform the creation of TPD? What ones? Why?

e. Were there any consultations, stakeholder engagements or public hearing for the TPD? Who was consulted and why (if relevant)? At what stage of the process were they consulted? Was all the feedback considered? (Why not? What were the grounds for disregarding some feedback?)

2. What sources of information/evidence did the European Commission draw on to inform TPD regulations?

a. How did they search for the information? Who did the searching? What was their expertise in relation to data sourcing/research/ evidence synthesis?

b. Were the sources of information vetted for bias and conflict of interest? If yes, who did the vetting and how?

c. How did the European Commission decide on what weight to accord to different elements of information?

3. What team or individuals represented the UK as a member state in the creation of the EU Tobacco Product Directive (TPD)?

a. In what capacity or how were they involved?

b. Were they assigned to the task by default, nominated, voted, employed, or volunteered?

c. What strategies did the European Commission adopt to check for conflict of interest in representatives of the member states for the regulatory committee for tobacco control?

4. How were decisions reached with respect to TPD regulatory measures?
   a. How were regulatory measures voted for by member states? Was it majority vote or some other means?
   b. Were there consensus of opinions on some measures? What measures? What do you think was the reason for consensus on those issues?
   c. Were there divisive opinions on any regulatory measure? What measures? How were decision made on such measures?
   d. Did the UK representatives vote on all regulatory measures? Are there regulatory measures currently in the TPD that UK representatives were opposed to during the regulatory process?

Appendix L: Interview guide for Public Health Scotland (PHS) representative

1. What was the role of PHS in e-cigarette regulation in the UK?

a. In what way, if any, was PHE involved in transposing the TPD to TRPR?
b. What aspects of the TRPR did PHS contribute towards?
c. To what extent did PHS follow the lead of Public Health England (PHE) when it came to their contribution to the TRPR?
d. Was their involvement in the form of a consultation? Whose views were sought? How did these views influence the transposition process?
e. At what stage of the regulatory process was PHS involved? Why?
f. What team or individuals within PHS were involved in the process? Why? Were they assigned by default or how were they selected? Were they in anyway assessed for conflict of interest?

2. What was the role of PHS in e-cigarette/ Nicotine vapor products (NVP) regulation in Scotland?

a. In what way, if any, was PHS involved in producing the Health (Tobacco, Nicotine etc. and Care) (Scotland) Act 2016? What aspects did PHS contribute towards?
b. Was their involvement in the form of a consultation? Whose views were sought? How did these views influence the regulatory process?
c. At what stage of the regulatory process was PHS involved? Why?
d. What team or individuals within PHS were involved in the process? Why? Were they assigned by default or how were they selected? Were they in anyway assessed for conflict of interest?

3. To what extent if any, does PHS currently regulate Nicotine vapor products/ e-cigarettes in Scotland?

a. Is PHS responsible for implementing any aspects of the Health (Tobacco, Nicotine etc. and Care) (Scotland) Act 2016? If yes, what aspects? What methods are used in implementing those methods? How were the methods decided on?

b. Is PHS responsible for implementing any aspects of the TRPR? If yes, what aspects? What methods are used in implementing those methods? What methods are used in implementing those methods? How were the methods decided on?
c. To what extent does PHS follow the lead of PHE on how it implements any aspects of e-cigarette regulation in Scotland and or the UK?

Appendix M: Interview guide for Interview of Nigerian stakeholders

1. What influencing factors identified in the US and or the UK may be relevant in Nigeria for e-cigarette regulation and policies? *(Summary list of UK/US influencing factors will be presented)*

a. What are the similarities in situation and context between the US/UK context VS Nigerian context?

b. What is the likelihood that the identified factors will influence e-cigarette regulation or policy in Nigeria? (**Probe:** Explain? Why?)

c. How do you feel the identified influencing factors will impact e-cigarette regulation in Nigeria? (**Probe:** Negatively or positively? Explain? Why?)

d. Are there influencing factors identified in the US and or the UK you feel Nigeria should leverage? (**Probe:** Which ones; Why? Explain? Would this factor be regarded as a barrier (to be overcome) or a facilitator (to be promoted)?)

2. What factors not already identified from the US and the UK may influence/determine e-cigarette regulations and policies in Nigeria?

a. What circumstances specific to Nigeria may lead to the influence of such factors when regulating e-cigarettes in Nigeria?

b. Are the influencing factors related to the sector for which you are a representing stakeholder? (**Probe:** How? Explain? Are your views of a technical nature?)

c. Which stakeholders do you think will influence e-cigarette regulations and policies in Nigeria? (**Probe:** How? Why? To what extent?)

d. What factors do you think will have the most influence on e-cigarette regulation and policies in Nigeria? (**Probe:** How? Why?)

e. Is there anything else you'd like to say about e-cigarette regulation in Nigeria?

CHAPTER T6
TOBACCO SMOKING (CONTROL) ACT
ARRANGEMENT OF SECTIONS
SECTION

CHAPTER T6

TOBACCO SMOKING (CONTROL) ACT

An Act to provide for the control of smoking in certain places and advertisement of tobacco in Nigeria.

{1990 No. 20}

[1st October, 1990; 1st June, 1990]

[Commencement. S.I. 7 of 1990. S.I. 18 of 1990]

1. Control of tobacco smoking

No person shall, as from the commencement of this, smoke tobacco in the places specified in the First Schedule to this Act.

[First Schedule]

2. Restriction on tobacco smoking advertisement

(1) In pursuance of this Act, no person shall advertise tobacco products to the general public in a bid to encourage tobacco smoking through any of the means specified in the Second Schedule to this Act unless the advertisement contains a warning that tobacco smoking is dangerous to health.

[Second Schedule]

(2) Pursuant to subsection (1) of this section, no tobacco industry, firm or association of individuals or any other body corporate shall sponsor or promote any of their products at any sports event sponsored or promoted by them.

3. Tobacco packages to contain certain information

(1) Except as provided by this Act, no package containing tobacco products meant for smoking shall be sold in Nigeria, unless the following rotating warnings are inscribed on the package, that is-

(a) "The Federal Ministry of Health warns that tobacco smoking is dangerous to health"; and
(b) "Smokers are liable to die young".

(2) Pursuant to subsection (1) of this section, it shall be unlawful for any person to sell any tobacco product in Nigeria unless the amount of the tar and nicotine contents of each unit of the product is stated on the package.

4. Penalties for smoking, etc., In prohibited areas

Any person who smokes tobacco contrary to the provisions of this Acts shall be guilty of an offence under this Act and shall be liable to conviction to a fine of not less than N200 and not exceeding N1,000 or to imprisonment to a term fo not less than one month and not exceeding two years or to both such fine and imprisonment.

5. Penalty for advertising, selling, etc., Of tobacco

(1) Any person who advertises, sells or offers for sale any tobacco product otherwise than in compliance with the provisions of this Act shall be guilty of an offence under this Act and shall be liable, on conviction, to a fine of not less than N5,000.

(2) Where an offence under this Act is committed by a officer of the body corporate or firm or other association of individuals -

(a) every director, manager, secretary or other similar officer of the body corporate;
(b) every partner or officer of the firm;
(c) every person concerned in the management of the affairs of the association; or
(d) every person who was purporting to act in any such capacity as aforesaid,

shall be guilty of an offence and shall be liable on conviction to a fine not exceeding N5,000 or to imprisonment for a term not exceeding three years or to both such fine and imprisonment as if he had himself committed the offence, unless he proves that the act or omission constituting the offence took place without his knowledge, consent or connivance.

6. Interpretation

In this Act, unless the context otherwise requires -

"tobacco" includes manufactured and unmanufactured tobacco of every description which is processed and used for smoking in pipes, cigars and cigarettes.

CAP. T6

Tobacco Smoking (Control) Act

7. Short title

This Act may be cited as the Tobacco Smoking (Control) Act.

SCHEDULES

FIRST SCHEDULE

[Section 1.]

(a) Cinema, theatre or stadium;
(b) Offices;
(c) Public transportation;
(d) Lifts;
(e) Medical establishments;
(f) Schools; and
(g) Nursery institutions.

SECOND SCHEDULE

Section 2 (1).]

(a) Newspapers;
(b) Magazines;
(c) Radio;
(d) Television;
(e) Cinema;
(f) Bill boards; and
(g) Handbills.

WHO FRAMEWORK CONVENTION ON TOBACCO CONTROL

Conference of the Parties to the WHO Framework Convention on Tobacco Control

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Electronic nicotine delivery systems

Report by WHO

INTRODUCTION

1. This document was prepared in response to the request made by the Conference of the Parties (COP) at its fifth session (Seoul, Republic of Korea, 12–17 November 2012) to the Convention Secretariat to invite WHO to examine emerging evidence on the health impacts of electronic nicotine delivery systems (ENDS) use and to identify options for their prevention and control, for consideration at the sixth session of the COP.[1] This report incorporates the December 2013 deliberations and scientific recommendations on ENDS by the WHO Study Group on Tobacco Product Regulation (TobReg), and analysis from a recent WHO survey on tobacco products.[2]

2. ENDS are the subject of a public health dispute among bona fide tobacco-control advocates that has become more divisive as their use has increased. Whereas some experts welcome ENDS as a pathway to the reduction of tobacco smoking, others characterize them as products that could undermine efforts to denormalize tobacco use. ENDS, therefore, represent an evolving frontier, filled

[1] See decision FCTC/COP5(10).

[2] The WHO tobacco products survey on smokeless, electronic nicotine delivery systems, reduced ignition propensity cigarettes, and novel tobacco products was sent to all WHO Member States. A total of 90 WHO Member States, including 86 Parties to the WHO FCTC, had responded to the survey as at 9 April 2014. These countries are: Australia, Austria, Bahrain, Bangladesh, Barbados, Belarus, Belgium, Belize, Bhutan, Bolivia (Plurinational State of), Botswana, Brazil, Brunei Darussalam, Cambodia, Canada, Chile, China, Colombia, Congo, Costa Rica, Croatia, Czech Republic, Djibouti, Dominica, Ecuador, Egypt, Estonia, Fiji, Finland, France, Gabon, Georgia, Ghana, Guatemala, Honduras, Hungary, Iceland, India, Indonesia, Iran (Islamic Republic of), Iraq, Jamaica, Japan, Jordan, Kenya, Kuwait, Lao People's Democratic Republic, Latvia, Lebanon, Lithuania, Malaysia, Maldives, Mali, Mauritania, Mongolia, Morocco, Myanmar, Netherlands, New Zealand, Nicaragua, Norway, Oman, Pakistan, Palau, Panama, Paraguay, Peru, Philippines, Poland, Qatar, Republic of Korea, Russian Federation, Slovakia, South Sudan, Spain, Sudan, Suriname, Sweden, Syrian Arab Republic, Thailand, Tonga, Tunisia, Turkey, Tuvalu, United Arab Emirates, United States of America, Uruguay, Uzbekistan, Viet Nam, and Zambia.

with promise and threat for tobacco control. Whether ENDS fulfil the promise or the threat depends on a complex and dynamic interplay among the industries marketing ENDS (independent makers and tobacco companies), consumers, regulators, policy-makers, practitioners, scientists, and advocates.[1] The evidence and recommendations presented in this report are therefore subject to rapid change.

PRODUCT DESIGN AND CONTENTS

3. ENDS, of which electronic cigarettes are the most common prototype, deliver an aerosol by heating a solution that users inhale. The main constituents of the solution by volume, in addition to nicotine when nicotine is present, are propylene glycol, with or without glycerol and flavouring agents.

4. Although some ENDS are shaped to look like their conventional tobacco counterparts (e.g. cigarettes, cigars, cigarillos, pipes, or hookahs), they also take the form of everyday items such as pens, USB memory sticks, and larger cylindrical or rectangular devices.

5. Battery voltage and unit circuitry differences can result in considerable variability in the products' ability to heat the solution to an aerosol and, consequently, may affect delivery of nicotine and other constituents, and may contribute to the formation of toxicants in the emissions.

6. User behaviour may affect nicotine absorption – length of puffs, depth of inhalation and frequency of use may be factors. However, while a faster, deeper puff increases nicotine delivery from a conventional cigarette, it might diminish it from ENDS due to cooling of the heating element.

7. In addition to manufacturer differences, some users modify products at home to alter delivery of nicotine and/or other drugs. Products vary widely in the ease with which they can be modified and the ease with which they can be filled with substances other than nicotine solutions.

THE ENDS MARKET

8. The use of ENDS is apparently booming. It is estimated that in 2014 there were 466 brands[2] and that in 2013 US$ 3 billion was spent on ENDS globally. Sales are forecasted to increase by a factor of 17 by 2030.[3] Despite this projection, transnational tobacco companies are divided about the prospects of the growth of ENDS sales and some companies have reported a slowdown in sales in some markets.[4,5,6] There are no data on ENDS use at the global level and for many countries. However, data mainly from North America, the European Union (EU) and Republic of Korea indicate that ENDS use at least doubled among both adults and adolescents from 2008 to 2012.[7] In 2012, 7% of EU citizens aged 15 years and over had tried electronic cigarettes. However, only 1% of the total

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[1] Abram DB. Promise and peril of e-cigarettes: can disruptive technology make cigarettes obsolete? Journal of the American Medical Association. 2014;311(2):135–6. doi:10.1001/jama.2013.285347.

[2] Zhu S-H, Sun JY, Bonnevie E, Cummins SE, Gamst A, Yin L, Lee M. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. Tobacco Control. 2014;23:iii3–iii9. doi:10.1136/tobaccocontrol-2014-051670.

[3] The tobacco industry at a crossroads: cigarettes growth falters as focus falls on alternatives. Euromonitor international. July 2013

[4] Evans P. E-cigarettes are the future? Not so fast, says BAT's boss. Wall Street Journal. 30 July 2014 (http://blogs.wsj.com/corporate-intelligence/2014/07/30/e-cigs-are-the-future-not-so-fast-says-bats-boss/)

[5] Prior A. Lorillard profit down as e-cigarette sales drop: electronic cigarette sales tumble 35%, offsetting slight increase in traditional cigarettes. Wall Street Journal. 30 July 2014 (http://online.wsj.com/articles/lorillard-profit-down-as-e-cigarette-sales-drop-1406720447).

[6] Wile R. Citi e-cigarettes: the e-cigarette boom is over. Business Insider. 15 May 2014 (http://www.businessinsider.com/citi-ecigarette-growth-slows-2014-5).

[7] Grana R, Benowitz N, Glantz SA. E-cigarettes: a scientific review. Circulation. 2014;129: e490–e492. doi:10.1161/CIRCULATIONAHA.114.008545.

population used them regularly.[1] In 2013, 47% of smokers and ex-smokers in the United States of America had tried e-cigarettes, but prevalence of established use was 4% in this group.[2] Users report that the main reasons for using ENDS are to reduce or stop smoking and because they can be used in smoke-free places.[3]

9. According to the recent WHO survey, ENDS availability is widespread. Slightly over half of the world's population live in 62 countries that report the availability of ENDS in their jurisdictions, 4% live in countries reporting that ENDS are not available, while the rest live in countries that did not respond concerning the availability of ENDS.

10. Recently, the transnational tobacco companies have entered the ENDS market. Some of them are aggressively competing with the independent companies to gain market share. Given the economic power of the tobacco industry, recent moves to sue other companies alleging patent infringement may be an indicator of how difficult it will be for ENDS to remain a business niche dominated by independent companies.

QUESTIONS RELATED THE USE OF ENDS

11. Questions have been articulated in three groups:

(a) health risks to users and non-users;

(b) efficacy in helping smokers to quit smoking and ultimately nicotine dependence; and

(c) interference with existing tobacco-control efforts and implementation of the WHO FCTC.

Health risks to users and non-users

12. Most ENDS products have not been tested by independent scientists but the limited testing has revealed wide variations in the nature of the toxicity of contents and emissions.

13. Health risks from nicotine inhalation are affected by several factors.

(a) The capacity of ENDS to deliver nicotine to the user varies widely, ranging from very low to levels similar to that of cigarettes, depending on product characteristics, user puffing behaviour and nicotine solution concentration.

(b) Nicotine is the addictive component of tobacco. It can have adverse effects during pregnancy and may contribute to cardiovascular disease. Although nicotine itself is not a carcinogen, it may function as a "tumour promoter".[4] Nicotine seems involved in fundamental aspects of the biology of malignant diseases, as well as of neurodegeneration.

[1] Attitudes of Europeans towards tobacco (Special Eurobarometer 385). European Commission, May 2012.

[2] Giovenco DP, Lewis MJ, Delnevo CD. Factors associated with e-cigarette use. American Journal of Preventive Medicine. Published online, 27 May 2014. doi: http://dx.doi.org/10.1016/j.amepre.2014.04.009.

[3] Grana R, Benowitz N, Glantz SA. E-cigarettes: a scientific review. Circulation. 2014;129: e490–e492. doi:10.1161/CIRCULATIONAHA.114.008545.

[4] Nicotine alters essential biological processes like regulation of cell proliferation, apoptosis, migration, invasion, angiogenesis, inflammation and cell-mediated immunity in a wide variety of cells including fetal, embryonic and adult stem cells, adult tissues as well as cancer cells.

(c) The evidence is sufficient to caution children and adolescents, pregnant women, and women of reproductive age about ENDS use because of the potential for fetal and adolescent nicotine exposure to have long-term consequences for brain development.[1]

14. The main health risk from nicotine exposure other than through inhalation is nicotine overdose by ingestion or through dermal contact. Since most countries do not monitor these incidents the information is very scarce. Reports from the United States and the United Kingdom nonetheless indicate that the number of reported incidents involving nicotine poisoning has risen substantially as the use of ENDS has increased. The actual number of cases is probably much higher than those reported.

15. Evidence concerning the health risks resulting from chronic inhalation of toxicants in aerosol to ENDS users are described below.

(a) Short-term effects of ENDS use include eye and respiratory irritation caused by exposure to propylene glycol. Serious short-term health problems may occur but are very rare.

(b) Given the relatively recent entry of ENDS into the market and the lengthy lag time for onset of many diseases of interest,[2] such as cancer, conclusive evidence about the association of ENDS use with such diseases will not be available for years or even decades.

(c) However, evidence based on the assessment of the chemical compounds in the liquids used in and aerosol produced by ENDS indicate:

(i) potential cytotoxicity of some solutions that have raised concerns about pregnant women who use ENDS or are exposed to second-hand ENDS aerosol.[3] Cytotoxicity was related to the concentration and number of flavourings used in the e-liquid;

(ii) the aerosol usually contains some carcinogenic compounds and other toxicants found in tobacco smoke at average levels of 1–2 orders of magnitude lower than in tobacco smoke, but higher than in a nicotine inhaler. For some brands, the level of some of these cancer causing agents, such as formaldehyde and other toxicants like acrolein have been found to be as high as in the smoke produced by some cigarettes;[4]

(iii) the range of size of particles delivered by ENDS is similar to that of conventional cigarettes, with most particles in the ultrafine range (modes around 100–200 nm) compared to the bigger size found in cigarette smoke. However, ENDS generate lower level of particles than cigarettes.[5]

(d) Therefore, it is very likely that average ENDS use produces lower exposures to toxicants that combustible products.

16. Evidence concerning the health risks resulting from inhalation of second-hand ENDS aerosol by non-users are described below.

[1] The health consequences of smoking – 50 years of progress. A report of the Surgeon General. Rockville (MD); US Department of Health and Human Services: 2014 (p.126).

[2] Including the lack of agreed early biomarker changes to assess potential harms.

[3] Bahl V, Lin S, Xu N, Davis B, Wang Y. Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. Reproductive Toxicology. 2012;34:529–37.

[4] Goniewicz ML, Knysak J, Gawron M, Kosmider L, Sobczak A, Kurek J et al. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. Tobacco Control. 2014;23(2):133–139. doi:10.1136/tobaccocontrol-2012-050859.

[5] Schripp T., D. Markewitz, E. Uhde, and T. Salthammer. Does e-cigarette consumption cause passive vaping? Indoor Air. 2013;23(1):25–31.

(a) Bystanders are exposed to the aerosol exhaled by ENDS users, which increases the background level of some toxicants,[1,2] nicotine[3] as well as fine and ultrafine particles in the air. Nevertheless the level of toxicants, nicotine and particles emitted from one ENDS is lower than that of conventional cigarette emissions.[4] It is not clear if these lower levels in exhaled aerosol translate into lower exposure, as demonstrated in the case of nicotine. Despite having a lower levels of nicotine than in second-hand smoke, the exhaled ENDS aerosol results in similar uptake as shown by similar serum cotinine levels.[5]

(b) It is unknown if the increased exposure to toxicants and particles in exhaled aerosol will lead to an increased risk of disease and death among bystanders as does the exposure to tobacco smoke. However, epidemiological evidence from environmental studies shows adverse effects of particulate matter from any source following both short-term and long-term exposures. The low end of the range of concentrations at which adverse health effects has been demonstrated is not greatly above the background concentration, which for particles smaller than 2.5 µm has been estimated to be 3–5 µg/m3 and increases with dose, which means that there is no threshold for harm and that public health measures should aim at achieving the lowest concentrations possible.[6]

17. In summary, the existing evidence shows that ENDS aerosol is not merely "water vapour" as is often claimed in the marketing for these products. ENDS use poses serious threats to adolescents and fetuses. In addition, it increases exposure of non-smokers and bystanders to nicotine and a number of toxicants. Nevertheless, the reduced exposure to toxicants of well-regulated ENDS used by established adult smokers as a complete substitution for cigarettes is likely to be less toxic for the smoker than conventional cigarettes or other combusted tobacco products. The amount of risk reduction, however, is presently unknown. The 2014 Surgeon General's Report concluded that non-combustible products such as ENDS are much more likely to provide public health benefits only in an environment where the appeal, accessibility, promotion, and use of cigarettes and other combusted tobacco products are being rapidly reduced.[7]

Efficacy in helping smokers to quit smoking and ultimately nicotine dependence

18. Although anecdotal reports indicate that an undetermined proportion of ENDS users have quit smoking using these products their efficacy has not been systematically evaluated yet. Only a few studies have examined whether the use of ENDS is an effective method for quitting tobacco smoking.

[1] Under near real-use conditions, e-cigarettes increased indoor air levels of polycyclic aromatic hydrocarbons, 1,2-propanediol, 1,2,3-propanetriol, glycerine, and aluminium.

[2] Schober W, Szendrei K, Matzen W, Osiander-Fuchs H, Heitmann D, Schettgen T et al. Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. International Journal of Hygiene and Environmental Health. 2014;217(6):628–37. doi:10.1016/j.ijheh.2013.11.003.

[3] Czogala J1, Goniewicz ML, Fidelus B, Zielinska-Danch W, Travers MJ, Sobczak A. Secondhand exposure to vapors from electronic cigarettes. Nicotine and Tobacco Research. 2014;16(6):655–62. doi: 10.1093/ntr/ntt203.

[4] McAuley TR, Hopke PK, Zhao J, Babaian S. Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. Inhalation Toxicology. 2012;24(12):850-7.

[5] Flouris AD, Chorti MS, Poulianiti KP, Jamurtas AZ, Kostikas K, Tzatzarakis MN et al. Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. Inhalation Toxicology. 2013;25(2):91–101. doi: 10.3109/08958378.2012.758197.

[6] WHO air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide: summary of risk assessment. Geneva: World Health Organization; 2006.

[7] The health consequences of smoking – 50 years of progress: a report of the Surgeon General. Atlanta (GA): US Department of Health and Human Services; 2014 (p. 874).

19. The evidence for the effectiveness of ENDS as a method for quitting tobacco smoking is limited and does not allow conclusions to be reached. However, the results of the only randomized control trial that compared use of ENDS, with or without nicotine, to use of nicotine patches without medical assistance in the general population, showed similar, although low, efficacy for quitting smoking.[1] A recent study also shows some, although limited, effectiveness in real-world conditions.[2]

20. At this level of efficacy, the use of ENDS is likely to help some smokers to switch completely from cigarettes to ENDS. However, for a sizeable number of smokers ENDS use will result in the reduction of cigarette use rather than in quitting. This will lead to dual use of ENDS and cigarettes. Given the likely greater importance of duration of smoking (number of years smoking) over intensity (number of cigarettes smoked per day) in generating negative health consequences, dual use will have much smaller beneficial effects on overall survival compared with quitting smoking completely.[3]

21. No ENDS product has yet been evaluated and approved for smoking cessation by a governmental agency, although the United Kingdom's Medicines and Healthcare Products Regulatory Agency is in the process of reviewing some of these products.

22. In considering ENDS as a potential cessation aid, smokers should first be encouraged to quit smoking and nicotine addiction using a combination of already approved treatments. However, at the individual level, experts suggest that in some smokers who have failed treatment, have been intolerant to it or who refuse to use conventional smoking cessation medication, the use of appropriately-regulated ENDS may have a role to play in supporting attempts to quit.[4,5]

Impact on existing tobacco-control efforts

23. Although ENDS present a range of potential benefits to smokers, there is an extensive and often heated debate about whether ENDS will prove to have a positive or negative impact on population health and particularly tobacco control. Areas of legitimate concern include avoiding nicotine initiation among non-smokers and particularly youth while maximizing potential benefits for smokers. Such concerns are referred to as the gateway and renormalization effects.

24. Gateway and renormalization concerns.

(a) The gateway effect refers to two potential circumstances:

(i) the possibility that children (and generally non-smokers) will initiate nicotine use with ENDS at a rate greater than expected if ENDS did not exist;[6] and

(ii) the possibility that once addicted to nicotine through ENDS children will switch to cigarette smoking.

[1] Bullen CB, Howe C, Laugesen M, McRobbie H, Parag V, Williman J et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. Lancet. 2013;382(9905):1629–37.

[2] Brown J, Beard E, Kotz D, Michie S, West R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. Addiction. Published online, 20 May 2014. doi:10.1111/add.12623.

[3] The health consequences of smoking – 50 years of progress: a report of the Surgeon General. Atlanta (GA): US Department of Health and Human Services; 2014.

[4] Fiore MC, Schroeder SA, Baker TB. Smoke, the chief killer – strategies for targeting combustible tobacco use. New England Journal of Medicine. 2014;370(4):297–9. doi: 10.1056/NEJMp1314942.

[5] Grana R, Benowitz N, Glantz SA. E-cigarettes: a scientific review. Circulation. 2014;129: e490–e492. doi:10.1161/CIRCULATIONAHA.114.008545.

[6] this This does not mean that use of ENDS by children in not a concern in itself.

(b) The renormalization effect refers to the possibility that everything that makes ENDS attractive to smokers may enhance the attractiveness of smoking itself and perpetuate the smoking epidemic. ENDS mimic the personal experience and public performance of smoking and their market growth requires marketing that is challenging commercial communication barriers erected to prevent the promotion of tobacco products.

(c) The likelihood and significance of these two effects occurring will be the result of a complex interplay of individual, market and regulatory factors and is difficult to predict. They can only be assessed with empirical data, which at present are virtually non-existent.

(d) The limited existing survey data from a handful of countries show that experimentation with ENDS is increasing rapidly among adolescents and that in itself is of great concern even if most of the young ENDS users also smoke. In fact, except in one case, the surveys show that there are few exclusive ENDS users who have never smoked (mostly around 1% of the population).[1,2,3] These data do not allow the conclusions to be drawn as to whether this is a sign of adolescent smokers switching to ENDS, an established pattern of dual use, or a temporary experimentation fashion. Therefore, in the absence of longitudinal data, existing evidence does not allow an affirmation or rejection of the role of ENDS in increasing nicotine addiction among adolescents above existing uptake rates, much less as to whether ENDS lead to smoking in these countries. Among adults the pattern of dual use seems also the predominant one, resulting in a reduction of smoked cigarettes and with few never smokers starting to use ENDS (below 1% of the population).[4,5]

(e) There are also very limited data from very few countries about the evolution of the smoking epidemic in the presence of the ENDS boom. In one country (United Kingdom), where tobacco-control measures are very strong and ENDS use is popular and growing, it seems that smoking prevalence, cigarette consumption as well as overall nicotine use continues to decrease gradually.[6] Whether these contrasting trends are causally related cannot be concluded from these data. At least for the United Kingdom, renormalization as measured by prevalence of smoking is not occurring currently. Whether this would be the case for other countries cannot be generalized from the existing data and needs to be proven empirically.

25. More specific public health questions related to the interaction between ENDS and tobacco-control efforts are discussed below.

26. Positioning the tobacco-control message: The entry of ENDS in the market has created challenges to the core message of tobacco control, which until now has been that tobacco use should not be started and if started it should be stopped.[7] The promotion of ENDS comes with at least one of

[1] Calculations based on Centers for Disease Control and Prevention reported data from the United States National Youth Tobacco Survey, contained in: Corey C, Wang B, Johnson SE, Apelberg B, Husten C, King BA et al. Notes from the field: electronic cigarette use among middle and high school students – United States, 2011–2012. Morbidity and Mortality Weekly Report;62(35):729–30.

[2] Lee S, Grana RA, Glantz SA, Electronic cigarette use among Korean adolescents: a cross-sectional study of market penetration, dual use, and relationship to quit attempts and former smoking. Journal of Adolescent Health. Published online, 22 November 2013. doi: http://dx.doi.org/10.1016/j.jadohealth.2013.11.003.

[3] Lukasz Goniewicz M, Zielinska-Danch W. Electronic cigarette use among teenagers and young adults in Poland. Pediatrics. Published online, 17 September 2012. doi:10.1542/peds.2011-3448.

[4] Sutfina EL, McCoy TP, Morrell HER, Hoeppner BB, Wolfson M. Electronic cigarette use by college students. Drug and Alcohol Dependence. 2013;131(3):214–221. http://dx.doi.org/10.1016/j.drugalcdep.2013.05.001.

[5] ASH UK fact sheet. Use of electronic cigarettes in Great Britain. April 2014. Available from: http://www.ash.org.uk/files/documents/ASH_891.pdf.

[6] West R, Brown J, Beard E. Smoking toolkit study. Trends in electronic cigarette use in England. Updated 4th April 2014. Available from: http://www.smokinginengland.info/latest-statistics/.

[7] de Andrade M, Hastings G, Angus K, Dixon D, Purves R. The marketing of electronic cigarettes in the UK. London: Cancer Research UK; November 2013.

the following messages or a combination of them: (a) try to quit smoking and if everything fails use ENDS as the last resort; (b) you do not need to quit nicotine addiction, just smoking; and (c) you do not need to quit smoking, use ENDS where you cannot smoke. Some of these messages are difficult to harmonize with the core tobacco-control message and others are simply incompatible.

27. The role of the tobacco industry: The future role of ENDS is strongly determined by the commercial interests of the industry that manufactures and sells ENDS. While there are "independent" ENDS companies that have reported no interest in perpetuating tobacco use, the tobacco industry involved in the production and sale of ENDS certainly is.

(a) The ENDS market, initially dominated by companies with no links to the tobacco industry, is increasingly owned by the tobacco industry. All main transnational tobacco companies sell ENDS and one of them is launching legal proceedings over patents against its rivals as they become increasingly aggressive in the battle for the fast-growing e-cigarette market. The increasing concentration of the ENDS market in the hands of the transnational tobacco companies is of grave concern in light of the history of the corporations that dominate that industry.

(b) It is unclear yet what this means for the ENDS market. However, if prior interest of the tobacco industry in reduced-risk products serves as a precedent, their interest lies in maintaining the status quo in favour of cigarettes for as long as possible, while simultaneously providing a longer-term source of profit should the cigarette model prove unsustainable. In addition, selling these products is intended to bring reputational benefits to these companies, as they can pretend to be part of the solution to the smoking epidemic.[1] ENDS may follow the trend of smokeless tobacco wherein the industry's historic interest in smokeless tobacco products outside some Nordic countries was both because they could be used in smoke-free environments and because they could be promoted to young, non-tobacco users to create a new form of tobacco use.[2]

28. Potential interference with smoke-free policies.

(a) Smoke-free policies are designed not only to protect non-smokers from second-hand smoke, but also to provide incentives to quit smoking and to denormalize smoking as adolescents are particularly vulnerable to visual cues and social norms.[3]

(b) The use of ENDS in places where smoking is not allowed

(i) increases the exposure to exhaled aerosol toxicants of potential harm to bystanders,

(ii) reduces quitting incentives, and

(iii) may conflict with the smoking denormalizing effect.

(c) Many ENDS look like smoking products and even if they do not resemble them, the exhaled vapour looks like tobacco smoke. ENDS are marketed to be used where smoking is prohibited and given the resemblance to tobacco products it is likely that their use where smoking is banned will make enforcing smoke-free policies more difficult.

(d) The fact that ENDS exhaled aerosol contains on average lower levels of toxicants than the emissions from combusted tobacco does not mean that these levels are acceptable to

[1] Peeters S, Gilmore AB. Understanding the emergence of the tobacco industry's use of the term tobacco harm reduction in order to inform public health policy. Tobacco Control. Published online, 22 January 2014. doi:10.1136/tobaccocontrol-2013-051502.

[2] Mejia AB, Ling PM. Tobacco industry consumer research on smokeless tobacco users and product development. American Journal of Public Health. 2010;100(1):78–87. doi: 10.2105/AJPH.2008.152603.

[3] Preventing tobacco use among youth and young adults. A report of the Surgeon General. Rockville (MD); US Department of Health and Human Services: 2012.

involuntarily exposed bystanders. In fact, exhaled aerosol is likely to increase above background levels the risk of disease to bystanders, especially in the case of some ENDS that produce toxicant levels in the range of that produced by some cigarettes.

29. The role of ENDS marketing (which falls into two categories: consumer marketing aimed at the general public, and stakeholder marketing aimed at policy-makers and public health bodies):

(a) ENDS are being marketed to consumers in many media and forms, including television commercials, sports and cultural sponsorship, celebrity endorsement, social networking, online advertising, point-of-sale displays, pricing strategies, and product innovation. Some marketing clearly emulates the very successful tobacco advertising asserting an independent identity and a lifestyle choice, aligning oneself with celebrities, fashionable and youthful places and activities. Some ENDS are marketed not only as socially acceptable but as socially superior. Unsubstantiated or overstated claims of safety and cessation are frequent marketing themes aimed at smokers. Some ENDS marketing also promotes long-term use as a permanent alternative to tobacco, and a temporary one in public places where smoking is banned. ENDS marketing activities have the potential to glamorize smoking and attracting children and non-smokers even if those are unintentional results. However, no empirical studies have been conducted to show whether the negative prospects of ENDS marketing are actually directly associated with attitudinal and behavioural changes among children and non-smokers consistent with the realization of such potential. Concerns have also been raised over the use of flavours in the marketing of ENDS. One recent study indicates that ENDS are marketed in 7764 unique flavours.[4] Although the role of ENDS flavours potential attractiveness has not been studied yet, expert opinion indicates that candy-like flavours could entice youths to experiment with ENDS and could also facilitate the development of tobacco dependence by enhancing the sensory rewards of ENDS use.[1] The tobacco industry's internal documents suggest that flavouring agents have played an important role in the industry's targeting of children and youth, and there is a concern that they could play the same role in the uptake of ENDS in these age groups.

(b) The marketing message to tobacco-control stakeholders is one of alignment of industry and public health interests based on the harm reduction potential of ENDS. This leads to a proposal of partnership between government and industry because industry claims a meaningful seat at the table in the so-called harm reduction debate.

CURRENT REGULATION AND POLICY: RESULTS OF THE WHO SURVEY

30. **Table 1** reflects the results of the 2014 WHO survey, showing the distribution of countries according to the regulatory approach taken to ENDS.

Type of ENDS	ENDS regulated as					Not regulated or unknown
	consumer product	therapeutic product	tobacco product	other	total	
With nicotine	14 (27%)*	12 (6%)	22 (10%)	11 (6%)	59 (49%)	135 (51%)
Without nicotine	23 (35%)	0 (0%)	18 (7%)	12 (2%)	53 (44%)	141 (56%)

* The figure in parentheses after the number of countries indicates the percentage of the world population living in these countries.

31. The sale of ENDS with nicotine is banned in 13 of the 59 countries that regulate them. However, the majority of these 13 countries report that ENDS are available to the public, probably through illicit trade and cross-border Internet sales.

[1] The scientific basis of tobacco product regulation: a WHO Study Group on Tobacco Product Regulation report. Candy-flavoured tobacco products: research needs and regulatory recommendations. Geneva; World Health Organization: 2007 (WHO Technical Report Series 945).

32. The survey also shows that:

(a) comprehensive advertising, promotion and sponsorship bans on ENDS are in place in 39 countries (in which 31% of the world's population live);

(b) use of ENDS in enclosed public places is banned in 30 countries (35%);

(c) premarket review is required by 19 countries (5%);

(d) vendor licences are required by nine countries (4%);

(e) policies on ENDS sales to minors were confirmed by 29 countries (8%). Where specified, minimum required age for purchase ranged from 18 to 21 years.

GENERAL CONSIDERATIONS

33. Smokers will obtain the maximum health benefit if they completely quit both tobacco and nicotine use. In fact, Article 5.2(b) of the Convention commits Parties not only to preventing and reducing tobacco consumption and exposure to tobacco smoke but also to preventing and reducing nicotine addiction independently from its source. Therefore, while medicinal use of nicotine is a public health option under the treaty, recreational use is not.

34. The rapid growth of ENDS use globally can neither be dismissed nor accepted without efforts to appropriately regulate these products, so as to minimize consequences that may contribute to the tobacco epidemic and to optimize the potential benefits to public health. Thus it is important to identify public health concerns and to consider these concerns when undertaking regulation and surveillance.

35. Regulation of ENDS is a necessary precondition for establishing a scientific basis on which to judge the effects of their use, and for ensuring that adequate research is conducted, that the public has current, reliable information as to the potential risks and benefits of ENDS, and that the health of the public is protected. Public health authorities need to prioritize research and invest adequately to elucidate evidentiary uncertainties as soon as possible. However, the greater responsibility to prove claims about ENDS scientifically should remain with the industry.

36. When designing a regulatory strategy for ENDS, governments should bear in mind the following general regulatory objectives:

(a) impede ENDS promotion to and uptake by non-smokers, pregnant women and youth;

(b) minimize potential health risks to ENDS users and non-users;

(c) prohibit unproven health claims from being made about ENDS; and

(d) protect existing tobacco-control efforts from commercial and other vested interests of the tobacco industry.

37. Because the product, the market and the associated scientific evidence surrounding ENDS are all evolving rapidly, all legislation and regulations related to ENDS should be adaptable in response to new scientific evidence, including evaluation of different models for ENDS regulation, as evidence accumulates.

38. Governments should consider that if their country has already achieved a very low prevalence of smoking and that prevalence continues to decrease steadily, use of ENDS will not significantly decrease smoking-attributable disease and mortality even if the full theoretical risk reduction potential of ENDS were to be realized.

SPECIFIC REGULATORY OPTIONS

39. In order to achieve the general regulatory objectives mentioned above, Parties that have not banned the sale of ENDS could consider the following non-exhaustive list of regulatory options, on the understanding that the advisability and feasibility at country level of each of these options will depend on a complex set of country-specific factors, including the existing regulatory frameworks and the legal exigencies of the regulatory process.

40. **Health claims.** Prohibit manufacturers and third parties from making health claims for ENDS, including that ENDS are smoking cessation aids, until manufacturers provide convincing supporting scientific evidence and obtain regulatory approval. The regulatory standard for cessation claims and approval as cessation aids should remain an appropriate body of evidence, based on well-controlled clinical trials. For ENDS products to be approved for smoking cessation by the suitable regulatory agency, the appropriate balance should be reached between providing accurate scientific information to the public about the risks of ENDS use and its potential benefits as compared with smoking. This balance can only be determined through scientifically tested audience messaging.

41. **Use of ENDS in public places**. Since the reasonable expectation of bystanders is not a diminished risk in comparison to exposure to second-hand smoke but no risk increase from any product in the air they breathe, ENDS users should be legally requested not to use ENDS indoors, especially where smoking is banned until exhaled vapour is proven to be not harmful to bystanders and reasonable evidence exists that smoke-free policy enforcement is not undermined. If smoke-free legislation is not fully developed according to Article 8 of the WHO FCTC and the guidelines for its implementation, this should be done as soon as possible.

42. **Advertising, promotion and sponsorship**. Given that the same promotional elements that make ENDS attractive to adult smokers could also make them attractive to children and non-smokers, Parties should contemplate putting in place an effective restriction on ENDS advertising, promotion and sponsorship. Some forms of ENDS promotion, however, may be considered acceptable by Parties if empirical evidence shows that ENDS might play a role in helping some smokers to quit without leading to increased ENDS use by minors and non-smokers who otherwise would not have used nicotine.

43. Any form of ENDS advertising, promotion and sponsorship must be regulated by an appropriate governmental body. If this is not possible, an outright ban on ENDS advertising, promotion and sponsorship is preferable to the implementation of voluntary codes on ENDS marketing, given the overwhelming evidence that similar codes for tobacco and alcohol products have failed to protect young people from such advertising.

44. Advertising, promotion and sponsorship of ENDS with or without nicotine, must, at a minimum:

(a) state clearly whether the product contains nicotine or may be used with nicotine solutions;

(b) not make them appealing to or target, either explicitly or implicitly, non-smokers or non-nicotine users, and must therefore indicate that ENDS are not suitable for use by people who do not currently consume tobacco products;

(c) not make them appealing to or target, either explicitly or implicitly, minors, including through the selection of media, location or the context in which they appear or through imagery that promotes sexual or sporting prowess;

(d) never promote ENDS for non-smokers, and their use should not be portrayed as a desirable activity in its own right;

(e) encourage smoking cessation and provide a quitline number if one exists;

(f) contain nothing that could reasonably be expected to promote the use of tobacco products, such as:

(i) the appearance or/and use of tobacco products;

(ii) the use of any brand name, design, colour, emblem, trademark, logo or trade insignia or any other distinctive feature that might be associated by the audience with a tobacco product;

(iii) the use of the words e-cigarette, electronic cigarette, or any other descriptor that might reasonably be expected to create confusion with the promotion of cigarettes and other combustible tobacco products;

(iv) showing ENDS products in ways that could reasonably be expected to promote tobacco products, including images of tobacco-like products;

(g) not contain health or medicinal claims, unless the product is licensed for those purposes by the appropriate regulatory agency. Electronic cigarettes and other nicotine-containing products should be presented only as an alternative to tobacco, and should include warnings that dual use will not substantially reduce the dangers of smoking;

(h) not undermine any tobacco-control measure, including by not promoting the use of ENDS in places where smoking is banned;

(i) include factual information about product ingredients other than nicotine and in a way that does not distort evidence of risks;

(j) not link these products with gambling, alcohol, illicit drugs or with activities or locations in which using them would be unsafe or unwise.

45. Advertising, promotion and sponsorship of ENDS that contain nicotine or may be used with nicotine solutions must:

(a) clearly state the addictive nature of nicotine and that these products are intended to deliver nicotine;

(b) Prohibit suggestions that ENDS have positive qualities as a consequence of the addictive nature of the product.

46. All authorized forms of ENDS advertising, promotion and sponsorship must be cleared by the appropriate authority prior to publication/transmission in order to proactively prevent inappropriate marketing, and then be monitored to assess compliance.

47. **Protection from vested commercial interests.** Transparency should be required from ENDS and tobacco companies advocating for and against legislation and regulation, both directly and through third parties. No matter what role the tobacco industry plays in the production, distribution and sale of ENDS, this industry, its allies and front-groups can never be considered to be a legitimate public health partner or stakeholder while it continues to profit from tobacco and its products or represents the interests of the industry. Article 5.3 of the WHO FCTC should be respected when developing and implementing ENDS legislation and regulations.

48. **Product design and information**. ENDS should be regulated to:

(a) minimize content and emissions of toxicants;

(b) ensure use of nicotine of pharmacological quality, when nicotine use is intended;

(c) standardize nicotine delivery at levels known to the consumers;

(d) minimize acute nicotine toxicity;

(e) impede product alteration to use of other drugs;

(f) ban ENDS solutions with fruit, candy-like and alcohol-drinks flavours until empirical evidence shows that they are not attractive to minors;

(g) require manufacturers and importers to disclose to governmental authorities information about the contents and emissions of ENDS; and

(h) require registration of manufacturers and importers with governmental authorities.

49. **Health warnings.** ENDS health warnings should be commensurate with proven health risks. In this regard, the following risk warnings could be considered: potential nicotine addiction; potential respiratory, eyes, nose and throat irritant effect; potential adverse effect on pregnancy (due to nicotine exposure).

50. **Surveillance and monitoring**. Governments are recommended to use or strengthen their existing tobacco surveillance and monitoring systems to assess developments in ENDS and nicotine use by sex and age.

51. **Sale to minors.** Retailers should be prohibited from selling ENDS products to minors, and vending machines should be eliminated in almost all locations.

REGULATORY FRAMEWORK

52. In order to implement the suggested general regulatory objectives as well as the specific regulatory options, Parties will need to consider the available national regulatory frameworks that could best provide solid regulatory grounds.

53. The applicability of many of the WHO FCTC provisions to the regulation of ENDS was reviewed in a report by the Convention Secretariat on this topic[1] presented at the fifth session of the COP.

ACTION BY THE CONFERENCE OF THE PARTIES

54. The COP is invited to note this report and to provide further guidance.

Appendix P: List of Publications

1. Weke, A. Smoking cessation: an update on the impact of COVID-19. Dental Health 2020; 59: 26-27.
2. Weke A, Holliday R. Electronic cigarettes: an update on products, regulation, public health approaches and oral health. Community Dental Health 2022; 39: 68-73.
3. Insan N, Weke A, Forrest S, Rankin J. Social determinants of antenatal depression and anxiety among women in South Asia: A systematic review & meta-analysis. PLOS ONE 2022; 17(2): e0263760. https://doi.org/10.1371/journal.pone.0263760
4. Insan, N., Weke, A., Rankin, J. et al. Perceptions and attitudes around perinatal mental health in Bangladesh, India, and Pakistan: a systematic review of qualitative data. BMC Pregnancy Childbirth 2022; 22, 293. https://doi.org/10.1186/s12884-022-04642-x
5. Holliday, R., McColl, E., Weke, A. et al. Vaping misrepresentations [Letter to the editor]. British Dental Journal 2022; 232, 840-841. https://doi.org/10.1038/s41415-022-4409-1
6. Holliday, R., Weke, A., McColl, E. Misleading and worrying [Letter to the editor]. British Dental Journal 2022; 235(4):231. DOI 10.1038/s41415-023-6189-7
7. Jackson, J., Weke, A., Holliday, R. Nicotine pouches: a review for the dental team. British Dental Journal 235, 643–646 (2023). https://doi.org/10.1038/s41415-023-6383-7