Understanding the role of evidence in e-cigarette regulation and policy development

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Abstract

Background: Public health recommendations should be informed by the best available evidence. E-cigarette policy has varied across jurisdictions, contrasting with the previous coordinated approach of international tobacco control communities. An understanding of such divergence may help inform future public health policy. Using e-cigarettes as a case study, this thesis examines the role and use of evidence in the development of public health recommendations.

Methods: This multi-methods case study focused on e-cigarette recommendations from the WHO, UK, Australia, and USA; and comprised: a document analysis of recommendations; a citation network analysis of the evidence cited and their conflicts of interest (COI); an analysis of the guideline development documents which described the processes for developing recommendations, including managing COI; expert interviews with individuals involved in developing recommendations; and triangulation across these data sources.

Results: Analysis of public health recommendations showed that different jurisdictions supported different e-cigarette policy approaches, with the UK following a 'harm reduction' approach, while the WHO, Australia, and USA followed a more 'precautionary' approach. Analysing the evidence cited by the recommendation documents revealed that substantial COI, such as pre-existing relationships between the e-cigarette and tobacco industries, were present within the cited evidence. Examination of the processes for collecting and managing COI, illustrated variation across public health bodies, often with a lack of transparency. Triangulating across the data demonstrated the myriad contextual factors (e.g., previous and current tobacco policies) influencing the role and use of evidence in the development of e-cigarette recommendations. I highlight how internal contextual factors (e.g., the remit of the document) were often influenced by external contextual factors (e.g., epidemiological features of smoking and vaping) and interact in subtle ways to frame the focus of recommendations and the evidence underpinning them.

Conclusion: Contextual factors are crucial in understanding divergence in e-cigarette recommendations across jurisdictions, with similar evidence used by public health bodies internationally. COI are common in the evidence base and a lack of standardisation in managing COI might threaten evidence-informed decision-making. This thesis suggests internal and external contextual factors interact and that this interplay may help explain the divergence in e-cigarette policy approaches.

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Publications and other outputs

The following publication, conference presentations and invited presentation have resulted from the research described in this thesis. My specific contribution to each element of the project is described in detail on page 16.

Publication

Smith MJ, Baxter AJ, Skivington K, McCann M, Hilton S and Katikireddi SV (2021) Examining the sources of evidence in e-cigarette policy recommendations: A citation network analysis of international public health recommendations. PLoS ONE 16(8): e0255604. https://doi.org/10.1371/journal.pone.0255604

Conference presentations

Smith MJ, Baxter AJ, Skivington K, McCann M, Hilton S and Katikireddi SV. Exploring e-cigarette policy recommendations and the role of evidence: A citation network analysis of international public health guidelines. *Lancet Public Health Conference*, 30th November 2019. I was presented with an Early Career Researcher award for my presentation.

Smith MJ, Skivington K, Katikireddi SV and Hilton S. Understanding the role of evidence and management conflicts of interest in e-cigarette regulation and policy: A qualitative interview study. *Society for Research on Nicotine and Tobacco International Conference*, 25th February 2021.

Invited presentation

Smith MJ, Skivington K, Katikireddi SV and Hilton S. Understanding the role of evidence in e-cigarette policy and recommendations: a multi-methods approach. *SPECTRUM (Shaping Public hEalth poliCies To Reduce IneqUalities and harM) Academy*, 29th June 2021.

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Lastly, I would like to thank my wonderful colleagues at Lloyds pharmacy, West Kilbride. I want to thank you for listening to my, sometimes longwinded thoughts over what is the quickest thirty minutes of the day, lunch.

Author's declaration

I declare that, except where explicit reference is made to the contribution of others, this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Printed Name: Marissa Johan Smith

Signature:

Contribution statements

Chapters 1-4

The writing and development of these chapters was led by me and I take full responsibility for it.

Chapter 5

I was responsible for the conceptualisation and development of the research question; defining the sample; coding the documents (30% of the documents were double-coded by my co-authors Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington); and leading the interpretation, with input from all co-authors. I drafted the first draft of the manuscript and revised it following feedback. All co-authors provided feedback on the interpretation of results and contributed to revising the manuscript.

Chapter 6

I was responsible for the conceptualisation and development of the research questions. I led data collection including data extraction for all citations; extraction of data from high-impact citations; Shiny app development; and extraction of data using the Shiny apps. I was responsible for the development and visualisation of network graphs; statistical analysis (including coding of blockmodelling and Fisher's exact tests); and qualitative analysis and interpretations of the documents (20% of the documents were double-coded by my co-author Dr Kathryn Skivington). I wrote the first draft of the manuscript and revised it following feedback. Co-author Andrew Baxter acted as the second reviewer for the data extraction and assisted with the statistical analysis, visualisation, and Shiny app development. All co-authors provided feedback on the

interpretation of results, contributed to revising the manuscript, and responding to reviewers' comments.

Chapter 7

I was responsible for the conceptualisation and development of the research question, defining the sample, and coding the conflicts of interest policies (40% of the documents were double-coded by my co-author Dr Kathryn Skivington). I conducted all expert interviews and coding of transcripts (30% of the transcripts were double-coded by my co-authors Professor Srinivasa Vittal Katikireddi, Dr Kathryn Skivington, and Professor Shona Hilton). I led the interpretation and sought input from co-authors. I wrote the first draft of the manuscript and revised it following feedback. All co-authors provided feedback on the research question, data interpretation and contributed to revising the manuscript, and responding to reviewers' comments.

Chapter 8

I was responsible for the conceptualisation and development of the research question; coding of the data (20% of the data were double-coded by my co-author Dr Kathryn Skivington) and; interpretation of results; I wrote the first draft of the manuscript and revised it following feedback. All co-authors provided feedback on the research question, interpretation of results and contributed to revising the manuscript.

Chapter 9

The writing and development of this chapter was led by me and I take full responsibility for it.

Acronyms and Abbreviations

AGREE II	Appraisal of Guidelines for Research Evaluation, Version II
ASH	Action on Smoking and Health
BAT	British American Tobacco
CDC	Centers for Disease Control and Prevention (USA)
COI	Conflicts of interest
COVID-19	Coronavirus
EBM	Evidence-based medicine
EBPM	Evidence-based policymaking
ENDS	Electronic Nicotine Delivery System
EU	European Union
EVALI	E-cigarette, or Vaping, product use Associated Lung Injury
FCTC	Framework Convention on Tobacco Control (WHO)
FDA	Food and Drug Administration (USA)
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICMJE	International Committee of Medical Journal Editors
MRC	Medical Research Council
NICE	National Institute for Health and Care Excellence
NHMRC	National Health and Medical Research Council (Australia)
NHS	National Health Service (UK)
NRT	Nicotine Replacement Therapy
PMI	Phillip Morris International
PHE	Public Health England
RCT	Randomised Control Trial
SPHSU	Social and Public Health Sciences Unit
SR	Systematic Review
TGA	Therapeutic Goods Administration (Australia)
THC	Tetrahydrocannabinol

TPD	Tobacco Products Directive
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

1 Introduction and structure of the thesis

1.1 Overview

In this introductory chapter, I briefly describe the background of the study in the setting of public health research and the rationale for the approach undertaken. The chapter concludes with a guide to the overall thesis and its structure.

1.2 Background to the thesis

Public health policies, guidelines, and recommendations aspire to be informed by the best available evidence. The evidence-based medicine (EBM) movement has demonstrated the benefits of using evidence for clinical decision-making (Sackett et al., 1996). Since the emergence of EBM, there has been an increasing interest among policymakers and public health researchers in pursuing evidence-based policymaking (EBPM) and more rigorous approaches to policy development have been sought (Norris et al., 2011; Parkhurst, 2017). However, efforts to understand the relationship between evidence and public health policy when the evidence base is limited and/or disputed (such as electronic cigarettes (e-cigarettes) and Coronavirus (COVID-19)) is limited. Furthermore, the transition from EBM to EBPM is not straightforward and this will be explored in Chapter 2.

This thesis examines the relationship between evidence and public health policy using a multi-methods case study approach, therefore providing a holistic analysis. Public health recommendation documents can be characterised as documents that contain recommendation(s) for health practice, public health, or health policy (Eccles et al., 2012). It is generally agreed that the process for developing public health recommendations should be transparent and lead to impartial decisions that improve health, based on the best available evidence (Woolf et al., 2012). Public health policies are comprised of recommendations that aim to improve population health (Centers for Disease Control and Prevention, 2015). Smith and Katikireddi (2013) state that "'policy' can also refer to an approach or broader direction (e.g., 'free-market policies') or a process, involving multiple stages (including implementation)" (p.198) – and can therefore be considered a broader term. It is argued that public health policies should also be developed through a transparent process, which results in a plan of action that sets out a vision of identified public health goals (Martin, 2008). In the context of public health, policies are often determined by the political or executive section of the

jurisdiction (e.g., the government), although public health bodies may be involved during their development. Public health guidelines can be defined as documents consisting of clinical, public health, and/or policy recommendations, and are often used as a guide for practitioners (World Health Organisation, 2014a). This thesis focuses on public health recommendations produced by public health bodies rather than public health policies produced by government departments or clinical guidelines produced by public health bodies. The former would be expected to be inherently political, while the latter are focused on clinical practice more than public health. Public health bodies instead tend to agree on the centrality of evidence for producing recommendations that are relevant for public health.

Using e-cigarettes as a case study to explore the relationship between evidence and public health policy is both pertinent and timely for various reasons. Unlike tobacco products, where most countries have coalesced around a series of regulatory approaches meant to shrink the market for the products over time, the development of alternative nicotine products, for example, e-cigarettes, has polarised the tobacco control debate. Their rapid proliferation, the limited evidence base on the long-term health effects, and their patterns of use among different population groups has led to controversial political and public health debates, with public health policymakers and researchers finding themselves with divergent views. As a result, a variety of regulatory approaches have been pursued. Therefore, the issue of e-cigarettes offers a highly relevant case through which to examine the relationship between evidence and public health policy. This is important as an understanding of how evidence can lead to different policy responses in different jurisdictions may help to inform effective policy across public health in the future.

1.3 Structure of the thesis

For this thesis, I have adopted a 'journal format' structure (University of Glasgow, 2020), as I was keen to publish the findings from my research as I progressed. The thesis is therefore built around four empirical chapters, each corresponding to a published or submitted article.

I briefly summarise below the content of each chapter.

Chapter 2 will examine relevant literature about the relationship between evidence and public health policy. The chapter introduces a philosophical and practical framework about how we interpret information in the decision-making process as presented by

Dobrow (2003). The chapter then introduces key concepts from public health and political science which are drawn upon in the remainder of the thesis.

Chapter 3 introduces the topic of e-cigarettes, the case study upon which this thesis focuses. The chapter discusses the emergence of e-cigarettes and examines the key arguments and debates surrounding e-cigarette products. The chapter concludes by reviewing the national and international e-cigarette policy jurisdictions selected for analysis.

Chapter 4 describes the methods used within the case study of e-cigarettes. A description of the data and analysis procedures is provided for the four different sources of data that are drawn upon: public health bodies' recommendations on e-cigarettes; development documents produced by the public health bodies; sources of evidence cited in the public health bodies' recommendation documents; and qualitative interviews with experts involved in developing e-cigarette recommendations.

Chapters 5-8 each comprise an article describing the work undertaken to address the research questions. As each article is intended to be a stand-alone output, inevitably there is some degree of duplication with the content covered in other parts of the thesis. Some minor formatting changes have been made to published versions in keeping with guidelines for thesis submission.

Chapter 5 explores the results of the document analysis of four jurisdictions' e-cigarette recommendations. It provides a description of the e-cigarette public health recommendations, highlighting the similarities and differences in recommendations across the four selected jurisdictions.

Chapter 6 examines the sources of evidence used by public health bodies when making e-cigarette public health recommendations. In particular, it explores the influential citations (used in 3+ recommendation documents) and highlights the presence and types of conflicts of interest (COI) and study funding in the evidence sources drawn upon by public health bodies.

Chapter 7 combines the data from the public health bodies' COI policies (detailing the processes for collecting and managing COI) and expert interview data. It examines how COI are collected and managed during the decision-making process.

Chapter 8 triangulates the data across the four data sources to understand how contextual factors influence the role and use of evidence in decision-making. To do so, the analysis draws upon Dobrow et al.'s (2004) conceptual framework for context-based evidence-based decision-making.

Chapter 9 summarises the empirical findings and reflects on the strengths and limitations of this thesis. The chapter then outlines the public health policy and academic implications, and contributions of the thesis as well as future research implications. The chapter ends by providing a conclusion.

While I led the conceptualisation, conduct, and writing up of each part of the thesis, I also benefited from the invaluable contributions of other researchers at the MRC/CSO Social and Public Health Science Unit (SPHSU). Their contribution is acknowledged in the contributions statements that prefaces the thesis (page 16) and in the authorship statement associated with each article. The overall work has been led by me and I take full responsibility for it.

2 Literature review: evidence and public health policy

2.1 Overview

This thesis aims to explore the relationship between evidence and public health policy and therefore begins by briefly defining and explaining why evidence is important in decision-making. Following this, the EBM movement is introduced and which has led to the resurgence of the evidence-based policy movement. Public health straddles both EBM and EBPM as they both use evidence to enhance care and population health (Kohatsu et al., 2004) and as such, both will be discussed in this chapter. The chapter then reviews the academic literature to understand the relationship between evidence and public health recommendations, including an examination of the decision-making context.

2.2 Evidence and public health policy

Within public health and other areas of social policy, there are calls to increase EBPM (Brownson et al., 2009; Parkhurst and Abeysinghe, 2016). Yet there is a lack of clarity as to what can be considered 'good evidence' for policymaking (Newman et al., 2013). Numerous discussions of best practice in the public health policy sector are derived from the EBM movement and the 'hierarchy of evidence' (Parkhurst and Abeysinghe, 2016). This section begins with a brief discussion of various definitions of evidence, followed by an examination of the EBM movement and the relationship between evidence and policymaking.

2.2.1 What is evidence and why is it important?

Before understanding the role and use of evidence in the development of public health policy and recommendations, it is worth considering what evidence is and why it is important. Evidence can be defined as facts (actual or asserted) in support of a conclusion, statement, or belief (Rychetnik et al., 2002; Oxman et al., 2009). It can take a variety of forms including published research (e.g., books and journal articles) and personal experiences and opinions (Oxman et al., 2009). Evidence also includes economic, behavioural, attitudinal, and anecdotal evidence together with the knowledge and expertise of both experts and lay persons (Juntti et al., 2009). Evidence

can provide a range of information, but by itself, it cannot tell researchers or decision-makers what to do with the results or how to proceed (Black, 2001; Department of Planning Monitoring and Evaluation, 2014). Factors such as the goals being pursued in a country or jurisdiction (e.g., whether to be smoke-free), expertise and experience of the decision-makers, and available resources need to be considered when decisions are being deliberated (Rycroft-Malone et al., 2004; Bowen et al., 2009).

Parkhurst (2017) states that the use of scientific evidence for public health decision-making is critical to avoid unnecessary harms and to help achieve key social policy goals. A commonly cited example of unnecessary harm is advice on avoidance of sudden infant death syndrome (SIDS). For decades, parents were urged to place their babies on their fronts when putting them to sleep (Gilbert et al., 2005). Dr Benjamin Spock in his book Baby and Child Care (1958) reported that the front sleeping position would reduce the risks of babies choking in their sleep if they were to vomit (Spock, 1958; Gilbert et al., 2005; Howick, 2015). This practice was encouraged despite growing evidence that if babies were put in the front sleeping position, they were at a higher risk of SIDS compared to those babies who slept on their backs. In 1991, the 'Back to Sleep' campaign was launched, which aimed to highlight the emerging evidence base and directly contradicted the advice of Dr Spock and other medical professionals (Dwyer and Ponsonby, 1996; Gilbert et al., 2005). Gilbert et al. (2005) explain the 'Back to Sleep' campaign was based on "the strongest evidence to date for a harmful effect of the front position" (p.883). The success of the 'Back to Sleep' campaign brought about a decrease in the number of SIDS cases in the United Kingdom (UK), with the number of SIDS deaths reduced by up to 40% within the first year of the campaign (Her Majesty's Stationery Office, 1993).

2.2.2 Evidence-based medicine

There has been a longstanding interest in the use of evidence to inform public policy (Bulmer, 1982; Sutcliffe and Court, 2005). The EBM movement has influenced evidence-based policy, particularly within public health (Lohr et al., 1998; Oliver and Pearce, 2017) and is therefore worthy of discussion. The EBM movement began in the early 1990s and was inspired by researchers including David Sackett, David Eddy, and Archie Cochrane (Djulbegovic and Guyatt, 2017). The purpose of EBM was to educate clinicians on the understanding and use of evidence and how to apply results from published literature to clinical practice (Evidence-Based Medicine Working Group, 1992; Rosner, 2012; Djulbegovic and Guyatt, 2017). Advocates of EBM recognise that scientific evidence needs to be integrated with other types of evidence, but they remain focused

on the use of the best evidence (Sackett, 1997; Sackett et al., 2000; Dobrow et al., 2004; Oliver and Pearce, 2017). One of the drivers of EBM was a response to the view that doctors know best from their own experience (Masic et al., 2008). Supporting the perspective of EBM is a view of evidence derived from epidemiology – the science that is traditionally seen as underpinning public health (Holland et al., 2007).

Epidemiology is the "study of the distribution and determinants of disease frequency" (MacMahon and Trichopoulos, 1996, p.1) or even more simply "the study of how often diseases occur in different population groups and why" (Coggon et al., 2003, p.81). By studying the pattern and distribution of disease and its determinants in a population, it helps plan and evaluate strategies to prevent illness and seeks to improve population health (Coggon et al., 2003).

Epidemiologists have developed a range of study designs that can be used to help make causal judgements. Causal thinking is central to epidemiology as it allows the prediction of future events, explanations of observed events, and choice of the correct intervention to achieve goals (Waldmann, 2010). This form of epidemiological thinking has been drawn upon by the EBM movement to create a well-known 'hierarchy of evidence'.

Since the 1980's there has been a growing emphasis on basing healthcare decisions on the 'best available evidence'. To assist in the interpretations and evaluation of research findings, evidence hierarchies have been developed which rank research according to its internal validity, i.e., its potential to identify cause-effect relationships within the studied population and setting robustly (Evans, 2003). Attention has also been focused on the quality of the scientific evidence, recognising that not all evidence is equal in its validity (Evans, 2003; Dobrow et al., 2004). The Canadian Task Force on the Periodic Health Examination authored the first hierarchy of evidence in 1979 and since then numerous different hierarchies have been developed (Canadian Task Force on the Periodic Health Examination, 1979; Sackett, 1986; Woolf et al., 1990). Sackett developed it further and in 1989 produced the hierarchy of evidence illustrated in Figure 2.1.

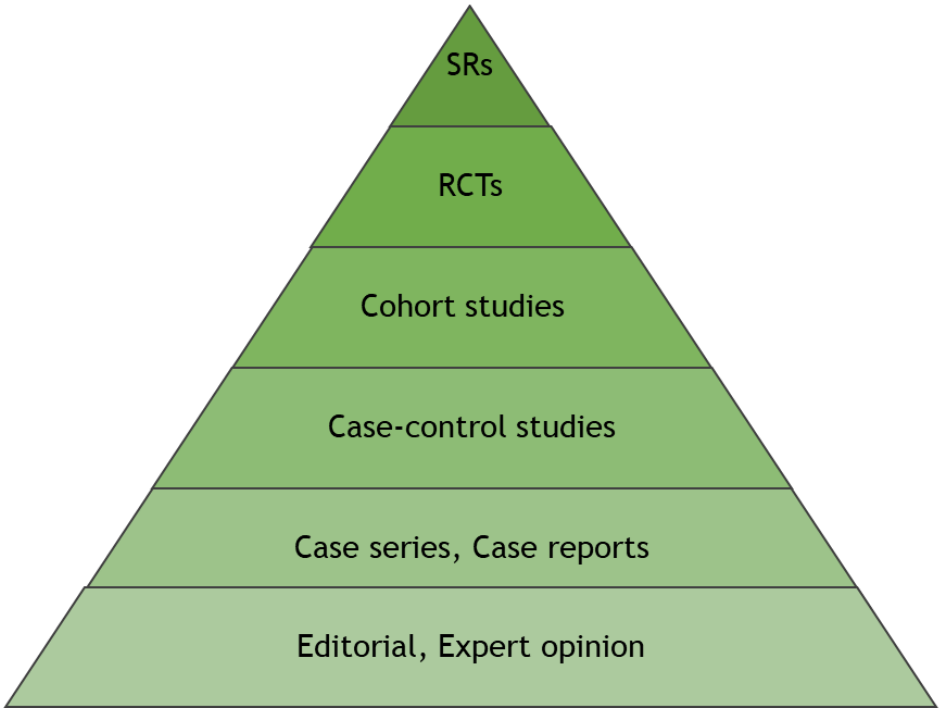

Figure 2.1: A hierarchy of evidence[1]

Key: RCTs=Randomised Controlled Trials; SRs=Systematic Reviews

The hierarchy of evidence includes numerous different types of studies used to evaluate treatment effects, starting from expert opinion at the lowest level, going up through case-control studies and randomised controlled trials (RCTs), to systematic reviews (SRs) at the top of the pyramid. SRs attempt to collect, merge and report the leading available evidence using a systematic and reproducible procedure (Pandis, 2011). RCTs are the most scientifically rigorous method of establishing causal effects and are regarded as the 'gold standard' for evaluating the effectiveness of interventions (Last, 2001; McGovern, 2001; Goodman and Thompson, 2018). EBM grades RCTs as one of the 'highest quality' forms of evidence. The grading of the quality of evidence deems higher-quality studies as those least susceptible to bias and that certain types of studies are less vulnerable to bias (Sackett et al., 1996; Haynes, 2002). The grading of evidence will be discussed in more detail in Section 2.3.3. SRs and RCTs are deemed both more reliable and more important to clinical decision-making compared to information that is gathered by other methods, such as observational studies and qualitative methods (Cohen et al., 2004; Fernandez et al., 2015). However, RCTs are expensive and not

[1] Reproduced from SACKETT, D., STRAUS, S., RICHARDSON, S., ROSENBERG, W. & HAYNES, R. 2000. *Evidence-Based Medicine: How to Practice and Teach EBM*, London, UK, Churchill Livingstone.

always feasible or ethical to conduct. Lower-level studies are not necessarily inferior; some have resulted in important scientific breakthroughs, including the discovery of penicillin (Pandis, 2011) and the 'Back to Sleep' campaign (Gilbert et al., 2005). Pandis (2011) states that the hierarchy of evidence "has helped in assessing the quality of evidence and has been pivotal in translating the available evidence into clinical practice" (p.546).

It is worth noting that the hierarchy of evidence does not capture all aspects of study validity. An important distinction is between internal and external validity:

> "There are two types of study validity. Internal validity is the degree to which the results of a study are correct for the sample of people being studied. External validity (generalisability) is the degree to which the study results hold true for a population beyond the subjects in the study or in other settings." (Rychetnik et al., 2004, p.539)

Thus, the hierarchy of evidence focuses only on internal validity and does not consider external validity. Despite the criticisms of the hierarchy of evidence, the development of such hierarchies have been influential to EBM but there is now more of an acknowledgement that diverse forms of evidence are needed (McAlister et al., 2000; Guyatt et al., 2002; Sheridan and Julian, 2016; Straus et al., 2018). However, many public health bodies and organisations which are responsible for producing evidence-based guidelines, including the World Health Organisation (WHO) (World Health Organisation, 2014b), National Institute of Health and Care Excellence (NICE) (National Institute for Health and Care Excellence, 2022) and Australian National Health and Medical Research Council (NHMRC) (National Health and Medical Research Council, 2016), retain a distinction between RCTs and other forms of evidence, reflecting the less potential for bias in RCTs.

2.2.2.1 Achievements and criticisms of evidence-based medicine

There have been many achievements of the EBM movement including the establishment of the Cochrane Collaboration, which produces high-quality reviews of published research (the Cochrane Collaboration will be discussed in more detail in Section 2.3.2.1) (Masic et al., 2008; Sheridan and Julian, 2016); setting methodological and publication standards for primary and secondary research (Simera et al., 2010); developing resources for critical appraisal such as Grading of Recommendations Assessment, Development and Evaluation (GRADE) (this will be discussed in more detail in Section

2.3.3.1) (Horsley et al., 2011; Djulbegovic and Guyatt, 2017); creating both national and international organisations for developing and updating clinical practice guidelines (Hill et al., 2011; Djulbegovic and Guyatt, 2017); and building the knowledge base for implementation and knowledge translation (McCormack et al., 2013).

The value of EBM has been persistently defended by its proponents; however, it has been criticised by many disciplines, including clinical practice (Carrhill, 1995; Miles and Loughlin, 2006; Wilson, 2010). According to Djulbegovic and Guyatt (2017), there are three main criticisms of EBM. Firstly, EBM encourages 'cookbook medicine' (Timmermans and Mauck, 2005), meaning the processes are algorithmic (Greenhalgh et al., 2014). Critics have argued that care for a particular patient "may not match what the best evidence seems to suggest" (Greenhalgh et al., 2014, p.3), therefore, it neglects the personal aspects of medical care and the focus is moved away from the individual patient (Miles et al., 2001a; Greenhalgh et al., 2014; Miles et al., 2015; McCartney et al., 2016). However, over time issues such as lived experiences, patient values, and acceptability of the intervention have been incorporated into the EBM mainstream. Secondly, critics suggested that EBM does not encourage intuitive and experiential thinking (i.e., expert judgement) (Greenhalgh et al., 2014). EBM argues for the use of high-quality and replicable research and as a result could be seen to diminish the role of expertise and thoughtful clinical decisions (Greenhalgh et al., 2014). Djulbegovic and Guyatt (2017) argue that "EBM does, in fact, highly value the critical role of expertise in health-care-delivery by emphasising the importance of judicious judgment in critical appraisal and decision-making" (p.420). Thirdly, critics have raised concerns about the strict adherence to the hierarchy of evidence (Figure 2.1), which is simplistic and constricted (Miles et al., 1997; Miles et al., 2000; Miles et al., 2001b; Worrall, 2002). To address critics' concerns, the GRADE framework was developed to highlight that other components matter too (e.g., external validity). The GRADE framework will be discussed in more detail in Section 2.3.3.1. Despite these criticisms, detractors have generally not argued that reliable evidence should not be central to decision-making and problem-solving.

2.2.3 Philosophical-normative and practical-operational orientations of determining what constitutes evidence

Policy advisers, academics, researchers, policymakers, and service providers have different perspectives on what constitutes evidence (Haynes, 2002; Department of

Planning Monitoring and Evaluation, 2014). Dobrow (2003) states the question of "what constitutes evidence?":

> "[…] is both philosophical and practical, firmly established in epistemology and ontology theorising how we relate to the world in terms of creation, interpretation and evaluation of information and knowledge […]" (p.12)

Dobrow (2003) distinguishes between the philosophical and practical aspects of evidence and argues that the two focus on different relationships between evidence and context (Figure 2.2). These two aspects will be discussed next.

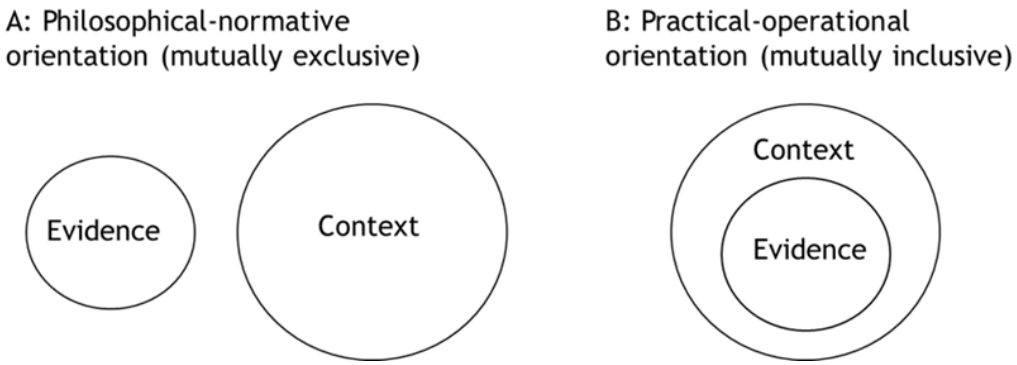

Figure 2.2: Two orientations for determining what constitutes evidence[2]

2.2.3.1 Philosophical-normative orientation

The philosophical-normative orientation focuses on the properties and characteristics of evidence (e.g., internal validity and rigour) and introduces the claim that some forms of evidence are to be preferred over others (Dobrow, 2003; Djulbegovic et al., 2009a). Those who adopt this perspective may refer to hierarchies of evidence. In this mindset evidence and context are considered competing priorities, meaning the focus is on what is considered as evidence and not context (Figure 2.2) (Dobrow, 2003). Therefore, from this perspective, what constitutes evidence is based on quality with the belief being that higher-quality evidence should lead, in turn, to higher-quality decisions (Dobrow, 2003).

[2] Reproduced from DOBROW, M. J. 2003. *Context-based evidence-based decision-making: Case study of evidence utlisation in the development of cancer screening policy*. Doctor of Philosophy University of Toronto.

Initially, the EBM movement supported the philosophical-normative orientation and as discussed previously, emphasised the use of evidence produced through systematic and rigorous research, while de-emphasising the use of expert judgement, unsystematic clinical experience, and patient and professional values (Evidence-Based Medicine Working Group, 1992). However, there is now recognition that scientific evidence alone is not sufficient to make decisions and needs to be integrated with other types of evidence and context.

The cancer screening literature provides an example of how the EBM movement has influenced the use of evidence. Eddy (2004) stated:

> "Direct [scientific evidence], the prototype, being the randomised control trial, is desirable over other types of indirect evidence." (p.14)

However, he also argued that:

> "It is rare that all outcomes of [cancer] screening can be learned from a single source. More commonly a policymaker must examine many sources and types of evidence to document the benefits of [cancer] screening and to estimate the magnitude of benefits, harms and costs." (p.13)

Similarly, the U.S. Preventative Services Task Force's Guide to Clinical Preventive Services (1996) stated:

> "The recommendations in this report are influenced largely by one factor, scientific evidence, recognising that other factors need to be considered." (Translating Science into Clinical Practice Recommendations section, para.1)

However, EBM proponents have acknowledged that broad disease and test-specific characteristics are required to evaluate cancer screening programs. Furthermore, in other areas of public health, we should go beyond what scientific evidence (e.g., RCTs) normally address, including patient acceptability, cost, and context (Chamberlain and Moss, 1996; Clark and Reintgen, 1996; Goldenberg, 2006; Greenhalgh et al., 2014).

2.2.3.2 Practical-operational orientation

The inclusion of other factors (such as context) when making decisions is the basis of the practical-operational orientation, which is now incorporated into EBM. This

orientation is context-based and "defines evidence less by its quality and more by its relevance, applicability, or generalisability to a specific context" (Dobrow et al., 2004, p.209). Therefore, this orientation argues that what constitutes evidence is context-based (Dobrow et al., 2004). It is argued that this perspective is more aligned with decision-making as it focuses on the variety of factors that contribute to an outcome and that evidence alone does not make decisions (Dobrow et al., 2004; Oxman et al., 2009). The focus is not solely on what should constitute evidence, but rather on understanding the relationship between evidence sources and the range of contextual factors that impact decision-making (Figure 2.2) (Dobrow, 2003). This orientation reflects the goal-orientation focus of decision-making, with the means (e.g., the intervention) varying according to the ends (e.g., the goal/outcome).

Tobacco control is an example where context is considered alongside evidence. For example, smoking prevalence might be considered a factor when developing recommendations and policies relating to the use of e-cigarettes as a smoking cessation tool. E-cigarettes could be a tool to help reduce prevalence among those who are unwilling or unable to quit smoking but the relative merit of this approach depends on how common smoking is in that population. The role of contextual factors in decision-making will be explored in more detail in Chapter 8.

2.2.4 Evidence-based policymaking

Following the rise of the EBM movement, there has been an increasing interest in the concept of EBPM (Oliver and Pearce, 2017). As discussed in Section 2.2.2, EBM was derived from clinical practice, whereas EBPM focuses on broader policymaking. The EBPM movement is based on the premise that policy decisions are better informed by available evidence and should include rational analysis (Sutcliffe and Court, 2005).

In public policymaking, evidence can be useful to support a wide range of decisions, for example, from changing the timing of traffic lights to decisions about going to war (Parkhurst, 2017). Although EBPM has been more recently widely considered and discussed, there is nothing new in the use of evidence to inform decisions (De Marchi et al., 2016). During the Second World War, science and policy began to be studied within the same framework; when it was considered conceivable to use scientific methods in order to advance policymaking (De Marchi et al., 2016).

2.2.4.1 Evidence-based policymaking in the UK

The resurgence of EBPM in the UK is attributed to the election of the Labour Party in 1997 (Wells, 2007; Andrews, 2017). To organise and promote this, they published the Modernising Government White Paper (1999) which detailed their changing approach to public policy. One of the changes identified in the document was ensuring that future policies were evidence-based. Another key UK Government text, 'Professional Policy-making for the Twenty-First Century' (1999) argued:

> "This Government's declaration that 'what counts is what works' is the basis for the present heightened interest in the part played by evidence in policymaking. The White Paper makes it clear that policy decisions should be based on sound evidence. The raw ingredient of evidence is information." (p.33)

Legrand (2012) explains that the appeal for 'sound evidence' was strengthened by the Better Policy-Making document published in 2001 (Bullock et al., 2001). This document requested the use of high-quality information and evidence and emphasised that modern policymaking required the "best use of evidence and the need to improve the accessibility of the evidence available to policy-makers" (Bullock et al., 2001, p.25). Following a speech given by David Blunkett, the then UK Education Secretary, in 2000, "What Works and Why" became the UK slogan for EBPM promotion (De Marchi et al., 2016).

2.2.4.2 Evidence-based policymaking in Australia and USA

The EBPM movement expanded its impact in other English-speaking countries, including Australia and the United States of America (USA) (De Marchi et al., 2016). According to Banks (2009), there are many Australian examples of policy reform that have been directed and supported by EBPM. This includes the reduction of tariffs on imports, the Higher Education Contribution Scheme, lifetime community rating on private health insurance, and national competition policy (Banks, 2009). A pivotal moment in terms of EBM in Australia was the establishment of the National Institute of Clinical Studies (NICS) in 2000. The aim of NICS was to encourage continuous improvement in clinical practice, by bridging the gap between researching findings and daily practice (National Institute of Clinical Studies, 2002). In 2007, the NICS was incorporated into the NHMRC. The purpose of this merger was to reinforce the conversion of research findings into

improvements to health care practice (National Health and Medical Research Council, 2006).

In the USA, the most symbolic event was the formation of the U.S. Coalition for Evidence-Based Policy in 2001 (Baron, 2018). The aim of this coalition was to advance the development and use of rigorous evidence in evidence-based policy (Baron, 2018). The types of rigorous evidence the coalition encourages, consist of RCTs to determine effectiveness based on evidence-based approaches that "have produced extraordinary advances in human health" (U.S. Coalition for Evidence Based Policy, 2002, p.7). The U.S. Coalition for Evidence Based Policy (2002) argues that "policy is often implemented in the absence of adequately rigorous and compelling research" (p.2).

2.2.4.3 What constitutes evidence?

Scientists and policymakers face many common challenges, most prominently constraints on their time. Any attempt by scientists "to collect and communicate evidence to policymakers involves distorting that evidence through simplification" (Botterill and Hindmoor, 2012, p.368). Cairney (2016) explains that these limitations are disguised by scientific consensus. A scientific consensus can be useful and effective in certain situations where the evidence is clear (e.g., the health effects associated with smoking) (Cairney, 2016). However, it is harder to develop a consensus on highly debated issues such as health inequalities, where a singular cause is difficult to identify (Cairney, 2016).

Occasionally, EBPM appears to be supported by policymakers in the same way as scientists. It has been reported that some governments, including in the UK, privilege certain types of evidence when providing funding for academic or scientific centres, to determine 'what works' (Boaz et al., 2008; Cairney, 2016). However, policymakers and scientists may not interpret the evidence in the same way (Botterill and Hindmoor, 2012). Policymakers often associate the word research with analysis or investigations and evidence is comprised of raw data and advice from experts (Lomas and Brown, 2009), whereas scientists associate the word evidence with research (Lomas and Brown, 2009). The nature of the policymaking process may require decisions to be made quickly. Policymakers' demand for information can sometimes be erratic and they often find it difficult to devote time to fully understand the evidence, nonetheless, they still make decisions (Cairney, 2016).

2.2.4.4 Criticisms of evidence-based policymaking

Greenhalgh and Russel (2009) detail several limitations of EBPM. They argue that EBPM makes numerous assumptions, including that the moral and ethical issues encountered by policymakers can be reduced to questions of 'best evidence'. Another assumption made is that the majority of policy questions will be answered if enough empirical research is conducted (Greenhalgh and Russell, 2009). In terms of practicality, EBPM presumes that reliable and complete evidence will clarify the best-suited solution (Greenhalgh and Russell, 2009).

Other criticisms of EBPM relate to the criteria used to evaluate evidence. Critics are concerned that advocates of evidence have a narrow view of what 'counts' as evidence (Cooper et al., 2009). Thus, certain types of evidence will be used to replace professional judgement and experience (Cooper et al., 2009). The selection of the 'right' evidence is a restricted view of what counts as valid knowledge. In choosing what is considered valid knowledge for policies, policymakers subtly alter their interpretation of reality (De Marchi et al., 2016). There are numerous interpretations the same evidence may carry and it is possible that multiple stakeholders will interpret the same evidence differently (De Marchi et al., 2016; Turner et al., 2017; Brownson et al., 2018).

Policymaking is not a process where evidence is applied to solve pre-existing problems that are awaiting solutions (Greenhalgh and Russell, 2009). It is in fact about defining what problems should be addressed, via deliberation and negotiation and using judgements to make the correct choice relating to the situation while being faced with persistent uncertainty (Lindblom, 1959). Social scientists have explained that there can be many ways to conceptualise evidence use other than simply the direct uptake or implementation of findings from a particular research study. Much writing on this subject refers to the work conducted by Carol Weiss, who in the 1970s classified seven distinct models of 'research utilisation'; these are summarised in Section 2.3.4.1.

2.3 Evidence into public health policies and recommendations

Prior to the EBM movement, policies and recommendations were primarily based on the consensus of experts. Experts would often make recommendations based on what they used in their practice and evidence they could easily remember or identify (Murad,

2017). Since the emergence of EBPM, there has been an increasing interest in pursuing evidence-based public health recommendations and more rigorous approaches to policy development have been sought (Norris et al., 2011; Parkhurst, 2017), though it is not always clear these have been adopted (Katikireddi et al., 2011). This section will start by discussing the purpose of public health policies and recommendations, followed by examining the role of evidence and its incorporation into public health policies and recommendations.

2.3.1 Public health recommendations

Public health recommendation documents can be characterised as documents that contain recommendation(s) for practice, public health, or health policy (Eccles et al., 2012). It is generally agreed that the process for developing public health recommendations should be transparent and lead to impartial decisions that improve health, based on the best available evidence (Woolf et al., 2012). According to EBPM advocates, recommendations should be based on, firstly, evidence-based research through SRs and secondly, a rational and scientific approach to the problems and their solutions (Kaiser and Miksch, 2009; Norris et al., 2011; Fink, 2013). However, evidence can be contested, limited, or rapidly developing, meaning the development of recommendations is not always straightforward (Grol, 2001; Burgers and van Everdingen, 2004; Raine et al., 2004; Kavookjian and Mamidi, 2008). One example of this is e-cigarettes - the case study for this thesis, which is discussed further in Chapter 3. There are numerous tools available for critically appraising and grading scientific literature and these will be discussed in the next two sections.

2.3.2 The role of evidence synthesis in the development of public health recommendations

Around the world, there is growing interest in ensuring that public health policies, guidelines, and recommendations are informed by the best available research evidence (World Health Organisation, 2012a). Evidence synthesis can be defined as “the contextualisation and integration of evidence on a particular topic including the findings of individual research studies” (Langlois et al., 2018, p.2). Syntheses can take the form of a SR and may collate and integrate qualitative and/or quantitative data (Langlois et al., 2018). Evidence syntheses involve the identification of all relevant studies, critical appraisal of their quality and synthesising the results using a transparent and reproducible process (Lavis et al., 2005; Akobeng, 2005; Langlois et al., 2018). Thus,

results of evidence syntheses are considered more reliable than results from a single study (Glenton et al., 2013).

Public health researchers and policymakers are interested in reviews of the effectiveness of public health recommendations, but they also require evidence on stakeholders' perceptions and views of policy options (Tricco et al., 2016; Langlois et al., 2018). To address this need for a wide array of knowledge and expertise, there is now a broad range of methods available for evidence synthesis to complement the traditional SR. A scoping review involves a mapping of the concepts underpinning a policy or public health issues and the main sources and types of evidence available (Langlois et al., 2018). Narrative reviews provide a qualitative summary of the literature on a topic (Smith et al., 2021a). In contrast, narrative synthesis is part of a larger review process that may include a systematic approach to searching for and quality appraising evidence, as well as the synthesis of this evidence (Popay et al., 2006). A meta-analysis statistically combines the results from multiple studies. In addition, rapid reviews are also being increasingly used to provide evidence to make informed decisions in both routine and emergency situations (Tricco et al., 2017).

Evidence syntheses can be utilised at various stages of the development of public health recommendations. They can be used, for example, to highlight policy and/or public health problems, to offer evidence about the implementation and impacts of policy options and to consider the diversity in populations and contexts (Oliver et al., 2015; Langlois et al., 2018). Synthesis and research evidence is only one part of the decision-making process and numerous other factors (such as contextual factors, financial constraints, pressure from stakeholders, and public opinions) influence public health recommendations (Lavis et al., 2005).

2.3.2.1 Infrastructures for synthesising evidence

Synthesis of research through SRs, particularly RCTs, has been central to EBM, EBPM, and health promotion and practice (Evidence-Based Medicine Working Group, 1992; McMichael et al., 2005). A wealth of knowledge has been accumulated by making use of the principles of systematic searching and appraisal of the literature, as illustrated by the Cochrane Library. The SRs in the Library aim to minimise bias through the use of transparent methods (ideally with a publicly available protocol), exhaustive searches of the available literature on a narrowly defined question and privileging studies with the greatest internal validity in the synthesis process (Higgins et al., 2022). In circumstances where included studies are highly comparable, this approach allows a combination of

outcomes across studies through statistical meta-analysis (Greenhalgh and Russell, 2006; Deeks et al., 2020; Smith et al., 2021a). The benefits associated with this approach are widely recognised within the medical and public health literature (McMichael et al., 2005).

The availability of high-quality evidence, in particular SRs, has facilitated the production of evidence-based guidelines to assist clinicians to provide high-quality medical care (Guyatt et al., 2008a; Hill et al., 2011). Within the UK, organisations such as NICE in England and the Scottish Intercollegiate Guidelines Network (SIGN) have adopted SR methods to determine the most effective treatments and methods to determine if such treatments are cost-effective (Scottish Intercollegiate Guidelines Network, 2019; National Institute for Health and Care Excellence, 2022).

2.3.3 Assessing evidence for the development of public health recommendations

Decision-making processes and the factors (criteria) that decision-makers need to consider vary for different types of decisions, including clinical recommendations and public health recommendations or decisions (Burford et al., 2012). The quality of the evidence is an important factor in the decision-making process and knowledge translation. Some standardised methods for assessing the quality of evidence have been developed (Djulbegovic et al., 2009b) and these are discussed in the next two sections (Sections 2.3.3.1 and 2.3.3.2). However, evidence assessment presents some challenges, for both public health and clinical interventions, including the issue that interventions typically have multiple effects, some intended positive effects but also possibly unintended negative effects (Oliver et al., 2019; Hilton Boon et al., 2021). In addition, there needs to be consideration of how certain we can be about the effects of an intervention based on the available evidence (Murad, 2017). Although evidence synthesis can provide a range of information, by itself, it cannot tell decision-makers what to do (Black, 2001; Department of Planning Monitoring and Evaluation, 2014; Cairney and Oliver, 2017). Furthermore, despite considering cost-effectiveness when synthesising evidence, in public health, costs may extend beyond financial and could include political considerations (e.g., liberty) (Gostin and Gostin, 2009; Hilton Boon et al., 2021).

2.3.3.1 GRADE

Decision-makers have used numerous different systems to determine the certainty (previously referred to as 'quality') of evidence resulting in inconsistency in public health recommendations and guidelines and a lack of transparency in their development (Atkins et al., 2004; Cruz et al., 2015; Murad, 2017). To unite the numerous different systems, the GRADE approach was developed in 2003 (Atkins et al., 2004; Schünemann et al., 2013). GRADE is a standardised and transparent framework for grading the certainty of evidence based on eight domains, rather than on study design alone, and provides a systematic approach for making recommendations in healthcare (Guyatt et al., 2011a; Balshem et al., 2011). It is the most widely adopted tool for grading the certainty of evidence and making recommendations, with numerous organisations worldwide, including the WHO, the Cochrane Collaboration, and NICE, employing this framework (Dijkers, 2013; BMJ Best Practice, 2017).

The GRADE approach has four levels of certainty in evidence: very low, low, moderate, and high (Table 2.1).

GRADE Ranking	**Definition**
High ⨁ ⨁ ⨁ ⨁	High certainty that the effect of the study resembles the actual effect
Moderate ⨁ ⨁ ⨁	Some confidence that the effect of the study will be similar to the true effect. However, there is a possibility that it could be different
Low ⨁ ⨁	Possibly the true effect will be considerably different from the estimated effect
Very low ⨁	The true effect of the study is expected to be entirely different from the pre-determined effect

Table 2.1: GRADE rankings of evidence and corresponding definitions[3]

GRADE details five domains for rating down the certainty of evidence: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Evidence from RCTs

[3] Based on material from GUYATT, G. H., OXMAN, A. D., KUNZ, R., FALCK-YTTER, Y., VIST, G. E., LIBERATI, A. & SCHÜNEMANN, H. J. 2008a. Going from evidence to recommendations. *BMJ,* 336, (7652), 1049-1051, GUYATT, G. H., OXMAN, A. D., VIST, G. E., KUNZ, R., FALCK-YTTER, Y., ALONSO-COELLO, P. & SCHÜNEMANN, H. J. 2008c. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ,* 336, (7650), 924-926.

starts at high certainty and due to the risk of residual confounding, evidence from observational data starts at low quality (Guyatt et al., 2008b; BMJ Best Practice, 2017). Guyatt et al. (2011b) describe the phenomenon of residual confounding as "when unmeasured/unknown determinants of outcome unaccounted for in the adjusted analysis are likely to be distributed unequally between intervention and control groups" (p.1314). There are occasions where the certainty in the evidence can be rated up when assessing evidence from observational studies. First, when there is a large magnitude of effect; second, when higher levels of exposure are associated with larger outcome effects (a dose-response gradient); and third, when residual confounding is likely to decrease rather than increase the magnitude of effect (Guyatt et al., 2008b; BMJ Best Practice, 2017).

Having determined the certainty of the evidence, recommendations and the strength of these are determined. The strength of a recommendation is determined by the balance between desirable (e.g., reduction in mortality and improvement in quality of life) and undesirable effects (e.g., increase in mortality and adverse effects on quality of life), resource use, quality of evidence, and variability in values and preferences (Atkins et al., 2004; Guyatt et al., 2008a; Guyatt et al., 2008c; Andrews et al., 2013; Cruz et al., 2015). Strong recommendations tend to be made when there is confidence that the desirable effects of a recommendation outweigh the undesirable effects (Atkins et al., 2004; Guyatt et al., 2008a; Guyatt et al., 2008c; Andrews et al., 2013; Cruz et al., 2015). Weak recommendations are generally made when the desirable effect most likely outweighs the undesirable effects but are uncertain (Atkins et al., 2004; Guyatt et al., 2008a; Guyatt et al., 2008c; Andrews et al., 2013; Cruz et al., 2015). Cruz (2015) argues that the GRADE system has several advantages over other methods, including guideline development by international experts, differentiation between the certainty and strength of the evidence, and the provision of clear interpretations of recommendations for stakeholders.

GRADE allows for limitations in bodies of evidence from RCTs and also the rating of observational studies as high-quality evidence (Guyatt et al., 2008b), whereas in the hierarchy of evidence this type of evidence sits further down the pyramid. GRADE, therefore, recognises the potential for observational studies to provide conclusive causal evidence, particularly relevant for harmful exposures (Djulbegovic and Guyatt, 2017).

Building on the GRADE approach for assessing the strength of recommendations (Guyatt et al., 2008a; Andrews et al., 2013), the GRADE working group, funded by the DECIDE

(Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence) project (Treweek et al., 2013) developed the Evidence to Decision (EtD) framework (Alonso-Coello et al., 2016b; Alonso-Coello et al., 2016a) to support the process of moving from evidence to recommendations. The main purpose of the EtD framework is to help decision-makers use evidence systematically and transparently to inform decisions (Alonso-Coello et al., 2016b). The EtD framework provides information on criteria that can impact recommendations (e.g., health benefits, harms, certainty in the best available evidence, cost, feasibility), helps decision-makers consider how these criteria may affect the final recommendation structure, and facilitates adaptation of recommendations and decisions to specific countries or jurisdictions (Alonso-Coello et al., 2016b; Schünemann et al., 2017).

2.3.3.2 AGREE II

The AGREE (Appraisal of Guidelines, Research and Evaluation) Collaboration wanted to develop a standardised method for grading guidelines (i.e., the process for assessing how transparent and useful the approach through which guidelines were being developed) and in 2003, the AGREE tool was published. The AGREE tool was replaced by AGREE II in 2010 and in 2013 the latter was updated to improve reliability, viability and usability (Cruz et al., 2015). The AGREE II tool has 23 items grouped into six domains (scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence) which are used to quantify the rating of a guideline (Brouwers et al., 2010; Cruz et al., 2015). Each of the 23 items is assessed on a seven-point Likert scale from one (strongly disagree - absence of information) to seven (strongly agree - guideline meets all conditions) (Brouwers et al., 2010; Cruz et al., 2015).

As discussed above, GRADE focuses on the grading of evidence, whereas AGREE II is drawn upon when grading guidelines. Both are important to discuss and relevant to the focus of this thesis.

2.3.4 Evidence utilisation

So far, this chapter has examined the key aspects of the literature on EBM and EBPM. To understand the relationship between evidence and the decision-making process, it is worth examining the different influences evidence may have on the process. The next subsection discusses models of research and knowledge utilisation (i.e., how evidence is used).

The research and knowledge utilisation literature are often used and cited interchangeably, but there is one important difference. Research utilisation focuses on the use of scientifically produced research, whereas knowledge utilisation is broader in scope and includes a range of other sources of data and information (Dobrow, 2003). This distinction is important, especially within my research, as it marks a progression from a narrow focus on the utilisation of scientific research, to a broader focus on the utilisation of knowledge, to an unrestricted focus on the utilisation of scientifically and non-scientifically produced information and knowledge in the support or, to justify a decision (Dobrow, 2003).

The definition of 'utilisation' has been subject to debate. Weiss (1979) has questioned what 'using research' actually means, stating that:

> "Much of the ambiguity in the discussion of 'research utilisation'- the conflicting interpretation of its prevalence and the routes by which it occurs-derives from conceptual confusion." (p.427)

Rich (1997) added that:

> "[…] it is essential that one be certain of what is meant by use and that the concept can be operationalised in a fashion which realistically provides a basis for evaluation, accountability and oversight." (p.12)

Social scientists are becoming more concerned about making their research useful for decision-makers (Smith, 2013a; Boswell and Smith, 2017), fostered by recent incentives within funding mechanisms. Weiss (1979) explains that there is an interest in whether social science research intended to influence public policy is actually 'used'. To understand the extent to which social science research has influenced public policy previously and learn how to make its contribution more valuable in the future, the concept of 'research utilisation' needs to be clarified (Weiss, 1979). The following section will explore the different influences evidence may have on the decision-making process.

2.3.4.1 Models of research utilisation

The work of Weiss has been particularly influential and provides a helpful framework for understanding the different ways evidence can influence the decision-making process (Table 2.2).

Model of evidence use	Explanation
Knowledge-driven	Regarded as one of the simplest ways of thinking about the connection between research and policy, this represents a direct, linear connection in which policy relevant research drives policy changes (for example, the development of the contraceptive pill)
Problem-solving	Decision-makers face a problem and draw upon evidence either by generating research or by drawing upon existing research to help solve that problem
Interactive	A back-and-forth dialogue occurs between those engaged in decision-making and a mixture of sources, including journalists, interest groups, academic researchers, administrators, and practitioners
Political	Research is drawn upon by those involved in the decision-making process to strengthen and support their existing position
Tactical	Decision-makers use research, not for its findings but typically, to demonstrate something is being done or to delay difficult decisions
Enlightenment	Research diffuses through various channels including mass media, conversations or articles, and shapes the way decision-makers think about an issue

Table 2.2: Different models for the utilisation of evidence in the decision-making process[4]

Utilisation can be instrumental (e.g., identifiable research/knowledge is used directly in the decision-making process), namely the knowledge-driven and problem-solving model, conceptual (accumulation of research/knowledge over time provides new idea/hypothesis leading to 'enlightenment' and is indirectly used in the decision-making process), or symbolic (research/knowledge is used as justification for tactical or political decisions in the decision-making process (Brownstein, 1978; Weiss, 1979)). The enlightenment model of evidence is thought to be the most important means through which evidence influences decision-making (Brownstein, 1978; Weiss, 1979).

[4] Based on material from WEISS, C. H. 1979. The Many Meanings of Research Utilization. *Public Administration Review,* 39, (5), 426-431.

Rich (1997) developed a framework for knowledge utilisation based on a three-stage approach. Rich (1997) described these stages as: 1) information pick-up, 2) information process, and 3) information application.

> "Information pick-up refers to the process by which information is retrieved or received by a given user." […] "Information process involves understanding the information, testing it for validity and reliability, testing it against one's own intuition and assumptions and transforming the information/data into a form that is useable […]", while "information application involves the decision of whether to use the available information which has been received." (Rich, 1997, p.21)

This framework for thinking about the process suggests that utilisation should be thought of as a series of events, incorporating the idea of stages that correspond to the different stages of the decision-making process (Rich, 1997). The process considers the introduction of research or knowledge into the decision-making process, instead of forcing utilisation to account for the use of research or knowledge through categories such as the previously discussed instrumental and conceptual/symbolic uses (Rich, 1997; Dobrow et al., 2004).

Dobrow et al. (2004) modified Rich's (1997) framework for the impact of the decision-making context on the utilisation of evidence. The three main stages of the process were identified as: the introduction of evidence, interpretation of evidence, and application of evidence. The introduction of evidence stage refers to how evidence is defined and the process by which evidence is brought into the decision-making process (Dobrow et al., 2004). This stage addresses issues relating to the availability and accessibility of evidence (Dobrow et al., 2004; Dobrow et al., 2006). Dobrow et al. (2004) argue that "the introduction of evidence is based on both the perceived conception of evidence and the operationalisation of that conception of evidence, subject to both internal and external contextual factors" (p.213). At the interpretation of evidence stage, evidence that has been introduced into the decision-making process is synthesised, evaluated and assessed on its quality and generalisability. Interpretation of evidence involves considering the validity and reliability of evidence (e.g., quality) and its applicability and relevance to a particular decision (e.g., generalisability) (Dobrow et al., 2004; Dobrow et al., 2006). The final stage of the process is the application of evidence. This is where evidence that has been introduced and interpreted is applied to support or justify a decision and recommendations are made. While at the interpretation stage individual sources of evidence are evaluated and

assessed, at the application stage collective sources of evidence are weighed and prioritised.

Although this framework addresses the different stages of evidence-based decision-making, it assumes a linear process. The stages in the framework do not always occur consecutively so the aforementioned stages may occur out of sequence as it is possible that evidence may be drawn upon to justify a policy position (e.g., moving from introduction to application) (Howlett et al., 2009; Howlett and Giest, 2015). Furthermore, policymakers are typically limited in their ability to implement the decisions they make, so a policy that is enacted is often altered by those responsible for its implementation (Lipsky, 2010). Despite these limitations, the framework presents a helpful way to explain the decision-making process.

2.3.5 The role of context in the development of public health recommendations

Evidence and context are two fundamental components of evidence-based decision-making (Dobrow et al., 2004). Having previously discussed the role and use of evidence in decision-making, this section of the thesis will address the role of context in decision-making. Context can be broadly defined as all the factors outside the decision-making process itself (such as political and social and scientific factors) that influence decision-making (Dobrow et al., 2004; Mirzoev et al., 2017). Plsek and Greenhalgh (2001) argue that the decision-making context is characterised by its complexity and comprises both the known and unknown and the certain and uncertain. It is not possible to fully account for all contextual factors that might have some potential influence or impact on a decision.

There are a variety of different frameworks and perspectives on what constitutes context in decision-making (Evans, 2001; Dobrow et al., 2004; Hudson and Lowe, 2009; Ricketts, 2010). One framework suggests a three-tier distinction between macro, meso, and micro levels of context and has been used in various policy analyses (e.g., Evans, 2001; Hudson and Lowe, 2009; Ricketts, 2010). There are similar interpretations of what defines macro-level (system-wide culture, politics, and system characteristics) and micro-level (individual attitudes, behaviours, and relationships). However, there have been differences in how the meso-level is interpreted. Ricketts (2010) interpreted it as organisations or policy actors, Evans (2001) as wider networks, and Hudson and Lowe (2009) as policy processes.

Another perspective was proposed by Pye and Pettigrew (2005) who distinguish between inner and outer context:

> "Inner context refers to factors from within the organisation e.g., structure, culture, power, and political characteristics; and outer, to factors external to the organisation such as industry sector, economic, political, and social context. This is a handy simplification, although may not be so easy to identify in practice, as these boundaries are sometimes permeable." (p.31)

Frameworks such as that of Bate et al. (2008) add to the category of inner contextual factors such as size, scale, and complexity of the organisational unit, degree of organisational stability, and prior financial and service performance. To the outer context, they add factors such as regulatory environment and market forces (Bate et al., 2008). However, settling on a definitive categorisation is problematic given that, as Squires et al. (2015) note "no one framework is sufficiently inclusive or comprehensive about what comprises context." (p.137)

Similarly, Dobrow et al. (2004) distinguish between internal and external contextual influences. The internal context refers to the environment in which a decision is made and includes factors related to the purpose of the decision-making activity, the role of participants, and the processes used to arrive at decisions (Dobrow et al., 2004). Several scholars argue that participants play a key role in what is considered evidence and how evidence is interpreted and applied (Champagne, 1999). Dobrow et al. (2004) argue that the most crucial internal contextual factor is related to the process of decision-making. The process includes purpose (the 'why'), participants (the 'who'), but fundamentally the structures and mechanisms of 'how' decisions are made (Dobrow et al., 2004). The external context accounts for the environment in which a decision is applied and includes epidemiological features of the health issue being addressed, extrajudicial factors (e.g., experiences in other jurisdictions that may help inform decision-making), and political factors (e.g., ideological, social, and economic issues) (Dobrow et al., 2004). Both internal and external contextual factors impact how evidence is weighed and how that evidence is utilised (Dobrow et al., 2004; Dobrow et al., 2006).

Even when there is general agreement on what constitutes evidence, the literature suggests that the same evidence when used in different decision-making contexts often leads to different decision outcomes (Lipskie, 1998; Walls et al., 2017). Based on my review of the various frameworks and perspectives as to how context is defined and how

it is addressed during decision-making, Dobrow et al.'s (2004) conceptual framework was particularly useful for my investigation of the decision-making process. Firstly, the three-stage approach allows for an examination of the various stages of the process individually (introduction, interpretation, and application), while also being able to examine the process as a whole. Secondly, due to the differentiation between internal and external contextual factors. They were not presented as having strict 'boundaries' compared to the three-tiered approach (macro, meso, and micro approach), where the factors are pre-defined. Finally, contextual factors were considered throughout the evidence utilisation not only at the application stage, which is where it is only considered in other frameworks. The importance of contextual factors in decision-making is explored in more detail in Chapter 8.

2.3.5.1 Applicability of public health interventions

It is challenging to determine whether a public health intervention is suitable for other settings. There has been an increasing interest in the generalisability (i.e., to which unspecified settings a study's findings could be generalised) and applicability (i.e., the likelihood that an intervention could be applied to a new, specific setting) of public health interventions. Researchers and decision-makers have argued that there is a lack of guidance on generalisability and applicability, with many noting insufficient information for the assessment of these in existing frameworks. Several statements (including CONSORT (Des Jarlais et al., 2004), TREND (Moher et al., 2001), and STROBE (Vandenbroucke et al., 2007)) have been developed to assist in the reporting of randomised trials and observational studies. However, these statements have received criticism for not reporting on contextual information (Dzewaltowski et al., 2004; Glasgow et al., 2006). Burchett et al. (2013) argued that there is a lack of guidance on how to assess whether findings from primary studies or SRs are generalisable to another setting. A number of frameworks have been proposed (such as Young and Borland, 2011; Burford et al., 2013; Cambon et al., 2013; Khorsan and Crawford, 2014; Munthe-Kaas et al., 2020; Moore et al., 2021) which offer as a starting point. However, there still appears to be a lack of consensus on the most appropriate method for assessing the applicability of public health interventions to other settings (Cambon et al., 2012; Cambon et al., 2013; Burchett et al., 2018; Moore et al., 2021).

2.3.6 Theories of policymaking

A wide variety of theories exist to explain the policy process and despite their diversity, none appear to be wholly satisfactory to describe the policy process. Many theories

highlight different sections of the policy process, therefore, it can be advantageous to draw on various theories to understand the policy process (Sabatier, 2007). This section will review some of the policy theories employed in the policy process that are of relevance to this thesis and help in our understanding of the relationship between evidence and public health policy.

2.3.6.1 Power and public policy

Prior to addressing any policy theories, the operation and place of power should be discussed. Policy theory is about the relationship between power and ideas. Dahl's (1957) view of power as 'one dimension' where an actor exerts power over another to act in a way that they would otherwise not, has been portrayed as incomplete. Bacharach and Baratz (1962) claimed that power is not simply about visible conflicts, it is also exercised covertly by keeping certain issues on the political agenda at the expense of letting others become dormant. Key issues on the political agenda may be regarded as 'safe', therefore, debates on these issues will receive policy attention. Hence, Bacharach and Baratz (1962) view power as two dimensional; decision-making (overt) and no decision-making (covert).

Lukes (2005) states that the two-dimensional view proposed by Bacharach and Baratz (1962) represents a major advance over the one-dimensional view. It incorporates the control over the agenda of politics and the ways in which potential issues are concealed from the political process. Lukes (2005) stated that we need to think of power broadly rather than narrowly – in three dimensions rather than two. Lukes (2005) adds a third dimension; the exercise of power that shapes people's preferences so that they are not aware of their own interests.

However, the third dimension of power has been critiqued as it suggests that 'true' interests (which are not determined by the individuals themselves) can be identified (Hay, 2002). Hay (2002) proposes that there are two uses of power: 'conduct shaping' (individuals' actions are directly influenced) and 'context shaping' (power structures are visible in institutions and organisations which structure human actions).

While acknowledging the importance of power in the policy process, this thesis seeks to understand the relationship between evidence (which can itself be viewed as an instrument of power (Armstrong, 1995)) and public health policy.

2.3.6.2 Institutions and institutionalism

In the past, the term institution may have referred to reputable organisations such as legislature, courts, and executives (Judge, 2005; Farrell, 2018). Now, it describes the formal and informal rules that guide action (Cairney, 2019a). Institutions are not just the buildings within which people compose policy - they are also the rules of performance that influence how they make policy (Cairney, 2019a). 'Institutionalism' is the term used to describe this focus on rules rather than the physical structure.

Historical institutionalism treats institutions as the formal rules and standard operating procedures (SOPs) that structure conflict or in other words structure and shape behaviour and outcomes (Farrell, 2018; Cairney, 2019a). A key term is 'path dependence' which can be described as when a commitment has been made to a particular institution and resources have been devoted to it and in turn, it will produce 'a return' over time (Pierson, 1993; Pierson, 2000). Therefore, it becomes increasingly difficult to reverse past institutional choices, because not following the rules and standards established by previous choices would not be effective and would become costly (Pierson, 1993; Pierson, 2000; Cairney, 2019a). A classic example of this is the QWERTY keyboard; it can only be understood by studying the development of the typewriter (David, 1985). Historical institutionalism is therefore neither a particular theory nor a specific method, it is best understood as an approach to studying policy (Steinmo, 2008).

In contrast, rational choice institutionalism seeks to model the policy process by addressing what proportions of political outcomes one can explain with reference to the choice of individuals pursuing their preferences under particular conditions (Hall and Taylor, 1996; Fioretos et al., 2016; Farrell, 2018). Preferences provide the motivations for individual action; however, the context within which they operate must also be considered. Cairney (2019a) explains that individuals know that actions have consequences in different contexts and this influences how they pursue their preferences. They act based on what they anticipate to happen and institutions often provide this. Institutionalism has been described as overly deterministic, it can explain stability, but is poor at explaining change and it cannot describe how and why institutions develop in the first place (Hall and Taylor, 1996; Fioretos et al., 2016; Farrell, 2018; Cairney, 2019a).

2.3.6.3 Multi-level governance

Multi-level governance is not regarded as a theory *per se* but draws attention to the ongoing changes in institutional capabilities (Hooghe and Marks, 2001; Bache and Flinders, 2004; Cairney, 2016; Cairney, 2019b). It can be described as the dispersion of power from national central government to other levels of government (hence multi-level) and non-governmental actors (hence governance rather than government) (Hooghe and Marks, 2001; Cairney, 2016; Cairney, 2019b). For example, the multi-level nature is illustrated by policies in Scotland being affected by the Scottish Government, UK Government, European Union (EU) and WHO. In addition, there is a diffusion of power from government to broader institutions of governance: quasi-autonomous non-governmental organisations (quangos), arms-length independent regulators, and private sector actors, amongst others (Rhodes, 1994). It is not only those who are formally delegated responsibilities that influence the complex world of governance; non-governmental interest groups (such as businesses, lobbyists, charities, and think tanks) that attempt to influence policymaking are included (Stoker, 1998; Hill, 2014). Two types of multi-level governance were identified by Hooghe and Marks (2003): 'type 1' is derived from federalism where there is a relatively clear separation of powers by territory - local, regional, national, global; and 'type 2' is comprised of an array of special purpose jurisdictions that accomplish specific tasks involving a wide range of organisations across various levels of government and the public and private sectors. From the 'type 1' approach, nation states retain the central role in defining collective goals. Nevertheless, local governments and non-state actors are viewed as having varying degrees of agency and the ability to influence policymaking. For example, regional levels of governance may be able to bypass the decision-making processes at the national level by defining problems in local terms, or, they might make effective coalitions at the global level, again avoiding the national level. However, these levels of governance remain dependent on national level governance, since it is the governmental frameworks that create the opportunities to bypass the national level, either by localising or globalising decisions (Bulkeley and Betsill, 2005).

Multi-level governance helps us describe policymaking in unitary and centralised systems such as the UK. The Westminster Model has been a traditional organising perspective for the study of the UK Government (Bache and Flinders, 2004; Cairney, 2019b). The Westminster Model suggests a centralised state in which there are clear lines of accountability and hierarchical control, whereas multi-level governance suggests a divided state in which control is replaced by influence within a political system with various lines of accountability (Bache and Flinders, 2004). It described not

only how the government was thought to work, but how it should work (Bache and Flinders, 2004). During the 20th Century, various problems arose relating to the Westminster Model, including its narrow conception of politics and domestic focus (Bache and Flinders, 2004). The influence of American and European political studies in the 1980s and 1990s presented new approaches and techniques that could be employed (Bache and Flinders, 2004). Political events such as the economic crisis of the 1970s also weakened the validity of the Westminster Model. Now, the Westminster Model has limited relevance as it does not help understand the inter-woven boundaries and institutional framework of the UK Government (Bache and Flinders, 2004). Cairney (2019b) argues that "multi-level governance, therefore, provides us with a new set of dictums when exploring policymaking." (p.6)

A value of multi-level governance is that power does not lie with one governmental authority, instead, it disperses vertically (across multiple levels of government) and horizontally (to a broad range of both state and non-state actors), suggesting multi-level relationships (Cairney, 2019b). Consequently, it is difficult to identify who has the power to make decisions and also who has the authority to do so (Bache and Flinders, 2004). As it is not clear who has authority, this has led to confusion amongst decision-makers. Hajer (2003) argues that the emergence of multi-level governance has resulted in policymaking now taking place in an 'institutional void', where the rules and norms by which politics is conducted and policy measures are agreed on are not apparent.

2.3.6.4 Policy transfer

Policy transfer describes the transfer of policy solutions or ideas from one setting to another (Evans, 2009). Various terms such as 'policy learning' (May, 1992), 'policy diffusion' (Majone, 1991), and 'policy convergence' (Bennett, 1991) have been identified in the literature, and transfer is an umbrella term (Evans, 2009; Cairney, 2019c). The actors involved in the policy transfer process are usually those involved in the policymaking process, such as civil servants, elected officials, and political parties (Dolowitz and Marsh, 1996; McCann and Ward, 2012). Cairney (2019c) states policy transfer often occurs as a result of pressure from other countries either directly (via coercion) or indirectly (by inspiring other countries to follow).

According to McCann and Ward (2012), multi-level governance studies indicate that international import and export of policies can take place at the local and regional levels. Hooghe and Marks (2003) add that multi-level governance may result in more

originality in policies as regions can compete with each other and have the opportunity to test new ideas.

There are typically three types of transfer. The first type is referred to as an action-orientation approach and occurs when there are dissatisfactions with a current policy and policymakers look elsewhere to see how the issues have been addressed, or policymakers look elsewhere for evidence to legitimise and support their existing policies (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009). The second type is direct coercion and this occurs when an organisation, nation, or supernational government directly coerces another government to adopt a policy; however, it has been argued that this is a rare occurrence (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009). The third type is indirect coercion which refers to the voluntary transfer of a policy and occurs when the importing country recognises the need to change (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009).

Policy transfer can range from the long-term decision to completely duplicate the substantive aims and institutions associated with a major policy change to pursuing a vague idea (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009).

For a policy to be successful, the importing country/government should study the exporting policy and contextual factors (such as social, economic, and political factors) (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009; Cairney, 2019c). This allows the importing country to understand if the policy worked as intended, why the policy was successful and if these successes are transferable (Dolowitz and Marsh, 1996; Dolowitz and Marsh, 2000; Evans, 2009). Cairney (2019c) argues that policy transfer may be evidence-informed; however, evidence alone is not the deciding factor in policy transfer.

2.3.6.5 A summary of theories of the policy process

This chapter section has described several influential theories of the policy process. Institutionalism focuses analysis on the role of the institution in influencing the actions of actors; however, it does not explain how and why institutions develop in the first place. Multi-level governance suggests there is a move from government to governance and increasing layers of governmental institutions, yet does not explain the policy process in itself. Policy transfer describes the importation and exportation of policies from one context to another. However, some have argued that pre-existing evidence alone does not determine the success of policies in other settings. These theories

illustrate several important aspects of the policy process, such as the rules that guide decision-making, the distribution of power across government levels, and why certain regulatory approaches may or may not be transferred to another setting. Therefore, in combination, they will assist when trying to understand the development of e-cigarette policies and recommendations.

2.4 Chapter summary

This chapter has provided an overview of the key literature underpinning this thesis by setting out the importance of evidence and examining a range of perspectives of what constitutes evidence. A separate disciplinary perspective provided by the influential EBM movement was then introduced. Key debates about EBPM, evidence-based public health policies and recommendations have been summarised, concluding that evidence and context are two central components of evidence-based decision-making. Lastly, the literature exploring the relationship between evidence and public health policy, mainly originating in the fields of social science and political science, was provided. An improved understanding of the relationship between evidence and public health policy could help in the development of a more responsive evidence base by researchers, plus improved methods to develop and harness evidence to improve policy and ultimately public health.

The following chapter examines tobacco control, the emergence of e-cigarettes and identifies gaps in this literature, highlighting the importance of alleviating such gaps.

3 Introduction to e-cigarettes as a case study

3.1 Overview

This chapter starts with a discussion of tobacco control and how evidence has influenced the development of international tobacco control policies. The chapter then explores the development and emergence of e-cigarettes – the case study for this inquiry. Next, the arguments and evidence used in the e-cigarette regulatory debates are examined. Following on from this, the role of commercial influences, particularly tobacco industry influences and COI in e-cigarette decision-making will be explored, before a discussion on the international and UK policies surrounding tobacco control and e-cigarette regulation. The chapter ends by highlighting the gaps in evidence and presents the research questions guiding this study.

3.2 Tobacco control

Tobacco control is an area of public health that is devoted to reducing the morbidity and mortality associated with tobacco use. The tobacco control community (including inter alia, public health researchers, clinicians, and decision-makers) has worked together to reduce tobacco use and has been successful in supporting the implementation of various policies and frameworks. However, the coherence of the tobacco control community has been challenged by the development of alternative nicotine products. This section will examine tobacco harm reduction and the influence of evidence on tobacco control policies, before moving on to discuss the emergence of e-cigarettes.

3.2.1 Tobacco harm reduction

Warnings about tobacco can be traced back to 1616 in King James I and VI's anti-smoking tract. King James I and VI argued that smoking is "harmefull to the braine and dangerous to the lungs" (Milne, 2011, p.89). It was in the 1950s that tobacco warning efforts came to prominence when scientific research proved there to be a relation between smoking and lung cancer (Doll, 2010). The publication of the Smoking and Health report by the Royal College of Physicians of London in 1962 and the U.S. Surgeon General Report in 1964 also documented the association between smoking and lung cancer (Royal College of Physicians, 1962; U.S. Department of Health Education and

Welfare, 1964). Consequently, there were tobacco harm reduction efforts, through which smokers were advised to switch from smoking cigarettes to smoking less harmful products, which, at the time included pipes and cigars (U.S. Department of Health and Human Services, 2014). Following the demonstration of the association between smoking and lung cancer in the 1950s and 1960s, tobacco companies introduced new types of cigarette products into the market, including 'light', 'filtered', and 'low tar' cigarettes (Pollay and Dewhirst, 2002; Fairchild and Colgrove, 2004). This approach was supported at the time by Professor Michael Russell, who argued that altering the ratio of tobacco to nicotine in cigarettes could be the route to safer smoking, specifically a low tar, medium-nicotine cigarette (Russell, 1976). However, research found that switching from traditional cigarettes to light or low tar cigarettes did not reduce the harm associated with smoking (National Cancer Institute, 2001; Gan et al., 2010). This was attributed to 'compensating behaviours', where smokers take deeper puffs when smoking or smoke more (Evans and Farrelly, 1998).

Over the last several decades, various other products have been introduced onto the market, most notably e-cigarettes. The introduction of e-cigarettes and their rapid emergence into the market will be discussed in Section 3.3.

3.2.2 Influence of evidence on tobacco control policies

As mentioned in Section 3.2.1, the health effects associated with smoking emerged in the 1950s and 1960s (Doll, 2010; Berridge, 2006; Berridge, 2007). By the 1990s, passive or environmental smoke was also found to have carcinogenic properties (Scientific Committee on Tobacco and Health, 1998). Since the development of the WHO Framework Convention on Tobacco Control (FCTC) (see Section 3.6.1 for more details), there have been a series of public policy efforts to reduce tobacco use and the harms associated with second-hand smoking (Smith, 2013a), for example, the introduction of the Smoking, Health and Social Care (Scotland) Act in 2006 (Scottish Parliament, 2016). In 2012, the UK was recognised as having the most advanced tobacco-control policies of all European countries, including product display restrictions (Cairney, 2007; Smith, 2013a). In 2016, the EU Tobacco Products Directive (TPD) was implemented, which placed further restrictions on tobacco products including the introduction of plain packaging. See Section 3.6.2 for more details on the EU TPD.

Other public health areas including alcohol and food have cited tobacco control as an example from which they can learn (Douglas et al., 2011). Tobacco-related research may be understood as a unique example of a 'knowledge-driven model' of the

relationship between research and policy: knowledge (originated from scientific research) helped to identify a noteworthy problem (the health harms caused by tobacco, first to active smokers and second to passive smokers) and assisted policymakers to decide how to respond (Smith, 2013b).

More recent tobacco-related research might be understood as an example of the 'problem-solving model', as researchers increase their focus on assessing which policy interventions are likely to be the more effective in reducing tobacco-related harms (Smith, 2013a). Larsen (2008) identifies a flaw with this framing: the failure to account for the significant delay between the recognition of the health effects associated with both active and passive smoking and the subsequent policy interventions introduced to prevent these effects. Caplan (1979) offers one possible explanation for understanding why there was a delay - there is a cultural and institutional divide. This divide separates researchers and policymakers, thus restricting the accessibility of evidence within policy (Caplan, 1979). However, focusing on differences between 'policymakers' and 'researchers' does not appear to help explain the delayed policy response to research relating to the damaging effects of tobacco as it side-lines the role of policymakers' values and judgements (Cairney, 2007). It also obscures the possible important role of actors who cannot be categorised as 'researchers' or 'policymakers' (e.g., journalists, corporate lobbyists, health advocacy groups, and government researchers) (Killoran and Kelly, 2010; Smith, 2013b).

The linear conception of the relationship between evidence and public health policy in the 'tobacco wars' does not differentiate between the numerous different types of evidence that can influence a policy change (Smith, 2013b). It is only recently that a substantial amount of the evidence required to achieve 'evidence-based' policies has emerged; however, gaps in the evidence base remain (Killoran and Kelly, 2010; Smith, 2013b). Furthermore, Chapman (2008) argues that the advances in tobacco control, including the ban on smoking in public places, went beyond the available evidence, although evidence supporting these policies did materialise.

Evidence has played an important role in advocating for tobacco control policies. However, it appears difficult to conclude that this situation represents an example of a rational, linear relationship between evidence and public health policy. Smith (2013b) argues that such linear descriptions are not only inaccurate but that commitments informed by such approaches can be used to restrict policy innovation.

3.3 Emergence of e-cigarettes

3.3.1 E-cigarettes: a new product

The tobacco control community has previously been unified regarding reducing smoking prevalence. However, the introduction of electronic nicotine delivery products (ENDS) to the market has resulted in the polarisation of many public health debates. ENDS is an umbrella term and numerous different products fall under this category: vapes, vaporizers, vape pens, e-cigarettes, and e-pipes. E-cigarettes are the most generic form of ENDS. In the 1960s, a patent was registered by Herbert A. Gilbert for the first "smokeless nontobacco cigarette" (U.S. Department of Health and Human Services, 2016). In 2003, 40 years later, Chinese pharmacist, Hon Lik developed the current form of the e-cigarette (Rom et al., 2014). An e-cigarette is comprised of a battery; a cartridge that stores propylene glycol and/or vegetable glycerine; nicotine and flavouring(s); and an atomiser or heating elements necessary to heat the e-liquid to create a vapour that can be inhaled through a mouthpiece and expelled similarly to tobacco cigarette smoke (Drope et al., 2017; Marques et al., 2021).

Since the development of the first e-cigarettes in 2003, there are now a variety of models or 'generations' available. First-generation e-cigarettes (sometimes referred to as 'cigalikes') were designed to mimic the look and feel of combustible cigarettes (Williams and Talbot, 2019). They are not rechargeable or refillable. Second-generation e-cigarettes are larger and are generally refillable using e-liquids (Grana et al., 2014). E-liquids are nicotine-containing liquid solutions that are consumed in e-cigarettes. However, some solutions may contain no nicotine, the composition of e-liquids is discussed in more detail in Section 3.4.1. Third-generation e-cigarettes (tanks or mods) are much larger than the previous generations and are refillable and rechargeable (Williams and Talbot, 2019; Centers for Disease Control and Prevention, 2020a). They are modifiable devices ('mods'), meaning the user can customise the substances in the device (National Academies of Sciences Engineering and Medicine, 2018). The fourth generation of e-cigarettes is called 'Pod Mod'. They contain a prefilled or refillable 'pod' or pod cartridge with a modifiable 'mod' system ('Pod-Mod') (Centers for Disease Control and Prevention, 2020a). Pod Mods are available in many shapes, sizes, and colours and the most common brands worldwide include JUUL and Suroin. Figure 3.1 illustrates the four generations of e-cigarette products available on the market.

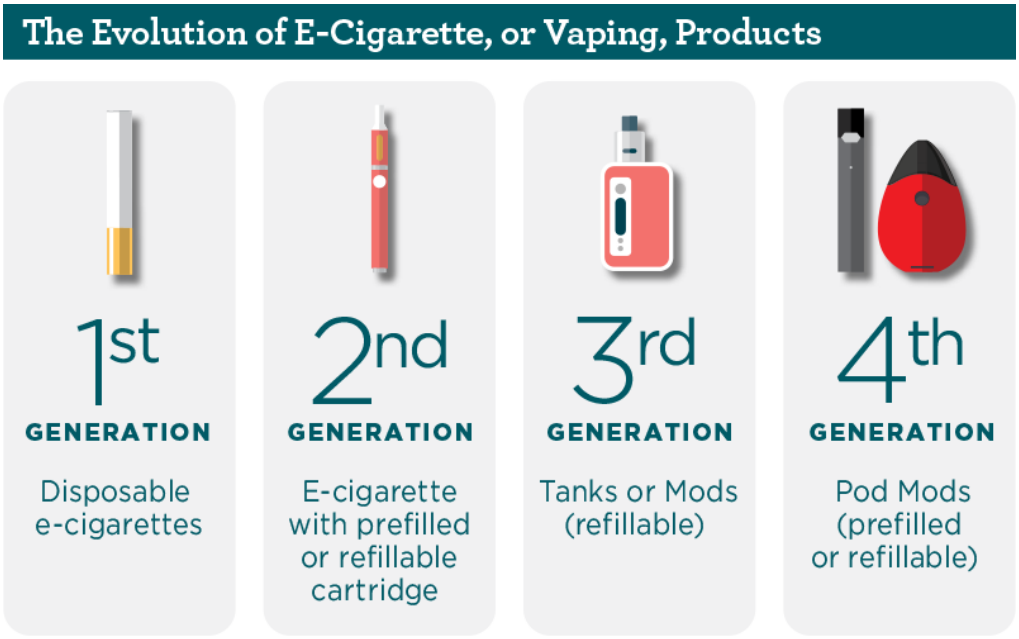

Figure 3.1: Illustration of the four generations of e-cigarette, or vaping products[5]

3.3.1.1 Heat not burn products

'Heat not burn' (HNB) products are electronic devices that, unlike e-cigarettes, contain tobacco and heat the tobacco to ~350°C and similar to e-cigarettes produce an inhalable aerosol (Simonavicius et al., 2019). Commercially available HNB products such as 'Glo' by British American Tobacco (BAT) or 'IQOS' (I Quit Ordinary Smoking) produced by Philip Morris International (PMI), include a charger; a holder; and tobacco sticks, plugs, or capsules (Caputi, 2017; Ratajczak et al., 2020; Simonavicius et al., 2019). Tobacco sticks are inserted into the holder and heated with an electronically controlled heating element. Other products, like 'iFuse' by BAT or 'Ploom Tech' by Japan Tobacco International, produce vapour from a non-tobacco source and pass it through a tobacco plug to absorb flavour and nicotine.

HNB products aim for a niche between combustible tobacco smoking and e-cigarettes that vapourise nicotine suspended in humectants (moisturising agents) (Caputi, 2017; Ratajczak et al., 2020; Simonavicius et al., 2019). Research has suggested that HNB products may be less harmful than combustible cigarettes (Titz et al., 2015; Lüdicke et al., 2017) However, other studies have found that risks of HNB include carbon monoxide

[5] TEXAS DEPARTMENT OF STATE HEALTH SERVICES. 2020. *What is Vaping?* [Online]. Texas Department of State Health Services, Tobacco Prevention and Control Bureau. Available: https://www.dshs.state.tx.us/Vaping/WhatisVaping/ [Accessed 27 January 2021]., reproduced with permission from Texas Department of State Health Service.

and formaldehyde exposure, as well as the potential for side-stream emissions (Wilkinson et al., 2015; Forster et al., 2015). Although HNB products are not the focus of this thesis they are pertinent to discuss given their presence on the market as an alternative nicotine product.

3.3.2 The rapid emergence of e-cigarettes

E-cigarettes were first manufactured in 2004 by the Chinese company Ruyan (Sanford and Goebel, 2014; Stimson et al., 2014). The e-cigarette market was not introduced into Europe and North America for another four years (Stimson et al., 2014). Since 2008, there has been a rapid increase in both the uptake and popularity of the products. They have become so popular that in 2014 the word 'vape', the term for using ENDS, was picked as the Oxford English Dictionary's Word of the Year (Correa et al., 2017). In 2019, the global value of the e-cigarette market was $11.73 billion and is expected to reach $21.4 billion by 2023 (The Business Research Company, 2020). As well as their market value, the increased number of e-cigarette users demonstrates the rapid emergence of e-cigarettes (Figure 3.2).

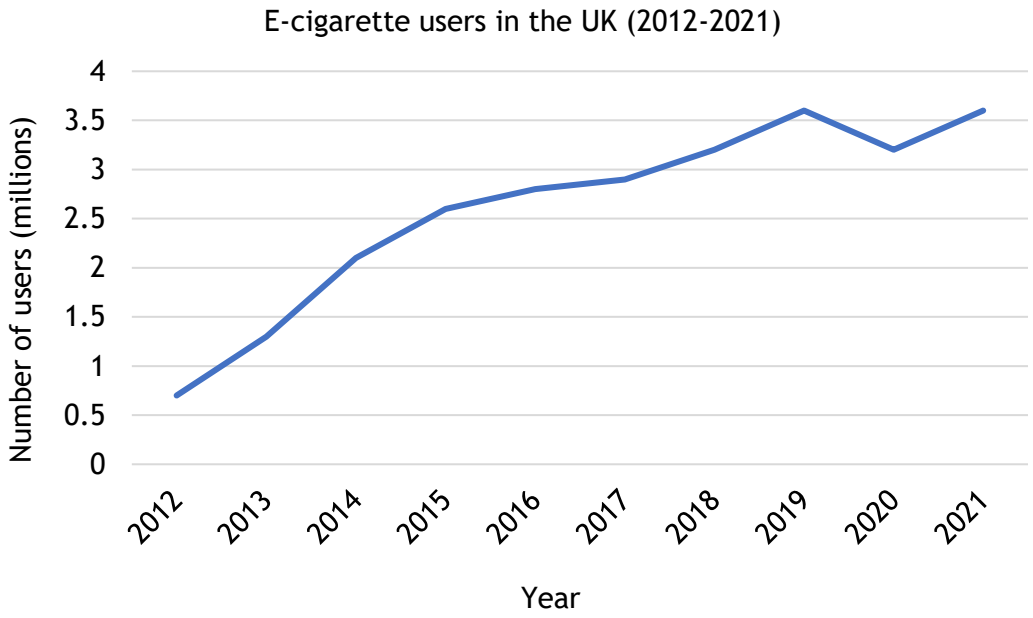

Figure 3.2: Number of e-cigarette users in the UK[6]

[6] Based on material from ACTION ON SMOKING AND HEALTH 2021. *Use of e-cigarettes (vapes) among adults in Great Britain*, Action on Smoking and Health. Available: https://ash.org.uk/wp-content/uploads/2021/06/Use-of-e-cigarettes-vapes-among-adults-in-Great-Britain-2021.pdf.

Action on Smoking and Health (ASH) (2021), a UK public health charity that works to eliminate the harm caused by tobacco, states that the use of e-cigarettes is largely confined to current and ex-smokers. As shown in Figure 3.2, the number of e-cigarette users grew from around 700,000 in 2012 to 3.6 million in 2019, falling to 3.2 million in 2020, before increasing again in 2021 to 3.6 million (Action on Smoking and Health, 2021).

This rapid emergence of e-cigarettes and the numerous generations and flavourings available has led to various concerns being raised including the risks, benefits, and safety of these products. The next section will review some of the current arguments and evidence in e-cigarette debates, including the toxicology of e-cigarettes and the arguments about the use of e-cigarettes as a harm reduction tool.

3.4 Arguments and evidence in the e-cigarette policy debate

Across the world, policy debates about tobacco control have been markedly altered by the rapid proliferation of e-cigarettes. The development and population exposure to e-cigarettes has created a 'moral quandary' (Loddenkemper and Kreuter, 2015). A range of regulatory approaches towards e-cigarette products have been pursued across the globe from being completely prohibited (e.g., Singapore, Lithuania) to being regulated as consumer products (e.g., UK, Spain, Italy), tobacco products (e.g., Malta), or medicinal devices (e.g., France, Netherlands, Finland) (Rose et al., 2015; Kennedy et al., 2017; Hawkins and Ettelt, 2019; Erku et al., 2020; Campus et al., 2021). Proponents and opponents of e-cigarettes remain divided on the evidence base and the appropriate approach for regulation. This section will examine some of the arguments and evidence used by different sides of the e-cigarette policy debate.

3.4.1 Are there health risks associated with e-cigarette use?

Research on the health effects of e-cigarettes is increasing. The toxicology of e-cigarettes is an area that has been extensively studied by various scientific bodies. E-cigarette operation does not involve combustion, therefore no smoke or other harmful combustion products, such as tar and carbon monoxide, are formed (Farsalinos and Polosa, 2014; Action on Smoking and Health, 2018). However, the content of e-cigarettes is a key concern. The variations in product design and e-liquid compositions among the variety of brands available affect the toxicants and chemicals released in the

aerosol and delivered to the user (Wang et al., 2019). E-liquids are available in a variety of nicotine concentrations, with levels ranging from 0 mg/mL (i.e., no nicotine) to over 59 mg/mL (Cheng, 2014; Kim et al., 2018; Erythropel et al., 2021) and a single e-liquid cartridge for some devices can contain the same amount of nicotine that is in a pack of 20 cigarettes (Willett et al., 2019). For general reference, combustible tobacco cigarette smokers absorb about 1 mg (range=0.3–2 mg) of nicotine systemically from smoking, which represents about 80 to 90 percent of the amount of nicotine inhaled (National Academies of Sciences Engineering and Medicine, 2018).

Research has identified a variety of chemical components in the cartridges, e-liquids, and aerosols of e-cigarettes (Herrington and Myers, 2015; Kucharska et al., 2016). Substances identified in e-liquids and aerosols include nicotine, tobacco-specific nitrosamines, aldehydes, metals, volatile organic compounds, phenolic compounds, polycyclic aromatic hydrocarbons, flavours, tobacco alkaloids, and drugs (such as amino-tadalafil and rimonabant) (Hadwiger et al., 2010; Cheng, 2014; Goniewicz et al., 2014; Orr, 2014; Margham et al., 2016; Flora et al., 2016; Takahashi et al., 2018; Wang et al., 2019). Despite concerns regarding the contents of e-cigarettes, research has found the levels of these compounds to be lower than those found in traditional cigarettes (Goniewicz et al., 2014; Orr, 2014; Cheng, 2014; Takahashi et al., 2018). Additionally, research by Goniewicz et al. (2014) showed that the carcinogenic compounds in e-cigarettes are 9-450 times lower than the levels found in traditional cigarettes and are comparable to the levels found in currently licenced nicotine-containing products. Although few studies have examined the effects of flavouring substances administered by inhalation, there are some chemicals that, although approved for ingestion, have adverse health effects when inhaled including diacetyl, acetylpropionyl, acetoin, cinnamaldehydes, and benzaldehyde (National Academies of Sciences Engineering and Medicine, 2018). Similarly, although second-hand vapour from e-cigarettes exposes bystanders to nicotine and other chemicals, research has shown the exposure to be much less than that which results from cigarette smoke (Czogala et al., 2014; Goniewicz et al., 2014; McEwen and McRobbie, 2016).

Concerns have also been raised about the risk of nicotine intoxication and fatal poisoning, particularly in young children if a high nicotine-content solution is ingested (Gupta et al., 2014; Gill et al., 2015; Bartschat et al., 2015). There have been incidents of children ingesting e-liquids used by parents/families to fill their e-cigarettes, leading to a large number of calls to poison centres and several cases of fatal nicotine ingestion (Quail, 2020). Data from published case reports state that the ingestion of 4mL of a 12mg/mL nicotine-containing solution would be lethal for an adult (Mayer, 2014). It is

argued that the risk of accidental poisoning in children due to e-cigarettes is not different from household devices and chemicals (Wagener et al., 2012).

Although existing research does not provide a definitive conclusion on the safety of e-cigarettes, research suggests that they are less harmful than tobacco products and are comparable in toxicity to approved nicotine replacement therapies (NRT) (Farsalinos and Polosa, 2014; McEwen and McRobbie, 2016). Concerning the long-term health effects, the UK's National Centre for Smoking Cessation and Training (2016) stated that although they do not know the long-term risks the "magnitude of any risks that may emerge from long-term e-cigarette use is likely to be small" (p.34). However, some researchers and public health bodies and organisations argue that much is unknown about the long-term health effects of e-cigarette use and we need focused research to study this (Rigotti, 2018; Darville and Hahn, 2019; Sapru et al., 2020).

3.4.2 Are e-cigarettes associated with lung injury?

In 2019, the USA reported a rise in people, particularly those under 30, being admitted to hospital suffering from pneumonia-like lung injuries; none were traceable to a microbial source, but all reported recently using e-cigarettes (Centers for Disease Control and Prevention, 2019; King et al., 2020). The Centers for Disease Control and Prevention (CDC) referred to the outbreak of severe lung illness as e-cigarette or vaping product use-associated lung injury (EVALI). All individuals with EVALI reported using e-cigarette products, most of whom reported using their e-cigarette devices to ingest tetrahydrocannabinol (THC), the primary psychoactive compound in cannabis (U.S. Department of Health and Human Services, 2016; Koslow and Petrache, 2020). Vitamin E acetate is strongly associated with EVALI and it has been added to THC cartridges by cost-cutting manufacturers who would claim that their products contained more THC than they did, as Vitamin E acetate increased the viscosity of the THC (King et al., 2020). It is important to note that not all EVALI cases have been associated with THC-containing products and that in certain individuals, nicotine-containing or flavoured e-cigarettes may also cause acute lung inflammation and injury (Schweitzer et al., 2015; Layden et al., 2020; King et al., 2020). King et al. (2020) argue that the use of e-cigarette products by adolescents is unsafe, regardless of whether they contain nicotine or THC, and the risks posed by these products are further heightened by the EVALI outbreak.

Other countries such as the UK and Australia were on alert for lung injuries caused by e-cigarette use after the outbreak in the USA. As of January 2020, there have been two

potential cases of EVALI (UK Government, 2020a), occurring during a similar time period to the USA outbreak. UK public health researchers argue that the EVALI outbreak could damage the reputation of e-cigarettes, as the UK has pursued a 'harm reduction' approach towards e-cigarettes (Hawkes, 2019). In Australia, which has taken a 'precautionary' approach towards e-cigarettes and where there are no confirmed reports of EVALI, public health researchers argued that the EVALI outbreak in the USA further entrenched the negative perception of e-cigarettes and therefore supported their regulatory approach (Munsif et al., 2020).

3.4.3 Are e-cigarettes a useful harm reduction tool?

Harm reduction is a strategy for reducing, but not eliminating risk and has been a pillar of public health practices, an example is the use of methadone and needle exchanges rather than eliminating intravenous drug use. However, harm reduction approaches are often controversial (including the example above) because opponents are concerned that they accommodate rather than eliminate risky behaviours (Thomas et al., 2020). Since the development of e-cigarettes, public health researchers and tobacco control advocates have debated the role of e-cigarettes as a harm reduction tool. Proponents of e-cigarette harm reduction believe e-cigarettes can play a role in eliminating smoking-related diseases and consider them to be a breakthrough in harm reduction development (Cahn and Siegel, 2011; Britton and McNeill, 2013; Hajek, 2014; Cox and Dawkins, 2018). Whereas opponents of the e-cigarette harm reduction debate argue that caution should be taken when endorsing e-cigarette products until crucial evidence becomes available (Chapman, 2014). E-cigarettes are popular among smokers due to their ability to replicate the behavioural and physical aspects of smoking (Rahman et al., 2015; Green et al., 2018). E-cigarettes are often termed a short-term tobacco harm reduction tool, as they do not contain tobacco or tar which are known to cause numerous smoking-related diseases, including cardiovascular disease. As there is no long-term evidence yet available, the debate about using them as a long-term tobacco harm reduction tool will continue. I explore the debate surrounding the use of e-cigarettes as a smoking cessation tool in Section 3.4.7, which is linked to the harm reduction debate.

3.4.4 Are e-cigarettes a gateway to youth smoking?

One of the main concerns and important debates concerning e-cigarettes is whether e-cigarettes increase tobacco smoking among adolescents, a gateway effect. Opponents of e-cigarettes argue that research has shown that adolescents who use e-cigarettes are

more likely to start smoking compared to those who do not (Dutra and Glantz, 2014; Moore et al., 2014; Barrington-Trimis et al., 2015; Bunnell et al., 2015; East et al., 2018; Khouja et al., 2020).

Another issue that has been raised relates to the increasing number of e-liquid flavours now available. In 2014 it was estimated there were 7,764 unique flavours, with an average of 242 new flavours being added per month (Zhu et al., 2014; Tierney et al., 2016). The vast majority of flavours are related to confectionery (e.g., candyfloss, marshmallow, vanilla, cola, bubblegum), and in 2020 it was estimated that there were over 15,000 different flavours available on the market (Henry et al., 2020; Campaign for Tobacco-Free Kids, 2020). The question being asked is if this variety of e-liquid flavours is attracting youths to try e-cigarettes. Research has shown that the variety of available flavours is one of the top reasons for experimentation with e-cigarettes among youths, in addition to peer influence and curiosity (Kong et al., 2015; Bold et al., 2016; Audrain-McGovern et al., 2016; Czoli et al., 2016; Zare et al., 2018). Compared to adults, youths are more likely to use sweet e-liquid flavoured e-cigarettes and their popularity among youths and the rates of prevalence have significantly increased in recent years (Stanton et al., 2016; Harrell et al., 2017). Research shows that youths perceived fruit and sweet flavoured e-cigarettes to be less harmful compared to tobacco flavour e-cigarettes (Ford et al., 2016; Pepper et al., 2016; Cooper et al., 2016). Harrell et al. (2017) argue that the elimination or restriction of flavoured e-liquids (particularly sweet and fruit flavours) could potentially aid youth and young adult prevention efforts. Already, Finland and several states in the USA (including Chicago and New York City) prohibit the sale of flavoured e-cigarettes (Emanuel, 2013; Ollila, 2020).

E-cigarette harm reduction proponents have disputed the gateway effect, arguing that the adolescent smoking prevalence continues to decline, therefore, e-cigarettes cannot be causing smoking among adolescents (Bauld et al., 2017; Chapman et al., 2019). Harm reduction proponents also argue that research has found that smoking more often preceded vaping rather than vice versa (i.e., most adolescents who had tried e-cigarettes are already smoking or have previously experimented with cigarette smoking) (de Lacy et al., 2017; West et al., 2019; Berry et al., 2019; Mendelsohn and Hall, 2020).

3.4.5 Are e-cigarettes re-normalising smoking?

Concerns over the renormalisation of smoking has been raised by numerous researchers and tobacco control advocates (including Fairchild et al., 2013; World Health Organisation, 2014a; Voigt, 2015). The renormalisation hypothesis suggests the growing

prevalence and visibility of e-cigarette use will undo 'decades of work' in tobacco control and shift social norms surrounding the extent to that smoking is once again seen as 'normal' behaviour (Hsu et al., 2013; Sæbø and Scheffels, 2017; Aleyan et al., 2018). This concern has been cited in policy documents in several countries (such as Australia and USA) as a rationale to support more restrictive policies (Hallingberg et al., 2020).

The Australian Government (2018) stated:

> "[…] the Department is concerned about evidence suggesting that e-cigarettes may provide a gateway to nicotine addiction or tobacco use (particularly among youth) and may re-normalise smoking. Rather than encouraging smokers to quit smoking, E-cigarettes may expand the nicotine market by attracting new smokers (particularly youth) who may otherwise be unlikely to initiate smoking with conventional cigarettes." (p.43)

Sæbø and Scheffels (2017) and Hallingberg et al. (2020) argue that the renormalisation hypothesis assumes cigarettes and e-cigarettes are viewed as similar to one another. E-cigarette products are evolving over time and as discussed in Section 3.3.1, new models no longer resemble traditional cigarettes compared to earlier generations. Therefore, this needs to be considered when discussing and evaluating the renormalisation debate (Sæbø and Scheffels, 2017; Hallingberg et al., 2020).

By contrast, some researchers argue that e-cigarettes may denormalise smoking through the social display of an alternative behaviour and cause some youth to not smoke who would otherwise have become smokers (Hallingberg et al., 2020). From this perspective, aligning e-cigarettes and tobacco regulation could result in the perception that the products are equal and potentially cause the renormalisation of smoking (Hallingberg et al., 2020).

3.4.6 Do e-cigarettes promote dual-use?

The issue of dual-use relates to whether e-cigarette users will continue to use both tobacco cigarettes and e-cigarettes for an extended period of time (Wills et al., 2015). Some researchers argue that from a population-level public health perspective, dual-use could provide an opportunity to reduce the burden of tobacco use if it represents a temporary stage before smokers switch to solely e-cigarette use or quit tobacco products completely (Wills et al., 2015; Nayak et al., 2016; Owusu et al., 2019).

Nayak et al. (2016) found that higher proportions of dual-users have a stronger intention to quit compared to cigarette smokers. Similarly, research by Nabi-Burza et al. (2019) showed that dual-users may have higher rates of contemplating smoking cessation than individuals who only smoke cigarettes, suggesting that dual-users may be using e-cigarettes for harm reduction or as a step towards cessation. However, it is possible that dual-use could prolong nicotine addiction and consequently inhibit smoking cessation among smokers who might otherwise quit smoking (Jha et al., 2013; U.S. Department of Health and Human Services, 2014; Wills et al., 2015; Hilton et al., 2016). Concerns about the dual-use of hazardous and reduced hazard products adds another layer of complexity to the e-cigarette debate.

3.4.7 Do e-cigarettes lead to smoking cessation?

Since the development of e-cigarettes, there has been an increase in the number of smokers who use and enquire about e-cigarettes when attempting to quit smoking (McRobbie et al., 2014; NHS, 2019b). Currently, available medications include NRT, Varenicline (Champix), and Bupropion (Zyban) (NHS, 2019a). There are several published RCTs evaluating whether nicotine-containing e-cigarettes increase smoking cessation compared to placebos, to financial incentives, and to behavioural therapy, or NRT (including Caponnetto et al., 2013; Bullen et al., 2013; McRobbie et al., 2014; Hartmann-Boyce et al., 2016; Hajek et al., 2019; Lee et al., 2019; Walker et al., 2020; Hartmann-Boyce et al., 2021).

A 2016 Cochrane review (Hartmann-Boyce et al., 2016) found that data from research by Caponnetto et al. (2013) and Bullen et al. (2013) support an effect of nicotine e-cigarettes on cessation when compared to placebo e-cigarettes, but has low certainty in the evidence due to the small number of trials (n=2), low event rates and wide confidence intervals (Hartmann-Boyce et al., 2016). The study by Bullen et al. (2013) compares e-cigarettes to standard NRT, which is the most relevant comparator for clinicians. Unfortunately, the trial design placed the NRT group at a disadvantage compared to the e-cigarette group, as the NRT group was given vouchers for purchasing patches while the e-cigarette group was provided with e-cigarettes (Bullen et al., 2013). The authors of the review (Hartmann-Boyce et al., 2016) were unable to determine if e-cigarettes were better than a nicotine patch for smoking cessation due to the low number of participants in the study. Furthermore, the review indicated that none of the studies, included in the review, found that smokers who used e-cigarettes short to mid-term (for two years or less) had an increased health risk compared to smokers who did not use e-cigarettes (Hartmann-Boyce et al., 2016).

Since the 2016 Cochrane review, three RCTs have been completed (Hajek et al., 2019; Lee et al., 2019; Walker et al., 2020). Hajek et al. (2019) conducted the largest RCT of e-cigarettes compared with NRT to date, finding that nearly twice as many participants quit smoking at one year in the vaping group (18.0%) compared to the NRT group (9.9%). Participants in the NRT groups were allowed to choose the NRT product they use, this included using combination NRT (i.e., using two forms of NRT together, which is the most effective way to use NRT (U.S. Department of Health and Human Services, 2020)) (Hajek et al., 2019). All three RCTs have found nicotine-containing e-cigarettes to be at least as effective as NRT and some found vaping was more effective (Hajek et al., 2019; Lee et al., 2019; Walker et al., 2020).

The 2014 and 2016 Cochrane reviews both demonstrated low certainty in the evidence regarding the efficacy of e-cigarettes as a smoking cessation tool (McRobbie et al., 2014; Hartmann-Boyce et al., 2016). A newly published Cochrane review (Hartmann-Boyce et al., 2021) found that nicotine e-cigarettes were superior to placebo e-cigarettes and at least as effective as NRT for smoking cessation, which is consistent with findings from other RCTs (Hajek et al., 2019; Lee et al., 2019; Walker et al., 2020). In addition, the review stated that there is moderate certainty in the evidence that nicotine-containing e-cigarettes increase the quit rate compared to NRT and non-nicotine-containing e-cigarettes (Hartmann-Boyce et al., 2021). As with the previous Cochrane reviews, there is imprecision due to the small number of trials, often with low event rates (McRobbie et al., 2014; Hartmann-Boyce et al., 2016; Hartmann-Boyce et al., 2021).

More evidence is required about the effects of e-cigarettes concerning smoking cessation, particularly due to the development of newer types of e-cigarette devices that have better nicotine delivery compared to older generations of e-cigarettes (Farsalinos et al., 2014; Tattan-Birch et al., 2021).

3.5 The influence of the tobacco industry and conflicts of interest in e-cigarette debates and decision-making

As discussed in Section 3.4, researchers and policymakers have raised various issues regarding the impact of e-cigarettes on tobacco-related outcomes at individual and population levels and the potential health effects associated with their use. In this next subsection, I examine the tactics of the tobacco industry, before moving on to discuss the role of the tobacco industry in the e-cigarette debate, allowing me to examine

some of the factors which have influenced the development and perceptions of e-cigarettes and subsequent policy recommendations. Following on from this, I will discuss the presence of COI in the tobacco control e-cigarette debate and how they have been found to influence decision-making.

3.5.1 Tactics of the tobacco industry

Many researchers believe that the tobacco industry was responsible for tobacco addiction and for "decades of deceit and actions that cost millions of lives" (Brownell and Warner, 2009, p.259). Robert Proctor was the first historian to extensively analyse the tobacco industry's internal documents. In his book the Golden Holocaust: Origins of the Cigarette Catastrophe and the Case for Abolition (2011) he describes the tobacco industry as:

> "Notorious masters of deception; they know how to manufacture ignorance and rewrite history. They know the power of images and how to twist these to violate common sense and pulmonary civility. They also know how to engineer desire and, of course, they'd like us to believe they don't want youngsters to smoke." (Prologue)

Proctor examined the ways in which the U.S. tobacco industry funded research. One example is the relationship between Virginian Commonwealth University and the tobacco company PMI. In 2007, PMI provided funding to the University in exchange for research, but the contract stipulated that PMI alone would have the power to decide the results of the research that would be published (Proctor, 2011).

There is a fundamental conflict between the tobacco industry's interests and public health policy interests. The marketing strategies and political influence of the tobacco industry have enabled them to falsify results and manipulate research to advance their ultimate goal of selling harmful products (Godlee et al., 2013; Goldberg and Vandenberg, 2021). Governments and public health researchers want to reduce smoking prevalence and the number of tobacco-related deaths. Due to the negative impact tobacco control policies have on the tobacco industry, the tobacco industry actively fights against these policies (World Health Organisation, 2012b; Clifford et al., 2014; Hill et al., 2019; Ikegwuonu et al., 2021). Consequently, many researchers, policymakers, and academics recognise the tobacco industry as a barrier to achieving global health and urge policymakers to commit themselves to the principles outlined in

Article 5.3 of the WHO FCTC (World Health Organisation, 2012b). See Section 3.6.1 for more information on Article 5.3 of WHO FCTC.

3.5.2 The tobacco industry and e-cigarettes

There is concern regarding the active interest that the tobacco industry has taken in e-cigarettes and is demonstrated by the change in the global market (Hastings et al., 2012; de Andrade et al., 2013). Prior to 2012, the e-cigarette market was dominated by small manufacturers; however, since then, large tobacco companies have produced their own products and have bought up small manufacturers (Pisinger et al., 2019; Tobacco Tactics, 2020). By 2018, BAT, Imperial Tobacco, Japan Tobacco International, Lorillard, and PMI all had their own 'flagship' e-cigarette brands and were expanding their global markets (Tobacco Tactics, 2020). For example, BAT launched 'Vype' in 2013 and Lorillard acquired the e-cigarette company 'blu ecigs' (Cision PR Newswire, 2012). A report by the WHO (2014a) concludes:

> "However, if the 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." (p.8)

The tobacco industry has been moving to build links with policymakers, public health researchers and other stakeholders. The tobacco industry planned to work with the Medicine and Healthcare products Regulatory Agency (MHRA) to produce a licensed e-cigarette that could be marketed as an alternative nicotine delivery device. In September 2014, Nicovations, a fully owned subsidiary of BAT, announced the acquisition of a medicinal licence for their product 'Voke' (Hendlin et al., 2017). The Voke inhaler is the first licensed non-electronic cigarette-like nicotine inhaler (Romeu, 2020). Then in 2015, they obtained a license for their 'E-Voke' electronic inhaler (Hendlin et al., 2017). de Andrade, Hastings and Angus (2013) argue that:

> "This is jeopardising Article 5.3 of the Framework Convention on Tobacco Control, which requires that development and implementation of public health policy should be completely protected from industry influence." (p.3)

In addition, the authorisation of such products legitimises the tobacco industry as a partner and producer of innovative alternative nicotine products, such as Voke, while ignoring the ethics of producing and profiting from addiction and its treatments (World Health Organisation, 2008; Romeu, 2020).

3.5.3 Conflicts of interest in e-cigarette debates

A conflict of interest occurs when "a set of circumstances that creates a risk that an individual's professional judgement or actions regarding a primary interest (e.g., validity of research) is, or could be, impaired or influenced by a secondary interest (e.g., financial gain)" (Institute of Medicine, 2009; Morse, 2015). COI can be classified into two broad categories: financial and non-financial. Financial COI are often the most evident and research has shown an association between financial relationships of the author and/or sponsor/funder and industry-favourable results, in tobacco research (Fabbri et al., 2018; Martínez et al., 2018; Hansen et al., 2019) and other public health topics (Vartanian et al., 2007; Bes-Rastrollo et al., 2013; Neltner et al., 2013; Lundh et al., 2017; Geiger and Cuzzocrea, 2017). Non-financial COI can range from personal, political, or religious beliefs, professional experiences, social relationships, or institutional relations (Bero and Grundy, 2016; Bou-Karroum et al., 2018; Napierala et al., 2018; Grundy et al., 2020). Intellectual COI are one sub-type of non-financial COI and can be defined as "academic activities that create the potential for an attachment to a specific point of view that could unduly affect an individual's judgment about a specific recommendation" (Guyatt et al., 2010, p.739).

Author COI may arise from influence on authors through financial payments from companies to researchers for consulting, advisory roles, and/or speaking and are reported in COI statements (Institute of Medicine, 2009). Although receipt of study funding (financial support from companies for conducting the research and is usually paid to the institution) is not always recorded as a conflict of interest for the author(s), it is associated with other concerns, including agenda setting (when a problem attains a high level of interest amongst policymakers) and sponsorship bias (the distortion of design and reporting of results of research to favour the sponsor's aims (Jefferson, 2020)) (Bero and Rennie, 1996; Lexchin, 2012; Boyd et al., 2012; Lundh et al., 2017).

In recent years, COI disclosure policies have become a regular part of scientific research (Dunn et al., 2016). The International Committee of Medical Journal Editors (ICMJE) guideline recommends that authors should disclose the study's funding source and any financial ties to industry, e.g., pharmaceutical or tobacco companies (Drazen et al.,

2010; International Committee of Medical Journal Editors, 2021). COI may threaten the integrity of scientific investigations, undermine the evidence base and risk threatening the trustworthiness of recommendations (Institute of Medicine, 2009). An important concern is that COI may act as a potential source of bias in the development of public health recommendations (Norris et al., 2011; Mendelson et al., 2011). COI may also be present among the evidence base that policy and decision-makers draw upon and this may lead to recommendations being distorted to favour a secondary interest. Thus, the management of COI in all stages of the process is essential for the development of high-quality recommendations (Qaseem and Wilt, 2019).

This thesis focuses on an individualised conception of COI - specifically in relation to research/ authorship and receipt of funding. This is the most common conception of COI used in the health literature, often drawing on the definition by Thompson (1993). COI can also be conceptualised at a broader e.g., institutional level, as in the conflict between commercial interests (on the part of the tobacco industry) and health goals (World Health Organisation, 2015). This broader conception of COI is relevant to the case study and the 'context' of policymaking in relation to e-cigarettes; however, this thesis draws upon an individualised conception of COI (see Section 3.8 for the research questions guiding this study).

Evidence has shown that tobacco research funded by the tobacco and/or pharmaceutical industry may be biased (Malone and Bero, 2003; Hong and Bero, 2006; Pisinger et al., 2019; Collin et al., 2021). Some journals no longer accept submissions with links to tobacco companies, a decision that has been criticised by some researchers who argue that these journals have passed a strong rule without enough evidence to justify it (Shaw et al., 2016). Given the misinformation and deception by the tobacco industry, which historically undermined public health policies (e.g., in the 1970s, the tobacco industry downplayed the harms associated with second-hand smoke), other researchers argue that there is potential for the e-cigarette industry to do the same; noting that these are often one and the same corporate entities (Barnes and Bero, 1997; Malone and Bero, 2003; Capps et al., 2020). There is concern among the scientific community that research and publications associated with the e-cigarette industry may hide COI, thus the results reported could be biased (Polosa, 2015; Pisinger, 2016; Kosmider and Anastasi, 2016; Capps et al., 2020). An example of this was the conclusion of the 2015 Public Health England (PHE) report, stating that e-cigarettes are ‘95% less harmful to health the normal cigarettes’ (Public Health England, 2015). This figure was based on expert opinion (a multi-criteria decision analysis), where a panel of 12 experts estimated the relative harm of various nicotine-containing products (Nutt et al., 2014).

The 95% figure was disputed because of the COI among the 12 experts (The Lancet, 2015). The Lancet (2015) argues that PHE strives to protect and improve the nation's health and to do should use the highest quality evidence; however, in the 2015 report, they have not.

While the evidence base remains disputed, there is a concern that public understanding of the potential health risks of e-cigarette use appears to be mediated by some researchers with links to the tobacco and e-cigarette industry. E-cigarette research funded by or associated with the tobacco and e-cigarette industry, even where the research and results are not affected or influenced, affects the public's trust and confidence in public health research (Capps et al., 2020).

3.6 Policy jurisdictions: national and international

For this thesis, I have adopted a case study approach (this will be discussed in more detail in Section 4.2) and have selected e-cigarettes as the focus of this enquiry. Jurisdictions around the world have adopted different policies when regulating e-cigarette products; however, it is not feasible to provide an in-depth examination of all regulatory approaches. As such, I have chosen to examine four jurisdictions which have relative importance for setting the agenda on tobacco control policies but have pursued different e-cigarette regulatory frameworks (WHO, UK, Australia, and USA.) The following sections discuss the e-cigarette regulatory approaches in each jurisdiction and the reasons for subsequent policies. I also draw on the EU as UK tobacco regulation has, up until 2020, been a mixture of domestic and EU law (Branston et al., 2021). This is followed by an illustration of a timeline of national and international tobacco control policies.

3.6.1 WHO policies

The WHO states that tobacco kills more than eight million people annually, with more than seven million of those deaths attributed to direct tobacco use, while approximately 1.2 million are among non-smokers exposed to second-hand smoke (World Health Organisation, 2020). To address the global tobacco epidemic the WHO developed the world's first public health treaty, the FCTC (World Health Organisation, 2003). It was adopted by the World Health Assembly in 2003 and legally entered into force in 2005. The international treaty provides a comprehensive strategy for member Parties to address and combat the tobacco epidemic. It details a range of evidence-

based measures to reduce tobacco demand (Articles 6-14) and supply (Articles 15-17) (World Health Organisation, 2003). It is worth noting that the UK, Australia, and USA have signed to be Parties to the FCTC; however, the USA has not ratified the framework (World Health Organisation, 2022). Between 2007 and 2014, it is estimated that nearly 22 million future premature smoking-attributable deaths were prevented as a result of the strong implementation of the FCTC (Levy et al., 2018). Similarly, Dubray et al. (2015) found that overall, countries with higher levels of implementation of the FCTC experienced greater decreases in current tobacco smoking between 2006 and 2009.

To assist parties to meet their commitment to the treaty and implement appropriate policies, in 2008 the WHO developed the MPOWER framework for tobacco control. This framework corresponds to WHO FCTC articles: Article 20 (**M**onitoring tobacco use and prevention policies); Article 8 (**P**rotect people from tobacco smoke); Article 14 (**O**ffer help to quit tobacco use); Articles 11 and 12 (**W**arn about the dangers of tobacco); Article 13 (**E**nforce bans on tobacco advertising, promotion and sponsorship); and Article 6 (**R**aise taxes on tobacco) (World Health Organisation, 2003; World Health Organisation, 2013).

Ngo et al. (2017) reported a reduction in smoking prevalence and cigarette consumption during 2007–2014 as a result of the implementation of the MPOWER framework. The FCTC has served as a powerful tool to initiate, support and advance national and global tobacco control policies. Evidence suggests that strong implementation of the FCTC and MPOWER framework can lead to significant reductions in tobacco use (Dubray et al., 2015; Ngo et al., 2017; Gravely et al., 2017).

Although numerous countries have been successful in implementing policies in line with the FCTC, many countries, particularly low and middle-income countries, are still facing challenges in moving tobacco control policies forward. This is due to the role and influence of the tobacco industry in tobacco control policies. Article 5.3 of the FCTC requires Parties to take action to protect health policy “from commercial and other vested interest of the tobacco industry” (World Health Organisation, 2003, p.7). Therefore, the strong implementation of Article 5.3 is of vital importance in fighting the tobacco epidemic and protecting public health policies from the tobacco industry (World Health Organisation, 2003; Hogg et al., 2016).

Concerning e-cigarettes, the WHO argues that e-cigarettes have the potential to normalise smoking in society and attract youths through branding and marketing (World Health Organisation, 2019). The WHO urges governments to implement legislation for

the effective regulation of e-cigarettes. According to the WHO (2021), tobacco control must remain focused on reducing tobacco use globally and e-cigarettes should be regulated to maximise the protection of public health. The WHO has published two reports on potential e-cigarette regulations that Parties should consider implementing (World Health Organisation, 2014a; World Health Organisation, 2016). In addition, the WHO states that the MPOWER framework and other regulatory measures can be applied to e-cigarettes (World Health Organisation, 2021).

3.6.2 UK policies

In the 1980s the UK was considered a 'laggard' in tobacco control (Cairney, 2019d). In 1988, a comparison between the UK and Norway was conducted (Baggott, 1988). Both countries implemented similar tobacco control measures, but in Norway, the measure had statutory weight, whereas the UK relied on less effective voluntary measures that arguably favoured the tobacco industry (Baggott, 1988; Cairney, 2019d). By 2007, the UK shifted from voluntary measures to more comprehensive statutory measures. Key policy changes include[7]:

- 2007: the rest of the UK banned smoking in all workplaces and public places;
- 2007: the legal age of sale of cigarettes increased from 16 to 18 years;
- 2008: UK became the first EU nation to introduce picture health warnings on all tobacco packaging;
- 2015: introduction of plain packaging (tobacco packages were to be dominated by health warnings and devoid of any logos);

[7] Based on information from BRITISH HEART FOUNDATION. 2018. *Timeline: 10 years of the fight against smoking* [Online]. British Heart Foundation. Available: https://www.bhf.org.uk/informationsupport/heart-matters-magazine/news/smoking-ban/10-years-of-the-fight-against-smoking [Accessed 24 November 2021], ACTION ON SMOKING AND HEALTH 2020. *Key dates in tobacco regulation 1962 — 2020*, Action on Smoking and Health. Available: https://ash.org.uk/wp-content/uploads/2020/04/Key-Dates.pdf.

- 2015: Scotland, England, and Wales banned smoking in private cars with children present; and

- 2016: EU TPD came into effect.

Since 1986, UK tobacco regulation has been a mixture of domestic and EU law (McHale et al., 2021). In 2014, the European Parliament created the TPD, which applied across the EU (European Commission, 2014). Member states of the EU were required to bring the Directive into effect by May 2016. Some of the regulations detailed in the EU TPD include ensuring e-cigarette nicotine containers do not exceed 10 mL; cartridges or tanks do not exceed 2 mL in volume; the nicotine concentration of an e-liquid is not higher than 20 mg/mL; and the addictiveness and toxicity are stated. E-liquids containing more than 20 mg/mL or making medical claims are required to be licensed as medicines by the MHRA (European Commission, 2014; Patterson et al., 2016). The TPD also included regulations requiring manufacturers to submit information on their products including all ingredients contained in and emissions resulting from the use of the product; information regarding the nicotine dose and uptake when the product is consumed under normal or reasonably normal conditions; and a description of all the components of the product (European Commission, 2014).

Concerning tobacco cigarettes, some of the TPD regulations include all packs of cigarettes must contain at least 20 cigarettes; health warnings must cover 65% of the front and back packaging of cigarettes; the size, font, and colour of brand name will be restricted; packaging must be green with large images of the harmful effects caused by smoking; and e-cigarettes must feature health warnings (European Commission, 2014; Action on Smoking and Health, 2017). In addition to bringing the TPD into force, all the devolved nations of the UK have taken steps to regulate smoking; Health (Tobacco, Nicotine, etc. and Care) (Scotland) Bill (2016); Public Health (Wales) Act (2017); and Health (Miscellaneous Provisions) Act (Northern Ireland) (2016).

In January 2020, the UK left the EU. As part of the Withdrawal Agreement (2019), the UK negotiated with its EU partners a transition period, including the application of EU law to the UK until December 2020 (this included the EU TPD) (Branston et al., 2021). The transition period allowed for negotiation of the future relationship between the UK and EU. As the UK, implemented the TDP (an EU law), the decision to leave the EU would impact tobacco regulations (Branston et al., 2021). Since January 2021, tobacco and e-cigarette products are regulated under the Tobacco Products and Nicotine Inhaling Products (Amendment) (EU Exit) Regulations (2020b). The regulations stated in

the Tobacco Products and Nicotine Inhaling Products (Amendment) (EU Exit) Regulations (2020b) are the same as those stated in the EU TPD (e.g., restrict the maximum volume of nicotine-containing e-liquid for sale in one refill container to 10mL).

3.6.3 Australian policies

Australia is globally recognised as a leader in tobacco control due to the implementation of progressive and innovative tobacco control strategies (Chapman and Wakefield, 2001; Freeman, 2019). Australia has largely adopted the principles outlined in the WHO FCTC and MPOWER framework (World Health Organisation, 2003; World Health Organisation, 2013; Freeman, 2019). Some of the tobacco control policies implemented include the prohibition of tobacco companies/brands sponsoring any event; high taxation of tobacco products; broadcast of impactful anti-smoking campaigns; and smoke-free laws prohibiting smoking in all public places. Up until 2012, tobacco packages sold in Australia displayed graphic health warnings and were not visible at the point of sale (Freeman, 2019). In 2012, Australia was the first nation to introduce plain packaging laws (Freeman, 2019; Hill et al., 2019). Since then, many countries including the UK, have implemented plain packaging. Internationally tobacco control advocates are advocating for plain packaging to become "a global standard in the fight against tobacco related-deaths" (Freeman, 2019, p.10).

Unlike the UK and USA where e-cigarettes can legally be sold, and although there are regulations, Australia does not have a legal market for nicotine-containing e-cigarettes. Nicotine, except in forms that are therapeutic or prepared for smoking, is regulated as a dangerous poison by the Therapeutics Goods Administration (TGA) and banned from sale in the country without premarket approval from the TGA (Douglas et al., 2015; Gartner and Bromberg, 2019; Berridge et al., 2021). However, there are currently two ways that Australians can legally purchase nicotine-contain e-cigarettes: through the personal importation scheme, or through a compounded pharmacy (Berridge et al., 2021). The personal import scheme enables Australians to ask a medical doctor to apply to the TGA to allow the importation of up to a three-month supply of nicotine for use in e-cigarettes for therapeutic purposes (Klein et al., 2020). Non-nicotine e-cigarettes are currently not regulated as a therapeutic good under the TGA and to date, no products have been approved by the TGA for registration as a medical device (Klein et al., 2020)

Australia's regulatory approach towards e-cigarettes has suppressed the market by preventing e-cigarette and tobacco companies from marketing their e-cigarette

products. Until an e-cigarette product receives approval from the TGA, this regulatory approach will continue to suppress the development of an e-cigarette market.

3.6.4 USA policies

The publication of the 1964 U.S. Surgeon General Report resulted in an increased public awareness of the dangers of tobacco use and increased governmental action to regulate the use, sale, and advertising of tobacco products (U.S. Department of Health Education and Welfare, 1964; Cummings, 2002; Paoletti et al., 2012). In this section, I will focus on federal-level regulations. Due to the complexity of the various state-level legislative processes and regulations, it is not possible within the scope of this study to explore each in detail. In the late 1960s and early 1970s, there was the first large-scale national counter-advertising campaign to educate the public about the risks associated with tobacco use. This campaign was run by the Federal Communications Commission under the Fairness Doctrine. The Fairness Doctrine, introduced in 1949, was a policy that required licensed broadcasters to dedicate airtime to discuss controversial topics of public interest and also allowed opportunities for discussion of contrasting views (U. S. Department of Health Human and Services, 1989; Paoletti et al., 2012). In 1971, the Fairness Doctrine campaign ended due to federal law prohibiting cigarette advertising on television and radio (Paoletti et al., 2012). The banning of advertising on television and radio is only one example of key tobacco control policies. Yong (2015) describes the USA as lagging in the implementation of several tobacco control initiatives, including a nationwide smoke-free policy. It is worth noting the complexity of policy development in the USA. Policies can be made at the federal, state, and county level, with considerable variation in state laws. In 2003, there was one US state with smoke-free law, this progressed to two states in 2005, seven states in 2007, 12 states in 2009, and 30 states in 2014 (ITC Project, 2020).

A pivotal moment in US tobacco control was the enactment of the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act), signed into law in 2009, giving the Food and Drug Administration (FDA) authority to regulate the manufacturing, distribution, and marketing of tobacco products. It also included restrictions on the marketing and sale of tobacco products to children. In 2016, the FDA's authority was extended to regulate all tobacco products including e-cigarettes. Another pivotal

moment in US tobacco control was the increase of the legal age of sale from 18 to 21. As of September 2021, the following regulations were in place[8]:

- Restriction on sale to underage persons: All 50 states have passed legislation prohibiting the sale of e-cigarettes to underage persons;

- Retail Licensure: 33 states[9] have passed legislation that requires a retail license to sell e-cigarettes over the counter;

- Smoke-Free Indoor Air Laws, including e-cigarettes: 16 states[10] have passed comprehensive smoke-free indoor air laws that include e-cigarettes; and

- E-cigarette tax: 30 states[11] tax e-cigarettes on a percentage of a specified cost.

3.6.5 Tobacco control policies and how they have changed

The timeline depicted in Figure 3.3 illustrates some of the major international and national tobacco control and other noteworthy publications and milestones within the four jurisdictions focused upon in this thesis. Some of these have been discussed previously, such as the publication of the Smoking and Health report by the U.S. Surgeon General Report in 1964. The timeline highlights how international and national tobacco control policies changed in response to evidence showing the association

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[8] Based on information from CENTERS FOR DISEASE CONTROL AND PREVENTION. 2020b. *STATE System E-Cigarette Fact Sheet* [Online]. Available: https://www.cdc.gov/statesystem/factsheets/ecigarette/ECigarette.html [Accessed 04 February 2021].

[9] Alabama, Alaska, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Hawaii, Idaho, Indiana, Iowa, Kansas, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, Ohio, Oregon, Pennsylvania, Rhode Island, Texas, Utah, Vermont, and Washington.

[10] California, Colorado, Connecticut, Delaware, Hawaii, Massachusetts, Minnesota, New Jersey, New Mexico, New York, North Dakota, Oregon, Rhode Island, South Dakota, Utah, and Vermont.

[11] California, Colorado, Connecticut, Delaware, Georgia, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oregon, Pennsylvania, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

between smoking and lung cancer in the 1950s and 1960s, through to the development of e-cigarettes, which resulted in the further modification of tobacco control policies to incorporate e-cigarette regulations.

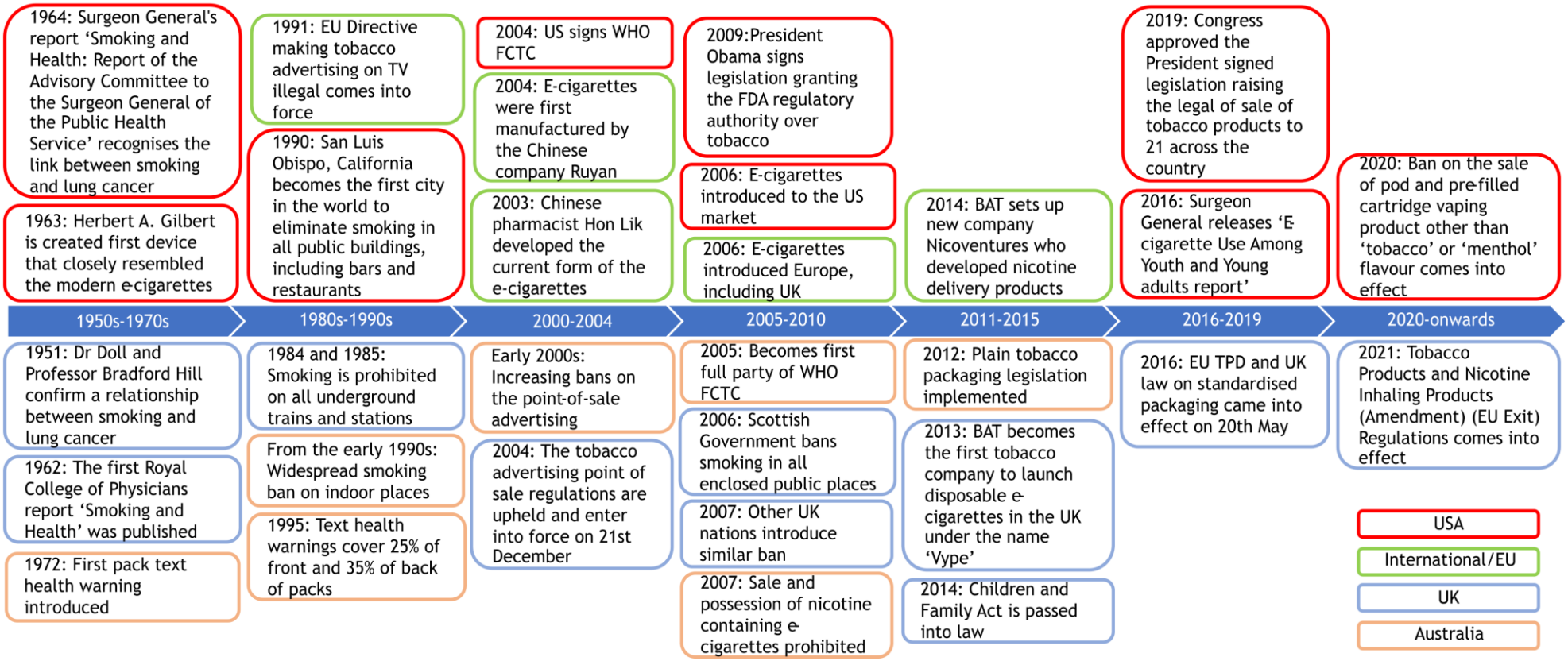

Figure 3.3: Timeline of major international and national tobacco control and e-cigarette policies and other noteworthy milestones[12]

[12] Based on material from CONSUMER ADVOCATES FOR SMOKE-FREE ALTERNATIVES ASSOCIATION. 2020. *Historical Timeline of Vaping and Electronic Cigarettes* [Online]. Available: https://casaa.org/education/vaping/historical-timeline-of-electronic-cigarettes/ [Accessed 27 January 2021], ACTION ON SMOKING AND HEALTH 2020. *Key dates in tobacco regulation 1962 — 2020*, Action on Smoking and Health. Available: https://ash.org.uk/wp-content/uploads/2020/04/Key-Dates.pdf.

3.7 Gaps in existing research

Chapters 2 and 3 have presented a summary of key academic literature relevant to the study of the relationship between evidence and e-cigarette public health policy. Researchers and academics within the field of public health have sought to improve the uptake of evidence in public health policy. An improved understanding of this could assist researchers in developing a more responsive evidence base and improved methods to develop and harness evidence to improve policy and ultimately improve public health. The issues discussed in Chapters 2 and 3 make the study of the relationship between evidence and public health policy particularly worthwhile for several reasons. First, the case study of e-cigarettes focused upon within this thesis is of substantive interest due to the diversity of regulatory approaches pursued, despite the limited evidence, and therefore worthy of investigation. Second, the relationship between evidence and public health policy is known to be sensitive to context, hence making a comparison of public health recommendations across four jurisdictions particularly warranted. Third, debates within public health have often revolved around how best to make decisions in the absence of evidence, therefore making an investigation of public health e-cigarette recommendations an important topic to examine.

Public health recommendations aspire to be evidence-based; however, the demand for evidence-based recommendations on e-cigarettes poses clear challenges for decision-makers. The novelty of these products and the absence of long-term epidemiological data mean only limited relevant evidence is available to guide public health recommendations (Zhu et al., 2014; Hawkins and Ettelt, 2019; Smith et al., 2021b). While there is the potential for evidence to resolve areas of clear disagreement, there needs to be a consideration as to why there are these areas of disagreement, and this leads to the question: ‘how can the same product be treated differently in different jurisdictions despite decision-makers having access to the same evidence?’

Few studies have attempted to answer why e-cigarette regulatory approaches diverge. Feldman (2016) suggested that a lack of a scientific consensus, economic and political interests, and the influence of courts as policymaking bodies were responsible for divergence between the USA, Japan, and China on e-cigarette regulation. Newman and Nurfaiza (2020) propose that some countries, like Singapore, have intentionally designed their e-cigarette regulatory approaches to achieve a particular outcome. Whereas other

countries, like Indonesia, have employed what they call “anti-design” to develop an approach where no policy objective was apparent (Newman and Nurfaiza, 2020). McKee (2019) proposed that the harm reduction approach taken in England is attributable to the dominance of respiratory physicians. Although, McKee (2019) states that it is important to acknowledge that some of the leading respiratory public health bodies and organisations do not share their views. Fairchild et al. (2019) propose that the proof of safety demands by USA policymakers were more strict than those of UK policymakers, leading to a USA regulatory environment that was less supportive of a harm reduction approach. While each of these studies may explain some divergence in regulations, none of these hypotheses stem from a detailed empirical analysis. The diverging cultural, economic, political, and institutional reasons are not accounted for in these explanations.

This thesis attempts to fill these knowledge gaps by firstly, exploring the similarities and differences in e-cigarette public health recommendations (Chapter 5). It is worth noting that while writing this thesis, several papers (Brady et al., 2019; Erku et al., 2020; Campus et al., 2021) examining the varying e-cigarette policy approaches across jurisdictions were published. I will discuss the findings of these studies in relation to my findings in Chapters 5 and 9, respectively. Secondly, this thesis investigates the sources of evidence drawn upon by public health bodies when developing e-cigarette recommendations (Chapter 6). Thirdly, I investigate the management of COI when developing e-cigarette public health recommendations (Chapter7), and finally, I explore the contextual factors influencing decision-making to help explain the divergence in regulations (Chapter 8). The next section details the research aim and questions guiding the study.

3.8 Research aim and questions

The overall research aim guiding my research is to understand how public health bodies prioritise and use evidence in developing e-cigarette public health recommendations by comparing regulatory development across four purposively selected jurisdictions (WHO, UK, Australia, and USA).

The research questions (RQ) guiding this study are:

RQ1: What are the similarities and differences in e-cigarette public health recommendations across diverse jurisdictions?

RQ2: What are the sources of evidence being used in public health bodies' e-cigarette public health recommendations and is the evidence cited differently across jurisdictions?

RQ3: What are the conflicts of interest and funding sources present within cited evidence drawn upon during the development of e-cigarette public health recommendations?

RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

3.9 Chapter summary

This chapter has provided an overview of the key literature surrounding the e-cigarette debate, therefore, providing a rationale for using e-cigarettes as a case study. Key public health arguments and debates surrounding e-cigarettes have been summarised, highlighting why the tobacco control debate has become polarised as a result of the development of e-cigarettes and how this may influence e-cigarette regulatory approaches. The role of the tobacco industry, including their marketing tactics and influences on scientific research was discussed, concluding that the tobacco and e-cigarette industries are often one and the same corporate entities and have been found to be influencing public health research. The previous and current tobacco and e-cigarette regulations within each of the four selected jurisdictions were summarised, providing a rationale as to why these jurisdictions were selected for this case study. Lastly, the gaps in this literature were identified before discussing the importance of alleviating such gaps.

The following chapter explains the need for a multi-methods case study approach to addressing the research questions and describes the methodology for the thesis.

4 Methodology

4.1 Overview and research questions

The aim of this thesis is to understand how public health bodies prioritise and use evidence in developing e-cigarette public health recommendations by comparing regulatory development across four purposively selected jurisdictions (WHO, UK, Australia, and USA).

This chapter describes the methods used for a more detailed analysis of the role of evidence in the development of public health recommendations. To investigate the relationship between evidence and public health policy, e-cigarettes have been investigated as a case study. An investigation solely focusing on the roles of evidence in the decision-making process risks neglecting the importance of contextual factors such as political and institutional factors. Therefore, a broader approach to understanding the decision-making process, while highlighting implications for the evidence-policy debate is needed.

A multi-methods approach, consisting of qualitative and quantitative data analysis, was adopted and four data sources were used to investigate the development of e-cigarette public health recommendations:

- A document analysis of public health bodies' e-cigarette recommendation documents;

- A document analysis of the public health bodies' development documents that detail the processes they follow to develop recommendations;

- A citation network analysis of the sources of evidence drawn upon by public health bodies' when developing e-cigarette recommendations; and

- A thematic analysis of in-depth interviews that were carried out with a range of experts (including academics, policymakers, and methodologists) who had been involved in the development of the recommendation documents.

Each of the four data sources were used in combination to answer the research questions guiding my study (Table 4.1) and are reported in subsequent chapters (Chapters 4-8).

Chapter	Research questions (RQ)	Document analysis of public health bodies' recommendation documents	Document analysis of public health bodies' development documents	Citation network analysis of the sources of evidence used in public health bodies' recommendation documents	Thematic analysis of expert interviews
5	RQ1: What are the similarities and differences in e-cigarette public health recommendations across diverse jurisdictions?	✓			
6	RQ2: What are the sources of evidence being used in public health bodies' e-cigarette public health recommendations and is the evidence cited differently across jurisdictions?			✓	
	RQ3: What are the conflicts of interest and funding sources present within cited evidence drawn upon during the development of e-cigarette public health recommendations?			✓	
7	RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?		✓		✓
8	RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?	✓	✓	✓	✓

Table 4.1: Research questions addressed in the thesis

4.2 Taking a case study approach

Case study research is an exploration of a phenomenon (a case) or multiple phenomena (cases) within a real-life context, through detailed, in-depth data collection involving multiple sources of information (Creswell, 2012). Case study research is best applied when the researcher addresses descriptive or explanatory questions (i.e., what happened, how, and why?) (Yin, 2009) and is appropriate, especially if context is relevant to the phenomenon (Schoch, 2019)- as was with my research.

Stake (1995) and Yin (2009) used different terms to describe a variety of case studies. Stake (1995) identifies case studies as intrinsic, instrumental, or collective. Yin (2009) categorises case studies as explanatory, exploratory, or descriptive. He also differentiates between single, holistic case studies and multiple-case studies. Definitions of the different types of cases are provided in Table 4.2.

Case study type	**Definition**
Intrinsic	An intrinsic case study is undertaken when attempting to learn about a unique phenomenon
Instrumental	An instrumental case study uses a case to gain a wider appreciation of an issue or phenomenon
Collective	The collective case involves studying multiple cases simultaneously or consecutively to produce a still wider appreciation of an issue
Explanatory	This type of case study explores cause-effect relationships and /or how events happen that are too complex for the survey or experimental strategies
Exploratory	This type of case study explores situations where there is no single outcome
Descriptive	This type of case study is used to describe an intervention or phenomenon within its setting

Table 4.2: Definition of different types of case studies[13]

[13] Based on material from STAKE, R. E. 1995. *The art of case study research,* Thousand Oaks, California, SAGE Publications, YIN, R. K. 2009. *Case study research: design and methods,* Thousand Oaks, California, SAGE Publications.

In my research, an instrumental case study approach to e-cigarette policy was taken to gain a deeper understanding of the role and use of evidence in decision-making.

When defining the case, each case must have a predefined boundary which clarifies the nature and time period covered by the case study. Additionally, the relevant social group, organisation, or geographical area of interest to the researcher(s); the types of evidence to be collected; and the priorities for data collection and analysis should be defined (Crowe et al., 2011).

Data collection in case study research can be extensive and time-consuming and typically involves drawing on multiple sources of evidence (Crowe et al., 2011; Shanks and Bekmamedova, 2018). Potential data sources may include, but are not limited to, interviews, documents, direct observation, participant-observation, archival records, and physical artefacts (Yin, 2009; Baxter and Jack, 2010). In case studies, rather than handling the multiple data sources individually they are combined in the analysis process (Baxter and Jack, 2010). Each data source contributes to the researcher's understanding of the whole phenomenon (Jacobsen and Hellström, 2002; Baxter and Jack, 2010). By combining multiple data sources, strength is added to the findings, as the data are woven together to promote a greater understanding of the case (Jacobsen and Hellström, 2002; Baxter and Jack, 2010). Further, they can capture unique features that may otherwise be lost in large-scale data and it is possible that these unique features might be vital to understanding the situation (Nisbet and Watt, 1984; Basias and Pollalis, 2018).

Yin (1994) proposed two types of analytic strategies: general strategy and specific strategy. The general strategy aims to “help an investigator to choose among different techniques and to complete the analytic phase of the research successfully” (Yin, 1994, p.103). Yin (1994) advises the researcher to ‘play with the data’ to develop “a systematic sense of what is worth analysing and how it should be analysed” (p.125) if they lack specific strategies. The researcher can then use specific strategies to analyse data after the general strategy step.

It is important to note that case study is not a method, rather a research strategy (Titscher et al., 2000; Hartley, 2004) or as defined by Stake (2000) “case study is not a methodological choice, but a choice of what is to be studied. By whatever methods we choose to study the case” (p.435). Case study as a research strategy is all-encompassing, meaning that a number of methods may be used- either qualitative,

quantitative, or both (Hartley, 2004; Yin, 2009). Therefore, a case study is defined through its theoretical orientation and interest in cases (either individual or multiple) and not through the research methods employed (Stake, 2000; Hartley, 2004).

While qualitative data usually dominates case studies, quantitative data are often included; however, this may result in limited insight into the selected case if used exclusively (Patton and Appelbaum, 2003; Schoch, 2019).

Using the case of e-cigarettes to explore the relationship between evidence and public health policy, I have employed a multi-methods approach, consisting of both qualitative and quantitative data and this will be discussed in the following section.

4.2.1 Using multi-methods for the case study

Multi-methods research allows different data sources and types of data to be analysed in combination with one another, resulting in both a broader and more in-depth understanding of the area of interest (Guest et al., 2013; Green et al., 2015). Therefore, using multi-methods brings a unique approach to analysing multiple perspectives within a phenomenon (Roller and Lavrakas, 2015). I selected multi-methods, comprising of both qualitative and quantitative research to answer the various research questions (see Table 4.1, p.87) and to gain an in-depth understanding of the relationship between evidence and policy.

Qualitative methods were selected for my research for several reasons. Firstly, qualitative inquiry is explanatory and offers the opportunity to employ inductive methods to enhance and develop theories from data (Mason, 2002; Maxwell, 2005). Inductive methods are especially useful when the research aims to describe, explore, investigate or explain a particular phenomenon (Williams, 2007; Mohajan, 2018). My study aimed to examine the similarities and differences in e-cigarette public health recommendations and the reasons why such recommendations were pursued. Therefore, the investigative nature of qualitative methods is best suited to answer this research question.

Secondly, qualitative research produces descriptions or details of an individuals' feelings, opinions, and experiences and interprets the meaning of their actions (for example, how this directs behaviours, attitudes, and values) (Denzin, 1989). Qualitative methods such as interviews can explore the 'how' and 'why' of a phenomenon in

greater detail (Green and Thorogood, 2004). Therefore, a qualitative approach to my research was thought to be most suitable to address the gaps identified in the literature (see Section 3.7) and answer the proposed research questions. My research questions required the study design to allow for individuals to give detailed descriptions of the decision-making process, including the role and use of evidence in this process. A qualitative approach provided the participants with the opportunity to do so.

Thirdly, qualitative research provides contextual information to data (Guba and Lincoln, 1998; Corbin and Strauss, 2008). It gives data in-depth meaning and purpose, for example, by remedying the gap between theory and local 'real-life' settings (see Chapter 8). Therefore, the investigative nature of qualitative methods is best suited to answer the research questions posed in this thesis.

To answer two of the research questions (RQ2 and RQ3, Table 4.1, p.87), I adopted quantitative research methods. Bryman (2012) defines quantitative research as "a research strategy that emphasises quantification in the collection and analysis of data" (p.35). This research method attempts to investigate the answers to the questions starting with, but not limited to, how many, how much, and to what extent (Rasinger, 2013). There are several advantages to conducting quantitative research which were relevant to my research. Numerical data obtained through quantitative research facilitates comparisons between samples (Yauch and Steudel, 2003). In relation to my study, this meant I could compare the sources of evidence drawn upon and the presence of COI across and within the selected jurisdictions.

In the case of my research, I aimed to examine the sources of evidence drawn upon by public health bodies when developing e-cigarette recommendations and to do this I required quantitative methods. However, this meant I did not have a direct connection with the authors (i.e., I was not able to understand the reasons for drawing upon these sources). To overcome this, I drew upon qualitative data (expert interviews) to explore the 'how' and 'why' questions proposed.

The following sections will describe the process for selecting the study jurisdictions before moving on to describe each of the methodological approaches used to analyse each data source, followed by an explanation of how two data sources (development documents and expert interviews) were compared, and finally how the four data sources were triangulated.

4.3 Selection of study jurisdictions

Four influential jurisdictions were purposively selected: WHO, UK (Scotland, England, Wales, and Northern Ireland), Australia, and USA. These jurisdictions were chosen due to their different e-cigarette regulatory frameworks and their relative importance for setting the agenda on policy recommendations for tobacco control and e-cigarettes, as discussed in Chapter 3.

Sub-national level bodies within the UK were included in the sample to investigate the diversity within a jurisdiction and allowed for exploration of the implications of multiple levels of government. The UK has four public health systems and they correspond to its four different political systems. Scotland, Wales, and Northern Ireland each have an autonomous legislature that makes health policy, while the UK Government directly runs England's National Health Service (NHS) (Bogdanor, 1999; Greer, 2016). This, therefore, makes the UK an interesting and complex case to examine. However, resources precluded the ability to include sub-national level bodies and multiple levels of government in all jurisdictions.

4.3.1 Identification of public health bodies' e-cigarette recommendation documents

Within each of the chosen jurisdictions, public health bodies that had produced public health recommendation documents, position, or policy statements on e-cigarettes were identified. A 'public health body' was defined as an organisation whose aims stated, or whose role within local/national/international policy is, to protect and improve the health of a population. Several public health bodies had been identified during the literature review stage of the research and through correspondence with experts in the field.

Additional public health bodies were identified using online searches. The online search for the public health bodies and recommendation documents was conducted between July and August 2019. As the literature surrounding e-cigarettes is continuously evolving, another online search was conducted in December 2019 to ensure no documents had been missed from the sample. Websites of public health bodies were searched for any publicly available documents using the key terms "e-cigarettes", "electronic cigarettes", "e-liquids", and "tobacco". Citation lists within the identified

documents were examined for additional relevant recommendation documents, position, or policy statements. The criteria for sample inclusion are shown in Table 4.3.

INCLUSION	EXCLUSION
Published as a report or in similar document form	Webpages, fact sheets, research articles, and media releases
Published between 2014-2019	Published before 2014 or after 2019
Published in English	Not in English
Published by a public health body	Medical organisations, patient organisations, pharmaceutical organisations, health charities, and government policy
Public health recommendations relating to e-cigarettes had to be made (e.g., regarding advertising and promotion of e-cigarette products)	Detailed only research recommendations
Provided at least two public health recommendations on e-cigarettes	Provided fewer than two public health recommendations on e-cigarettes

Table 4.3: Criteria for including documents in the sample

Through snowballing from websites, policy documents, and personal networks, a list of relevant experts within each jurisdiction was compiled. These experts were emailed with a list of the documents making up the sample and asked to provide details of any recommendation documents, positions, or policy statements they believed to be influential that were not included in the original sample. The search strategy is presented in Figure 4.1. See Appendix A for the detailed search strategy of the sampling of public health recommendation documents.

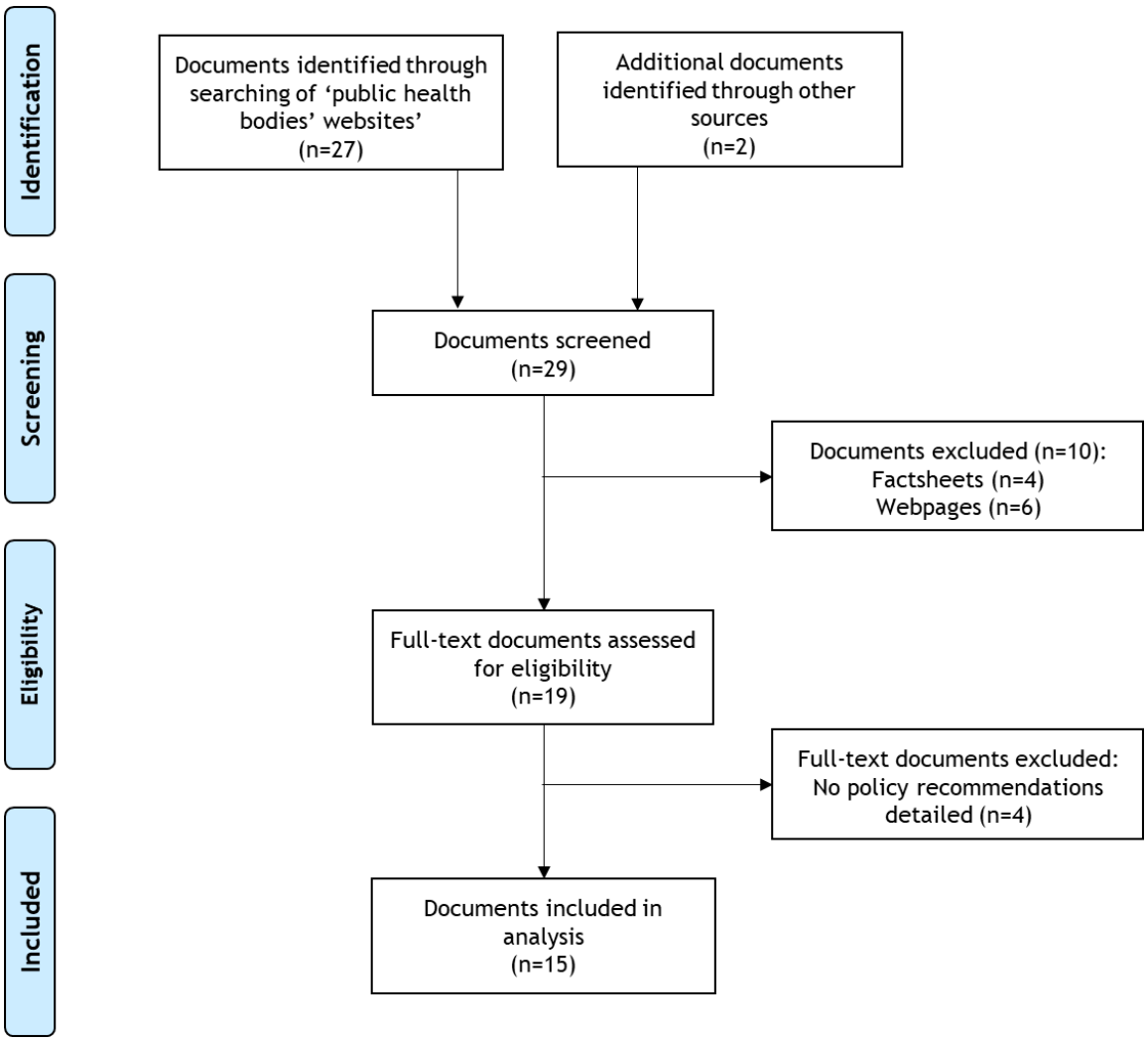

Figure 4.1: PRISMA Flow Chart of the strategy used to identify the public health bodies' recommendation documents

4.4 Document analysis of public health bodies' e-cigarette recommendation documents

Document analysis is a form of qualitative research in which both printed and electronic documents are reviewed or evaluated (Bowen, 2009). Similar to other qualitative analytical methods, document analysis involves the examination and interpretation of data to extract meaning, gain understanding and develop empirical knowledge, taking into account the context (i.e., the environment which influences policy decisions), and the purpose for which it was produced (Corbin and Strauss, 2008). Documents can serve a variety of purposes in terms of research including providing background and context; highlighting additional questions to be asked; supplementary data; a way of tracking changes and developments; and verification of findings from other data sources (Bowen,

2009). Document analysis combines the elements of content analysis and thematic analysis (Bowen, 2009). Content analysis can be defined as the organisation of data/information into categories related to the research question(s) (Hsieh and Shannon, 2005). In contrast, thematic analysis involves the examination of patterns within data, with the emerging themes becoming the focus of the analysis.

Document analysis has been used as a stand-alone method but is often conducted in combination with other qualitative research methods as a means of triangulation. I conducted triangulation across the four data sources, which are described in more detail in Section 4.9.

4.4.1 Research questions

The research question guiding this section of the study was:

RQ1: What are the similarities and differences in e-cigarette public health recommendations across diverse jurisdictions?

This section of the study also contributed to answering the following research question:

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

4.4.2 Analytical approach

Documents were qualitatively analysed using thematic analysis. The steps involved were: 1) familiarisation with the data; 2) generating initial codes; 3) searching for themes; 4) reviewing themes; 5) defining and naming themes; and 6) writing the report (Braun and Clarke, 2006). Reading of the included documents was first conducted to establish familiarity with the data. Coding of the documents was initially conducted using deductive coding, based on an adapted version of the WHO MPOWER framework for tobacco control (World Health Organisation, 2013), supplemented by inductive codes. See Section 3.6.1 for more information on the WHO MPOWER framework.

The adapted MPOWER framework comprised:

- **M**onitoring e-cigarette use and prevention policies;

- **P**rotecting people from passive vaping;
- **O**ffering to help quit tobacco use and use of e-cigarettes as a smoking cessation tool;
- **W**arning about the danger of tobacco and e-cigarette use;
- **E**nforcing bans on e-cigarette advertising, promotions and sponsorship; and
- **R**aising taxes on e-cigarette products.

A full list of the coding framework is shown in Appendix B. Using NVivo 12 descriptive coding was then completed for all the recommendation documents. The coding was refined and a framework was created to summarise the descriptive coding. Data was coded under multiple themes when it was thought to be appropriate. The frameworks allowed familiarity to be gained with the data. Both the framework and a sample (30%) of the coding were double-checked by two experienced researchers (Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington). Following the initial coding, thematic analysis was conducted, making comparisons across documents and jurisdictions. In addition to examining patterns in the data, I paid attention to contradictory data during the analysis.

4.5 Document analysis of public health bodies' development documents

4.5.1 Research questions

This section of the study contributed to answering the following research questions:

RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

4.5.2 Identification of public health bodies' development documents

To examine the processes followed by public health bodies in order to develop recommendations, various development documents or manuals produced by selected public health bodies were identified. Websites of the included public health bodies were searched for any publicly available documents or manuals detailing the process used to develop their recommendations. If a document or manual was not publicly available, the public health body was contacted via email and asked to provide any details on the process used to develop recommendation documents.

As I was interested in the processes for disclosing, collecting, and managing COI, I aimed to include documents that addressed COI in the development process. I called a document detailing the processes for collecting and managing COI a "COI policy". Two of the public health bodies' COI policies were emailed to me previously when contacting them about their development documents. For the remaining public health bodies, I searched their respective development documents to see if they contained or cross-referenced (e.g., included a hyperlink to the document(s)) a COI policy). If a COI policy was not included or cross-referenced, the public health bodies' websites were searched for any publicly available COI policies. Following this, if a COI policy was not publicly available, the public health body was contacted via email and asked to provide any details on the process(s) to disclose, collect and manage COI.

4.5.3 Analytical approach

The development documents and COI policies were qualitatively analysed using thematic analysis following the six-step process described by Braun and Clark (2006). Reading of the included documents was first conducted to establish familiarity with the data. Coding of the documents was initially conducted using deductive coding, based on the GRADE EtD Framework (Alonso-Coello et al., 2016b), with inductive codes iteratively added. In doing so, this allowed for exploration of public health bodies' processes for developing recommendations and how evidence influences the development process. For details relating to the disclosure, collection, and management of COI, I drew upon standards and recommendations proposed by the Institute of Medicine (IOM) (Institute of Medicine, 2009; Institute of Medicine, 2011) and ICMJE (International Committee of Medical Journal Editors, 2021). A full list of the

coding frameworks for the development documents and COI policies is shown in Appendix C and Appendix D, respectively. Using NVivo 12, descriptive coding was then completed for all the development documents and COI policies. The coding was refined and frameworks were created to summarise the descriptive coding (one for the development documents and one for the COI policies). Data were coded under multiple themes when it was thought to be appropriate. The frameworks allowed familiarity to be gained with the data. The development document framework and a sample (30%) of the coding were double-checked by two experienced researchers (Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington). The COI policies framework and a sample (40%) of the coding were double-checked by Dr Kathryn Skivington. In addition to examining patterns in the data, I paid attention to contradictory data during the analysis.

4.6 Citation network analysis of the sources of evidence used in recommendation documents

A citation "represents the citing author's use of the cited work and indicates an influence of the cited work on the author's new work and as such a flow of knowledge from the cited to the citing works' authors" (Zhao and Strotmann, 2015, p.1). Citation analysis measures the importance or impact of an author, an article, or a publication by counting the number of times cited in other works. Network analysis can be used to study patterns of connections between documents, where a citation is considered a link between documents in the network (Aksnes et al., 2019; Lefebvre et al., 2020). It has been applied in several social sciences to study research impact, knowledge flows, and knowledge networks (Zhao and Strotmann, 2015). Network analysis is a set of techniques derived from network theory (Hevey, 2018) and is used to examine the relationship among entities, such as persons, organisations, or documents (Marsden, 2015). In my research, I utilised network analysis to investigate the relationship between public health bodies' e-cigarette recommendation documents by examining the sources of evidence (citations) within each document.

4.6.1 Research questions

The two research questions used to guide this section of the research were:

RQ2: What are the sources of evidence being used in public health bodies' e-cigarette public health recommendations and is the evidence cited differently across jurisdictions?

RQ3: What are the conflicts of interest and funding sources present within cited evidence drawn upon during the development of e-cigarette public health recommendations?

This section of the study also contributed to answering the following research question:

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

4.6.2 Analytical approach

4.6.2.1 Data extraction

The analytical process started by manually extracting all the cited references from the recommendation documents into an Excel spreadsheet, where each cited document was given a unique identifier (across all recommendation documents). I conducted all of the data extraction, and a random sample of 10% was independently double-checked by a second author (Andrew Baxter, PhD Researcher at SPHSU). These were imported into R (v 3.6.1; R Core Team, 2019), cleaned and organised, and deduplicated before constructing a two-mode adjacency matrix (see Section 4.6.3 for more details) charting unique citations across recommendation documents (Wasserman and Iacobucci, 1991). One recommendation document was removed as it did not include any references.

Based on exploratory visualisation of the full network and a pragmatic decision between the supervisory team and myself, it was decided that visualisations and more detailed analysis should focus on high-impact citations (citations cited across three or more of the recommendation documents) as this was more manageable. From these, I manually extracted study type and COI and funding statements (this included authors' financial ties and commercial funding). Within the literature, COI and study funding are sometimes reported separately; receipt of study funding from a commercial entity is not always considered a conflict of interest by the author(s) (Boyd et al., 2012), but the ICMJE recommends declaring such funding as a potential COI (International Committee of Medical Journal Editors, 2021). Both author declarations of interest and study funding

statements were classified as COI, including declarations of financial relationships with commercial entities and industry influence. COI statements in the publications were assessed and supplementary material (such as ICMJE forms) were checked (by myself) when referenced and available. If an author did not provide a COI statement in the manuscript and did not refer to supplementary material elsewhere, this was classified as 'no mention' of COI.

The potential for COI is present in all areas of public health. As described in Chapter 3 COI may threaten the integrity of scientific investigations, undermine the evidence base and risk threatening the trustworthiness of recommendations (Institute of Medicine, 2009; Norris et al., 2011; Mendelson et al., 2011). Thus, the management of COI in all stages of the process is essential for the development of high-quality recommendations (Qaseem and Wilt, 2019). In addition to examining the presence of COI in the influential citations, the COI declared within the other citations were examined as this would deepen our understanding of the diffusion of industry-funded and industry-supported evidence in public health recommendation documents.

To retrieve information and categorise each of the citations, a Shiny interactive web app (Figure 4.2) was created by Andrew Baxter (PhD Researcher at SPHSU) under my direction. I was responsible for setting goals, determining the details to be extracted, testing, and providing feedback. The Shiny app displayed each citation extracted author and title, recorded publication type, and searched SCOPUS to identify journal-published articles. Shiny is an R package that allows the creation of interactive web applications, combining the statistical power of R and the interactivity of the modern web (Chang et al., 2019). It is an efficient alternative to spreadsheets and printed visualisations as it saves space and time in the construction, automation, and distribution of data visualisation and statistical analysis (Chang et al., 2019; Columbus, 2019). Citations were categorised (by myself) by type to provide insight into the different types of evidence being drawn upon by public health bodies when making e-cigarette recommendations.

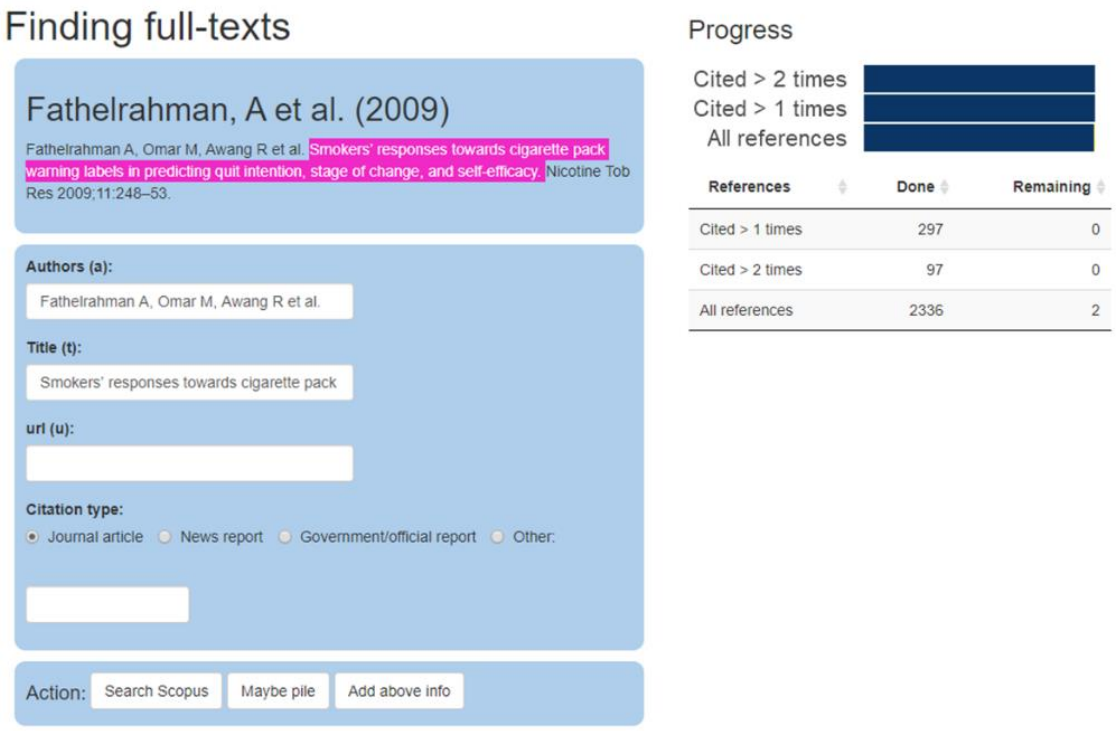

Figure 4.2: Screenshot of the Shiny app used to categorise each citation and to find the full text of all journal articles

Declaration of COI is an increasingly common requirement for journal publications (e.g., Nature Electronics, 2018; Elsevier, 2021). Therefore, analysis focused on cited journal article texts as I would be able to extract COI details. Journal articles were defined as journal publications consisting of an academic study or information (e.g., essay) concerning a particular topic/discipline. Cited journal article texts were then imported with search results into a second Shiny app (Figure 4.3), also developed by Andrew Baxter (PhD Researcher at SPHSU) under my direction, to read and code for the presence or absence of COI or funding statements and the types of conflict present. Full texts for each available article were retrieved and the phrases "Funding", "Interests", "Conflict*", and "Declar*", with the 100 characters preceding it and the 300 characters following it extracted. I also checked supplementary material (such as ICMJE forms) if the Shiny app detected the authors' reference to these. A random sample of 10% was independently double-coded by a second author (Andrew Baxter, PhD Researcher at SPHSU) and there was full agreement on the second coding.

Figure 4.3: Screenshot of the Shiny app used to extract COI and funding statements

4.6.3 Network graphs

I constructed bipartite network graphs using R and igraph (software for creating and manipulating graphs and analysing networks) (Csardi and Nepusz, 2006). Network graphs are visual illustrations of interconnections between a set of entities (Marsden, 2015). A bipartite network is a type of network comprised of two sets of nodes, in which an edge can only connect an agent to an artefact (Neal et al., 2021). Figure 4.4 illustrates a simple bipartite graph (left) and to-node adjacency matrix (right).

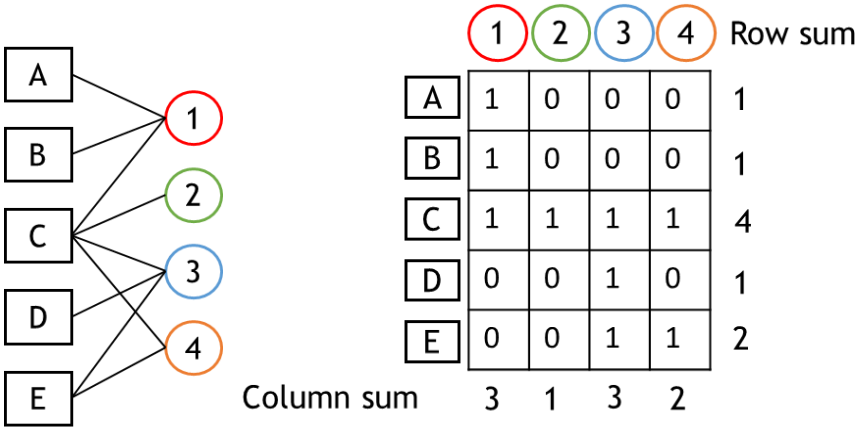

Figure 4.4: Example of a bipartite graph and matrix[14]

The bipartite graph shows five agents (squares) and their connections to four artefacts (circles). The bipartite matrix shows the pattern of agent-artefact connections using 0s and 1s. Recommendation documents and references were plotted as separate classes of nodes; edges denoted citation of a reference in a recommendation document. Bipartite network graphs were used to visualise and investigate the relationship between public health bodies' e-cigarette recommendation documents and the sources of evidence (citations) within each document. The Fruchterman-Reingold force-directed algorithm (Fruchterman and Reingold, 1991) was used for placing nodes to visualise the closeness of recommendation documents-document connection through the number of shared references. In force-directed layouts, nodes are represented as points that are electrically charged and apply repulsive forces against each other. Edges connect these points simulating a spring-force, attracting adjacent nodes (Gibson et al., 2012; Kobourov, 2013). The model iteratively determines the resulting forces that act on the nodes and tries to move the nodes closer to an equilibrium where all forces add up to zero and the position of the nodes stays stable (Gibson et al., 2012; Kobourov, 2013). The initial network graph plotted all citations across all recommendation documents (that included citations), coloured by the number of times cited.

Three further graphs of high-impact citations were constructed, coloured by the number of times cited, type of publication, and type of COI. Publication types were classed as basic science research without human subjects (e.g., examination of aerosols and e-

[14] Reproduced from NEAL, Z. P., DOMAGALSKI, R. & SAGAN, B. 2021. Analysis of Spatial Networks From Bipartite Projections Using the R Backbone Package. *Geographical Analysis,* DOI: 10.1111/gean.12275.

liquids), SR, non-systematic review, longitudinal observational study, cross-sectional observational study, and RCT.

4.6.3.1 Statistical analysis

To analyse whether recommendation documents drew upon similar evidence, bipartite stochastic block models were used to detect clustering within the citation network (Larremore et al., 2014). The method aims to detect if there are groups of documents that are similar based on their connections to other documents in the citation network. Recommendation documents which drew upon similar sources of evidence were examined and groups of recommendation documents by the strength of connection were created. The clustering of evidence sources was determined by their co-occurring citations in recommendation documents. A series of block models were fitted, with between 1 and 10 blocks (referred to as 'groups' for the remainder of the thesis) of recommendation documents and between 1 and 15 blocks (referred to as 'clusters') of evidence sources (Larremore et al., 2014). Log-likelihood was used to identify the number of blocks that best fitted the structure of the citation network and selected the number of blocks based on model fit, parsimony, and interpretation of the recommendation document membership. Clusters were examined to determine which recommendation documents drew upon similar sources of evidence. Fisher's exact tests were conducted to determine whether the proportion of COI was differently distributed across recommendation groups and reference clusters (as several count values were low).

4.6.3.2 Qualitative analysis

In addition to examining the type of publication and type of conflict of interest of the subset of influential citations, I conducted in-depth qualitative analysis to determine if the interpretation of the citations varied across recommendation documents. I began the analysis by creating a framework containing each of the influential citations and the recommendation documents that cited that source. I then reviewed each recommendation document, firstly establishing the reference style used (e.g., Harvard or Vancouver) to assist in finding where in the document the reference was cited. To investigate the interpretation of the citations, the surrounding text of when the reference was cited within the recommendation document was examined. This was done each time the reference was cited. Coding was initially developed inductively using descriptive codes. These codes were refined during the coding process, with

additional codes added, to ensure that all important aspects of the interpretation were captured within at least one code. The text was firstly coded based on the topic area discussed (e.g., e-cigarettes as a smoking cessation tool) and secondly by the interpretation (e.g., may have benefits). Where COI were declared in a cited document, it was recorded whether this was assessed in the recommendation document. The coding was an iterative process and was discussed at team meetings to help refine and adapt the framework. A full list of the coding framework is shown in Appendix E. A random sample of 20% was independently double-coded by Dr Kathryn Skivington and any disagreements were discussed and clarified.

4.7 Thematic analysis of expert interviews

The final data source was qualitative interviews with experts involved directly and indirectly in the development of the recommendation documents included in the sample.

4.7.1 Research questions

This section of the study contributed to answering the following research questions:

RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

4.7.2 Rationale for interviews with experts

Expert interviews are beneficial when it is difficult or impossible to gain access to a particular topic/situation (Smith, 2006; Bogner et al., 2009). Bogner et al. (2009) define an expert as a person with technical, process, and interpretive knowledge in relation to their areas of expertise. Experts have inside and in-depth knowledge or privileged access to information relating to the development, implementation, or control of solutions/policies, strategies, or decision processes (Meuser and Nagel, 2009; Van Audenhove and Donders, 2019). There are three different types of expert interviews:

- Explorative: applied in an un-investigated field for explorative purposes;

- Systematising: reconstruction of experts' 'objective knowledge' in a specific field; and

- Theory-generating: in addition to experts' 'objective knowledge', also includes the reconstruction of implicit knowledge of actions and interpretations.

Bogner et al. (2014) differentiate between technical knowledge, process knowledge, and explanatory knowledge. Technical knowledge is very specific data in a topic area (e.g., data, facts, technical information, business facts, statistics) (Bogner et al., 2014). Process knowledge refers to knowledge about processes, interactions, and routines in the topic area in which the expert is involved (Bogner et al., 2014). For example, in policy analysis, this will often relate to policy and decision-making processes (Van Audenhove and Donders, 2019). Explanatory knowledge can be defined as the subjective relevance, points of view, interpretations, meaning, and explanations held by the expert (Bogner et al., 2014; Kaiser, 2014). Kaiser (2014) adds the idea of context knowledge, defining it as "knowledge about the context, power, and interest structure interfering in solving societal conflicts" (Based on translation by Van den Bulck et al., 2019). This fourth type of knowledge is an interesting distinction from process knowledge as the decision-making process is highly influenced by the context. The influence of context on decision-making will be examined in Chapter 8. These types of expert knowledge correspond to different types of interviews (Table 4.4).

Type of expert interview	**Type of knowledge**
Exploratory interview	Technical knowledge
Systematising interview	Process knowledge
	Context knowledge
Theory-generating interview	Explanatory knowledge

Table 4.4: Type of interview according to the type of knowledge[15]

[15] Based on material from BOGNER, A., LITTIG, B. & MENZ, W. 2014. *Interviews with experts: a practical introduction,* Wiesbaden, Germany, Springer, KAISER, R. 2014. *Qualitative expert interviews,* Wiesbaden, Germany, Springer.

Semi-structured expert interviews were chosen as a way to have two-way communication between myself as a researcher and those experts involved in the development of public health recommendations. I conducted systematising expert interviews to access knowledge about the decision-making process to gain in-depth insights into the role and use of evidence in decision-making. Interviews provided an approach to question the motives relating to a particular position on e-cigarettes and the processes by which their position was informed. The latter is important for establishing an understanding of the role of evidence in public health bodies' recommendations. Furthermore, interviews allowed for the 'informal' aspects of the decision-making process to be investigated and discussed.

Expert interviews were chosen to develop an in-depth understanding of the decision-making process as they help ensure key areas are explored within every interview while also allowing the collection of rich data (Mason, 2002). The interviews allowed the participants' views, understandings, experiences, and perceptions of the decision-making process to be obtained, the semi-structured nature of the interaction allowing additional unexpected topics to be explored.

Three main benefits of expert interviews were relevant to my research. Firstly, expert interviews can be an advantageous method for interpreting documents (Richards, 1996). Within the setting of my research, the interviews with experts were an opportunity to question participants on their organisation's e-cigarette recommendations and the processes by which these recommendations were developed. Secondly, they can provide rich in-depth data that supply first-hand accounts of experiences and the outcome of events (Richards, 1996; Bogner et al., 2009). For my research, it allowed for a better understanding of the e-cigarette debate and the processes undertaken in the development of e-cigarette recommendations from the perspective of different expert groups. Thirdly, expert interviews can reveal information that is not recorded elsewhere or that is not available for public release (Richards, 1996; Audenhove, 2007). In terms of my research, this offered insights into the sources of evidence drawn upon, how evidence was transferred to recommendations, and how contextual factors are addressed in the decision-making process.

4.7.3 Sampling and inclusion criteria

Interviews with experts are important as their views on the development of e-cigarette recommendations, the role of evidence, management of COI, and addressing of

contextual factors when developing recommendations may differ across the four selected jurisdictions. Views may also differ between expert types. All participants recruited for this research were considered to be influential in the development of public health recommendations.

Before starting recruitment, a list was created of all the experts influencing the recommendations being made. Experts were grouped into the following categories: academics, policymakers, and methodologists (i.e., people with expertise in applying evidence to produce recommendations). The aim of this exercise was to assist in the purposeful selection of participants and to ensure that diversity (by expert type and jurisdiction) in the sample was achieved. Purposive sampling is a technique that is used in qualitative research as it allows for the identification and selection of information-rich cases while effectively using minimal resources (Patton, 2002; Creswell and Plano Clark, 2011; Palinkas et al., 2015).

The inclusion criteria for the expert interviews were individuals involved in the development of the e-cigarette recommendation documents and/or contributed to the recommendations (e.g., produced a specific section or chapter). If author/contributor names were not published in the recommendation document, I contacted the relevant public health body, stated the purpose of my research, and asked if someone would be willing to take part in the study. Alongside purposive sampling, snowball sampling was also used, whereby participants were asked to recommend additional respondents from their knowledge of the field and involvement in the decision-making process. Snowballing sampling is a technique in which the researcher identifies a sample of participants relevant to the research and these sampled participants introduce/propose other potential participants who meet the inclusion criteria (Bryman, 2012). Snowballing sampling is a useful technique as it allowed for potential participants to be identified who are relevant to the study. Although there needs to be consideration that the identified participants may not meet the inclusion criteria, this was not the case in this study.

Gaining access to experts can be difficult and there was a limited number of individuals available for recruitment, this was factored into the research when determining the sample size. With this in mind, as well as the limited time available, it was decided that the study should aim for between 15 and 20 participants. This, in combination with the two document analyses (analysis of recommendations documents and analysis of development documents) and the citation network analysis, would generate a

considerable amount of data that would allow for an in-depth analysis and triangulation of the four data sources. There were several difficulties with recruitment, these are discussed below in Section 4.7.5.2.

4.7.4 Ethics and confidentiality

The research received ethical approval from the University of Glasgow's College of Medicine and Veterinary Science research committee (reference 200180098) (Appendix F). All participants were contacted by myself and provided with a participant information sheet (Appendix G), which contained my contact information as well as the supervisory team. Consent was obtained for interview participation and the use of quotations in publications and presentations (Appendix H).

A participant information sheet and consent form were provided to each participant prior to the interview, which contained information about the project and the confidentiality that participants could expect. This was discussed further at the outset of each interview, and I assured participants that all data would be pseudonymised. I highlighted that only the research team would have access to the recording and transcripts.

At the beginning of each interview, I discussed the participant information sheet with the participants and confirmed that they had read and signed the consent form. I then checked they were satisfied and had no outstanding queries, and during this discussion I reiterated that they could withdraw from the research at any time. For those participants who had read the consent form, but had not returned it to me, verbal consent was taken. Where this occurred, these participants signed and returned the consent form shortly after the interview had finished.

Following the interview, participants were provided with a copy of their transcript to review and were asked for any amendments that were required to ensure their anonymity (for example, indicating sections of the transcript that should be made not for quotation). No ethical issues arose during or after the interviews.

4.7.5 Data collection

4.7.5.1 Recruitment and access

Recruitment took place between June 2019 and June 2020. In the initial email to potential participants, I provided an overview of the research and asked if they would be willing to have an informal discussion about the e-cigarette debate. Most of the experts contacted agreed to either a telephone or a Zoom/Skype call. The aim of this initial meeting was to build a relationship with the expert. As a result of these initial meetings, seven experts agreed to take part in the research. Some of the experts were not able to participate; however, they provided me with other potential participants and allowed me to use their name as a way of gaining access. Snowball sampling resulted in the recruitment of another three participants. A combination of initial discussions and snowball sampling resulted in the recruitment of a total of 10 participants.

For three of the public health bodies, I emailed the public health body directly asking if they would be able to put me in touch with a suitable participant. Each public health body provided a potential participant, although it took several points of contact before a participant was identified. One of my supervisors provided details of two potential participants, I made contact through email, copying in my supervisor and both agreed to take part in the research. During recruitment, I was mindful of maintaining diversity in the sample (e.g., across expert types and jurisdictions). Unfortunately, due to the COVID-19 pandemic, I was not able to obtain as much diversity in the sample as I had hoped. The impact of the pandemic on recruitment is discussed in the following section and in Section 9.3.4.

4.7.5.2 Recruitment: Problems encountered

Overall recruitment was largely successful; however, some difficulties did occur. There were instances where a potential participant was not able to participate and recommended an additional respondent, but on examination, the additional respondent was not involved in the development of the recommendation document. Recruitment of expert interviews proved to be difficult after March 2020, due to the COVID-19 pandemic. Before March 2020 I completed 10 interviews and planned to recruit a minimum of five more participants. Due to the COVID-19 pandemic, numerous academics and policymakers returned to clinical work and this impacted the

recruitment for this research. I continued recruitment by emailing potential participants and public health bodies; however, there was a delay in response or no response. Of those who did respond, most were not able to take part in the research. Like the academics and policymakers who I wanted to interview, I too returned to clinical work as a pharmacy dispenser, a job I had only left a few months prior, and this impacted the time I was able to spend on recruiting potential participants.

Following a discussion with my supervisors, it was decided to extend recruitment to June 2020. Between March 2020 and June 2020, I was able to recruit five more participants, taking the sample size to 15. Overall, considerable hours were dedicated to the recruitment; however, due to time constraints, it was decided that recruitment had to end in June 2020.

4.7.5.3 Participant characteristics

In total, 15 Interviews were conducted between January and June 2020. Table 4.5 provides a list of participants by sector. All participants authored/contributed to at least one document included in the sample and several of the participants authored/contributed to more than one document included in the sample. Due to confidentiality, it is not possible to provide further details of the breakdown of participants beyond the broad sector. Eleven of the interviews were conducted by video call (using Skype/Zoom platforms) and four by telephone (all recorded using the SPHSU's digital recording system).

Sector	Number of participants
Academic	8
Policymaker	5
Methodologist	2

Table 4.5: Participant by sector

4.7.5.4 Development of interview schedule

Initially, interview schedules were developed based on the results of the document analysis and GRADE EtD framework (Alonso-Coello et al., 2016b). These were then tailored to two different interview schedules for expert interviews: academics (Appendix I) and policymakers and methodologists (Appendix J). These interview schedules were framed around similar key topics but probed in different areas

depending on the category of experts. Academics were probed more about tobacco control, e-cigarette regulation, and the development process whereas policymakers and methodologists were questioned on the development process and briefly on e-cigarettes.

The interview schedules were adapted after the first two interviews, to incorporate questioning on the management of COI and how evidence is translated into recommendations. This was done to gain insight into how this part of the process is undertaken by different public health bodies. The questions in the interview schedules were not asked in order, but rather the guide was used as a prompt for discussion and to ensure that no key areas were skipped or excluded.

Some interviews took a broadly narrative approach, with participants describing the process of developing a recommendation document from the initial idea through to evidence collection and recommendations made. Other participants discussed their experiences and gave examples from various documents.

During data collection, a fieldwork diary was maintained, and notes were written up immediately after the interview had been conducted. In this diary, I recorded my thoughts regarding the data collection and discussions I had with participants. This diary allowed me to reflect not only on the interviews but also on my own progress.

4.7.5.5 Recording and transcribing

I conducted all of the interviews from my University office. Online interviews were digitally recorded using an Olympus digital recorder and telephone interviews were recorded using the Unit's digital recording system. Interviews were transcribed verbatim, checked and pseudonymised. I transcribed two recordings; the rest of the interviews were transcribed by a professional transcription service, subject to a confidentiality agreement. To ensure the accuracy of the transcriptions, I listened to the interviews in full. Interviews lasted between 34 minutes and 84 minutes (median 53 minutes). The interview which lasted 34 minutes was limited in time due to another meeting the participant had to attend. Following the interview, participants were provided with a copy of their transcript to review and were asked for any amendments that were required to ensure their anonymity (e.g., indicating sections of the transcript that should be made 'not for quotation').

4.7.6 Analytical approach

The framework method is a systematic approach that identifies commonalities and differences in qualitative data, defines relationships, and builds conclusions (Spencer et al., 2003a). In my research, the framework method was selected for analysis of the qualitative interviews as a useful way to explore and relate information gathered from a range of experts. The seven-stage process of the framework methods was used for analysis (Gale et al., 2013). These stages were: 1) transcription; 2) familiarisation (re-listening to audio recordings and reading and checking transcripts); 3) generation of initial codes (transcripts were coded based on the GRADE EtD Framework (Alonso-Coello et al., 2016b) and before using Nvivo 12, two transcripts were coded by hand); 4) development of a working analytical framework after coding the first few transcripts and comparison of the label among reviewers (myself and Professor Shona Hilton) to agree on the set of codes to use in the subsequent transcripts; 5) application of the analytical framework (codes were refined throughout the coding process, additional codes added, ensuring that all the important aspects were depicted by at least one code); 6) inserting data from the remaining transcripts into the framework (further confirmed or adjusted by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington to ensure consistency); and 7) interpretations of data so that the characteristics of and differences between data were identified. The coding was an iterative process and was discussed at team meetings to help refine and adapt the framework. A full list of the coding framework is shown in Appendix K. I conducted all of the coding and 30% of the transcripts were double-coded by Professor Shona Hilton, Professor Srinivasa Vittal Katikireddi, and Dr Kathryn Skivington.

During the analysis, fieldwork notes were re-read on several occasions, this was to review the initial impressions about the interview data and, also, to help identify potential explanations for the findings. I used the 'Memo' function within NVivo to note emerging findings for further consideration and also by writing notes in the fieldwork diary.

4.8 Comparison across two data sources

To answer the research question guiding this section of the research I compared data from two data sources: 1) COI policies produced by the public health bodies'; and 2) qualitative interviews with experts.

4.8.1 Research question

The research question guiding this section of the study was:

RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?

4.8.2 Analytical approach

The purpose of employing multi-methods for this section of the study was to elicit several important viewpoints regarding the collection and management of COI during the development of e-cigarette public health recommendations. The published public health bodies' COI policies describe the intended methods of the process and are more amendable to transparent analysis but were not always available and may not explain real-world implementation. Therefore, I analysed both data sources.

Having analysed each of the COI policies and expert interview transcripts individually as described in Sections 4.5.3 and 4.7.6, respectively, the analyses were synthesised.

The data from the COI policies and the data relating to COI from the interview transcripts were merged and a large data synthesis framework was produced in NVivo 12. This also allowed for a more comprehensive overview of all the data. A full list of the coding framework is shown in Appendix L. Within this framework, descriptive summaries of the data were generated and allowed for cross-comparisons to be made between the data sources. The framework highlighted where there was consensus or disagreement around the disclosure, collection, and management of COI during the development of e-cigarette public health recommendations.

4.9 Triangulating across data sources

Triangulation refers to using multiple sources of data or multiple approaches to investigate one set of research questions (Mason, 2002; Salkind, 2010). Bowen (2009) explains that by examining the data obtained from different methods, the researcher can verify findings across the data sources. In this way triangulation through combining methods allows triangulation across data, therefore, strengthening the study by combining methods while ameliorating, although not entirely overcoming, the

limitations of any single method pursued in separation (Patton, 2002). This can reduce the potential biases (Patton, 2002; Bowen, 2009) and gain deeper insights into the phenomenon under examination.

To examine the contextual factors influencing the development of e-cigarette recommendations I triangulated data across all four sources: 1) public health bodies' recommendations documents; 2) development documents produced by the public health bodies'; 3) sources of evidence used in the public health bodies' recommendation documents; and 4) qualitative interviews with experts.

4.9.1 Research question

The research question guiding this section of the study was:

RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

4.9.2 Analytical approach

Following the individual analysis of the four data sources, with the analytical approaches described above, a further stage of analysis was undertaken across all four data sources, using thematic analysis. Spencer et al. (2003b) state that thematic analysis of data should be conducted as an iterative process, starting close to the data and moving further away as the analysis progresses. Conducting triangulation across the four data sources allowed me to examine data obtained from different analytical methods, find new meanings to the data and verify findings across data sources.

This triangulation of data was guided by the conceptual framework set out by Dobrow et al. (2004) which discussed three key components of a policy decision: evidence; context; and utilisation. Dobrow et al.'s (2004) conceptual framework for context-based evidence-based decision-making discussed the three key components of policy decision-making and acknowledges the influence of contextual factors on the process. By drawing upon this framework, I was able to gain a deeper understanding of the numerous contextual factors influencing the role and use of evidence in the decision-making process and in turn, answer the research question guiding this section of the study.

Dobrow et al.'s (2004) framework was refined in 2006 to acknowledge the three layers of policy objectives: effectiveness, appropriateness, and implementation (Dobrow et al., 2006). In the refined framework, Dobrow et al. (2006) attempt to unpick the types of evidence used in the decision-making process. Whereas Dobrow et al.'s (2004) framework focuses in more detail on context and the influence of contextual factors on the decision-making process. As this was the focus of part of this thesis, the analysis is structured with reference to Dobrow et al.'s (2004) framework (Figure 4.5).

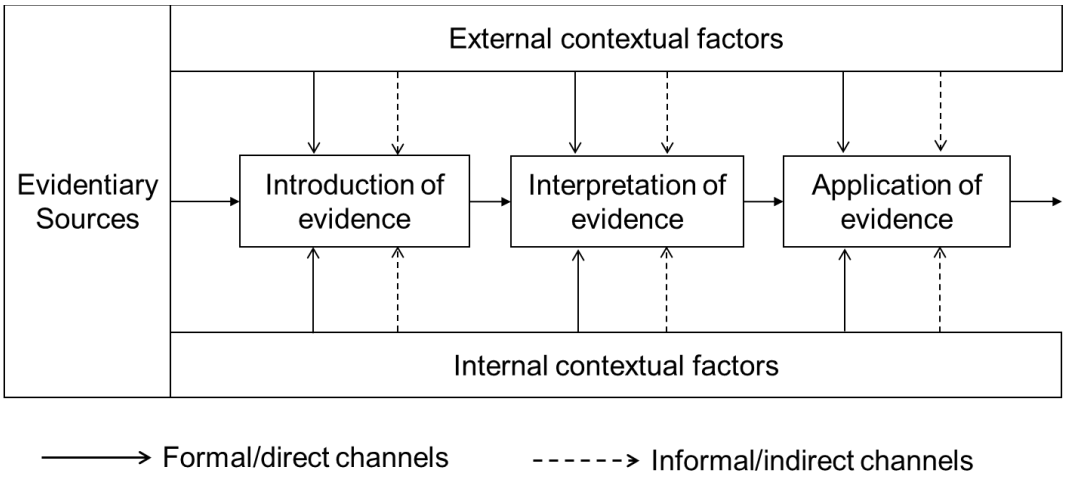

Figure 4.5: Conceptual framework for context-based evidence-based decision-making[16]

Utilisation was understood to mark the critical interaction between evidence and context. Utilisation was based on a three-stage process model developed by Rich (1997), which addressed: introduction of evidence, how evidence is identified and brought to the decision-making table; interpretation of evidence, how the internal and external validity of evidence is evaluated; and application of evidence, the influence each source of evidence has on the decision outcome.

Having coded each of the data sources individually, the analyses were synthesised and the codes were mapped onto the Dobrow conceptual framework (Figure 4.6).

[16] Reproduced with permission from Evidence-based health policy: context and utilisation M.J Dobrow and R.E Upshur, 2004, Social Science and Medicine, 58, p.216. Copyright [2004] by Elsevier.

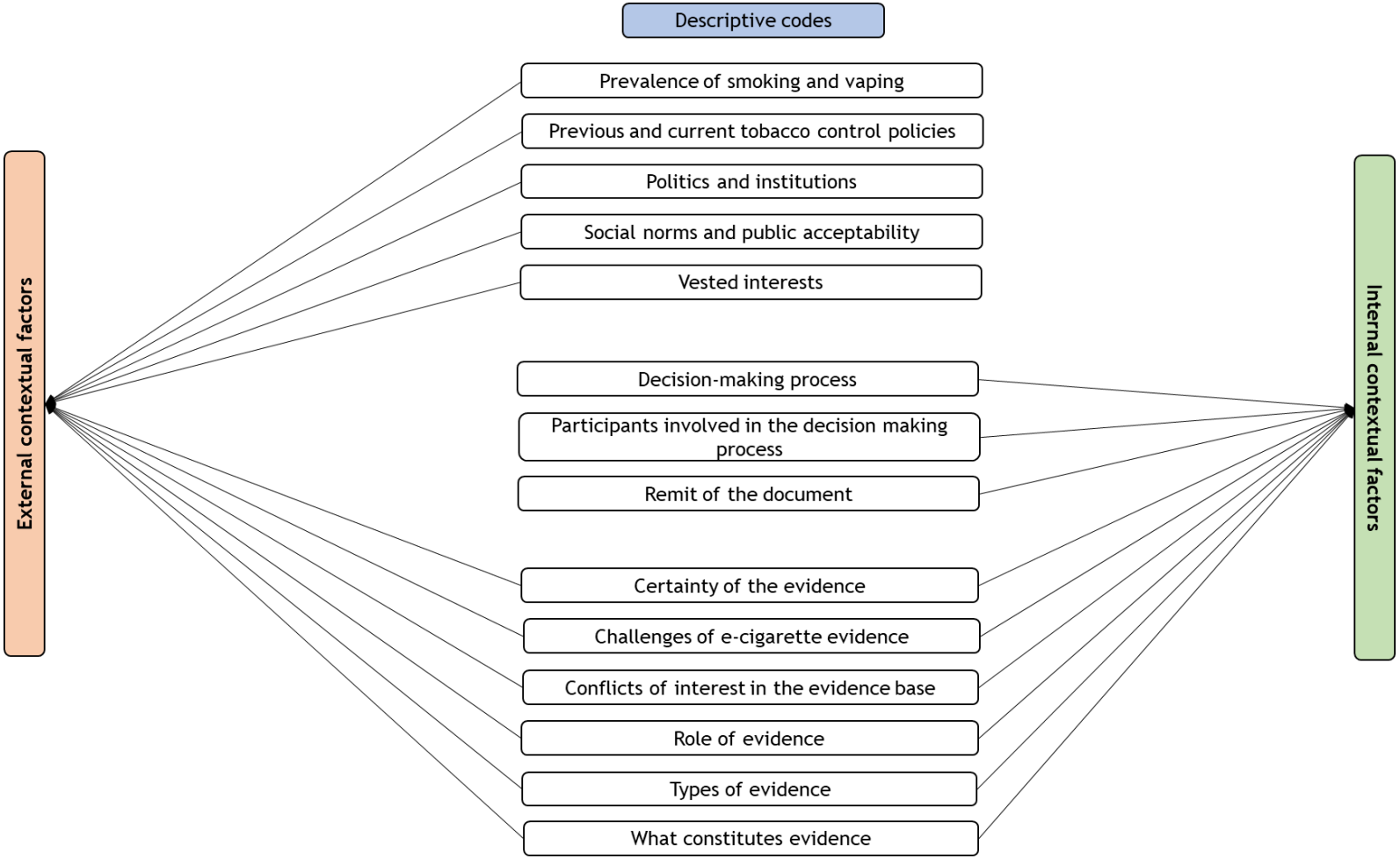

Figure 4.6: Coding process for integrating recommendation documents, development documents, and expert interviews

Three large data synthesis frameworks based on Dobrow et al.'s (2004) conceptual framework, one from each stage of evidence utilisation were produced in NVivo (Appendix M). The framework and a sample (20%) of the coding were double-checked by Dr Kathryn Skivington.

This also allowed for a more comprehensive overview of all the data. Within this framework, descriptive summaries of the data were generated and allowed for cross-comparisons to be made between the data sources. It highlighted where there was consensus or disagreement around evidence use, as well as showing how contextual factors influenced and were addressed during the decision-making process.

4.10 Reflexivity

Reflexivity can be defined as "an awareness of the researcher's role in the practice of research and the way this is influenced by the object of the research, enabling the researcher to acknowledge how he or she affects both the research processes and outcomes" (Symon and Cassell, 2012, p.72). Researcher positioning including personal characteristics such as age; gender; personal experiences; beliefs; biases and theoretical, political, and ideological stances; and emotional responses may impact the collection and interpretations of the data (Horsburgh, 2003; Primeau, 2003; Kosygina, 2005; Berger, 2013). In qualitative research, being reflective of one's own biases and standpoints is a strength rather than a weakness of the method. It reflects that the researcher is being transparent and reflexive throughout the study processes in data collection, data analysis, and the dynamics of managing the relationships with participants in terms of power and self-identification (Saunders, 2011). My perspectives and views have arguably impacted upon all aspects of the research process, from the decision to study the topic, to data collection and the analysis process. Throughout this research, I was conscious of my own standpoints, and during the data collection process I noted down my reflections as part of the fieldwork notes (Easterby-Smith et al., 2015).

Prior to undertaking this research, I completed a master's in Forensic Toxicology, during which I examined the nicotine concentration in a variety of e-liquids. It was during this project that my interest in tobacco control and more specifically e-cigarettes grew. Although my dissertation did not involve an examination of the different regulatory approaches to e-cigarettes, when reviewing the literature, it was evident that different

regulatory approaches were being adopted worldwide. This further prompted my curiosity about why different e-cigarette regulatory approaches were being pursued globally. Based upon this, when designing my PhD research project, I felt that there was an opportunity for research to examine what the different regulatory approaches were and to better understand the process for developing public health policies as this may provide insights into why different approaches are pursued.

Interview data are jointly constructed, arising from the interaction between interviewer and participant (Mishler, 1991). Prior to conducting the interviews, I had carried out a review of published e-cigarette recommendation documents produced with and across four jurisdictions. This allowed me to be aware of the policy background before conducting the interviews and thereby create an interview schedule that would best utilise the time spent with participants. In addition, this meant that I was better prepared for the interviews, and I was able to position myself to the participant as a credible researcher which in turn helped increase the chance of recruitment and the quality of interview data obtained.

I sought to interview a range of experts across the four selected study jurisdictions. I was aware that my own professional background (including working in a pharmacy where I work with patients who want to quit smoking) would make me more understanding of those who took the viewpoint that e-cigarettes should be used as a smoking cessation tool, as I have interacted with patients who have been successful in quitting smoking by using e-cigarettes and the interview data may sometimes reflect this. For example, in early interviews, I found that when interviewing someone who was supportive of e-cigarettes, I was less likely to explore the reasons for this compared to someone who wasn't. Upon re-reading my fieldwork notes and interview transcripts I became aware of this and during the rest of the interviews I tried to explore reasons for supporting e-cigarettes through questioning and prompts.

Within public health, qualitative research has mostly focused on exploring the perspectives of patients or other potentially vulnerable groups. In this setting, there have been issues of interviewers having greater power over the participants (Karnieli-Miller et al., 2009; Nimmon and Stenfors-Hayes, 2016). In my research, it was the reverse, where participants could be considered 'elite' (Kezar, 2003; Desmond, 2004; Smith, 2006). Smith (2006) and Kezar (2003) argue that there has been a lack of appraisal of the literature relating to the definitions of 'elites'. Elite interviews are

characterised by power relationships being either more equal or reversed, since many participants occupy high-level positions within their respective organisations (Smith, 2006; Harvey, 2011). During the expert interviews, I was concerned about my accent and my position as a young and inexperienced researcher (in particular the power dynamic). As discussed in Section 4.7.5, I arranged initial informal discussions with potential participants to help build a rapport with them. Therefore, it is possible that the responses of participants could have been influenced by their knowledge of me from the informal discussions. Participants may have been likely to perceive me in a different manner compared to someone with who they had no previous relationship with. It was during the initial discussions that I was most aware of the power dynamic. However, when it came to interviewing the experts, I felt that the dynamic had shifted to a similar level. After the first few interviews, I became more aware of this positioning and tried to use this to draw out a more comprehensive exploration of the issue of e-cigarettes and the development process.

Prior to conducting the interviews, I was concerned about keeping the interviews 'on track'. I was contacting individuals who are considered to be experts in the topic area. Although I was grateful to them for taking the time to speak to me and share their knowledge on the topic area, I was concerned and nervous about interjecting when the interview went off-topic. Throughout all the interviews, I was aware of how I asked questions and the speed at which I would ask them. For interviews with participants outside the UK, I felt that due to my Scottish accent I had to change the speed at which I spoke so that I would be more clearly understood. I did not change my accent, but it was something that I identified as being potentially impactful to the interviews. In addition, I found that if I used my position as a novice researcher, especially when interviewing people outside of the UK, participants would explain things in more detail and provide the background to their answers. During the initial interviews, I found it difficult to negotiate the feeling of nervousness and concerns about the flow of the interview. As a result, the data produced in later interviews is richer and more detailed. In the interviews, I tried to place these concerns aside and focus on the aim of the interviews, which was to gather the participants' views and experiences. As I conducted more interviews and become more confident with the interview schedule these feelings subsided.

Many of the issues discussed above have impacted the analysis process. While I have attempted to ensure that no findings in this thesis are based on the information given to

me outside the data collection process, the informal discussions with participants indicated areas worthy of exploration. Through the course of the research, I have achieved a greater understanding of different aspects of the decision-making process. It is possible that my deeper understanding of the process may have impacted the analysis of the data. For example, my knowledge, understanding, and views of the processes to manage COI may have influenced how I analysed the data, particularly when participants discussed a less restrictive approach to managing COI. I have sought to minimise this by ensuring I pay attention to the full range of data (not only the interviews but also the other data sources) within my analyses.

4.11 Chapter summary

This chapter has outlined the methodological approaches taken to investigate the case study of e-cigarettes. Six main approaches have been described: first, a document analysis of e-cigarette recommendations; second, a document analysis of public health bodies' development documents; third, citation network analysis of the sources of evidence drawn upon in the selected e-cigarette recommendations; fourth, qualitative expert interviews; fifth, comparison across the public health bodies' development documents and expert interviews; and finally, triangulation of the four data sources (public health bodies' recommendations documents, development documents produced by the public health bodies', sources of evidence used in the public health bodies' recommendation documents and qualitative interviews with experts). Chapter 5 will examine the similarities and differences in e-cigarette recommendations across the four selected jurisdictions. Chapter 6 will focus on the citation network analysis of the sources of evidence drawn upon and the presence of COI. Chapter 7 compares data from two data sources: 1) development documents; and 2) expert interviews to investigate the collection and management of COI during the development of e-cigarette recommendations. Lastly, Chapter 8 will triangulate the four data sources to investigate how contextual factors influence the role and use of evidence in the development of e-cigarette recommendations.

5 Exploring e-cigarette public health recommendations: A comparative document analysis of four jurisdictions

5.1 Title, authorship and publication details

This article has been revised following peer review comments and an edited version of this article has been submitted to Public Health and Practice; a decision is pending.

Smith MJ, Skivington K, Hilton S and Katikireddi SV. Exploring e-cigarette recommendations: A comparative document analysis of four jurisdictions.

The overall work has been led by me and I take full responsibility for it. In this chapter, I use the terms 'we' and 'our' to recognise all authors.

The background and methods section of the manuscript have been edited to reduce repetition within the thesis and to add cross-reference across different chapters. The results have been expanded to include details that were included in the submitted manuscripts appendices.

5.2 Abstract

Objectives: The coherence of the tobacco control community has been challenged by the development of alternative nicotine products, particularly e-cigarettes. This study therefore explores e-cigarette recommendations made by public health bodies across four diverse jurisdictions.
Study Design: Document analysis of e-cigarette public health recommendations.
Methods: We purposively selected four diverse jurisdictions (WHO, UK, Australia, and USA) and identified published public health recommendation documents which focused on e-cigarettes. We conducted thematic analysis using NVivo 12 and coded using an adapted version of the WHO MPOWER framework alongside inductive codes.
Results: There were 228 recommendations made in 15 documents across 11 public health bodies (two from the WHO, eight from the UK, two from Australia, and three from the USA). Recommendations were found to fall within a spectrum of options

ranging from ‘harm reduction’ to ‘precautionary’. Public health bodies in the UK have adopted a ‘harm reduction’ approach, particularly when discussing the use of e-cigarettes as a smoking cessation tool. The WHO and public health bodies in Australia and USA have adopted a more ‘precautionary’ approach, arguing against the use of e-cigarettes as a smoking cessation tool until research has been undertaken. Recommendations agreed on two broad areas: protection of minors and prohibiting or restricting advertising, promotion, and marketing of e-cigarettes.
Conclusion: The rapid proliferation of e-cigarettes has polarised the debate and led to different regulatory approaches within the tobacco control community, with proponents of e-cigarettes adopting a ‘harm reduction’ approach and calling for less regulation, and opponents seeking stronger ‘precautionary’ regulation.

5.3 Background

Over the years the tobacco control community has worked well together to reduce tobacco use and has successfully supported the implementation of policies and frameworks, most notably the WHO FCTC (World Health Organisation, 2003). It has been suggested that the coherence of the international tobacco control community has been disrupted by the development of alternative nicotine products, particularly e-cigarettes (Hasselbalch, 2015; Weishaar et al., 2019). This has led to controversy within the tobacco control community, with policymakers and public health researchers taking different positions on the potential implications of e-cigarettes and their regulation (McKee and Capewell, 2015; Avdalovic and Murin, 2015; Middlekauff, 2015; Hawkins and Ettelt, 2019; Smith et al., 2021b).

E-cigarettes are a relatively new technology and there is no long-term evidence available on the direct health consequences (Callahan-Lyon, 2014; Kaisar et al., 2016; Chaffee, 2019). Against this background of limited evidence, it is clear that different jurisdictions have pursued different strategies and adopted different regulatory approaches. For example, in Singapore e-cigarettes are completely prohibited; in the UK and Italy they are considered consumer products; in Malta they are classified as tobacco products; and in France and Finland they are regulated as medicinal devices (Rose et al., 2015; Kennedy et al., 2017; Erku et al., 2020; Campus et al., 2021).

Due to the rapid emergence of e-cigarettes, numerous public health bodies across the world have released reports, guidelines, and statements on their position on e-cigarettes. However, few studies have carried out detailed comparisons e-cigarette of

policy approaches across diverse jurisdictions (Kennedy et al., 2017; Brady et al., 2019; Erku et al., 2020; Campus et al., 2021). This research, therefore, aims to explore e-cigarette public health recommendations being made by public health bodies across four diverse jurisdictions, focusing on the similarities and differences.

5.4 Methods

As discussed in Chapter 3, we purposively selected four influential jurisdictions to examine in this research: WHO, UK, (Scotland, England, Wales, and Northern Ireland), Australia, and USA. Sub-national level bodies within the UK were included in the sample to investigate the diversity within a jurisdiction, therefore making the UK an interesting and complex case to examine. However, resources precluded the ability to include sub-national level bodies and multiple levels of government in all jurisdictions.

Within each of the chosen jurisdictions, we identified public health bodies that had produced public health recommendation documents, position statements, or policy statements on e-cigarettes. See Section 4.3.1 for more details on the identification of the sample.

Documents were qualitatively analysed using thematic analysis following the six-step process described by Braun and Clark (2006). Coding of the documents was conducted using deductive coding, based on an adapted version of the WHO MPOWER framework for tobacco control (World Health Organisation, 2013). See Section 4.4.2 for more details on coding.

5.5 Results

The 15 included documents were published between 2014 and 2019 and their aims are summarised in Table 5.1. Some of the earlier documents may have been revised or replaced to accommodate new and updated evidence, which may account for the differences in recommendations.

Public health body	Recommendation document	Aim
INTERNATIONAL		
World Health Organisation	Electronic nicotine delivery systems (2014a)	Created in response to a request made at the Conference of the Parties (COP) in 2012. Aims to examine the emerging evidence on the health impacts of ENDS and to provide recommendations for their prevention and regulation.
	Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)	Created in response to a request made at the COP in 2014. Aims to review ENDS and ENNDS, consider methods to measure the contents and emission of ENDS/ENNDS, and assess specific policy options.
UK		
National Institute for Health and Care Excellence	Stop smoking intervention and services [NG92] (2018)	To provide guidance, assistance, and recommendations for health professionals with links to stop smoking services and to members of the public.
NHS Health Scotland	Smoke-free prisons and e-cigarettes (2016)	To provide guidance and recommendations on introducing first generation e-cigarettes for the sale in the prison Canteen system.
	Consensus statement on e-cigarettes (2017)	Prior to the publication of this statement, NHS Health Scotland had not released a consensus statement relating to e-cigarettes. This document aims to use current evidence to clarify the benefits and harms of using e-cigarettes.
Public Health England	E-cigarettes: an evidence update (2015)	To provide an update of the evidence relating to e-cigarettes and provide policy implications based on the findings.
	Use of e-cigarettes in public places and workplaces (2016)	To provide guidance on the development of evidence-based policies.
	Evidence review of e-cigarettes and heated tobacco products (2018)	This report is the fourth in a series of reports on e-cigarettes and updates the PHE 2015 report on e-cigarettes. Aims to summarise the evidence relating to e-cigarettes and the new 'heat-not-burn' tobacco products.
	Vaping in England: an evidence update (2019)	This report is the fifth in a series of reports and focuses on the prevalence and characteristics of e-cigarettes use among young people.

		Aims to summarise evidence to support e-cigarette regulation and policy in England.
Public Health Wales	E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)	This statement updates the 2013 position statement, considering changes in legislation and research evidence, and provides recommendations tailored to different population groups.
Australia		
National Health and Medical Research Council	National Health and Medical Research Council CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)	To provide an overview of the current evidence related to e-cigarettes, which will assist consumers and policymakers understand the current evidence on the safety and efficacy of e-cigarettes.
Public Health Association Australia	E-cigarettes policy position statement (2018)	To provide an overview of the current evidence relating to e-cigarettes and recommendations regarding the regulation of e-cigarettes in Australia.
USA		
American Public Health Association	Supporting Regulation of Electronic Nicotine Delivery Systems (2018b)	This statement updates the 2014 position statement. Provides an overview of e-cigarettes, and e-cigarette use in the US population and proposes Federal, State, and Local regulations that should be taken.
U.S. Department of Health and Human Services	E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)	To provide an in-depth review of e-cigarettes to illustrate what is known and not known about these products.
U.S. Food and Drug Administration	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 (2016)	To extend the FDA authority to include e-cigarettes and other tobacco products under the Family Smoking Prevention and Tobacco Control Act and detail what restrictions will be applied to these products.

Table 5.1: Background and aim(s) of the 15 analysed public health recommendation documents, drawn from four jurisdictions

Below, we present an illustration of the number of recommendations made under each of the codes (Table 5.2). ‘Monitor e-cigarette use and prevention policies’ (M of the MPOWER framework) was the most commonly discussed, with the fewest recommendations made about ‘raising taxes on e-cigarette products’ (R of the MPOWER framework).

The ‘minors’ code included recommendations where minors were the target population for the recommendation and their protection was key. The ‘other’ code included recommendations we feel that is important but does not fit within other codes. See Appendix B for an illustrative example of each code.

The following section will discuss the e-cigarette regulatory spectrum, a key theme in the results, and the varying approaches contained within the spectrum.

Recommendation document	M	P	O	W	E	R	Minors	Other
World Health Organisation (2014a)	3	1	2	2	6	0	4	1
World Health Organisation (2016)	15	1	1	5	1	1	4	0
National Institute for Health and Care Excellence (2018)	0	0	3	0	2	0	0	0
NHS Health Scotland (2016)	0	1	1	0	0	0	0	0
NHS Health Scotland (2017)	1	0	2	0	0	0	1	0
Public Health England (2015)	2	0	2	2	0	0	1	0
Public Health England (2016)	3	4	2	0	2	0	3	0
Public Health England (2018)	12	0	7	6	0	1	3	0
Public Health England (2019)	3	0	4	0	0	0	3	0
Public Health Wales (2017)	2	2	2	2	1	0	5	0
National Health and Medical Research Council (2017)	1	1	1	0	0	0	1	0
Public Health Association Australia (2018)	2	0	1	0	1	0	1	0
American Public Health Association (2018b)	4	2	0	0	1	1	2	0
U.S. Department of Health and Human Services (2016)	17	10	1	12	12	3	12	5
U.S. Food and Drug Administration (2016)	3	0	0	1	2	0	1	0
Total	68	22	29	30	28	6	41	6

Table 5.2: A heat map illustrating the number of recommendations made by each recommendation document in each of the MPOWER, minors, and other coding themes[1]

[1] M=Monitor e-cigarette use and prevention policies; P=Protect people from passive vaping; O=Offer to help quit tobacco use and the use of e-cigarettes as a smoking cessation tool; W=Warn about the dangers of tobacco and e-cigarette use; E=Enforce bans of e-cigarette advertising, promotion and sponsorship; R=Raise taxes on e-cigarette products

5.5.1 Regulatory spectrum

Analysis suggests that e-cigarette public health recommendations fall within a spectrum of options. The spectrum ranges from a singular focus on a 'harm reduction' approach at one end to a singular focus on a 'precautionary' approach at the other end (Figure 5.1).

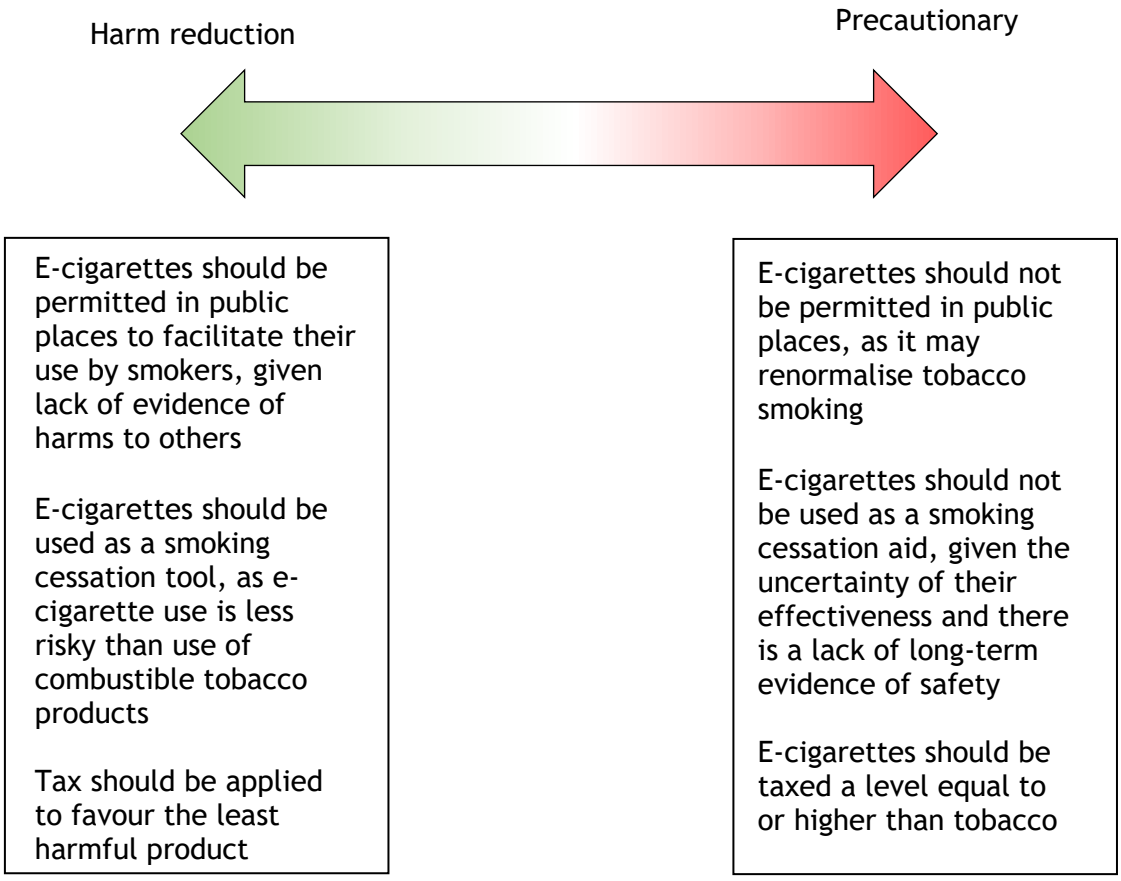

Figure 5.1: A representation of the regulatory spectrum towards e-cigarette regulation

The main difference between the two ends of the spectrum is the population which the recommendations are focused. The 'precautionary' approach generally focuses on the health effects e-cigarettes pose to non-smokers, particularly youths and young people. In contrast, the 'harm reduction' approach focused on the potentially positive health effects e-cigarettes pose to conventional smokers.

In the next two sections, we will discuss the environment in which e-cigarette use should be permitted, the use of e-cigarettes as a smoking cessation tool, and taxation of e-cigarette products (M, P, O, W and R of the MPOWER framework) in relation to a 'harm reduction' and 'precautionary approach'.

5.5.1.1 'Harm reduction' approach

Harm reduction, in general, can be described as a way to reduce the negative health effects of health behaviours by making less harmful products available for use as a substitute for more harmful products (Hawk et al., 2017).

A key theme of the 'harm reduction' approach was the environment in which e-cigarette use should be permitted. Analysis demonstrated that disagreement arises across the jurisdictions, particularly concerning the inclusion of e-cigarettes in smoke-free legislation/ indoor use. Public health bodies in the UK (PHE (2016), NHS Health Scotland (HS) (2017) and Public Health Wales (2017) argue against the inclusion of e-cigarettes in smoke-free policies. However, there are nuances in the recommendations made by these UK public health bodies. PHE (2016) states:

> "E-cigarette use is not covered by smoke-free legislation and should not routinely be included in the requirements of an organisation's smoke-free policy." (p.8)

The NHS Health Scotland (HS) (2017) argues that exposure to second-hand vapour should be minimised and Public Health Wales (2017) state that the restrictions on the use of e-cigarettes in enclosed public spaces are voluntary. In contrast, the WHO and Australian and USA public health bodies have pursued a 'precautionary approach' on this issue which will be discussed in the next section.

The 'harm reduction' approach acknowledges that smokers become addicted to nicotine and cannot easily stop smoking. It is therefore desirable to encourage smokers to switch to a less harmful product (e.g., e-cigarettes) so that harms arising from combustible tobacco are minimised. Several UK public health bodies (PHE, NICE, NHS HS, and Public Health Wales) have recommended smokers who cannot or do not want to quit smoking should switch to e-cigarettes as they are less harmful than using tobacco products (Public Health England, 2015; Public Health England, 2016; NHS Health Scotland, 2016; NHS Health Scotland, 2017; Public Health Wales, 2017; Public Health England, 2018; National Institute for Health and Care Excellence, 2018; Public Health England, 2019).

> "Encouraging smokers who cannot or do not want to stop smoking to switch to EC could be adopted as one of the key strategies to reduce smoking-related disease and death." (Public Health England, 2015, p.6)

> "Although most e-cigarettes contain nicotine, which is addictive, vaping carries less risk than smoking tobacco. Thus, it would be a good thing if smokers used them instead of tobacco." (NHS Health Scotland, 2017, p.1)

Taxation is a means by which governments can impose a mandatory charge on particular products in the marketplace (Cox et al., 2020). Typically the main goal of taxation is to increase government revenue, although it can also be used to discourage consumption of specific products like e-cigarettes (Cox et al., 2020). PHE (2018) argue that e-cigarettes should be taxed at a lower rate than tobacco products. In turn, this would decrease their price, make them more affordable compared to tobacco products, discourage uptake and reduce smoking prevalence. However, lower taxation may increase their appeal among youths.

> "Depending on emerging evidence on their relative risk to combustible tobacco and EC, regulatory levers such as taxation and accessibility restrictions should be applied to favour the least harmful options alongside continued efforts to encourage and support complete cessation of tobacco use." (Public Health England, 2018, p.24)

Notably, the WHO (2016) which has adopted a strong 'precautionary' approach towards e-cigarettes, as discussed in the next section, argues for tobacco products to be taxed at a level that would deter youth appeal and initiation. Nevertheless, the WHO (2016) also argues that tobacco products should be taxed at a level higher than e-cigarettes to reduce smoking prevalence-which aligns with the 'ham reduction' approach.

> "In parallel, combustible tobacco products should be taxed at a higher level than ENDS/ENNDS [electronic non-nicotine delivery systems] to deter initiation and reduce regression to smoking." (World Health Organisation, 2016, p.6)

5.5.1.2 'Precautionary' approach

Various public health bodies (the WHO, Public Health Association Australia (PHAA), American Public Health Association (APHA) and U.S. Department of Health and Human Services) argue that e-cigarette use should not be permitted indoors and should be included in smoke-free legislation (World Health Organisation, 2014a; World Health Organisation, 2016; U.S. Department of Health and Human Services, 2016; American

Public Health Association, 2018b; Public Health Association Australia, 2018). By making recommendations to address this they are discouraging the use of e-cigarettes and aligning them with tobacco products. Inclusion in smoke-free legislation would force e-cigarette users outside, thus encouraging vapers to quit.

> "Prohibiting by law the use of ENDS/ENNDS in indoor spaces or at least where smoking is not permitted." (World Health Organisation, 2016, p.7)

Some public health bodies such as the WHO, NHMRC, and U.S. Department of Health and Human Services have adopted a strong 'precautionary approach' relating to the prohibition of e-cigarettes indoors, arguing that the health effects associated with passive vaping are still emerging (World Health Organisation, 2014a; World Health Organisation, 2016; U.S. Department of Health and Human Services, 2016; National Health and Medical Research Council, 2017).

> "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." (World Health Organisation, 2014a, p.11)

The WHO, NHMRC, PHAA, and APHA have adopted a strong 'precautionary' approach towards e-cigarettes as a smoking cessation tool. They argue that there is insufficient evidence to support claims about using e-cigarettes as a cessation aid and there is a lack of long-term evidence on safety (World Health Organisation, 2014a; World Health Organisation, 2016; National Health and Medical Research Council, 2017; Public Health Association Australia, 2018; American Public Health Association, 2018b).

> "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." (World Health Organisation, 2014a, p.11)

> "There is currently insufficient evidence to conclude whether e-cigarettes can assist smokers to quit." (National Health and Medical Research Council, 2017, p.1)

Some public health bodies argue that e-cigarettes should be taxed at the same rate as tobacco products (U.S. Department of Health and Human Services, 2016; American Public Health Association, 2018b). A potential consequence of imposing similar taxation on e-cigarette products would be increasing their price, decreasing their affordability, and ultimately reducing consumer demand- which aligns with the 'precautionary' approach. Although taxing e-cigarettes can depress sales and even act as a deterrent to initiation, it can also impede reducing smoking prevalence as smokers may be more likely to continue using tobacco products.

> "Taxing ENDS/ENNDS at a level that makes the devices and e-liquids unaffordable to minors in order to deter its use in this age group." (World Health Organisation, 2016, p.6)

However, as noted previously, the WHO (2016) document detailed recommendations relating to the taxation of tobacco products, stating that tobacco products should be taxed at a higher level than e-cigarette products. Based on this, it could be argued that in relation to taxation, the WHO falls towards the middle of the regulatory spectrum.

5.5.1.3 Similarities in policy approaches

While the other themes (M, P, O, W, and R of the MPOWER framework) highlighted differences in policy approaches, all four selected policy jurisdictions have consolidated around a shared policy priority of protecting the health of minors ('minors' of the framework) and the need to prohibit or restrict the advertising, promotion, and marketing (E of the MPOWER framework) of e-cigarettes. The M and W of the MPOWER framework also included recommendations that highlighted the similarities in policy approaches.

Of the 15 documents, only two documents did not discuss the protection of minors. The NICE (2018) document focused specifically on smoking cessation and the NHS HS (2016) document focused on the use of e-cigarettes in prisons. Although the other documents make varying recommendations on how to protect minors there is a consensus that e-cigarette use among minors should be monitored and access to e-cigarette products should be regulated.

> "ENDS should feature alongside other health-harming substances e.g., tobacco and alcohol, in all health education for children and young people and be presented as harmful to health." (Public Health Wales, 2017, p.1)

'Advertising, promotion and marketing' of e-cigarettes was also a recurrent theme. Prohibition or restricting the advertising, promotion, and marketing of e-cigarettes is not discussed in all the documents, but those that do discuss the topic argue that restrictions should be in place. The WHO, Public Health Wales, APHA, and U.S. Department of Health and Human Services argue that there should be regulations, some of which are explicitly aimed at protecting minors, these include banning flavoured e-cigarette solutions, plain packaging, restricting internet sales, and introducing taxes on e-cigarette products that are at the same rate as tobacco products to discourage youths from purchasing the products (World Health Organisation, 2014a; World Health Organisation, 2016; U.S. Department of Health and Human Services, 2016; Public Health Wales, 2017; American Public Health Association, 2018b).

> "There should be restrictions on the advertising of ENDS in all media that would be regularly viewed by children and young people." (Public Health Wales, 2017, p.1)

> "Advertising and promotion of e-cigarettes should be prohibited and consistent with tobacco advertising prohibitions." (Public Health Association Australia, 2018, p.4)

> "Regulating packaging, including requiring minimum package sizes, mandating child-resistant packaging and requiring health warnings; and prohibiting self-service displays." (U.S. Department of Health and Human Services, 2016, p.242)

5.5.2 Regulation in the face of uncertainty

All the documents included in this research provided at least two public health recommendations on e-cigarettes. There were differing statements on what was an adequate level of evidence required before making any recommendations. Although there is a lack of long-term evidence of the health effects, safety, and efficacy of e-cigarettes, public health bodies in the UK argued there was sufficient evidence to make recommendations. In contrast, the WHO and public health bodies in Australia and USA

argued that the lack of evidence warranted the 'precautionary approach'. While e-cigarette use may carry less risk, there are still unknown potential harmful effects that can be caused by using e-cigarette products, therefore, it would be in the public interest to regulate these products.

> "Health authorities and policy-makers should act to minimise harm to users and bystanders and to protect vulnerable groups such as young people, until evidence of safety, quality and efficacy can be produced." (National Health and Medical Research Council, 2017, p.1)

5.6 Discussion

Our study analysed e-cigarette public health recommendation documents and highlights the agreement and divergence among the tobacco control community. We found there to be much agreement on the need to protect minors and the regulation of e-cigarette advertising. However, there is divergence concerning the potential harms and benefits of e-cigarettes, the use of e-cigarettes as a smoking cessation tool, and the inclusion of e-cigarettes in smoke-free legislation. Recommendations were found to fall within a spectrum of options ranging from 'harm reduction' to 'precautionary'. Three topics illustrated a split between the recommendations supported by public health bodies: 1) locations where e-cigarette use should be permitted; 2) e-cigarettes being a medicinal product used for smoking cessation; and 3) the rate at which e-cigarette products are taxed. Public health bodies in the UK are against the inclusion of e-cigarettes in smoke-free policies. While the WHO and public health bodies in Australia and the USA argued that e-cigarettes should not be permitted indoors and should be included in smoke-free legislation. The divergence of opinion is also reflected in the debate about whether e-cigarette use should be used as a smoking cessation tool. Public health bodies in the UK adopt a 'harm reduction' approach in relation to e-cigarettes being used as a smoking cessation tool. In contrast, the WHO and public health bodies in Australia and USA have pursued a 'precautionary' approach, arguing against their regulation as a smoking cessation tool. Taxation was the least commonly discussed topic, with UK public health bodies stating that taxation should favour the least harmful products (i.e., e-cigarettes) and US-based organisations arguing that e-cigarettes should be taxed at a rate equal to that of tobacco products. While the WHO stated that e-cigarettes should be taxed at a level that deters use among youths and at a lower rate than tobacco products to reduce smoking prevalence.

Regardless of the regulatory approach taken towards e-cigarettes, globally all public health bodies still have the same goal; to reduce tobacco use and related harms.

Previous research has often focused on documenting e-cigarette policies and regulations, with less detailed qualitative approaches. Tremblay et al. (2015) summarised current and proposed e-cigarette regulations across US states and Kennedy et al. (2017) summarised the regulatory approaches across 68 countries. Brady et al. (2019) conducted a scoping review of international e-cigarette policy recommendations published between 2011-2017. Although our research differed from these studies in terms of the document sample and time period examined, all four studies found there to be a focus on protecting youths. However, only Brady et al. (2019) discussed finding a consensus on restrictions on marketing and advertising of e-cigarettes, a similar finding to our research. Additionally, we all found there to be variation in regulations: Tremblay et al. (2015) found variation within a jurisdiction (e.g., US state-level), whilst Kennedy et al. (2017), Brady et al. (2019), and our research found variation across jurisdictions. Although our research focuses on a smaller sample of documents from four jurisdictions, we conducted an in-depth examination of e-cigarette regulatory approaches by highlighting the similarities and differences. Furthermore, our study involved a qualitative analysis examining e-cigarette recommendations of international public health bodies published between 2014-2019, therefore providing a more up-to-date analysis compared to the aforementioned studies.

Erku et al. (2020) examined the nicotine vaping products (including e-cigarettes) policy positions of health and medical organisations across Australia, New Zealand and the UK. They found that the majority of public health bodies, charities, and government agencies in the UK and New Zealand supported nicotine vaping products as a 'harm reduction' tool (Erku et al., 2020). In contrast, organisations in Australia raised concerns about the lack of clear evidence and addicting non-smoking youths to nicotine (Erku et al., 2020). The results of our research also agree with Erku et al. (2020) finding the UK to be more supportive of e-cigarette use and Australia taking a 'precautionary' approach. Although Erku et al. (2020) included similar jurisdictions in their sample, our sample included USA and the WHO, therefore, providing an international and global perspective to the e-cigarette regulation debate. Further by including the WHO we were able to gain insights into how international leaders might position themselves in the debate and might influence setting the agenda on policy recommendations for tobacco control at a national level.

A recent study by Campus et al. (2021), involved a comparative public policy analysis of the regulatory and incentivising approaches towards e-cigarettes across 97 countries. While Campus et al. (2021) provided a more current analysis of e-cigarette policy approaches, they did not discuss sub-national regulation or focus on specific jurisdictions. Our research focused on four jurisdictions and included sub-national level bodies within the UK, therefore, allowing for a broader comparison across jurisdictions of policy approaches towards e-cigarettes. Similar to our study, Campus et al. (2021) discussed e-cigarette regulations in relation to a regulatory spectrum, and the various regulatory approaches (including the advantages and disadvantages of the approach), pursued in each of the 97 countries. In doing so, they do not examine the nuances in the recommendations/regulations made. Furthermore, Campus et al. (2021) do not report or discuss any regulations concerning smoke-free legislation or use indoors. They were either not examined as they were not included in the regulation approaches discussed or it was not a topic the authors felt was worthy of exploration. In contrast, our study found this to be an area where there was divergence in recommendations and was worthy of discussion. Our study builds on the literature by showing that the diversity in e-cigarette recommendations is also reflected in public health recommendation documents, not only across jurisdictions but also within documents produced in the same jurisdiction. The results from our study in comparison to previous research are discussed in more detail in Section 9.2.1.

This research had a number of strengths. We purposively identified different jurisdictions for investigation, systematically identified recommendation documents for consideration, and carried out detailed qualitative coding (with double-coding of a sample), drawing on the existing WHO MPOWER framework for tobacco control. However, some limitations should be noted when interpreting the findings. Firstly, the timing and remit of the chosen documents differ and this inevitably influences the recommendations being made. We attempted to consider the likely implications of these factors in our analysis, but we note that doing so is difficult, particularly since the policy background may have evolved during the time period covered by the documents (2014-2019). Secondly, although we employed multiple approaches to identify and include all relevant documents, it is possible that we may have missed some recommendation documents, position, or policy statements that were not made publicly available. Thirdly, this research focuses on the end-product of the recommendation documents. We are therefore reliant on the actual text included in the published documents and do not have access to any interim documents or authors' views which might provide insight into the decision-making process. Fourthly, our exploration of e-

cigarette public health recommendation did not include consideration of access or licencing/retailing of e-cigarettes, which also varies across jurisdictions and has been considered by other researchers (e.g., Tremblay et al. (2015)). This reflects both the limitations of the MPOWER framework in considering different approaches to e-cigarette regulation, and also our decision to focus on 'policymaking' at the level of public health bodies who haven't addressed these aspects of regulation in developing recommendations on e-cigarettes. Finally, government policy documents were not included due to the scope of the study. We were particularly interested in public health bodies which typically aspire to be evidence-based (or at least evidence-informed), rather than government departments which would be expected to be subject to greater political influences, are less transparent and less easy to interrogate. However, broader government policies are likely to shape the perspectives of public health bodies.

This research highlights several areas of research that could contribute to understanding e-cigarettes and public health recommendation documents. An important gap is the need to better understand not only how public health bodies differ in their approach towards e-cigarettes, but also why. Firstly, an investigation of the views of those involved in producing recommendation documents would be informative to explore if different approaches are a result of prioritisation of different goals, different local circumstances, or differences in the interpretation of the available evidence base across jurisdictions. Secondly, an examination of public health recommendations on HNB products would be informative. Thirdly, an examination of the sources of evidence drawn upon and how it is used when making e-cigarette recommendations would help deepen our understanding of the role of evidence in tobacco control.

5.7 Conclusion

Public health bodies in the UK presented e-cigarettes as a 'harm reduction' tool and supported regulations that would encourage smokers to switch to e-cigarettes. In contrast, concerns about addicting non-smokers and youths to e-cigarettes, the lack of evidence on the safety, and long-term health effects continue to cause concern among public health bodies in Australia and USA. The WHO has generally pursued a 'precautionary' approach towards e-cigarettes. However, in relation to the taxation of e-cigarettes they pursue both a 'harm reduction' and 'precautionary' approach. A scientific and political consensus may emerge as the evidence base improves and long-term evidence becomes available, allowing public health bodies to better balance the

extent to which they pursue ‘harm reduction’ or ‘precautionary’ approaches. Using e-cigarettes as a case study, we have shown that public health bodies, across jurisdictions, are pursuing different approaches to achieving the same goals- to reduce tobacco use and related harms.

Authorship statement

MS conducted the structured search of public health websites, identified relevant documents, conducted all analysis, and wrote the first draft of the manuscript. KS and SVK double-coded 30% of the documents. KS, SH, and SVK supervised MS and provided feedback on the manuscript.

Declarations of interest

No conflicts of interest.

Ethics approval

Ethical approval was not required for this research.

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6 Examining the role of evidence in e-cigarette policy recommendations: A citation network analysis of international public health recommendations

6.1 Title, authorship and publication details

This manuscript has been published:

Smith MJ, Baxter AJ, Skivington K, McCann M, Hilton S and Katikireddi SV (2021) Examining the sources of evidence in e-cigarette policy recommendations: A citation network analysis of international public health recommendations. PLoS ONE 16(8): e0255604. https://doi.org/10.1371/journal.pone.0255604

The overall work has been led by me and I take full responsibility for it. In this chapter, I use the terms 'we' and 'our' to recognise all authors.

The background and methods section of the manuscript have been edited to reduce repetition within the thesis and to add cross-references across different chapters. The results have been expanded to include details that were included in the submitted manuscripts appendices.

6.2 Abstract

Background: Public health policies and recommendations aim to be informed by the best available evidence. Evidence underpinning e-cigarette policy recommendations has been necessarily limited due to the novelty of the technology and the lack of long-term epidemiological studies and trials. Some public health bodies have actively encouraged e-cigarette use whilst others have raised concerns over introducing new health risks and renormalising tobacco smoking. Using citation network analysis, we investigated the author COI and study funding statements within sources of evidence used by public health bodies when making recommendations about e-cigarette policy.
Methods: We conducted citation network analysis of public health recommendation documents across four purposively selected diverse jurisdictions: WHO, UK, Australia,

and USA. We extracted all citations from 15 public health recommendation documents, with more detailed data collected for influential citations (used in 3+ recommendation documents). We analysed the relationships between the sources of evidence used across jurisdictions using blockmodelling to determine if similar groups of documents were used across different jurisdictions. We assessed the frequency and nature of COI.
Results: 1700 unique citations were included across the 15 public health recommendation documents, with zero to 923 citations per document (median=63, IQR=7.5-132). The evidence base underpinning public health recommendations did not systematically differ across jurisdictions. Of the 1700 citations included, the majority were journal articles (n=1179). Across 1081 journal articles published between 1998-2018, 200 declared a conflict of interest, 288 contained no mention of COI, and 593 declared none. COI were reported with tobacco (3%; n=37 journal articles of 1081), e-cigarette (7%; n=72), and pharmaceutical companies (12%; n=127), with such conflicts present even in the most recent years. There were 53 influential citations, the most common study type was basic science research without human subjects (e.g., examination of aerosols and e-liquids) (n=18) followed by SR (n=10); with RCT being the least common (n=4). Network analysis identified clusters of highly cited articles with a higher prevalence of COI.
Conclusion: Public health bodies across different jurisdictions drew upon similar sources of evidence, despite articulating different policy approaches to e-cigarettes. The evidence drawn upon, including the most influential evidence, contained substantial COI (including relationships with e-cigarette and tobacco industries). Processes to explicitly manage COI arising from the underlying evidence base may be required when developing public health recommendations.

6.3 Background

Public health policies and recommendations aim to be informed by the best available evidence (Norris et al., 2011; Fink, 2013). The quality of evidence is a key element of decisions making and several frameworks, such as GRADE, have been developed to assist in the assessment of evidence (Burford et al., 2012). It is generally agreed that the process for developing public health recommendations should be transparent and lead to impartial decisions that improve health, based on the best available evidence (Woolf et al., 2012).

As discussed in Chapter 3, given the rapid development of the evidence base, the issue of e-cigarettes offers a highly relevant case through which to investigate how such evidence informs public health recommendation documents. As illustrated by the findings in Chapter 5, different policy, regulatory and public health approaches are being pursued and this may be due to the different sources of evidence drawn upon (Hawkins and Ettelt, 2019). Alternatively, it is possible that decision-makers may be drawing on a similar evidence base, whilst, still making different recommendations either due to prioritisation of different goals or adaptation to their jurisdiction (Parkhurst, 2017). Citation network analysis can identify whether recommendation documents draw on similar or different sources of evidence. Using these methods, we can explore if there are underlying structures in how research evidence is used to develop recommendation documents.

The potential for COI is present in all areas of public health. Such conflicts may threaten the integrity of scientific investigations, undermine the evidence base and risk threatening the trustworthiness of recommendations (Institute of Medicine, 2009). An important concern is that COI amongst policymakers or decision-makers may act as a potential source of bias in the development of public health recommendations (Norris et al., 2011; Mendelson et al., 2011). COI may also be present among the evidence base which policymakers and decision-makers draw upon and this may lead to recommendations being distorted to favour a secondary interest. While both of these aspects of COI are important, our focus in this paper is on the latter. The impact of COI within the underlying evidence base could potentially differ across jurisdictions too. If some jurisdictions draw on different sources of evidence than others, this may mean that secondary interests may have a greater effect in some areas than others. Alternatively, if some key papers influence recommendation documents across all jurisdictions, the presence of COI in these papers may favour secondary interests in all jurisdictions. Thus, the management of COI in all stages of the process is essential for the development of high-quality recommendations (Qaseem and Wilt, 2019). The presence of study funding from a commercial entity and/or COI among the authors of articles forming the evidence base may induce bias and contribute to differences in recommendations concerning e-cigarettes. The tobacco industry, in particular, has a long history of reporting industry favourable results (Pisinger et al., 2019). In response to this Article 5.3 of the WHO FCTC focuses on limiting its influence on public health policy (see Section 3.6.1 for more details on the WHO FCTC).

Our research investigates the sources of evidence, including the types of evidence, used by public health bodies across four diverse jurisdictions when making e-cigarette policy recommendations. Further, we examine the author COI and study funding statements within these sources, to deepen our understanding of the diffusion of industry-funded and industry-supported evidence in public health recommendation documents.

6.4 Methods

For this analysis, we drew upon the same jurisdictions as described in Section 4.3. The contrasting e-cigarette policy and public health approaches (as shown in Chapter 5) provides an opportunity to investigate the sources of evidence drawn upon by public health bodies when developing e-cigarette recommendations. The same public health bodies' recommendation documents were used for this analysis. Please refer to Section 4.3.1 for details on how the recommendation documents were identified and Table 5.1, p.126 for the list of recommendation documents.

Citation analysis measures the importance or impact of an author, an article, or a publication by counting times cited in other works, and network analysis can be used to study patterns of connections between documents, where a citation is considered a link between documents in the network (Aksnes et al., 2019). We extracted all citations from the recommendation documents (Table 5.1, p.126) into an Excel spreadsheet, giving each cited document a unique identifier. These were imported into R (v 3.6.1; R Core Team, 2019) and a two-mode adjacency matrix charting unique citations across recommendation documents was constructed (Wasserman and Iacobucci, 1991).

Citations cited across three or more of the recommendation documents were selected for more detailed analysis to visualise high-impact citations. From these, study type and COI and funding statements (this included authors' financial ties and commercial funding) were manually extracted.

To retrieve information and categorise each of the citations, a Shiny interactive web app (Figure 4.2, p.101) was created to display each citation, extract author and title, record publication type, and search SCOPUS to identify journal-published articles. Citations were categorised by type to provide an insight into the different types of evidence being drawn upon by public health bodies when making e-cigarette recommendations. Analysis focused on cited journal article texts as we would be able to extract COI details. Cited journal article texts were then imported with search results

into a second Shiny app (Figure 4.3, p.102) to read and code for the presence or absence of COI or funding statements and the types of conflict present. See Section 4.6.2.1 for more details on data extraction.

We constructed bipartite network graphs using R and igraph (Csardi and Nepusz, 2006). The initial network graph plotted all citations across all recommendation documents, coloured by the number of times cited. Three further graphs of high-impact citations were constructed, colouring by the number of times cited, type of publication, and type of conflict of interest. See Section 4.6.3 for more details on the construction of network graphs.

To analyse whether recommendation documents drew upon similar evidence, bipartite stochastic block models were used to detect clustering within the citation network (Larremore et al., 2014). We examined which recommendation documents drew upon similar sources of evidence and created groups of recommendation documents by the strength of the connection. See Section 4.6.3.1 for more information on how the block models were fitted to the recommendation documents and evidence sources.

In addition, to examining the type of publication and type of conflict of interest of the subset of influential citations, we conducted an in-depth qualitative analysis to determine if the interpretation of the citations varied across recommendation documents. See Section 4.6.3.2 for more information on the qualitative analysis stage of this study.

6.5 Results

A total of 1700 unique citations were included across the 15 public health recommendation documents, with zero to 923 citations per recommendation document (median=63, IQR=7.5-132) (Table 6.1). The NHS HS (2017) document did not include any citations and therefore was not included in further analysis.

Jurisdiction	Public health body	Recommendation document	Number of citations in document
International	World Health Organisation	Electronic nicotine delivery systems (2014a)	30
		Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)	89
UK	National Institute for Health and Care Excellence	Stop smoking intervention and services [NG92] (2018)	9
	NHS Health Scotland	Smoke-free prisons and e-cigarettes (2016)	5
		Consensus statement on e-cigarettes (2017)	0
	Public Health England	E-cigarettes: an evidence update (2015)	178
		Use of e-cigarettes in public places and workplaces (2016)	11
		Evidence review of e-cigarettes and heated tobacco products (2018)	404
		Vaping in England: an evidence update (2019)	82
	Public Health Wales	E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)	6
Australia	National Health and Medical Research Council	National Health and Medical Research Council CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)	69
	Public Health Association Australia	E-cigarettes policy position statement (2018)	6
USA	American Public Health Association	Supporting regulation of Electronic Nicotine Delivery Systems (2018b)	86
	U.S. Department of Health and Human Services	E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)	923
	U.S. Food and Drug Administration	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 (2016)	63

Table 6.1: Number of citations within each of the 15 selected public health recommendation documents

The year of publication of the 1700 citations ranged from 1947-2019 (median=1994, IQR=1981-2007). Citations were categorised by type; the most common was journal article (n=1189), followed by Government/official report (n=267). E-cigarette company press releases (n=3) and commentaries on papers (n=1) were the least common. Table 6.2 shows further details on the types of citations.

Year of publication	**Number of studies (n=1700)**
Pre 1990	39 (2·3%)
1990-1999	75 (4·4%)
2000-2009	230 (13·5%)
2010 onwards	1331 (78·3%)
No date	25 (1·5%)
Type of citation	
Book	15 (0·9%)
Comment	1 (0·1%)
Conference proceedings	11 (0·6%)
E-cigarette company	3 (0·2%)
Government/official report	267 (15·7%)
Journal article	1179 (69·4%)
News report	72 (4·2%)
Other	4 (0·2%)
Policy think tank	4 (0·2%)
Public health website	39 (2·3%)
Social media	5 (0·3%)
Statistical report	85 (5·0%)
Tobacco company	15 (0·9%)
Type of conflict of interest	**Number of declarations (across 1135 accessible journal articles)**
Declared none	326 (27·6%)
No mention	594 (50·2%)
Pharmaceutical	38 (3·2%)
E-cigarette	128 (10·8%)
Tobacco company	72 (6·1%)
Tobacco control advocate	25 (2·1%)

Table 6.2: Year of publication and type of citation for all 1700 unique citations and number of COI stated in 1135 accessible journal articles

Table 6.3 illustrates the distribution of types of citation across all recommendation documents and across the four jurisdictions. Statistical reports were classified as reports that specifically detailed statistics (e.g., the number of youths using e-cigarette

products or the number of e-cigarette users, etc.). Of note, there were 15 citations that included COI with tobacco companies. COI associated with tobacco companies were classified when an author stated that they had worked and/or received payment from a tobacco company and/or when research was funded by a tobacco company (e.g., "Tanvir Walee is an employee of Fontem Ventures B.V and Josie Williams is an employee of Imperial Tobacco Group. Girish Sharma, Rebecca Savioz, and Claire Martin received a personal fee from Fontem Venture B.V.") (Walele et al., 2016, p.192).

Type of citation	Number of citations	Subset cited across jurisdictions			
		WHO	UK	Australia	USA
Book	15	0 (0%)	0 (0%)	0 (0%)	15 (1.5%)
Comment	1	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Conference proceeding	11	0 (0%)	9 (1.4%)	1 (1.4%)	1 (0.1%)
E-cigarette company press release	3	0 (0%)	0 (0%)	0 (0%)	3 (0.3%)
Government/ official report	267	15 (13.4%)	104 (16.1%)	11 (14.9%)	154 (15.0%)
Journal article	1179	81 (72.3%)	458 (70.8%)	60 (81.1%)	744 (72.1%)
News report	72	6 (5.4%)	14 (2.2%)	0 (0%)	52 (5.0%)
Other	4	0 (0%)	1 (0.2%)	0 (0%)	3 (0.3%)
Policy think tank	4	1 (0.9%)	0 (0%)	0 (0%)	3 (0.3%)
Public health website	39	1 (0.9%)	20 (3.1%)	1 (1.4%)	17 (1.6%)
Social media	5	1 (0.9%)	1 (0.2%)	0 (0%)	3 (0.3%)
Statistical report	85	3 (0.9%)	37 (5.2%)	1 (1.4%)	48 (4.7%)
Tobacco company	15	4 (0.9%)	3 (0.5%)	0 (0%)	8 (0.8%)
Total	1700	112	647	74	1,032

Table 6.3: Distribution of types of citation across all recommendation documents and across the four jurisdictions

6.5.1 Conflicts of interest over time

Of the 1179 cited journal articles, 44 texts were unavailable and therefore were excluded from the analysis. Between 1965-1997 the majority of articles cited had no mention of COI, therefore, more detailed analyses of distributions of COI were restricted to publications post-1998. This demonstrates the reporting of COI has improved over time, as shown in Figure 6.1. Across the remaining journal articles (n=1081), there was a total of 1142 declarations of COI (Figure 6.1). The number of declarations refers to individual authors, therefore there are multiple declarations within each article. Figure 6.2 illustrates the number of journal articles published between 1998-2018.

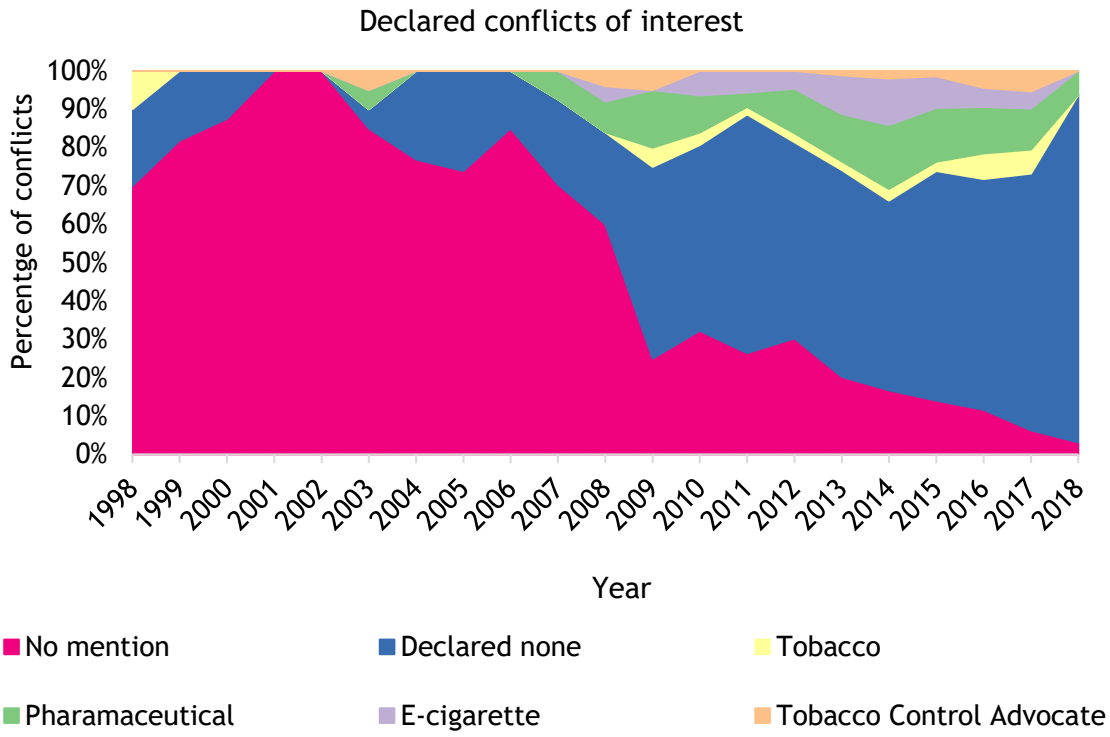

Figure 6.1: Percentage of declared COI across citations between 1998-2018

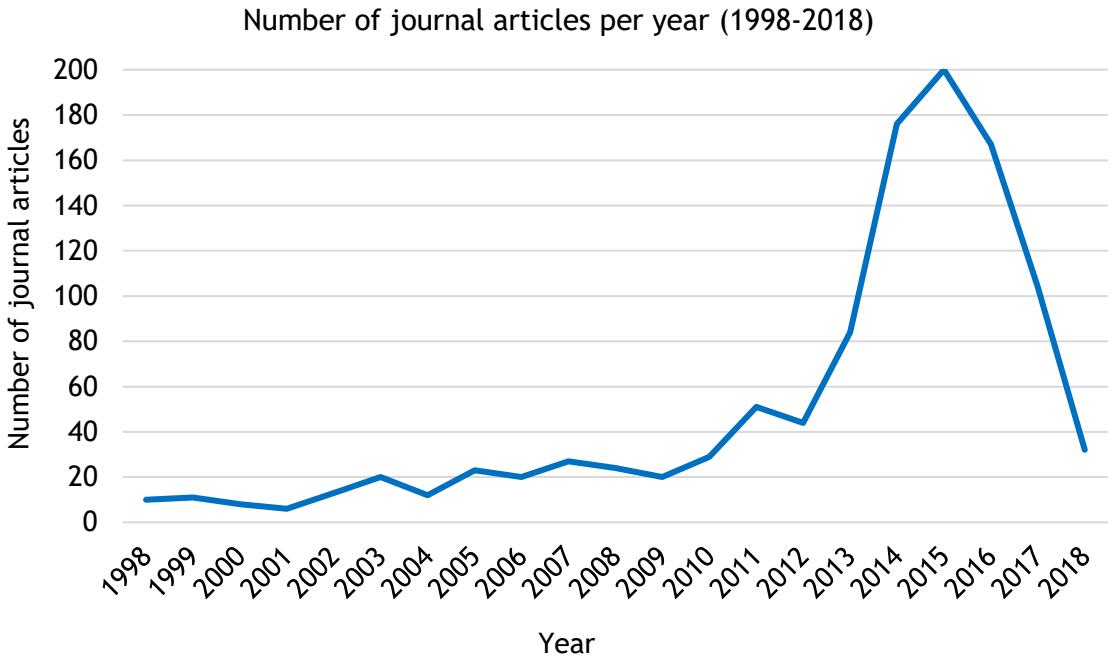

Figure 6.2: Distribution of the number of journal articles published between 1998-2018

Out of the 1081 journal articles published between 1998-2018, 288 contained no mention of COI, 593 declared no COI, and 261 declared COI. The reporting of COI has substantially improved over time, as shown in Figure 6.1. COI with e-cigarette

companies first appear in 2008. The number increased over the next two years in 2012, 4% of articles declared COI with e-cigarette companies (2 articles of the n=45 articles published), followed by 11% of articles in 2013 (9 of n=85), finally peaking in 2014 with 13% of articles (24 of n=183). Following the peak in 2014, the number of articles that declared COI with e-cigarette companies reduced in 2017 to 5% (5 of n=106), and in 2018 to zero (0 of n=32). COI associated with the tobacco industry were first visible in 1982. There is a consistent presence of tobacco company COI between 2009-2013, with the number increasing in 2015 to 3% of articles (5 articles of the n=204) to 7% of articles (12 of n=167). Overall, 3% of articles (37 of the 1081 articles published between 1998-2018) had tobacco, 7% (n=72) e-cigarette, and 12% (n=127) pharmaceutical COI.

6.5.2 Network graphs

The network graph in Figure 6.3 illustrates how sources were cited across the 14 recommendation documents. The NHS HS (2017) document did not include any citations, therefore, is not shown in Figure 6.3. Several recommendation documents are clustered in the centre of the graphs, sharing most of their citations with other recommendation documents. The FDA (2016) document shared few references with other recommendation documents, therefore is distinctly detached from the other documents.

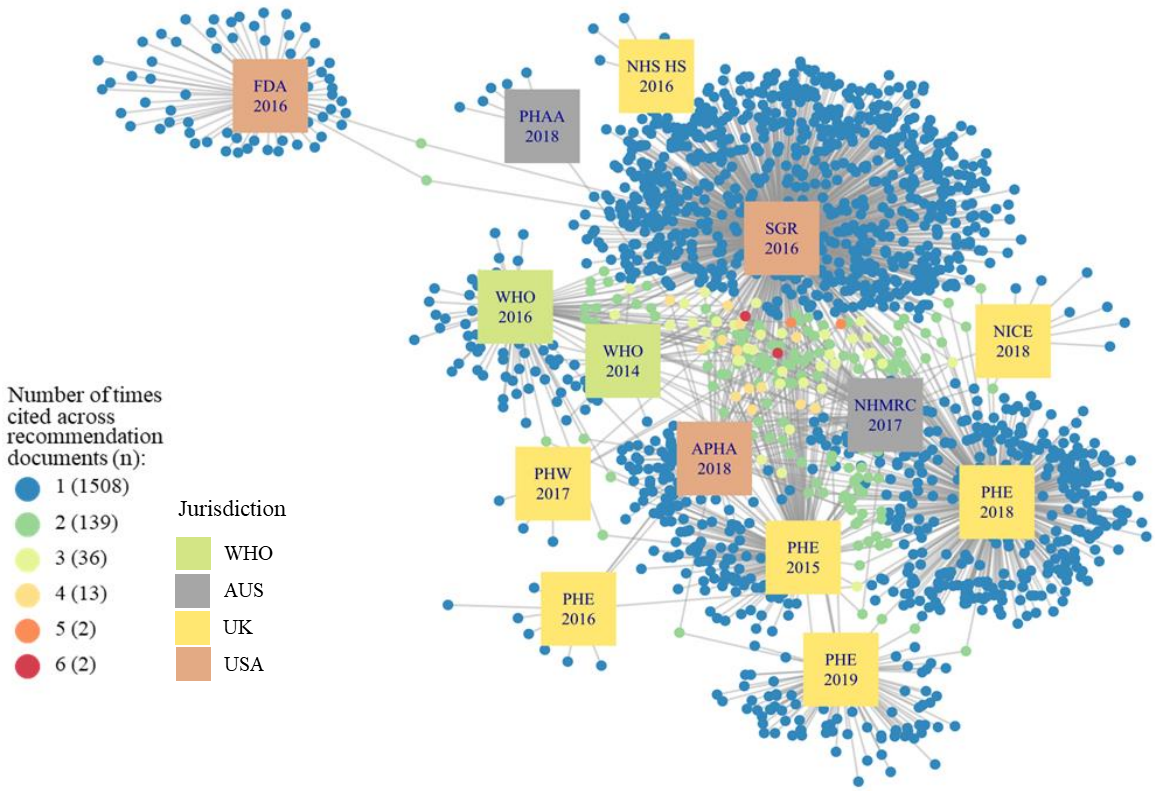

Figure 6.3: Citation network illustrating the 1700 evidence sources cited in 14 recommendation documents[18]

[18] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

As shown in Figure 6.3 there are a large number of citations appearing in only one or two of the recommendation documents; 1508 (89% of 1700 citations) were cited by only one recommendation document. The number of citations per recommendation document varied (zero to 923 citations) meaning that documents with fewer citations provided less information to the citation network compared to documents with more citations. Only three recommendation documents cited over 100 citations and the U.S. Department of Health and Human Services: A Report of the Surgeon General (SGR) (2016) included 923 citations, more than double the number of citations in the PHE (2018) document. There was a total of 53 citations across three or more recommendation documents (Figure 6.4). The PHAA (2018), NICE (2018), PHE (2018), and PHE (2019) documents were on the periphery of this network, sharing fewer citations in common than the other documents. The SGR (2016) document was the most central, sharing citations with all other documents in the sample. The NHS HS (2017) document did not include any citations in the document and FDA (2016) does not cite any of the 53 influential citations therefore, these two documents are not shown in Figures 6.4-6.6.

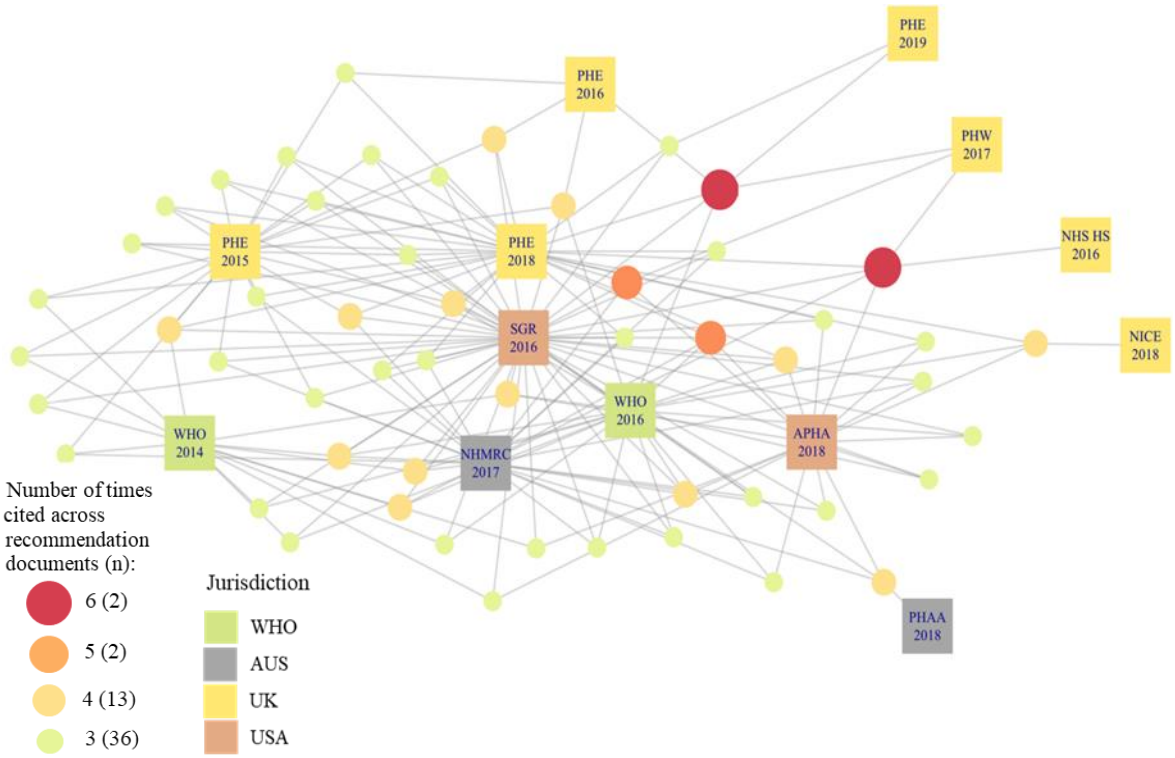

Figure 6.4: Citation network for the 53 most highly cited citations across 13 recommendation documents[19]

We explore the study type of each of the 53 citations (Figure 6.5). The most common study type was basic science research without human subjects (e.g., examination of aerosols and e-liquids) followed by SRs; with RCT being the least common.

[19] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

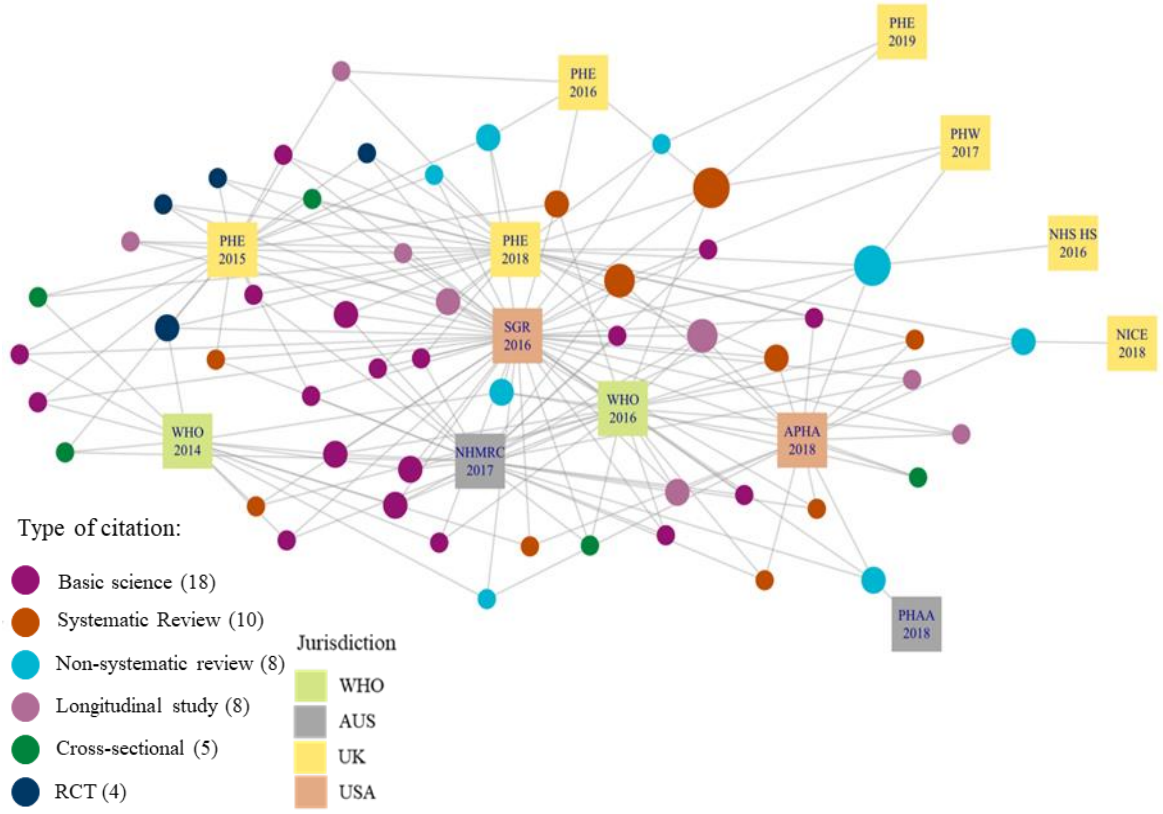

Figure 6.5: Citation network showing the study design of the 53 highly cited citations across 13 recommendation documents[20]

We also explored the type of COI declared by each of the 53 influential citations (Figure 6.6). COI were coded into five categories; details of each category are shown in Table 6.4. Out of the 53 influential documents, 13 citations declared a conflict of interest, 14 made no explicit mention of COI, and 26 declared none (Figure 6.6).

[20] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

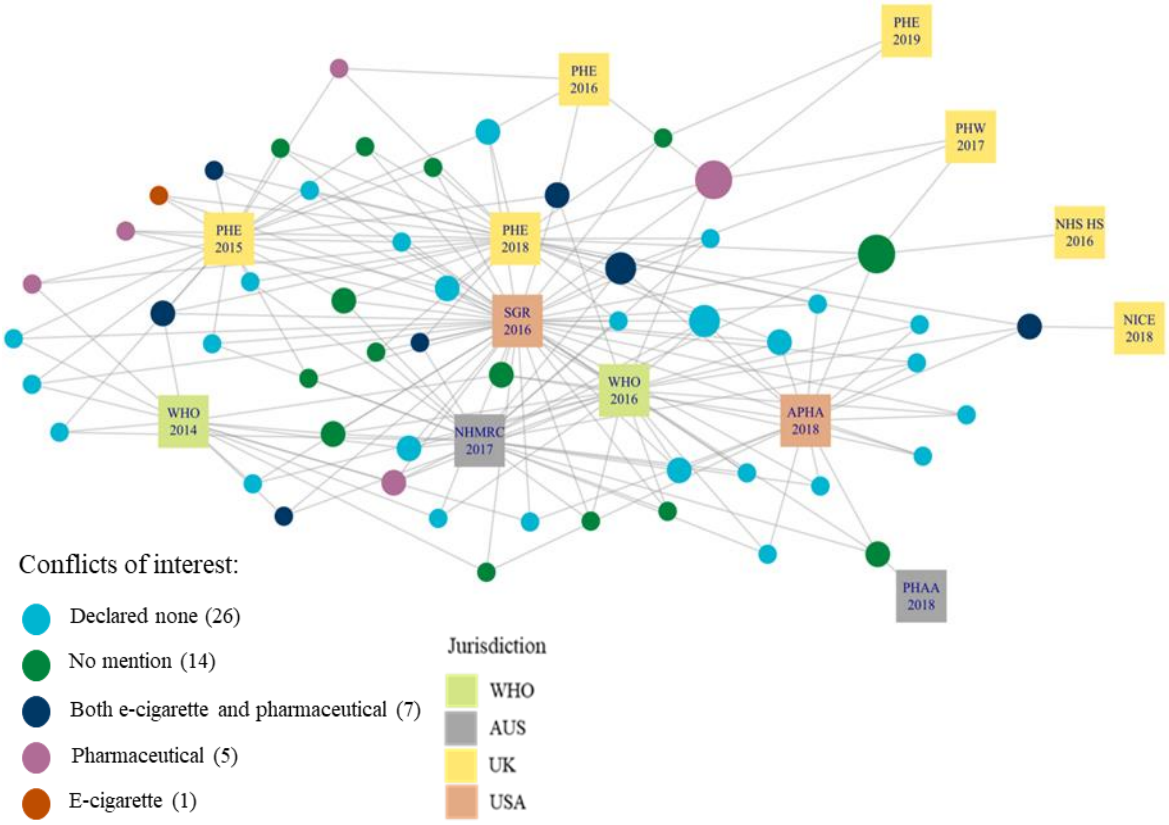

Figure 6.6: Citation network showing the COI of the 53 highly cited citations across 13 recommendation documents[21]

[21] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

Type of conflict of interest	Definition	Example from literature
Declared none	Authors declared no COI.	"The authors have no conflict of interest to declare." (Behar et al., 2014, p.207)
No mention	There was no mention of authors' COI by authors.	N/A
Pharmaceutical	Study was fully or partially funded by a pharmaceutical company and/or authors had received financial payments from companies for consulting, advisory roles, speaking, travel expenses, etc. from the pharmaceutical industry.	"MLG received a research grant from Pfizer and served as an advisory board member to Johnson manufacturers of smoking cessation medications." (Levy et al., 2018, p.24)
Both e-cigarette and pharmaceutical	Study was fully or partially funded by a pharmaceutical company and e-cigarette company and/or authors had received financial payments from companies for consulting, advisory roles, speaking, travel expenses, etc. from the pharmaceutical industry and e-cigarette industry.	"MLG received research funding from Pfizer, manufacturer of stop smoking medication and was funded by the UK Centre for Tobacco Control Studies (UKCTCS) during the study. AS received research funds and travel expenses from Chic Group Ltd., manufacturer of electronic cigarettes in Poland. Other authors declare no conflicts of interest." (Czogala et al., 2014, p.661)
E-cigarette	Study was fully or partially funded by e-cigarette manufacture and/or authors had received financial payments from companies for consulting, advisory roles, speaking, travel expenses, etc. from the e-cigarette industry.	"This study was conducted in Celerion (Lincoln, Nebraska), funded by the LOEC, Inc. d/b/a blu ecigs." (Yan and D'Ruiz, 2015, p.33)

Table 6.4: Definition of the five conflict of interest categories and an example of each type

Table 6.5 shows the distribution of COI declared in 53 influential citations.

Jurisdiction	Public health body	Not containing COI		Containing COI			Total	Proportion with COI
		None declared	No mention	Pharmaceutical	Both e-cigarette and pharmaceutical	E-cigarette		
International	WHO	20	7	4	5	0	36	25%
UK	NHS HS	0	1	0	0	0	1	0%
	NICE	0	0	0	1	0	1	100%
	PHE	21	13	10	9	2	55	38%
	PHW	0	1	1	1	0	3	67%
Australia	NHRMC	12	8	1	2	0	23	13%
	PHAA	0	1	0	0	0	1	0%
USA	APHA	11	4	0	2	0	17	12%
	FDA	0	0	0	0	0	0	0%
	SGR	21	14	3	6	1	45	22%

Table 6.5: Distribution of COI declared in 53 influential citations[22]

[22] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

6.5.3 Statistical analysis

Citations in only one recommendation document did not 'connect' any recommendation nodes together, therefore, blockmodelling was fitted to the network of citations included in more than one recommendation document, comprising 192 evidence sources (11% of 1700 citations). Bipartite modelling was used to allow the fitting of independent clusters of recommendation documents and citations. We identified four possible models for further analysis (Table 6.6). The best-fitting model contained four groups of recommendation documents (Groups 1-4) and five clusters of cited references (Clusters 5-9) (Figure 6.7). The log-likelihood for this model was -2601·83 and indicated a much better fit than fewer recommendation groups. There was a less clear differentiation between the number of clusters for evidence sources, with comparable likelihoods across a range of numbers of groups of recommendation documents.

Reference (x)	Recommendation document (y)	Log-likelihood
3	3	-2664·26
4	4	-2626·90
5	4	-2601·83
6	6	-2559·27

Table 6.6: Combinations of models identified for further analysis and corresponding log-likelihood

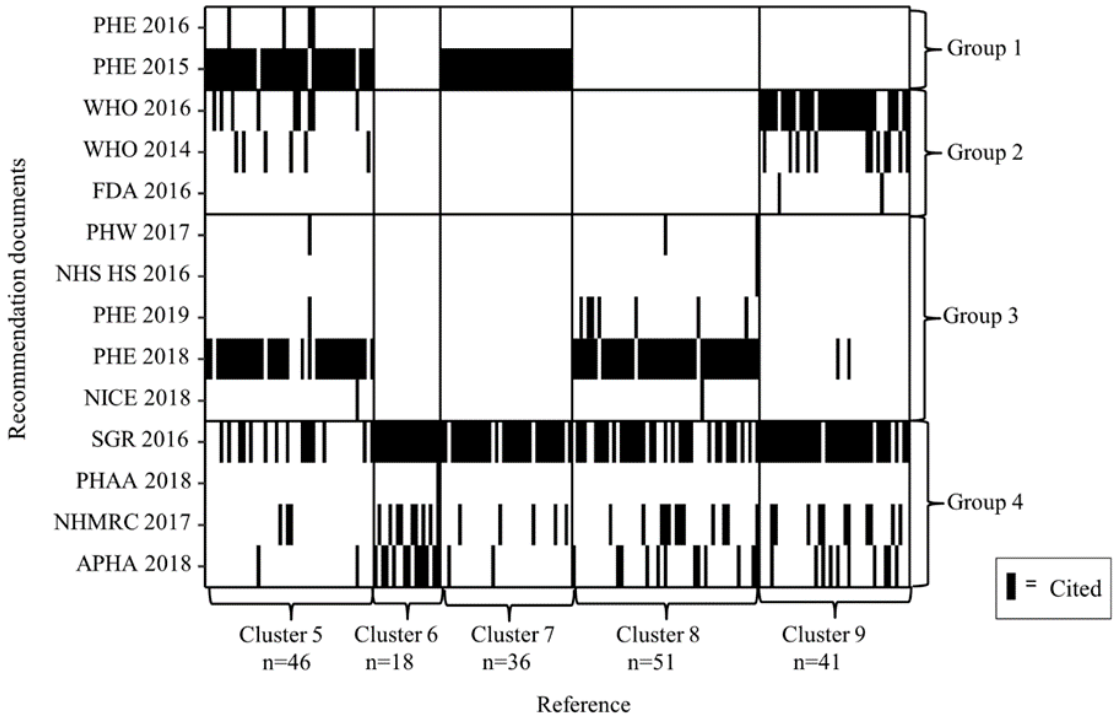

Figure 6.7: Clustering of recommendation documents by the number of shared references[23]

Each black rectangle in Figure 6.7 represents that a recommendation document (in the row) included a citation for the evidence source (in the columns, the citation labels are omitted for presentation). Where black lines appear in the same column on more than one row, this highlighted that there was a common reference across the recommendation documents in those rows. Recommendation Group 1 contained PHE (2015) and PHE (2016) documents, they drew on evidence from reference Cluster 5 (n=46) and 7 (n=36). Recommendation Group 2 contained the two WHO documents and FDA (2016) document, they exclusively drew on evidence from reference Clusters 5 and 9 (n=41). Recommendation Group 3 contained Public Health Wales (2017), NHS HS (2016), PHE (2018), PHE (2019), and NICE (2018) (five of the seven UK recommendation documents included), they drew upon evidence from reference Clusters 5, 8 (n=51) and 9. The recommendation documents in Group 4 (SGR (2016), PHAA (2018), NHMRC (2017), and APHA (2018b)) drew upon evidence clusters that were used by all other

[23] APHA=American Public Health Association; FDA=U.S. Food and Drug Administration; NHMRC=National Health and Medical Research Council (AUS); NHS HS=NHS Health Scotland; NICE=National Institute for Health and Care Excellence (UK); PHAA=Public Health Association Australia; PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

recommendation groups. This group corresponds with a central core of recommendation documents in Figure 6.4, p.153: SGR (2016), NHMRC (2017), and APHA (2018b). The evidence in Cluster 5 was used by recommendation documents across all four groups. The evidence in Cluster 8 was used exclusively by Groups 3 and 4, corresponding to the more central recommendation documents in Figure 6.4, p.153: Public Health Wales (2017), PHE (2018), SGR (2016), NHMRC (2017) and APHA (2018b). The evidence in Cluster 6 was drawn on exclusively by Group 4 and the evidence in Cluster 7 was drawn up exclusively by Group 1. In summary, the blockmodelling uncovered elements of the literature that were common across all policy jurisdictions, as well as some that are distinct to different jurisdictions. In addition, there were similarities in evidence used by jurisdiction (e.g., two recommendation groups (Groups 1 and 3) were exclusively UK and all UK public health bodies fall within these two groups).

Investigating the distribution of COI statements across recommendation groups, we saw clear differences in proportions of evidence sources declaring or not declaring the presence or absence of COI (Table 6.7). Groups 2 and 4 are drawing on more conflicted evidence sources than Groups 1 and 3 (representing all UK documents), with more than half of the evidence drawn upon by Group 2 declaring a conflict of interest. Group 3 includes fewer references not reporting COI statements and has low rates of declared COI. Groups 1 and 3 draw on evidence that has a lower proportion of COI and also, draw on evidence that has a higher proportion of 'None declared'. Results from the Fisher's exact test highlighted that these differences in distributions of COI are not random but represent clear distinctions in evidence used by recommendation documents.

Recommendation group	Type of conflict of interest			Fisher's exact test
	None declared	No mention	Declared a conflict of interest	
1	76 (53·1%)	22 (15·4%)	45 (31·5%)	p=0·02
2	30 (34·9%)	11 (12·8%)	45 (52·3%)	
3	40 (56·3%)	6 (8·5%)	25 (35·2%)	
4	36 (41·8%)	10 (11·6%)	40 (46·6%)	

Table 6.7: Type of conflict of interest by the number of times cited within recommendation group and results of the fisher's exact test[24]

In addition to examining the variation of COI across the recommendation groups, we also found distinct patterns of distribution of COI across reference clusters (Table 6.8). Clusters 6 and 7 have up to twice as many COI (and lower proportions of 'No mention') compared to the other clusters. Cluster 8 has the highest proportion of 'No mention' and the second highest proportion of 'None declared'. Cluster 5 which is drawn upon by all recommendation groups, but not all recommendation documents (FDA (2016), NHS HS (2016), and PHAA (2018)), has the second highest proportion of 'No mention' compared to other clusters. Results from the Fisher's exact test suggested that these differences in distributions of COI are not due to random chance but represent clear distinctions in evidence used by recommendation documents.

[24] Group 1: PHE 2015 and PHE 2016; Group 2: WHO 2014, WHO 2016, and FDA 2016; Group 3: PHW 2017, NHS HS 2016, PHE 2018, PHE 2019, and NICE 2018; and Group 4: SGR 2016, PHAA 2018, NHMRC 2017, and APHA 2018

Reference cluster	Type of conflict of interest			Fisher's exact test
	None declared	No mention	Declared a conflict of interest	
5	43 (45·7%)	17 (18·1%)	34 (36·2%)	p=0·00050
6	28 (37·8%)	2 (2·7%)	44 (59·5%)	
7	13 (27·1%)	4 (8·3%)	31 (64·6%)	
8	40 (48·8%)	16 (19·5%)	26 (31·7%)	
9	58 (65·9%)	10 (11·4%)	20 (22·7%)	

Table 6.8: Type of conflict of interest by the number of times cited within reference cluster and results of the Fisher's exact test

6.5.4 Interpretation of evidence

We conducted further analysis on the 53 influential citations and found that the interpretation of several citations differed across the recommendation documents. For example, in relation to the study by Hartmann-Boyce et al. (2016), PHE (2018) stated e-cigarettes had a positive effect on smoking cessation. In contrast, Public Health Wales (2017) and the NHMRC (2017) stated that there were low levels of confidence in the study findings, but e-cigarettes were likely to help in smoking cessation. The SGR (2016) stated, "the majority of currently available scientific evidence does not support the recommendation to use e-cigarettes for the cessation of cigarette smoking" (p.183) and the APHA (2018b) stated e-cigarettes "alone are not any more effective than other strategies." (p.9)

In addition, we explored the 13 of the 53 highly cited citations that declared COI and found that the presence of COI was not explicitly taken into account when it was presented as evidence in any of the recommendation documents. The NHMRC (2017) was the only document that highlighted the importance of considering COI of authors when reviewing the evidence base.

6.6 Discussion

Public health bodies across four jurisdictions vary in their approach to citing evidence to justify their recommendations, with some citing numerous sources whereas others not

indicating the evidence used to develop their recommendations. There was considerable overlap in the sources of evidence drawn upon by public health bodies when making e-cigarette recommendations. However, this evidence was used to articulate different policy approaches; the UK adopting a 'harm reduction' approach and the WHO, Australia, and USA adopting a 'precautionary' approach. Most of the evidence cited was not shared across the recommendation documents, with relatively few influential citations. We also found that there are sources of evidence that are only cited by one recommendation document, which is most likely due to the remit of the document. For example, the NICE (2018) document focused on stop smoking interventions and services, whereas the SGR (2016) document focused on e-cigarette use among youths and young adults. Therefore, it is not surprising that they did not share many references.

Our analysis demonstrated that some evidence influencing public health recommendation documents stems from research where COI are not declared or where important conflicts exist. A substantial proportion of cited evidence contained pharmaceutical (12%; n=journal articles of 1081), e-cigarette (7%; n=72), or even tobacco (3%; n=37) COI, including amongst the most influential research featuring across multiple recommendation documents. While reporting of COI has substantially improved over time, there is still a substantial proportion of articles that do not explicitly report potential COI. The presence of COI associated with e-cigarette companies coincides with the introduction of e-cigarettes into the European and US market in 2006 and 2007, respectively. Several journals will no longer accept submissions of articles that have ties with the tobacco industry (The PLoS Medicine Editors, 2010; Godlee et al., 2013). Therefore, it is surprising to see the presence of COI involving tobacco companies as recently as 2017.

Furthermore, using blockmodelling, our study highlighted differences in proportions of evidence sources declaring or not declaring the presence or absence of COI. We found that UK recommendation documents drew on less conflicted evidence sources compared to other recommendation documents, such as those in Groups 2 (e.g., WHO (2014a)) and 4 (e.g., NHMRC ((2017)). It is interesting to note that the UK draws on less conflicted data when producing e-cigarette recommendations and it may have been expected that they would have drawn on more conflicted data as they are pursuing the use of e-cigarettes as a smoking cessation tool. The use of less conflicted data could be a result of stricter COI policies; however, we are not able to determine this as it is outside the scope of our study.

Several studies have investigated the relationship between industry COI and/or funding and research outcomes (Stuckler et al., 2016; Lundh et al., 2017; Miller et al., 2017; Fabbri et al., 2018). Results from these studies demonstrated that funder interference is common across public health and can have an effect on the research agenda and can influence the results reported (e.g., reporting of industry favoured results). Miller et al. (2017) and Fabbri et al. (2018) argue that disclosure of COI and funding should be mandatory. Our research adds to the literature by demonstrating that the sources of evidence drawn upon by public health bodies when developing recommendation documents are subject to COI, including even the most concerning COI – funding from the tobacco industry. The results from our study in comparison to previous research are discussed in more detail in Sections 9.2.2 and 9.2.3.

Our study has several strengths. We systematically identified e-cigarette recommendation documents from four purposefully selected jurisdictions. We carried out a detailed investigation of the citations included in the 15 recommendation documents (with independent validation of data extraction). The use of citation network analysis to investigate and illustrate the sources of evidence drawn upon by public health bodies when making recommendations is a relatively novel method that highlights the inter-relationships between the evidence used by different public health bodies. The method of citation analysis has several strengths including its unobtrusiveness and reliability. Unlike data obtained from interviews or questionnaires, citations are unobtrusive as they do not require the cooperation of a participant/respondent and they are unreactive (Bornmann and Daniel, 2008).

However, some limitations should be noted. First, we examined only citations in relation to the types of research and COI rather than the quality of evidence and broader forms of evidence use. Second, it is highly likely that we are underestimating the presence of COI as we are reliant on what has been declared within each article and how COI are interpreted. Bindslev et al. (2013) and Rasmussen et al. (2015) showed that COI are often not declared, with Rasmussen et al. (2015) finding that almost half of all authors had undisclosed COI in clinical trials. Third, we are only examining citations, not how frequently a citation is used in the citing article, and it is possible that in some cases citations may reflect critiques of presented evidence rather than evidence use. However, we conducted further analysis of the 53 most influential citations and found no examples of this. Fourth, we investigated the COI within journal articles and influential citations. Several of the citations analysed were SRs and it is worth noting that individual COI within the studies incorporated into the SRs are not included in

declaration statements for the overall SR. Fifth, we examined only one case study (e-cigarettes) and there is a need for further research to investigate COI in recommendations for other public health areas. Finally, each of the recommendation documents included in the sample was produced at a specific time and to address slightly different remits. This is likely to lead to some divergence in the type and number of citations included, making comparison more challenging. Despite these limitations, our study draws on international data and investigates a priority for public health policy. Therefore, it is likely to be of interest to both policymakers and researchers internationally. Our findings about COI have important implications for public health policy, including highlighting a need for mechanisms to be implemented to guard against the undue influence of such COI. While we cannot establish that cited evidence which included COI definitively influenced decision-making, it is noteworthy that recommendation documents did not transparently record and consider COI in the underlying evidence base. Greater transparency in recommendation documents when drawing on evidence featuring COI may be warranted.

Our research highlights several areas of research that contribute to understanding the sources of evidence used in public health recommendations. There is a need to better understand the process used by different public health bodies when creating recommendations and how recommendation committees handle evidence where vested interests exist. To address this, an investigation of the views of those involved in the development of public health recommendations to explore the development process, the role of evidence, how COI are managed during the development process, and how contextual factors influence the development of recommendations. This would help to deepen our understanding of the development process and the role of evidence in public health recommendations. Our study was not able to determine and understand why different public health organisations have pursued different policy approaches based on the evidence. Further, more detailed analysis involving policy stakeholders may be required to understand this. The variation in the number of citations per recommendation document (e.g., six of 15 documents (40% of the sample) cited 11 or fewer citations from the total 1700 citations) impacted the visualisation of the citation network. The aim of our research was to investigate the sources of evidence used by public health bodies when making e-cigarette policy recommendations and COI within these sources rather than to investigate the quantity of citations included within a recommendation document. Future research could usefully explore how citations reflect the development of e-cigarette recommendations.

6.7 Conclusion

Public health recommendations aspire to be evidence-informed. Our study shows that the evidence relied upon when developing policy recommendations is subject to COI. The presence of COI could threaten the validity of the evidence base, therefore, shaping subsequent policy recommendations resulting in inappropriate public health actions. Using e-cigarettes as a case study we have demonstrated the need for robust methods to manage evidence derived from industry funding or incorporating industry COI within public health recommendations. These COI extend to even the most concerning industries, such as tobacco, and an urgent debate is needed about whether such evidence should inform public health policy.

Authorship statement

MS and SVK conceived the idea for the study. All authors contributed to the study design. MS led the data collection, analysis, and wrote the first draft. AB acted as second reviewer for the data extraction and assisted with the statistical analysis, visualisation, and app development. All authors critically revised the manuscript and approved the final version of the paper.

Declarations of interest

No conflicts of interest.

Data availability

All code used for the citation network analysis is available online at https://github.com/marissasmith8/Citation-Network-Analysis (archived at https://osf.io/P3KAU/). Categorisation of citation and retrieval of conflicts of interest statements was conducted using a purpose-built Shiny app in R. Code for the Shiny apps and archived input and output data are available at https://osf.io/w37dq/ and https://osf.io/rvu8k/.

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7 Development processes for e-cigarette public health recommendations lacked transparency in managing conflicts of interest

7.1 Title, authorship and publication details

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Smith MJ, Katikireddi SV, Hilton S and Skivington, K. Development processes for e-cigarette public health recommendations lacked transparency in managing conflicts of interest

The overall work has been led by me and I take full responsibility for it. In this chapter, I use the terms ‘we’ and ‘our’ to recognise all authors.

The background and methods section of the manuscript have been edited to reduce repetition within the thesis and to add cross-references across different chapters. The results have been expanded to include details that were included in the submitted manuscripts appendices.

7.2 Abstract

Objectives: To investigate how decision-makers collect and manage conflicts of interest (COI) when producing e-cigarette recommendations.
Study Design and Setting: Public health bodies that had produced e-cigarette recommendations were identified from four purposively selected jurisdictions (WHO, UK, Australia, and USA). We analysed their COI policies and conducted 15 interviews with guideline methodologists, policymakers and academics in guideline development groups.
Results: Only five of ten public health bodies had a publicly available COI policy. Participants discussed the importance of those involved in the development process declaring COI. However, there were differences in who had to report COI, the time period asked about, and what and how declarations are made. COI policies and

participants discussed a range of approaches for managing COI, from limiting involvement to disqualification from the recommendation development process. Participants considered the current processes for collecting and managing COI insufficient due to their open interpretation and possibility for partial declarations of interest.

Conclusion: The management of COI varies across public health bodies, with little standardisation and lack of transparency. To improve the collection and management of COI, and ultimately increase the trustworthiness of recommendations, decision-makers should draw upon a comprehensive and accessible COI policy.

7.3 Background

COI may threaten the integrity of scientific investigations, undermine the evidence base, and risk threatening the trustworthiness of public health policies, guidelines, and recommendations if not appropriately managed (Thompson, 1993; Institute of Medicine, 2009). An important concern is COI may be present among the evidence base which decision-makers draw upon and this may lead to recommendations being distorted to favour a secondary interest (Norris et al., 2011; Mendelson et al., 2011; Miller et al., 2017; Nejstgaard et al., 2020). In recent years, COI disclosure policies have become a routine part of scientific research (Dunn et al., 2016). The ICMJE guideline recommends that authors should disclose the study's funding source and any financial ties to industry e.g., pharmaceutical or tobacco companies (Drazen et al., 2010; International Committee of Medical Journal Editors, 2021). In addition, COI amongst decision-makers may act as a potential source of bias in the development of public health recommendations and clinical and public health guidelines (Norris et al., 2011; Mendelson et al., 2011; Nejstgaard et al., 2020). There is recognition that managing COI is a requirement of trustworthy recommendations; however, the identification and management of COI remains challenging (Wang et al., 2018). While both of these aspects of COI are important, our focus in this paper is on the latter.

The tobacco industry has historically undermined public health policies (e.g., in the 1970s, the tobacco industry downplayed the harms associated with second-hand smoke) and has a long history of selectively reporting industry favourable results (Brandt, 2012; Pisinger et al., 2019), as discussed in Section 3.5.3. To address the global tobacco epidemic the WHO developed the FCTC, with Article 5.3 of this focusing on limiting the tobacco industries' influence on public health policy (World Health Organisation,

2012b). See Section 3.6.1 for more details on the WHO FCTC. There is concern among the scientific community that it is possible the e-cigarette industry may similarly hide COI and report biased results (Polosa, 2015; Pisinger, 2016; Kosmider and Anastasi, 2016; Munafò, 2016; Pisinger et al., 2019; Capps et al., 2020); noting that these are often the same corporate entities (Barnes and Bero, 1997; Malone and Bero, 2003; Capps et al., 2020).

As discussed in Chapter 3 the issue of e-cigarettes offers a highly relevant case through which to investigate the collection and management of COI during the decision-making process due to the rapidly developing evidence base and range of vested interests and the potential influence of vested interests on public health policies and recommendations. The management of COI during the guideline-development process could impact the regulatory approaches that are pursued.

This study investigates how public health bodies across four diverse jurisdictions collect and manage COI during the development of e-cigarette public health recommendations.

7.4 Methods

This study employs a multi-method case study approach to how public health bodies collect and manage COI during the development of public health recommendations. For this analysis, we drew upon the same jurisdictions as described in Section 4.3. Two data sources were drawn upon: 1) COI policies produced by the selected public health bodies'; and 2) 15 qualitative interviews with experts working in one of the study jurisdictions included in the study (the WHO, UK, Australia, and USA) (see Table 4.5 p.111). We analysed each of the COI policies and expert interview transcripts individually as described in Sections 4.5.3 and 4.7.6, respectively and the analyses were synthesised. For more details on how the two data sources were combined see Section 4.8.2.

7.5 Results

Five of the public health bodies had a formal COI policy, either publicly available or provided on request (Table 7.1).

In total, 15 interviews (eight academics, five policymakers, and two methodologists) were conducted between January and June 2020. All participants authored/contributed to at least one of the public health bodies' e-cigarette recommendation documents included in the sample and several of the participants authored/contributed to more than one recommendation document included in the sample (Table 7.1).

Jurisdiction	Public health body	Recommendation document	COI policy available	Source of COI policy
International	World Health Organisation	Electronic nicotine delivery systems (2014a)	Yes	In development document (World Health Organisation, 2014b)
		Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)		
UK	National Institute for Health and Care Excellence	Stop smoking intervention and services [NG92] (2018)	Yes	Mentioned in the development document and a hyperlink provided to the public health bodies website (National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019)
	NHS Health Scotland	Smoke-free prisons and e-cigarettes (2016)	No. Personal communication with the public health body indicated no policy was publicly available.	Not applicable
		Consensus statement on e-cigarettes (2017)		
	Public Health England	E-cigarettes: an evidence update (2015)	No. Personal communication with the public health body indicated no policy was publicly available.	Not applicable
		Use of e-cigarettes in public places and workplaces (2016)		
		Evidence review of e-cigarettes and heated tobacco products (2018)		
		Vaping in England: an evidence update (2019)		
	Public Health Wales	E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)	Yes	Sent by a representative of public health body when enquiring about development document (Public Health Wales, 2019)

Australia	National Health and Medical Research Council	National Health and Medical Research Council CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)	Yes	Mentioned in the handbook and directed to online handbook (National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019)
	Public Health Association Australia	E-cigarettes policy position statement (2018)	No. Personal communication with the public health body indicated no policy was publicly available.	Not applicable
USA	American Public Health Association	Supporting Regulation of Electronic Nicotine Delivery Systems (2018b)	Yes	Sent by a representative of public health body when enquiring about development document (American Public Health Association, 2018a)
	U.S. Department of Health and Human Services	E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)	No. Personal communication with the public health body indicated no policy was publicly available.	Not applicable
	U.S. Food and Drug Administration	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 (2016)	No. Personal communication with the public health body indicated no policy was publicly available.	Not applicable

Table 7.1: Titles of 15 recommendation documents and source of five COI policies, drawn from 10 public health bodies across four policy jurisdictions

7.5.1 Conflicts of interest policies

There are subtle differences between the public health bodies' definition of the term 'conflict of interest' (Table 7.2). The APHA talks explicitly about the potential gain and the NHMRC discusses direct and indirect interests (American Public Health Association, 2018a; National Health and Medical Research Council, 2018). Whereas others include a broader definition (e.g., the WHO talk more generally about judgement being impaired or influenced (World Health Organisation, 2014b)).

Jurisdiction	Public health body	Definition of the term conflict of interest
International	World Health Organisation (World Health Organisation, 2014b)	"A conflict of interest is a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest" (Institute of Medicine, 2011). "Any interest declared by an expert that may affect or reasonably be perceived to affect the expert's objectivity and independence in providing advice to WHO." (p.57)
UK	National Institute for Health and Care Excellence (National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019)	"A conflict of interest arises when the judgement of someone involved in the work of NICE may be compromised, by the financial or other considerations set out in this policy." (National Institute for Health and Care Excellence, 2019, p.4)
	Public Health Wales (Public Health Wales, 2019)	"A set of circumstances by which a reasonable person would consider that an individual's ability to apply judgement or act, in the context of delivering, commissioning, or assuring taxpayer funded health and care services is, or could be, impaired or influenced by another interest they hold." (p.7)
Australia	National Health and Medical Research Council (National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019)	"Interests are any direct or indirect pecuniary or non-pecuniary interest." (National Health and Medical Research Council, 2018, p.4)
USA	American Public Health Association (American Public Health Association, 2018a)	"Conflict of interest or bias means any financial interest or potential for gain that (1) could impair the individual's objectivity; or (2) could create an unfair competitive advantage for the individual or for the individual's business partner(s), employer, spouse or partner, ancestors, children, grandchildren, great grandchildren, siblings (whether by whole or half-blood), and the spouses of children, grandchildren, great grandchildren." (p.2)

Table 7.2: Definition of conflict of interest by public health body

7.5.2 Disclosure of the conflicts of interest

Details on the types of information required varied across the public health bodies' COI policies (Table 7.3).

Jurisdiction	Public health body	What are the type of financial COI considered?	What are the type of non-financial COI considered?	Is the time period of disclosure considered?	About whom is the COI collected	Is the financial and/or non-financial COI of the individuals' personal relationships considered?
International	World Health Organisation (World Health Organisation, 2014b)	Paid employment. Paid consultancy or speaking engagement, honoraria, advisory role, and board membership. Research grant or salary support. Equity/stock or shares. Patent or royalties.	Publications, trials, systematic review. Member of an advisory board, committee, organisations, and advocacy group.	No	Members of the development groups, systematic review teams, methodologists, and external review groups (if they represent themselves).	Yes. "Both personal financial interest and the interests of the individual's immediate family members (defined as the pose or partner with whom one a close personal relationship and the children)." (p.63)
UK	National Institute for Health and Care Excellence (National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019)	Paid employment. Paid consultancy or speaking engagement, honoraria, advisory role, and board membership. Research grant or salary support. Equity/stock or shares. Patent or royalties.	Development of related guidelines and standards, educational material. Publications, trials, systematic reviews. Member of an advisory board, committee, organisations, and advocacy group.	Yes. 12 months before joining an advisory committee or during the period of membership of an advisory committee.	All committee members (such as practitioners, topic experts, and lay persons) and anyone who has direct input into the guideline including the developer, the evidence review team, and the expert witnesses.	Yes. Family financial interest. "Family member refers to spouse or partner living in the same residence as the individual as well as children and adults (who may or may not be living in the same residence) for whom the individuals is legally responsible." (National Institute for

						Health and Care Excellence, 2017, p.13)
	Public Health Wales (Public Health Wales, 2019)	Paid employment. Paid consultancy or speaking engagement, hospitality, honoraria, and sponsorship. Sponsorship or funding. Any connection with a voluntary, statutory, charitable, or private body. Endorsement of events run by third parties. Equity/stock or shares. Patent or royalties. Gifts.	Membership of committees, organisations (including those who have dealings with the NHS), and advocacy groups.	Yes. 12 months (for gits only). "An interest will remain on the public register for a minimum of 6 months and no more than 12 months after the Board Secretary has been informed that the interest has expired. A record of historic interests will be retained by the Trust for a minimum of 6 years after the date on which it expired." (p.30) (Unclear when it has expired)	All employees (this includes, Non-Executive Directors, Secondees, Agency workers, those with honorary contracts, those working in or with bodies hosted by Public Health Wales, advisors to the Board, Committees, and other decision-making bodies).	Yes. "All employees and Non-Executive Directors must also declare any interests held by spouses, civil partners or close family members or persons or bodies with which they are connected." (p.12)
Australia	National Health and Medical Research Council	Paid employment. Paid consultancy or speaking engagement,	Development of related guidelines and standards and	Yes. Over the past three years	Chair and other members of the development group.	Yes. "Financial interests by the member or their immediate family

	(National Health and Medical Research Council, 2018, National Health and Medical Research Council, 2019)	honoraria, advisory role, board membership, and directorship. Research grant or salary support. Patent or royalties. Equity/stock or shares. Gifts.	educational material. Publications, trials, systematic reviews. Member of advisory boards, committees, organisations, and advocacy groups.			members (partner and dependent children).” (National Health and Medical Research Council, 2018, p.4)
USA	American Public Health Association (American Public Health Association, 2018a)	Paid employment. Paid travel, consultancy, or speaking. Research grant or salary support (received or pending). Equity/stock or shares. Patent or royalties.	Not reported	12 months	All guideline developers, executive board members, governing councillors, and Special Primary Interest Group members.	Yes. Individual’s spouse or partner.

Table 7.3: Disclosure of conflicts and relationships of interest

All five public health bodies collected details on financial COI and there was consistency in their categorisation (for example, paid employment and stocks/shares) (World Health Organisation, 2014b; National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019; National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019; Public Health Wales, 2019; American Public Health Association, 2018a).

Among those that included details on non-financial COI (the WHO, NHMRC, NICE, and Public Health Wales) there was broad agreement on what constitutes this type of COI (for example, member of a committee or organisation) (World Health Organisation, 2014b; National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019; National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019; Public Health Wales, 2019). The APHA did not provide details on non-financial COI, in keeping with their definition of COI (Table 7.3) (American Public Health Association, 2018a).

Interviewees generally agreed on the importance of disclosing COI.

> "I definitely think that in the report it [COI] should be fully disclosed. The audience should be made aware about it." (Academic, USA)

When asked about the types of COI required to be disclosed (e.g., financial), participants stated that there should be full disclosure, whether these be financial or personal, by those involved in the development of recommendations. In doing so this could help prevent the underreporting of COI and potential influence that may occur.

> "To limit the scope for introducing bias to simply to where you have a connection, financial connection to tobacco industry or vaping industry or whatever, is pretty reductive. Actually, there are lots of influences on people's lives that would influence how they view research or how they wish to see the world and they are all kinds of conflicts of interest." (Academic, UK)

There was a substantial difference in the time for disclosure (Table 7.3), the NHMRC required only potential interests within the last three months, whereas NICE, Public Health Wales, and APHA required disclosure of potential COI within the last 12 months and, the WHO did not specify a time frame (World Health Organisation, 2014b; National

Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019; National Institute for Health and Care Excellence, 2017; National Institute for Health and Care Excellence, 2019; Public Health Wales, 2019; American Public Health Association, 2018a). Participants highlighted that such variations can negatively impact the reporting process:

> "There are potential pitfalls with declaration and that depends on what is expected in terms of the time frame and this can result in underreporting conflicts of interest." (Methodologist, International)

7.5.3 Process for collecting and managing conflicts of interest

There is variation in the format and process for disclosure, as well as the management of COI (Table 7.4).

Jurisdiction	Public health body	How are COI disclosed?	Is disclosure of COI required before involvement in the development process?	Who reviews the disclosure of COI?	Is there a procedure of exclusion if COI report?	Are there any COI specifically prohibited?	Is there a penalty for non-disclosure?
International	World Health Organisation (World Health Organisation, 2014b)	Form	Yes	The responsible technical officer and director with input from the officer of compliance, risk management, and ethics (CRE) as required. Disclosure of methodologist, systematic review team, and external review groups by a steering committee with input from CRE as required.	Yes	Not stated	Not stated
UK	National Institute for Health and Care Excellence (National Institute for Health and Care Excellence, 2017; National	Form initially and then by email before each meeting, orally at the start of each meeting	Yes	For committee members the chair reviews. If there is disagreement between the chair and member of the committee the relevant NICE director.	Yes	Not stated	Not stated

	Institute for Health and Care Excellence, 2019)						
	Public Health Wales (Public Health Wales, 2019)	Form when first employed and updated when a new interest arises or annually.	Yes	Board and committee members	Not stated	Yes. “Direct or indirect financial incentives from private providers other than those allowed by Competition and Markets Authority guidelines.” (p.13) Restrictions on hospitality. “Any money, gift or consideration as an inducement or reward from a person or organisation holding or seeking to hold a contract with Public Health Wales.” (p.17) “Under no circumstances may ‘linked deals’ be agreed, whereby sponsorship is linked	

						to the purchase of particular products or to supply from particular sources." (p.24)	
Australia	National Health and Medical Research (National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019)	Via email to the relevant Secretariat or through the Committee centre or verbally at a meeting (recorded in the meeting minutes)	Yes	The Chief Executive officer or delegates. The chair of the guideline group has the final decision.	Yes	Not stated	Yes
USA	American Public Health Association (American Public Health Association, 2018a)	Form	Not reported	Board and committee members	Yes	Not stated	Yes

Table 7.4: Process for disclosing and recording COI

Most interview participants discussed that they were required to fill out a form disclosing any COI before their involvement in the development process. However, one participant stated that when declaring COI with their public health body there was no written process but "a verbal declaration at the beginning of every meeting about conflicts of interest" (Academic, UK). It is worth highlighting that the public health body that this participant worked with did not have a publicly available COI policy.

Although COI disclosure has become common practice, participants argued that there is a blurring of what is acceptable which has resulted in partial/hidden COI in disclosures, particularly concerning the tobacco/vaping industry.

> "There are partial declarations of interest, so you'll get people saying, I've done work for [vaping company], but they won't say [vaping company] is actually a tobacco industry body." (Academic, Australia)

While one participant stated that, in their experience, those involved in developing recommendations are not "in any way, shape or form conflicted" (Policymaker, Australia), others reported that no action was taken when COI were declared.

> "[Conflicted individuals] weren't prevented from taking part in the [development] process, they just had to declare their conflicts of interest." (Academic, Australia)

This statement was not consistent with the public health body's COI policy that this participant was associated with. Based on further discussion with the participant, they reported that the COI were not considered during the decision-making process. Nonetheless, the most common approach discussed by participants was to limit the involvement of conflicted individuals, so that conflicted individuals were only allowed to participate in certain stages of the development process and excused from others.

> "It is kind of limited involvement and limited to the discussion and giving an opinion on the evidence, providing insight about the evidence but not making judgement about how to interpret this evidence and how to develop a recommendation accordingly." (Methodologist, International)

Exclusion of individuals with specific relationships was mentioned only by Public Health Wales and this related to direct or indirect financial incentives, restrictions on hospitality and money/gifts rewards, or incentives (Public Health Wales, 2019). When asked about the exclusion of individuals with specific relationships, participants often discussed industry relationships (e.g., pharmaceutical, tobacco, and vaping industries). We found there to be three different approaches to handling industry COI. The majority of participants stated that any industry COI were excluded from the development process.

> "[Public health bodies and organisations] are banning anybody who has spoken at forums on vaping, or nicotine because they think that these have a slant in favour of vaping." (Academic, USA)

However, one participant stated that the public health body they worked with did not always exclude individuals who declared industry COI.

> "[Conflicted work and individuals] don't lack credibility automatically, but you take a very careful look to see if they are being influenced." (Policymaker, USA)

One participant explained that the public health body they worked with took a completely different approach to managing COI, stating that "the quality of the study and credibility of the scientists over-rides any perception of a conflict of interest" (Policymaker, USA). However, it was not further made clear how this 'credibility' was defined.

Although processes are in place to increase the transparency of COI disclosure, overall participants lamented the "appalling lack of transparency in terms of conflicts of interest" (Academic, Australia). Despite disclosure of COI becoming more accepted within the scientific and policy communities policies are open to interpretation and participants argued that this is "not a perfect system" (Policymaker, USA).

7.6 Discussion

Our study shows that there is general agreement about the importance of disclosing COI. However, public health bodies across four jurisdictions vary in their approach to collecting and managing COI, with some not detailing a COI policy at all, even in

relation to tobacco control. Further, definition of the term 'conflict of interest' varies. Our analysis demonstrated there to be varied approaches to handling COI, ranging from total exclusion of conflicted individuals, limited involvement and simply declaring COI but being able to continue participating in the development process. The variation in COI policies was discussed by participants who ultimately argued that the current processes for collecting and managing COI are insufficient and that all COI should be disclosed.

Previous studies (including Mendelson et al., 2011; Guyatt et al., 2010; Eccles et al., 2012; Qaseem and Wilt, 2019; Traversy et al., 2021) have examined the presence and management of COI in the development process, finding there to be high rates of COI among those involved. Eccles et al. (2012) gave insight into how they believe COI should be managed during guideline development, arguing that participants involved in guideline development should disclose all potential COI, consistent with the views of our study participants. Guyatt et al. (2010), Mendelson et al. (2011), Qaseem and Wilt (2019), and Traversy et al. (2021) examined the COI management process in specific guidelines and suggest that explicit processes can be used by guideline development panels to declare COI and mitigate their effects (such as limited involvement). In addition, they argue the disclosure should include all past and current potential COI, and if COI are identified those individuals should abstain from discussion of recommendations, similar to many views of the participants in our study. However, only half of the public health bodies in our study detailed a COI policy, and research by Norris et al. (2011) similarly found that only 46% of the 37 surveyed organisations had a COI policy directly related to health care guidelines. This suggests that the absence of COI policies could result in the underreporting of COI by individuals involved in the development process (Norris et al., 2011; Neuman et al., 2011; Norris et al., 2012; Bindslev et al., 2013). Even a decade after Guyatt et al.'s (2010) research, which offered a potential solution by developing a strategy to resolve the tension between incorporating the expertise and knowledge of conflicted guideline developers, we are still seeing research highlighting a lack of an agreed process for collecting and managing COI. The results from our study in comparison to previous research are discussed in more detail in Section 9.2.4.

Decision-makers should consider how to balance the competing goals of incorporating diverse knowledge and expertise into the development process while minimising the potential influence of COI (Jones et al., 2012; Viswanathan et al., 2014). Using a standard for collecting COI (e.g., ICMJE) may support transparency and trustworthiness

in recommendations produced. Therefore, we recommend that public health bodies' that produce public health recommendations should ensure that their processes for collecting and managing COI are publicly available, as this will improve the transparency and trustworthiness of the recommendations produced and also, of the public health body themselves.

The collection and management of COI remains challenging and future research could examine how both financial and non-financial COI declared by those involved in the development process, impacts their decision-making, assessment of the certainty of evidence, the inclusion of specific studies (such as those that declare COI or industry funding/sponsorship), and the translation of evidence of into recommendations. This is important for understanding how COI relates to the evidence used in policy recommendations.

Our study has several strengths. We systematically identified publicly available COI policies and transparently coded the COI policies based on standards by ICMJE (International Committee of Medical Journal Editors, 2021) and IOM (Institute of Medicine, 2009; Institute of Medicine, 2011). By combining multiple data sources, the data are woven together to promote a greater understanding of the processes for collecting and managing COI during the guideline development process (Jacobsen and Hellström, 2002; Baxter and Jack, 2010). However, some limitations should be noted. Firstly, the results are based on studying a single topic (e-cigarettes) in a specific international context and therefore we excluded public health bodies that deal with other public health topics. Secondly, we are limited by the public health bodies' available COI policies. We contacted public health bodies directly if their COI policy was not available on their website. By not providing details of the policy, it could be argued that this impacts the transparency of the process as no such policy exists. However, participants discussed having to declare COI, even when the public health body did not have a publicly available COI policy. Third, the findings from this research rely on the perceptions of a limited number of key experts per jurisdiction. Although the experts were selected due to their knowledge of the development process and the e-cigarette debate, their views may not comprehensively or accurately describe the public health development process in their jurisdictions.

7.7 Conclusion

COI represent a potential threat to the trustworthiness, credibility, and utility of public health recommendations. It is concerning that some public health bodies either do not have or are unable to share their COI policy. The variation in COI policies can result in the incomplete reporting of potential COI and divergent declarations across public health bodies. There is a lack of transparency in the process, which could translate into a decrease in trust and credibility of recommendations produced. Decision-makers should consider how to balance the competing goals of incorporating diverse knowledge and expertise into the development process while minimising the potential influence of COI. Ultimately, public health bodies should have a well-defined and robust process to assess and manage COI.

Authorship statement

Marissa J. Smith: Conceptualisation, Methodology, Formal analysis, Investigation, Data Curation, Writing- Original draft preparation, Visualisation. **S. Vittal Katikireddi**: Conceptualisation, Writing - Review & Editing, Supervision. **Shona Hilton**: Conceptualisation, Writing - Review & Editing, Supervision. **Kathryn Skivington**: Conceptualisation, Validation, Writing - Review & Editing, Supervision.

Declarations of interest

No conflicts of interest.

Ethical approval

Ethical approval was received from the University of Glasgow's College of Medicine and Veterinary Science research committee (reference 200180098).

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8 Contextual influences on the role of evidence in e-cigarette recommendations: a multi-method analysis of four national and international jurisdictions

8.1 Title, authorship and publication details

An edited version of this article has been submitted to Evidence and Policy; a decision is pending.

Smith MJ, Skivington K, Katikireddi SV and Hilton, S. Contextual influences on the role of evidence in e-cigarette recommendations: a multi-method analysis of international and national recommendations

The overall work has been led by me and I take full responsibility for it. In this chapter, I use the terms ‘we’ and ‘our’ to recognise all authors.

The background and methods section of the manuscript have been edited to reduce repetition within the thesis and to add cross-references across different chapters. The results have been expanded to include details that were included in the submitted manuscripts appendices.

8.2 Abstract

Background: Decision-making takes place within divergent contexts, with countries having different political, social, cultural, and economic systems. E-cigarette policy has varied across jurisdictions, contrasting with the previous coordinated approach of international tobacco control communities.
Aims and objectives: Using a multi-methods case study approach of four purposively selected jurisdictions (WHO, UK, Australia, and USA), we investigated the external (e.g., previous and current tobacco policies) and internal (e.g., participants involved in the decision-making process) contextual influences on the role of evidence in the development of e-cigarette recommendations.

Methods: Structured by Dobrow et al.'s (2004) conceptual framework for context-based evidence-based decision-making, thematic analysis was employed to analyse recommendation documents, guideline development documents and interview data (aided by NVivo 12), and citation network analysis was employed to analyse sources of evidence drawn upon by the public health bodies.
Findings: Myriad of contextual factors influenced the role and use of evidence in the development of e-cigarette recommendations. We found a complex interplay between internal and external factors – for example, recommendation documents' remit (internal factor) were influenced by various external factors (e.g., epidemiology and policy history), with decisions made over time having reshaped the external context. We therefore propose a modified version of Dobrow et al.'s (2004) framework, highlighting the interplay between internal and external contextual factors.
Discussion and conclusion: This research suggests internal and external contextual factors and that they should not be considered in isolation when considering how recommendations are developed and may help explain why different policy approaches are pursued concerning public health topics, particularly e-cigarettes.

8.3 Background

Evidence and context are two fundamental components of evidence-based decision-making (Dobrow et al., 2004). Within public health and other areas of social policy, there are calls to increase the use of evidence in decision-making, yet there is a lack of clarity as to what can be considered 'good evidence' for decision-making (Brownson et al., 2009; Newman et al., 2013; Parkhurst and Abeysinghe, 2016). Evidence can be defined as facts (actual or asserted) in support of a conclusion, statement, or belief (Rychetnik et al., 2002; Oxman et al., 2009). It can take a variety of forms including published research (e.g., books and journal articles) and personal experiences and opinions (Oxman et al., 2009). Parkhurst (2017) argues that the use of evidence for public decision-making is critical to avoid unnecessary harm and to help achieve key social policy goals. However, evidence can be contested, limited or rapidly developing, meaning policies are often made under situations of considerable uncertainty as has been the case with e-cigarettes (Grol, 2001; Burgers and van Everdingen, 2004; Raine et al., 2004; Kavookjian and Mamidi, 2008).

Researchers and policymakers can have different perspectives about what constitutes evidence and how evidence should be utilised. As discussed in Section 2.2.3, Dobrow et

al. (2004) distinguish between the philosophical and practical aspects of evidence. The "philosophical-normative orientation" focuses on the properties and characteristics of evidence (e.g., validity and rigour) and introduces the claim that some forms of evidence are to be preferred over others (Dobrow, 2003; Djulbegovic et al., 2009a). Therefore, what constitutes evidence is based on methodological rigour with the supposition being that higher-quality evidence should lead, in turn, to higher-quality decisions (Dobrow et al., 2004). In contrast, the 'practical-operational orientation' is context-based and "defines evidence less by its quality and more by its relevance, applicability or generalisability to a specific context" (Dobrow et al., 2004, p.209). This perspective proposes that evidence is subjective, with different perspectives producing different explanations for the same decision outcome (Achinstein, 2001). It is argued that this perspective is more aligned with decision-making as it focuses on the variety of factors that contribute to an outcome and that evidence alone should not determine decisions (Dobrow et al., 2004; Oxman et al., 2009).

The two aforementioned orientations describe different perspectives of evidence and context. However, they do not define or describe what constitutes context. Context can be broadly defined as all the factors that influence policy decision-making (Pettigrew, 1985; Dobrow et al., 2004; Mirzoev et al., 2017). Dobrow et al.'s (2004) conceptual framework for context-based evidence-based decision-making can provide insights into the numerous contextual factors influencing the role and use of evidence in the decision-making process.

Dobrow et al. (2004) distinguish between external and internal contextual influences. The external context accounts for the environment in which a decision is applied and includes epidemiological features of the health issue being addressed, extrajudicial factors, and political factors (Dobrow et al., 2004). External factors play a role in decision-making; however, they are uncontrollable and cannot be manipulated by decision-makers. The internal context refers to the environment in which a decision is made and includes factors related to the purpose of the decision-making activity, the role of participants, and the processes used to arrive at decisions (Dobrow et al., 2004). Both internal and external contextual factors impact how evidence is weighed and how that evidence is utilised (Dobrow et al., 2004; Dobrow et al., 2006).

Dobrow et al. (2004) argue the most crucial aspect of the development of evidence-based policies is the interaction between evidence and context. Even when there is agreement on what constitutes evidence, research has shown that the same evidence,

utilised in different contexts can lead to different decision outcomes (Lipskie, 1998; Walls et al., 2017). A current example of this might be e-cigarette policies and recommendations. As discussed in Chapter 3, the issue of e-cigarettes offers a highly relevant case through which to investigate the role and use of evidence in public health recommendations, due to the rapidly developing evidence base and the potential influence of vested interests on public health policies and recommendations.

This paper aims to identify and explore how different contextual factors influence the role of evidence in the development of e-cigarette recommendations across four jurisdictions (WHO, UK, Australia, and USA). Both facilitators and barriers to the use of evidence are analysed and in doing so context is considered to comprise external and internal issues. Due to the lack of agreement in the literature as to what exactly represents the context for decision-making (Mirzoev et al., 2017) and the inability to fully account for all the factors that may influence or impact decision-making (Dobrow et al., 2004), we focus on how context influences the role of evidence in the development of e-cigarette recommendations and how it may contribute to different policy approaches.

8.4 Methods

This study employs a multi-method case study approach to understand the role of evidence and external and internal contextual factors in the development of public health recommendations. Four data sources were drawn upon: 1) 15 public health bodies' e-cigarette recommendation documents; 2) seven development documents produced by the public health bodies; 3) sources of evidence cited in the public health bodies' recommendation documents; and 4) 15 qualitative interviews with experts working in one of the study jurisdictions included in the study (WHO, UK, Australia, and USA) (see Table 4.5, p.111).

All four data sources were coded and analysed individually (see Chapter 4 for the analysis of the individual data sources).

Triangulation was carried out across all four data sources and was guided by the conceptual framework set out by Dobrow et al. (2004) which discussed three key components of a policy decision: evidence, context, and utilisation. See Section 4.9.2 for more details on how the data were triangulated and synthesised.

8.5 Results

Of the 10 public health bodies, 15 recommendation documents and seven development documents were identified through online searching of the public health bodies' website (Table 8.1).

Jurisdiction	Public health body	Recommendation document	Development document
International	World Health Organisation	Electronic nicotine delivery systems (2014a)	WHO Handbook for Guideline Development (2014b)
		Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)	
Australia	National Health and Medical Research Council	National Health and Medical Research Council CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)	Guidelines for Guidelines Handbook (2016)
	Public Health Association Australia	E-cigarettes policy position statement (2018)	No development document available. Personal communication with public health body where the stated that a Special Interest Group (SIG) will propose a new policy position statement and draft it. National Office and the Vice President, Policy, review for content and consistency with our existing policy position statements. The draft is then made available to all Public Health Association Australia members to review and comment on. The final draft is approved by the Board, and formally voted on and adopted by the annual general meeting.
UK	National Institute for Health and Care Excellence	Stop smoking intervention and services [NG92] (2018)	Developing NICE guidelines: the manual (2022)

	NHS Health Scotland	Smoke-free prisons and e-cigarettes (2016)	No development document available. Personal communication with public health body where they indicated it was an 'in person' development process, with no relevant formal development documentation.
		Consensus statement on e-cigarettes (2017)	
	Public Health England	E-cigarettes: an evidence update (2015)	Knowledge strategy: Harnessing the power of information to improve the public's health (2013)
		Use of e-cigarettes in public places and workplaces (2016)	
		Evidence review of e-cigarettes and heated tobacco products (2018)	
		Vaping in England: an evidence update (2019)	
	Public Health Wales	E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)	Process for developing Position Statements for Public Health Wales (2016)
USA	American Public Health Association	Supporting Regulation of Electronic Nicotine Delivery Systems (2018b)	American Public Health Association Policy statement development process (2019)
	U.S Department of Health and Human Services	E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)	Development process detailed in the recommendation document

	U.S. Food and Drug Administration	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 (2016)	No development document available. Public health body indicated it was an 'in person' development process.

Table 8.1: Titles of the 15 recommendation documents and seven development documents, drawn from 10 public health bodies across four jurisdictions

We begin with an overview of the results from the citation network analysis followed by an overview of the results from the document analysis of the e-cigarette recommendation documents. Analysis of contextual influences on the development of public health recommendations is structured by internal and external context and is followed by identification of potential interactions across these two contexts.

Our analysis of the sources of evidence drawn upon by public health bodies using citation network analysis found public health bodies to be introducing similar sources of evidence into the decision-making process (see Chapter 6 or (Smith et al., 2021c)). However, this evidence was used to articulate different policy approaches, with the UK pursuing a 'harm reduction' approach and the WHO, Australia, and USA pursuing a 'precautionary' approach. For example, six of the recommendation documents (WHO (2016), PHE (2016), PHE (2018), PHE (2019), Public Health Wales (2017), and SGR (2016) all cited McNeill et al. (2015) (Appendix E). We discuss the interpretation of the evidence in more detail in Section 8.5.1.2. However, as stated above the jurisdictions included in our study have pursued differing regulatory approaches towards e-cigarettes. Although this examination of the sources of evidence highlighted an overlap in the evidence sources used, it did not indicate the reasons for the divergence in recommendations and regulatory approach. In order to try and understand and explain the divergence, we examined what other factors in addition to evidence being cited plays a role in decision-making.

It is clear that evidence is a key factor in the decision-making process and "should be absolutely central in policymaking" (Policymaker, UK). However, other factors need to be considered during the process as this may impact the policy or recommendations pursued within a jurisdiction.

> "[Evidence] is not the whole story, it has to be contextualised to what's going to be realistic." (Academic, Australia)

> "It is important to consider how contextual factors can modify the benefits and harms of an intervention and how various barriers and facilitators can affect implementation and impact." (World Health Organisation, 2014b, p.153)

8.5.1 External contextual factors

In this study, we identified the epidemiological features of smoking and vaping and political and institutional factors as external contextual factors influencing the development process.

8.5.1.1 Epidemiological features of smoking and vaping

Epidemiological data have been used to draw attention to the growing rate of e-cigarette use. US participants discussed that the prevalence of vaping has increased among young people, highlighting a problem, and this caused concern among policymakers and public health researchers. In other words, epidemiological data highlighted a problem (increasing use of e-cigarettes among youths) and helped to frame the issues (a youth epidemic).

> "In the US context, it is really increasing the prevalence among young people. This is something that we see here, and the data (on youth prevalence) is really strong, it is increasing. It is increasing, the vaping among young people is increasing, we see not only increase in experimentation, but we see that the daily use pattern among the young people, many of those never smoked tobacco cigarettes." (Academic, USA)

In contrast, in the UK, this is not being seen. Policymakers and public health researchers are still monitoring e-cigarette use among youths; however, they are focusing on the use of e-cigarettes as a smoking cessation tool due to the prevalence of smoking among adults.

> "The priority for us arguably is adult smoking cessation. Whereas in other countries including many low and middle-income countries where smoking rates are still quite low and youth prevention is a big priority for them there are going to be worried about youth and if that's your focus then the natural response is to ban or heavily restrict the products." (Academic, UK)

As a result, e-cigarettes are being framed in two different ways. Data and evidence relating to the epidemiology of smoking and vaping (an external context factor) provide a basis for goals to be prioritised and policy to be developed accordingly. In turn, this will influence the remit of the recommendation document (internal context factor),

subsequent interpretation of evidence, and framing of policy goals. Therefore, this highlights the connection between external and internal contextual factors.

> "The problem's priority is determined by its importance and frequency (i.e., burden of disease, disease prevalence or baseline risk)." (World Health Organisation, 2014b, p.124)

> "Another use of epidemiological reviews is to describe relationships between epidemiological factors and outcomes – a review on associations. If an epidemiological review has been carried out, information will have been gathered from observational studies on the nature of the problem." (National Institute for Health and Care Excellence, 2022, p.85)

8.5.1.2 Maintaining and interacting policy positions

Previous tobacco control policies are important to consider when developing e-cigarette policies and recommendations, as they provide insights into what policies have been successfully implemented and what future goals are (e.g., reducing smoking prevalence within a timeframe).

> "The position statement must pay due regard to current legislation and policy, outlining how the organisation's proposed position aligns with the existing policy context." (Public Health Wales, 2016, p.4)

> "In order to develop guidelines that identify and promote effective practice, it is important to understand the current context. Context can include [...] legislative or regulatory frameworks." (National Institute for Health and Care Excellence, 2022, p.33)

In our examination of the interpretation of the 53 influential evidentiary sources, we found there to be broadly similar interpretations of the evidence. Interpretation of evidence involves considering the validity and reliability of evidence (e.g., risk of bias) and its applicability and relevance to a particular decision (e.g., generalisability) (Dobrow et al., 2004; Dobrow et al., 2006). We found that the framing of the interpretation of the evidence was in line with previous tobacco control policies, particularly a jurisdiction's 'stance' on e-cigarettes. Four of the recommendation documents (WHO (2016), PHE (2015), PHE (2016), and SGR (2016)) cite McRobbie et al.

(2014). Analysis showed that the recommendations documents that cited McRobbie et al. (2014) broadly interpreted the evidence the same but framed it in different ways. For example, the WHO (2016), which has adopted a 'precautionary approach', stated the result of the study show e-cigarettes "had a similar, although low, efficacy for quitting smoking, the overall quality of the evidence was low" (p.4). In contrast, PHE (2015) and PHE (2016), who have adopted a harm reduction approach, emphasised the potential of e-cigarettes as a smoking cessation tool.

> "Recent studies support the [McRobbie et al. 2014] Cochrane Review findings that EC [e-cigarettes] can help people to quit smoking and reduce their cigarette consumption." (Public Health England, 2016, p.13)

The UK, Australia, and USA have implemented various successful tobacco control policies over the last few decades and participants noted that it is important for new policies' to pay attention to these. Australian participants in particular spoke of the importance of these previous policies when developing and applying new policies.

> "I think in Australia, our response has been a little bit ego-driven, wanting to recognise the success of previous tobacco control measures. There's a real sense of responsibility to not undermine those successes, like plain packaging, like the excise increases." (Policymaker, Australia)

Although it is important to acknowledge previous and future tobacco control policies and goals, acknowledgement of new evidence that may alter policies is equally as important, especially in an area such as e-cigarettes where evidence is rapidly developing.

> "We're open to the fact that new evidence might come to hand which means we have to change our minds. And I think that's the essence of good science, is the willingness to change your mind when new evidence comes to hand that suggests that what you thought yesterday is not going to apply today or tomorrow." (Academic, Australia)

Policy transfer could impact evidence utilisation and policies and recommendations pursued in a jurisdiction. Participants discussed how the public health body they worked with considered other jurisdictions' e-cigarette regulations to learn about regulations they could either pursue or use this as an indication of why not to pursue the same

regulations. For example, Australian participants discussed New Zealand's regulatory approach towards e-cigarettes and why this is an approach they would not be transferring.

> "E-cigarettes aren't going to solve all tobacco control problems by flooding the market with these devices, completely unregulated, which is what New Zealand has done, which is very frightening, and they're now retroactively putting in legislation in place." (Academic, Australia)

> "In New Zealand, I think we've been a little more like the UK in terms of a wider, open free-ranging debate. We've been looking at their approach and looking at what works for us here in our country." (Academic, Australia)[25]

In addition, participants also discussed what would happen if the regulatory position was to change. For example, if e-cigarettes were to become more readily available, though still regulated there would be potential repercussions of this that could not be controlled.

> "That's one of the big concerns in Australia is if you take a more liberal approach and that liberal approach includes advertising and marketing of those products to adults, then you will see an upswing in the use by youth because you cannot isolate advertising just to adults." (Policymaker, Australia)

Peters (2016) states that the assumption is that once an institution selects a policy approach, it is likely to persist with that approach unless there are strong pressures to divert from that approach. This approach was discussed by one Australian participant:

> "We had the pre-existing statement that was about the precautionary approach typically when we go to do these things unless there's really strong evidence of a need to change that position. We didn't necessarily go into it with a clean slate, I'll be honest about that. There wasn't necessarily a discussion about, let's only support precautionary approaches, but there was a general sense that that was the position that had been supported by the

[25] This participant worked with both Australian and New Zealand public health bodies.

> overarching and that they would need to come up with a very strong and robust argument for changing that position." (Policymaker, Australia)

Our analysis also highlighted the asymmetric power relationships of some public health bodies within a jurisdiction, particularly PHE within the UK. Policies, reports, and recommendations produced by PHE are cited by and drawn upon by other public health bodies thus may be considered to be influential to other institutions. As shown in (Appendix E) McNeill et al. (2015) (i.e., the PHE (2015) recommendation document) was cited by six of the other recommendation documents (WHO (2016), PHE (2016), PHE (2018), PHE (2019), Public Health Wales (2017), and SGR (2016)). This was also reflected in discussions with the participants.

> "A lot of people are concerned that the UK relies way too much on that original Public Health England report, about 95% [the PHE 2015 stated that e-cigarettes were 95% less harmful than cigarettes]. I don't think that that conclusion was worth all of the reliance it received at the time and has continued to receive." (Policymaker, USA)

Similarly, political feasibility will be influential, as there needs to be a consideration as to whether the recommendations produced within the document are feasible and will be supported by decision-makers, those in community settings, and other public health officials who will be implementing the policies.

> "The committee should also judge to what extent it will be feasible to put the recommendations into practice." (National Institute for Health and Care Excellence, 2022, p.179)

Political feasibility and policy transfer (external factors) will shape the decision-making process by indicating what the tobacco control goals are of each jurisdiction and if the policy will be feasible and supported. This, in turn, influences the remit of the document (internal factor), evidence utilisation, and framing of the policy, highlighting the joint interaction of external and internal contextual factors in the decision-making process.

8.5.2 Internal contextual factors

In this study, we refer to internal contextual factors as the remit of decision-makers and documents, participants involved in the decision-making process, and influence of vested interests.

8.5.2.1 The remit of the document

The recommendation documents included in this study have slightly differing remits. Some focused on the broader topic of e-cigarettes (e.g., WHO (2014a)), while others focused on narrower topics (such as the use of e-cigarettes in the workplace). Dobrow et al. (2004) argue that the conception of evidence could be broadened or narrowed in response to the remit of the document, resulting in the introduction of different evidentiary sources. The introduction of evidence refers to the process by which evidence is brought into the decision-making process and addresses issues relating to the availability and accessibility of evidence (Dobrow et al., 2004; Dobrow et al., 2006). However, results from the citation network analysis highlighted that the remit of the document did not markedly alter the introduction of different evidentiary sources, as we found there to be considerable overlap in the sources cited. For example, the SGR (2016) document focuses on e-cigarette use among youths and young adults, and the PHE (2019) document focuses on the use of e-cigarettes in the workplace. Yet, there is an overlap in the sources of evidence they draw upon. An indication that despite different remits being pursued similar evidence sources can be drawn upon.

An examination of how the remit of the document is defined, found most frequently it is an external organisation which determines the remit. The remit of NICE documents are determined by NHS England or the Department of Health and Social (National Institute for Health and Care Excellence, 2022). Another participant discussed that the remit of documents produced by the public health body they worked with was determined by their funder.

> "This [the remit] is determined by the [UK organisation] and they fund us. In the tender, they outlined the areas they wanted us to cover, for example, vulnerable populations, pregnancy, mental health, etc." (Academic, UK)

In contrast, one participant stated that the remit of the document produced by the public health body they worked with is stipulated by the US Government.

> "The original authority from the government was only for cigarettes, smokeless tobacco, roll your own tobacco, and cigarette tobacco. […] A few years later we were asked to expand this to everything else, e-cigarettes, cigars, pipes, hookah, dissolvable products, anything that met the statutory definition of a tobacco product." (Policymaker, USA)

This shows that the remit of the document (internal factor) can be influenced by political factors, highlighting the interplay between internal and external contextual factors in the decision-making process.

8.5.2.2 What constitutes evidence?

Analysis of the development documents (see Table 8.1, p.198 for details on the development documents) shows there to be variation in what constitutes evidence (Appendix N).

The WHO (2014b) discussed only drawing explicitly on formal types of evidence (e.g., peer-reviewed studies) while, other public health bodies (such as the NHMRC (2016) and PHE (2013)) considered both formal and informal (e.g., grey literature) types of evidence in the development process.

> "Recommendations in WHO guidelines should be based on a systematic review of the scientific literature guided by specific key questions about the intervention, exposure, or approach under consideration. Non-systematic reviews and low-quality systematic reviews should not inform WHO guidelines […]." (World Health Organisation, 2014b, p.93)

Participants discussed their own ideas of what constitutes evidence in the decision-making process and indicated that drawing upon published SRs or conducting a SR was considered the typical approach. This highlighted that decision-making participants are able to influence the use of evidence by expressing personal values, interests, beliefs, or biases towards different evidentiary sources.

> "The standard for developing guidelines these days is to use systematic reviews." (Methodologist, International)

Participants discussed the importance of SRs; however, like the development document participants discussed drawing upon other types of evidence.

> "Narrative review of the papers of the evidence I thought were more comprehensive in my opinion." (Academic, USA)

> "Another body of evidence that is relevant is those are done in cells, cell line studies or studies that are done with rodent models, with mice and rats. However, translating those to the human population is highly problematic." (Academic, UK)

The NICE (2022) development document states that in some instances there may be a lack of evidence in relation to the topic being addressed therefore other types of types can be drawn upon. This point was raised by participants who discussed using different types of evidence due to the lack of evidence.

> "I didn't conduct a systematic review partly because there was so little evidence to review at all." (Policymaker, UK)

8.5.2.3 Participants involved in the decision-making process

Our analysis shows the influence of interpersonal relationships, potential COI, and individual responsibilities on decision-making and the use of evidence. The process for managing the COI of participants involved in the development process varied across public health bodies. It was mentioned by several public health bodies (the WHO (2014b) and the NHMRC (2016)) and participants that to allow transparency in the decision-making process, individuals who disclose COI were not allowed to participate.

> "The people who are putting the policy together aren't in any way, shape, or form conflicted." (Policymaker, Australia)

In contrast, one participant stated that the public health body they worked with required individuals to declare any COI; however, no further action was taken.

> "[Conflicted individuals] weren't prevented from taking part in the [development] process, they just had to declare their conflicts of interest." (Academic, Australia)

This statement was not consistent with the COI policy of the public health body which this participant worked with.

Most commonly, individuals who declare COI can be involved in the development process but were excused from certain other stages of the process.

> "It is kind of limited involvement and limited to the discussion and giving an opinion on the evidence, providing insight about the evidence but not making judgement about how to interpret this evidence and how to develop a recommendation accordingly." (Methodologist, International)

> "A conflicted individual being present but not taking part in any discussions or decision making related to the specific area or issue." (National Health and Medical Research Council, 2016)

8.5.2.4 Vested interests

Vested interests were influential in the decision-making process, not only concerning the utilisation of evidence but also in relation to those permitted to participate in the decision-making process. Drawing on the public health bodies' development documents, citation network analysis, and interview data there were differences in the involvement of the tobacco industry in the decision-making process (this included drawing upon tobacco industry data and involving representatives of the tobacco industry in the decision-making process).

Concerning drawing upon industry (including e-cigarette companies) data during the development process, most participants stated that they "excluded tobacco industry data" (Academic, USA) and that research funded by or associated with industry "should not be part of the formal literature" (Academic, Australia). Conversely, two participants stated industry associated data could be drawn upon.

> "That evidence [tobacco industry evidence] isn't just excluded automatically, we include it, but we make it very, very clear, when we're presenting to the committee and when we're writing things up, which bits of evidence are related to tobacco organisation." (Methodologist, UK)

Results from the citation network analysis suggested that some evidence influencing public health recommendation documents stems from research where important conflicts exist, such as industry (including pharmaceutical, tobacco, and e-cigarette) associated COI.

Regarding the involvement of the tobacco industry in the development process, there were differences across the jurisdictions. Within the UK some participants reported the tobacco industry was excluded from being involved in the development of recommendations and policies. However, this was not the case in all UK documents.

> "Nobody can claim they weren't allowed to participate in the debate, apart from the tobacco industry because they were systematically excluded from the whole process from start to finish." (Policymaker, UK)

Another UK participant stated that the tobacco industry could not be stopped from responding to consultations and voicing their opinions; however, their responses were dealt with separately. When it comes to classifying tobacco organisations, they "aren't officially stakeholders, they're responders, so they are given a different status" (Methodologist, UK). Although they are allowed to be part of the process and introduce evidence, it is handled differently compared to other stakeholders.

> "When the comments from stakeholders are all gathered in, all those comments go straight to the commissioning team, internally. They would go through and very carefully take out all the tobacco organisation and would look at them to see whether there was anything that was important that we needed to address." (Methodologist, UK)

Several Australian participants stated that the tobacco industry should not be involved in the development of public health recommendations. In doing so, this would restrict the industry's involvement in the decision-making process. One policymaker explained their public health body has internal processes on "how to safeguard the development of policies from those groups [tobacco industry]" (Policymaker, Australia). These processes included the organisation "being very acutely aware of the influence that the tobacco industry can have [on the development of policies] and "not investing or having any interactions with the tobacco industry" (Policymaker, Australia).

Similarly, the WHO (2014b) stated that those involved in the decision-making process should not be conflicted.

> "The majority of members of the GDG [guideline development group] should have no conflicts of interest, either financial or nonfinancial. Individuals with financial conflicts of interest should generally not be members of GDGs. This applies especially to individuals with substantial financial interests in an intervention under consideration in the guideline." (World Health Organisation, 2014b, p.71)

However, this was not a total restriction, as the same document also stated:

> "If the GDG [guideline development group] must include some members with financial and/or intellectual conflicts of interest, every effort should be made to balance the perspectives of these individuals in the group. This can be achieved by selecting people whose opinions are known to differ, including a variety of stakeholders." (World Health Organisation, 2014b, p.71)

Although participants included e-cigarette companies when discussing the tobacco industry, they did discuss that this was not a general classification. The "[e-cigarette companies] are tobacco companies" (Academic, USA); however, "the lines have gotten blurred" (Academic, USA) meaning that e-cigarette industry data are drawn upon when developing policies and recommendations. Participants argued that e-cigarette and tobacco companies should be treated the same.

> "You can't really disentangle it [the vaping industry] anymore from the tobacco industry. I think we had romantic notions a few years ago that somehow the vaping industry and the tobacco industry were separate entities and I don't think that holds up anymore. […] At the beginning, they [tobacco companies] weren't involved and now they are, I mean they bought them [e-cigarette companies] all up. So they are all the same and need to be treated that way too." (Academic, Australia)

While it is important to engage a variety of individuals in the decision-making process, it needs to be considered that those individuals may have their own agendas on how to frame policy goals and recommendations in line with their values and beliefs.

> "Although we have to be aware that stakeholders might have their own kind of angles that they are trying to push." (Methodologist, UK)

Paying attention to contextual factors during all stages of the development process can help decision-makers understand factors that affect the reach, relevance, implementation, outcome, and generalisation of policy recommendations.

> "To develop guidelines that identify and promote effective practice, it is important to understand the context." (National Institute for Health and Care Excellence, 2022, p.33)

8.6 Discussion

Cross-jurisdiction comparison revealed that there is considerable policy divergence relating to e-cigarettes despite similar evidence drawn upon. Public health decision-making does not take place in a vacuum (Walt, 1994; Barker, 1996; Murray, 2011; Buse et al., 2012; Hinrichs-Krapels et al., 2020) and our analysis highlights the various contextual factors influencing the decision-making process. Internal contextual factors (e.g., the remit of the document and participants involved) were found to influence the decision-making process. However, they did not highlight why differing e-cigarette policy approaches are being pursued. Analysis of the external factors suggests their importance in the framing of policy goals; these included differences in the epidemiology and the need to be consistent with broader institutional and political contexts. Considering the findings with respect to evidence utilisation, we have amended Dobrow et al.'s (2004) conceptual framework (Figure 8.1).

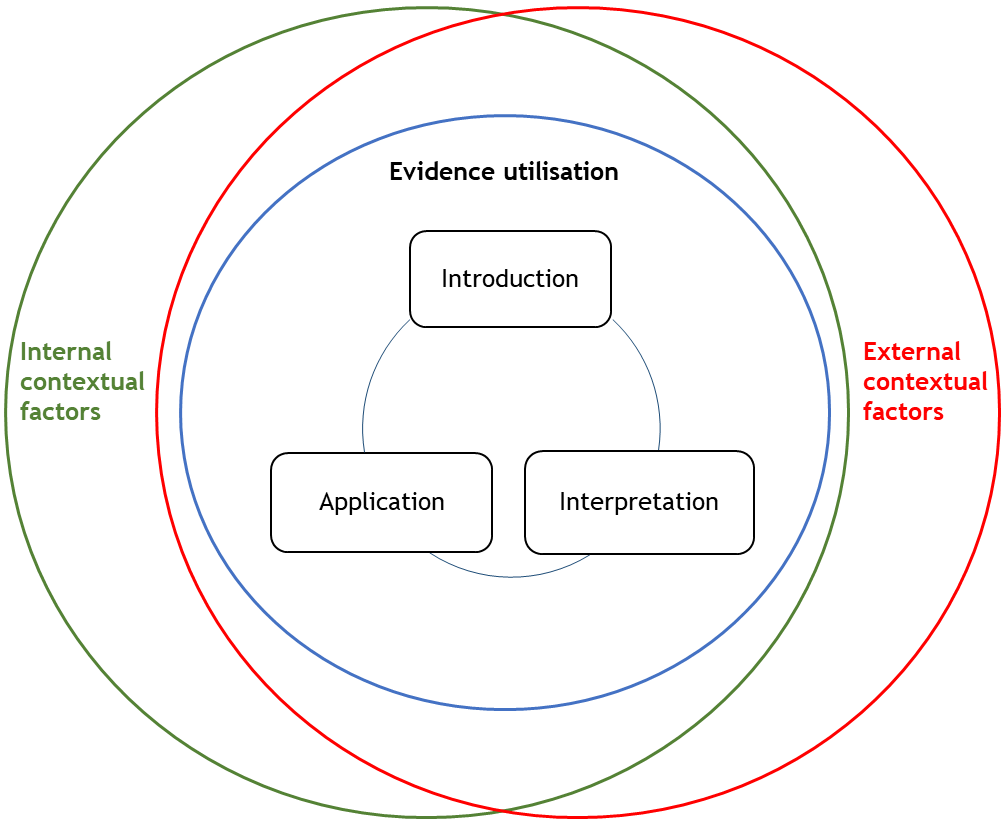

Figure 8.1: A modified conceptual framework for the influence of external and internal contextual factors in the development of e-cigarette policies and recommendations

Although the framework has been modified, the basic elements of the framework are the same as in the original model (see Dobrow et al., 2004). The main modification is that this framework acknowledges the interplay between external and internal contextual factors. For example, the remit of the document (internal factor) is influenced by various external factors (e.g., epidemiology and policy history), and over time decisions are made that will reshape the external context. This reflects the inherent complexity of decision-making and highlights the methodological challenge in understanding how the different elements (decision-making participants, processes, and context) are intertwined (Walt and Gilson, 1994; Walt et al., 2008; Hinrichs-Krapels et al., 2020). Considering the three-stage process model of evidence utilisation (i.e., introduction, interpretation, and application of evidence) together with the external and internal contextual factors, our modified conceptual framework essentially shows how the three elements (evidence utilisation, internal contextual factors, and external contextual factors) overlap resulting in evidence-informed decision-making. Within the evidence utilisation element of the framework, we have shown the process not as sequential as it is possible that evidence may be drawn upon to justify a policy position (e.g., moving from introduction to application).

Our findings suggest that although evidence is a key factor, context forms an important set of influences on evidence-based public health decision-making, which is consistent with other similar studies (Dobrow et al., 2004; Dobrow et al., 2006; Hutchinson, 2011; Hutchinson et al., 2011; Mirzoev et al., 2013; Mirzoev et al., 2017). Previous research (Ricketts, 2010; de Savigny et al., 2012; Mirzoev et al., 2017) has illustrated the interplay between factors across macro, meso, and micro levels. Although we describe contextual factors as external and internal, our study highlights the complexity of decision-making by showing the variety of contextual factors influencing decision-making and the subtle ways in which internal and external contextual interact to frame the focus of public health recommendations and the evidence chosen to underpin them. Our findings are broadly similar to findings from similar studies, as we did not find any indication of the dominance of contextual influences at any of the three stages of evidence utilisation (de Savigny et al., 2012; Ricketts, 2010; Hutchinson et al., 2011; Mirzoev et al., 2017). The results from our study in comparison to previous research are discussed in more detail in Section 9.2.5.

Our study had a number of strengths. We purposively identified different jurisdictions for investigation, systematically identified recommendation and development documents for consideration, and carried out detailed qualitative coding (with double-coding of a sample of each). In addition, we conducted 15 in-depth expert interviews with individuals involved in developing e-cigarette recommendations (with double-coding of a sample of each). Another strength of this study was the data from different perspectives generated by employing multi-methods. By combining multiple data sources, the data are woven together to promote a greater understanding of the case (Jacobsen and Hellström, 2002; Baxter and Jack, 2010). Triangulation of four data sources has enriched our analysis by moving beyond demonstrating the existence of different framings of the e-cigarette policy debate, to highlighting the contextual factors influencing the decision-making process. Further, we were able to capture the interplay between internal and external contextual factors, a unique feature that was able to provide a vital understanding of the role and use of evidence in the development of e-cigarette policies and recommendations.

Though, some limitations should be noted when interpreting the findings. Firstly, the small sample size of expert interviews and the limited number of each expert type interviewed due to the COVID-19 pandemic makes it difficult to understand the diversity of arguments made within these different expert groups. However, as discussed above, the use of multiple data sources has allowed for a deeper understating of the role and

use of evidence in decision-making. Secondly, it is argued that when employing multi-methods it is not enough to simply compare different data from different methodological sources, without understanding the data collection process of each (Fielding and Fielding, 1986; Flick, 2004). In our study, we analysed each data source individually, paying attention to the data collection processes, and then synthesised the data sets to analyse issues from these varying perspectives with reference to the different data collection processes (see Chapter 4 for more details).

Our study highlights several areas of research that contribute to understanding the role and use of evidence in public health recommendations. Our research focussed on the case study of e-cigarettes and future research could be conducted to determine if these findings are generalisable to other areas of public health, potentially including the global COVID-19 pandemic. In the absence of long-term evidence on COVID-19, global policies and recommendations have focused on behavioural changes (e.g., social distancing) and uptake of vaccines to help to reduce the number of cases and spread of the virus. Based on our analysis future research could investigate the contextualisation of evidence from the pandemic when developing policies and recommendations.

8.7 Conclusion

A greater understanding of contextual influence is helpful in appreciating the complexity of decision-making and the fact that policymakers wrestle with myriad different factors (including evidence, politics, and policy ambitions) when developing public health recommendations, especially on novel public health issues (such as e-cigarettes and COVID-19), where the evidence base is still emerging.

Authorship statement

Marissa J. Smith: Conceptualisation, Methodology, Formal analysis, Investigation, Data Curation, Writing- Original draft preparation, Visualisation. **Kathryn Skivington**: Conceptualisation, Validation, Writing - Review & Editing, Supervision. **S. Vittal Katikireddi**: Conceptualisation, Writing - Review & Editing, Supervision. **Shona Hilton**: Conceptualisation, Writing - Review & Editing, Supervision.

Declarations of interest

No conflicts of interest.

Ethical approval

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9 Thesis discussion

9.1 Introduction

This chapter provides a summary of the most important and original research findings from this thesis which aimed to understand how public health bodies prioritise and use evidence in developing e-cigarette public health recommendations by comparing regulatory development across four purposively selected jurisdictions (WHO, UK, Australia, and USA).

I will show how this thesis has answered each of my five research questions and highlight how this work contributes to the existing literature.

Importantly, this thesis has shown that across the four diverse jurisdictions studied, there was considerable overlap in the sources of evidence drawn upon by public health bodies when making e-cigarette recommendations and there was consensus about the need to protect public health, particularly that of youths and young adults. However, there were also differences in the priorities and regulatory approaches adopted towards e-cigarettes which suggested that other contextual factors were important (including epidemiological features of smoking and vaping, previous and current tobacco policies, the remit of decision-makers and policy documents, and which participants were involved in the decision-making process).

Furthermore, this thesis has highlighted the prevalence of COI among the sources of evidence used by public health bodies when developing recommendations and that the approaches public health bodies use to collect and manage COI vary, with little standardisation and often a lack of transparency. This suggests the need for more comprehensive and accessible COI policies that will improve the disclosure, evaluation, and management of COI.

Overall, this thesis has shown that contextual factors, including those related to the decision-making process (such as the presence and management of COI), influence how public health bodies prioritise and use evidence when developing e-cigarette recommendations. These internal and external contextual factors and the interplay between them may therefore help explain the diverging regulatory approaches towards e-cigarettes.

This chapter also reflects on the strengths and limitations of the thesis. The chapter then outlines the public health policy and academic implications and contributions of this thesis, as well as recommendations for future research. The chapter ends by providing a conclusion.

9.2 Summary of empirical findings

Prior to considering the implications of this thesis for practice and research, I summarise my findings in relation to each of the five research questions of the thesis and discuss these in the context of previous research.

9.2.1 RQ1: What are the similarities and differences in e-cigarette public health recommendations across diverse jurisdictions?

Based on the document analysis, it can be concluded that there are areas of agreement and divergence among the tobacco control community regarding the regulation of e-cigarettes. I found that recommendations diverge in the relation to the harms and benefits of e-cigarettes, the inclusion of e-cigarettes in smoke-free legislation, the use of e-cigarettes as a smoking cessation tool, and taxation of e-cigarette products. However, policymakers remain united on the protection of minors and the regulation of e-cigarette advertising. Public health bodies in the UK are against the inclusion of e-cigarettes in smoke-free policies. While the WHO and public health bodies in Australia and the USA argued that e-cigarettes should not be permitted indoors and should be included in smoke-free legislation. The divergence of opinion is also reflected in the debate about whether e-cigarettes should be used as a smoking cessation tool. Public health bodies in the UK pursued a 'harm reduction' approach concerning e-cigarettes being used as a smoking cessation tool. In contrast, the WHO and public health bodies in Australia and USA have pursued a 'precautionary' approach, arguing that e-cigarettes should not be used as a smoking cessation tool.

Governments have a range of options as to how they tax particular products and concerning e-cigarettes; there has been debate around the implications and benefits of introducing taxes on e-cigarettes. By increasing the level of tax imposed on e-cigarettes; their affordability would decrease resulting in reduced demand for the products and help stop initiation, particularly among youths (Kenkel, 2016). However, in doing so this would make it more difficult for tobacco smokers to switch to alternative,

less harmful products (Pesko et al., 2016). Taxation of e-cigarette products was the least commonly discussed topic and similarly, there was divergence in the best approach to adopt. UK public health bodies stated that taxation should favour the least harmful products (i.e., e-cigarettes). In contrast, US public health bodies argue that e-cigarettes should be taxed at a rate equal to that of tobacco products. There are a range of options that governments can pursue in relation to taxing e-cigarette products and there has been debate around the implications and benefits of introducing taxes on e-cigarettes. While the WHO stated that e-cigarettes should be taxed at a level that deters use among youths and at a lower rate than tobacco products to reduce smoking prevalence. By increasing the level of tax imposed on e-cigarettes their affordability would decrease resulting in reduced demand for the products and helping stop initiation, particularly among youths (Kenkel, 2016). However, in doing so this would make it more difficult for tobacco smokers to switch to alternative, less harmful products (Pesko et al., 2016).

Both approaches apply restrictions on e-cigarettes and tobacco products; however, in different ways. Adopting a 'harm reduction' approach does not require weak regulation of e-cigarette products, instead, it ensures that e-cigarette products are available as a smoking cessation tool for smokers who are unwilling or unable to quit smoking, meaning that the negative health effects caused by smoking can be reduced while minimising any exposure (resulting in potentially positive health effects) among non-smokers and youths. While the 'precautionary approach' adopts stronger e-cigarette regulations to prevent initiation and use of e-cigarettes among non-smokers and youths.

My research shows the variation in e-cigarette public health recommendations across four diverse jurisdictions. However, it did not attempt to shed light on which regulatory stance towards e-cigarettes should be considered best practice. While this question motivates many public health researchers and tobacco control advocates, it is too early to determine which regulatory approach yields the best results concerning key areas of debate (e.g., decreasing tobacco smoking prevalence). A 'harm reduction' or 'precautionary' approach might be better able to improve population health, but it is possible that the lack of consensus may reflect the optimal approach differing across jurisdictions. For example, in a country where adult smoking is low, but the prevalence of adolescent smoking is rapidly increasing, a 'precautionary' approach might be preferred. Evidence around safety, dual-use with tobacco cigarettes, youth initiation, long-term health effects, and smoking cessation were constantly put forward to justify one position or another. A scientific and political consensus may emerge as the evidence

base improves, allowing public health bodies to better balance the extent to which they pursue 'harm reduction' or 'precautionary' approaches. Using e-cigarettes as a case study I have demonstrated the complexity of public health decision-making and the differences in e-cigarette recommendations. Despite public health bodies all focusing on the same goals- to reduce tobacco use and related harms.

Several studies (Tremblay et al., 2015; Kennedy et al., 2017; Brady et al., 2019; Erku et al., 2020; Campus et al., 2021), largely published after my research was conducted, have examined the e-cigarette regulatory approaches pursued across different countries. Tremblay et al. (2015) summarised current and proposed e-cigarette regulations across US states, ranging from 2004-2014 (analysis conducted in 2014). They extracted details, including the level of regulation and description of regulation, finding six types of regulations: access; use; licensure; marketing and advertising; packaging; and taxation (Tremblay et al., 2015). Tremblay et al. (2015) found there to be a principal focus on youth protection and that regulations relating to the sale to and use by minors are enacted most frequently, whereas packaging requirements, regulations addressing taxation, and marketing or advertising were infrequent. In addition, they found variation in state-level regulations and an absence of federal regulations. Although my research differed from that of Tremblay et al. (2015) concerning the document sample and time period examined, we both found a focus on protecting youths. Furthermore, we both found there to be variation in regulations, Tremblay et al. (2015) within a jurisdiction (e.g., US state-level), my research across jurisdictions. My study involved an examination of e-cigarette policy recommendations published between 2014-2019, therefore, providing a more up-to-date analysis compared to Tremblay et al. (2015).

Kennedy et al. (2017) summarised the regulatory approaches, product classifications, and regulatory domain of e-cigarettes across 68 countries. They identified policies through Ministry of Health websites and broad web searches, finding that many countries regulate e-cigarettes using current regulations and not new legislation (Kennedy et al., 2017). My research broadly aligns with Kennedy et al. (2017) in relation to finding a range of regulatory approaches and the protection of minors by implementing age purchase regulations. However, they do not examine in detail the approaches pursued. They instead focus on how e-cigarettes are regulated (e.g., through an existing or new law), how e-cigarettes are classified (e.g., medical), and what regulatory domains are being applied (e.g., advertising/promotion, sale, and health warnings) (Kennedy et al., 2017). Kennedy et al. (2017) found that a third of the

countries included in the study do not have regulations written specifically for e-cigarettes, instead they applied existing tobacco control policies to the products. I found this to be the case with the FDA, where their authority has been extended to regulate all tobacco products (including e-cigarettes) and as a result, their tobacco control policy now includes e-cigarettes. In contrast, the other public health bodies included my research all produced new recommendations for e-cigarette products. Although my research focuses on a smaller sample of documents from four jurisdictions, I conducted an in-depth examination of e-cigarette regulatory approaches by highlighting the similarities and differences.

It is worth noting that while writing Chapter 5 of this thesis, several papers examining the varying e-cigarette policy approaches across jurisdictions were published (Brady et al., 2019; Erku et al., 2020; Campus et al., 2021). This had implications when attempting to publish this chapter. While this negatively impacted the perceived novelty of my document analysis, it is part of a bigger study and assists in understanding why different policy approaches have been pursued.

Brady et al. (2019) conducted a scoping review of international e-cigarette policy recommendations published between 2011-2017. The results from my study broadly agree with Brady et al. (2019) finding a consensus on preventing youth access to e-cigarettes and restrictions on marketing and advertising of e-cigarette products. My study involved a qualitative analysis examining e-cigarette policy recommendations of international public health bodies published between 2014-2019, therefore, providing a more up-to-date analysis compared to Brady et al. (2019).

Erku et al. (2020) examined the nicotine vaping products (including e-cigarettes) policy positions of health and medical organisations across Australia, New Zealand, and the UK. They found that the majority of public health bodies, charities, and government agencies in the UK and New Zealand supported nicotine vaping products as a 'harm reduction' tool (Erku et al., 2020). Whereas organisations in Australia raised concerns about the lack of clear evidence and non-smoking youths becoming addicted to nicotine (Erku et al., 2020). The results of my research also agree with Erku et al. (2020) finding the UK to be more supportive of e-cigarette use and Australia taking a 'precautionary' approach. Although Erku et al. (2020) included similar jurisdictions in their sample, my sample included USA and WHO, thereby providing an international and global perspective to the e-cigarette regulation debate. Further, by including the WHO I was able to gain insights into how international experts might position themselves in the

debate and might influence setting the agenda on policy recommendations for tobacco control at a national level.

A recent study by Campus et al. (2021), involved a comparative public policy analysis of the regulatory and incentivising approaches towards e-cigarettes across 97 countries. The study aimed to inform future policy decisions relating to the regulation of e-cigarettes. While Campus et al. (2021) provided a more current analysis of e-cigarette policy approaches (analysis conducted in 2020), they did not discuss sub-national regulation or focus on specific jurisdictions. My research focused on four jurisdictions and included sub-national level bodies within the UK, therefore, allowing for a broader comparison across jurisdictions of policy approaches towards e-cigarettes. Campus et al. (2021) discussed e-cigarette regulations in relation to a regulatory spectrum, similar to my study, and discussed the various regulatory approaches (including the advantages and disadvantages of the approach), pursued in each of the 97 countries. In doing so, they do not examine the nuances in the recommendations/regulations made. Furthermore, Campus et al. (2021) do not report or discuss any regulations concerning smoke-free legislation or use indoors. They were either not examined as they were not included in the regulation approaches discussed or it was not a topic the authors felt was worthy of exploration. In contrast, my study found this to be an area where there was divergence in recommendations and was worthy of discussion.

By examining the e-cigarette policy recommendations of international public health bodies published between 2014-2019, this thesis provides a more up-to-date analysis compared to the above-mentioned studies. The research builds on the literature by showing that the diversity in e-cigarette recommendations is also reflected in public health recommendation documents, not only across jurisdictions but also within documents produced in the same jurisdiction. Regardless of the regulatory approach taken towards e-cigarettes, globally all public health bodies still have the same goal; to reduce tobacco use and related harms. E-cigarette regulatory policies vary widely by jurisdiction and the classification of e-cigarette products appears to shape the type of regulations that are made.

Policymakers might want to consider developing policy approaches and solutions that facilitate harm reduction for certain population groups (e.g., smokers), while simultaneously protecting the health of other population groups (e.g., non-smoking adults and youths). A balance of e-cigarette policies for each jurisdiction might allow for the achievement of certain policy goals and objectives. Policymakers would need to

determine which goals and objectives to prioritise, and which ones cannot be optimally achieved.

9.2.2 RQ2: What are the sources of evidence being used in public health bodies' e-cigarette public health recommendations and is the evidence cited differently across jurisdictions?

The citation network analysis demonstrated that public health bodies across four jurisdictions vary in their approach to citing evidence, with some citing numerous sources (e.g., the SGR (2016) document cited 923 sources). Whereas others did not indicate the sources of evidence used to develop their recommendations (e.g., the NHS HS (2017) document). Most of the evidence cited was not shared across the recommendation documents, with relatively few influential citations. We also found that there are sources of evidence that are only cited by one recommendation document, and this is most likely due to the remit of the document.

The network graph (see Figure 6.3, p.151) illustrated how sources were cited across the 14 recommendation documents. A large number of citations appeared in only one or two of the recommendation documents; 1508 (89% of 1700 citations) were cited by only one recommendation document. The number of citations per recommendation document varied (zero to 923 citations) meaning that documents with fewer citations provided less information to the citation network compared to documents with more citations. Only three recommendation documents cited over 100 citations and the SGR (2016) document included 923 citations, more than double the number of citations in the PHE (2018) document.

In addition, I analysed the 53 most influential citations (sources cited across three or more recommendation documents). Analysis of study type demonstrated that basic science research without human subjects (e.g., examination of aerosols and e-liquids) was most common. Since the development and introduction of e-cigarettes to the market, there have been numerous concerns about the products. Basic science research can investigate a variety of components of e-cigarette products. Public health bodies may be drawing on this study type more as they are investigating the components and chemical composition of e-cigarette products which are fuelling some of the main health concerns around the safety of the products. Reviews were also prominent among the highly cited citations but often non-systematic (n=8), as well as SRs (n=10). There

are sources of evidence that are only cited by one recommendation document, and this is most likely due to the remit of the document.

Using bipartite blockmodelling I was able to analyse whether the recommendation documents drew upon similar evidence. The blockmodelling uncovered sources of evidence that were common across all policy jurisdictions. For example, public health bodies from the UK, Australia, and USA drew upon similar sources. However, this evidence was used to articulate different policy approaches; the UK adopted a 'harm reduction' approach, while the WHO, Australia, and USA adopted a 'precautionary' approach.

9.2.3 RQ3: What are the conflicts of interest and funding sources present within cited evidence drawn upon during the development of e-cigarette public health recommendations?

In addition to examining the sources of evidence, the citation network analysis was able to highlight the presence of author COI and study funding in the evidence cited. The analysis clearly shows that some of the evidence influencing public health recommendation documents stems from research where COI are not declared or where important conflicts exist. A substantial proportion of cited evidence contained pharmaceutical (12%; n=127 journal articles of 1081), e-cigarette (7%, n=72), or even tobacco (3%; n=37) COI, including amongst the most influential research featuring across multiple recommendation documents. While reporting of COI has substantially improved over time, there is still a substantial proportion of articles that do not explicitly report potential COI.

These findings are broadly in line with Stuckler et al. (2016), Miller et al. (2017), Lundh et al. (2017) and Fabbri et al. (2018) who argue that funder interference is common in public health and can have an effect on the research agenda and research outcomes. For example, Stuckler et al. (2016) examined whether the sugar industry influenced the updating of WHO sugar intake guideline and found that industry influenced guideline development. Miller et al. (2017) studied funder (e.g., industry, government, or charity) interference in international addiction science, finding interference to be common, particularly by governments. In contrast, Lundh et al (2017) investigated the influence of industry sponsorship on drug and device studies vs non-industry sponsorship and found that industry sponsorship resulted in a more favourable conclusion compared to non-

industry sponsorship. Fabbri et al. (2018) explored the influence of industry sponsorship and found that it can impact research agendas. While the broad themes within the aforementioned studies were similar to my results, my results differed from Stuckler et al. (2016) possibly due to the area of focus. Stucker et al. (2016) focused on the sugar industry, whereas I examined any COI across different types of commodities, sectors, and industries. In contrast, Bindslev et al. (2013) and Rasmussen et al. (2015) examined author COI in guideline development and clinical trials, respectively. Both studies showed that COI are often not declared, with Bindslev et al. (2013) demonstrating that COI among guideline authors were common but rarely disclosed and Rasmussen et al. (2015) finding that almost half of all authors had undisclosed COI in clinical trials. Unlike my research, none of the above-mentioned studies provides an in-depth exploration of author COI and study funding. My research adds to the literature by demonstrating that the sources of evidence drawn upon by public health bodies when developing e-cigarette recommendation documents are subject to COI, including even the most concerning COI – funding from the tobacco industry.

Although my research was not able to establish that cited evidence which included COI definitively influenced decision-making, it is noteworthy that recommendation documents did not transparently record and consider COI in the underlying evidence base. Therefore, greater transparency in recommendation documents when drawing on evidence featuring COI may be warranted.

9.2.4 RQ4: How are conflicts of interest disclosed, managed, and collected during the development of e-cigarette public health recommendations?

Analysis of the data from the development documents (including COI policies) and expert interviews allowed me to investigate how COI are disclosed, collected, and managed during the development process. I examined the presence of COI policies and found that of the ten public health bodies included in this study, only five public health bodies have a publicly available COI policy. My research shows that there is general agreement about the importance of disclosing COI. However, public health bodies across four jurisdictions vary in their approach to collecting and managing COI. Examination of how public health bodies define the term ‘conflict of interest’ indicated there to be slight variation. For example, the APHA talks explicitly about the potential gain, and the NHMRC discusses direct and indirect interests (National Health and Medical Research

Council, 2018; American Public Health Association, 2018a), whereas other public health bodies include a broader definition. I found there to be consistency across public health bodies in what constituted financial and non-financial COI, but there was variation in who is required to declare conflicts. Furthermore, I found there to be a substantial difference in the time period covered for disclosure. For example, the NHMRC required only potential interests within the last three months and the WHO did not specify a time frame (World Health Organisation, 2014b; National Health and Medical Research Council, 2018; National Health and Medical Research Council, 2019). Variation in time frame for disclosure was also raised but participants, who argued that such variation can negatively impact the reporting process. Despite the variation in the public health bodies' COI policies, there was agreement among the participants that everyone involved in the development of policies and recommendations should disclose any COI. In my examination of the approaches for handling COI, I found there to be varied approaches ranging from the total exclusion of conflicted individuals, limited involvement and just declaring COI but being able to continue participating in the development process. One participant discussed that conflicted individuals were required to declare any COI; however, no further action was taken. Interestingly, this was not consistent with the COI policy of the public health body which this participant worked with the process. The variation in COI policies was widely discussed by participants who ultimately argued that the current processes for collecting and managing COI are insufficient, and further that all COI should be disclosed - in doing so this would increase transparency in the process and prevent the underreporting of COI.

Numerous studies (including Guyatt et al., 2010; Mendelson et al., 2011; Eccles et al., 2012; Qaseem and Wilt, 2019; Traversy et al., 2021) have examined the presence and management of COI in the decision-making process, finding there to be high rates of those involved in the development process with COI. Eccles et al. (2012), who examined various aspects of the development process (including identifying topics for guidelines and the processes for managing COI), gave insight into how they believe COI should be managed during guideline development, arguing that participants involved in guideline development should submit a disclosure of all potential COI, a point that was also argued by the participants in my study.

Similar to my study, Guyatt et al. (2010), Mendelson et al. (2011), Qaseem and Wilt (2019), and Traversy et al. (2021) examined the COI management process in specific guidelines. Guyatt et al. (2010) discuss the American College of Chest Physicians' Antithrombotic Guideline and how COI were collected and managed during its

development, Mendelson et al. (2011) examined COI in cardiovascular clinical practice guidelines, and Qaseem and Wilt (2019) study how Clinical Guidelines Committee of American College of Physicians collected and managed COI. While Traversy et al. (2021), examined the best practices for managing COI in four international organisations; the WHO, NICE, United States Preventative Services Task Force, and the American College of Physicians. All four suggest that explicit processes can be used by guideline development panels to declare COI and mitigate their effects (such as limited involvement). In addition, they argue the disclosure should include all past and current potential COI, and if COI are identified those individuals should abstain from discussion of recommendations, similar to the views elicited in my study. Despite focusing on different organisations and guidelines, the results from Guyatt et al. (2010), Mendelson et al. (2011), Qaseem and Wilt (2019), and Traversy et al. (2021) align with the results from my study.

Although the results from the aforementioned studies broadly align with my study, it is worth highlighting the differences. Eccles et al. (2012) discussed how COI should be disclosed and managed but did not focus on a specific guideline or set of guidelines. In contrast, my study identified and examined a sample of public health bodies' publically available COI policies. In doing so, I was able to discuss the various aspects of the policies and compare the COI policies across the public health bodies. Furthermore, using expert interviews I was able to go beyond stating what should happen and discuss what does happen. In comparing research by Guyatt et al. (2010), Mendelson et al. (2011), and Qaseem and Wilt (2019) to my study, my findings broadly agree but my methodological approach has allowed for an in-depth analysis of COI. As mentioned above, I have been able to compare across public health bodies and through expert interviews and elicit various, sometimes diverging, views on how COI should be and are managed.

Traversy et al. (2021) drew upon the Guidelines International Network (GIN) for analysing the management processes and stated that they represent a rigorous approach for disclosing and managing COI in guideline development. Although they examined processes for managing conflicted individuals, they do not look at other important aspects of the process (e.g., time period for disclosure). Furthermore, they do not compare across the included organisations, instead, they compare the processes against the GIN approach. Although this is worthy of exploration, my study offers a comparison across policies and jurisdictions.

A concerning finding from my study was that only half of the public health bodies had a COI policy publically available. Research by Norris et al. (2011) similarly found that only 46% of the 37 surveyed organisations had a COI policy directly related to health care guidelines. This finding along with results from my study suggests that the absence of COI policies could result in the underreporting of COI by individuals involved in the development process (Norris et al., 2011; Neuman et al., 2011; Norris et al., 2012; Bindslev et al., 2013). There has been a consistent interest in the collection and management of COI in the development process across a range of public health topics, as can be seen in the aforementioned studies. It is noteworthy, that even a decade after Guyatt et al. (2010) research, we are still seeing research highlighting a lack of agreed processes for collecting and managing COI.

COI represent a potential threat to the trustworthiness, credibility, and utility of public health policies and recommendations and it is concerning that some public health bodies either do not have or are not able to share how they collect and manage COI. The variation in COI policies can result in the underreporting of COI and lack of transparency in the process, resulting in a decrease in trust and credibility of policies and recommendations. Given the concerns about COI, particularly industry COI, robust, transparent, and well-defined processes for collection, assessing, and managing COI when developing public health recommendations are necessary.

9.2.5 RQ5: What contextual factors influence the role and use of evidence in the development of e-cigarette public health recommendations and how do they do so?

As found in Chapters 5 and 6, the cross-jurisdiction comparison revealed that there is considerable divergence in relation to e-cigarette regulatory approaches despite similar evidence being drawn upon. Public health decision-making is complex and does not take place in a vacuum and my analysis shows that there are a variety of factors influencing decisions. Internal contextual factors (e.g., the remit of the document and participants involved) were found to influence the decision-making process. However, they did not indicate why differing e-cigarette policy approaches are being pursued. Analysis of external factors indicated their importance in the framing of policy goals; these included differences in the epidemiology and the need to be consistent with broader institutional and political contexts.

My application and refinement of Dobrow et al.'s (2004) conceptual framework on context-based evidence-based decision-making represents a novel contribution to the scientific literature, with my research highlighting the two-way interaction between internal and external contextual factors and the interaction between different jurisdictions. As described in Chapter 8, the analysis demonstrated numerous instances where this interplay occurred, for example, the remit of the document (internal factor) is influenced by various external factors (e.g., epidemiology and policy history), and over time, decisions are made that will reshape the external context. As a result, I modified Dobrow et al.'s (2004) conceptual framework (see Figure 8.1, p.212) to acknowledge the interplay between external and internal contextual factors. In doing so, this reflects the inherent complexity and messiness of decision-making and highlights the methodological challenge of understanding how the different elements (decision-making participants, processes, and context) are intertwined (Walt and Gilson, 1994; Walt et al., 2008; Hinrichs-Krapels et al., 2020).

In line with previous research (Dobrow et al., 2004; Dobrow et al., 2006; Hutchinson, 2011; Hutchinson et al., 2011; Mirzoev et al., 2013; Mirzoev et al., 2017) the findings demonstrate that context forms an important set of influences on evidence-based public health decision-making. Several studies (including Ricketts, 2010; de Savigny et al., 2012; Mirzoev et al., 2017) have illustrated the interplay between factors across macro, meso, and micro levels. Ricketts's (2010) analysis was restricted to one document (the Jamaica National Policy for Persons with disabilities), whereas Mirzoev et al. (2017) examined six public health policies across two jurisdictions, a more comparable sample to my study. Ricketts (2010) and Mirzoev et al. (2017) both studied the policymaking process using the macro-meso-micro framework, finding that contextual factors (such as individual values and politics) are influential in the policymaking process. Although my study found individual values and politics to be influential, Ricketts (2010) and Mirzoev et al. (2017) did not find epidemiological factors to be influential and this is most likely due to the cases they studied. While my study suggests that epidemiological factors were an influential factor in determining whether a policy is required and/or should be adopted.

In contrast, de Savigny et al. (2012) examined the influence of context on the success of consumer discount vouchers on insecticide treated nets for malaria prevention and found context to impact the uptake of the scheme. Contextual factors were categorised differently by de Savigny et al. (2012) compared to my study. de Savigny et al. (2012) followed an approach adopted by the business sector and categorised context factors as

human resources, governance, financing, informatics, technologies, and service delivery. de Savigny et al. (2012) found governance to be an influential factor; however, it was not as influential as other factors such as stakeholder engagement. In contrast, my study found political factors to be influential and they were often discussed as to why certain policy approaches were or were not adopted. This difference between my study and de Savigny et al. (2012) could be attributed to the case selected (e-cigarettes vs discount vouchers) and the jurisdictions (low-income country vs high-income country).

Hutchinson et al.'s (2011) research examined the development of Malawi's Co-trimoxazole prophylaxis national policy, meaning they were able to examine individual networks of those involved. Their study is broadly similar to my analysis, as we both used a case study to examine the role of context in developing public health policies across jurisdictions. Hutchinson et al. (2011) argue that although evidence is important, alone it does not drive the decision-making process and that contextual factors such as government structures are influential to the process. Similarly, the analysis of external factors (such as multi-level governance) suggests their importance in the framing of policy goals, these included differences in the epidemiology and the need to be consistent with broader institutional and political contexts. Furthermore, Hutchinson et al. (2011) found that networks of the individuals involved in the development of the policies was influential to the process. Although I found decision-making participants' beliefs and values to be influential, I was not able to explore the beliefs, values, and relationships of specific individuals. While my study involved an analysis of 15 recommendation documents and there would be numerous people involved in the development of each document. Therefore, it would not have been feasible to examine individual networks. Despite using two different case studies, I focused on e-cigarettes and Hutchinson et al. (2011) focused on Co-trimoxazole preventive therapy, we both found context to be influential in the decision-making process.

Although I describe contextual factors as external and internal, my study highlights the complexity of public health decision-making and the methodological challenges to understanding how the different elements are intertwined, by showing the variety of contextual factors influencing decision-making. Furthermore, I highlight the subtle ways in which internal and external contextual factors interact to frame the focus of policy recommendations and the evidence chosen to underpin them. These findings are broadly similar to findings from similar studies, as I did not find any indication of the

dominance of contextual influences at any of the three stages of evidence utilisation (Ricketts, 2010; Hutchinson et al., 2011; de Savigny et al., 2012; Mirzoev et al., 2017).

My study highlights the variety of contextual factors influencing decision-making and also how these contextual factors interact to frame policy goals, allowing for a greater understanding of contextual influence and helps appreciate the complexity of public health decision-making. Decision-makers wrestle with myriad different factors including evidence, politics, cultural norms, and policy ambitions when developing public health policies and recommendations, especially on novel public health issues (such as e-cigarettes and COVID-19) where the evidence base is still emerging.

9.3 Reflections on methods

The purpose of this thesis was to investigate the relationship between evidence and public health policy and the role of context in the development of public health policies and recommendations. In order to investigate this, I utilised a multi-methods case study approach, with e-cigarettes selected as the topic of inquiry. In this section, I discuss the key strengths and limitations, some of which could not be anticipated at the outset, of the methodological approach adopted.

9.3.1 Case study approach to the research

This thesis aims to explore the relationship between evidence and public health policy and the influence of contextual factors in the decision-making process. In order to do so, I selected a case study approach. E-cigarettes were chosen as a case study due to the perceived variation in approaches across public health bodies, despite all bodies claiming to be evidence-based. Therefore, the issue of e-cigarettes offers a highly relevant case through which to investigate the relationship between evidence and public health policy.

A focus on only one case study topic provides limited opportunity to investigate how the role of context might matter across different public health topics. However, my research has provided insights into how context is influential to the decision-making process in relation to e-cigarettes specifically. To better understand the role of context, this would ideally require the study of multiple diverse case studies focused on different public health issues. Furthermore, e-cigarettes were purposively selected and

therefore cannot be considered a representative example of the decision-making process. The extent that which the findings from this thesis may be transferable to other areas of public health policy and other settings is unclear, a weakness of the case study approach (Yin, 2009). However, this thesis highlights the dependent nature of the evidence-policy relationship, which aligns with previous research that has investigated the decision-making process in other areas of public health policy. Thus, this strengthens confidence that similar processes may operate elsewhere (Hill and Varone, 2017; Boswell and Smith, 2017; Kano and Hayashi, 2021) and mitigates such a weakness.

An important aspect of a case study is the use of multi-methods to collect data that leads to obtaining rich data (Basias and Pollalis, 2018). My research employed multi-methods and in doing so rich data from different sources were obtained. Using multi-methods allows for an in-depth study of a phenomenon through the analysis of multiple perspectives (Denzin and Lincoln, 1998; Roller and Lavrakas, 2015). By employing multi-methods, my research was able to explore the relationship between evidence and public health policy and contribute to our understanding of how public health policies and recommendations are developed when the evidence base is limited (e.g., lack of long-term evidence), and when the topic area is continuously evolving (as was the case with e-cigarettes). In addition, using multi-methods allowed me to deepen my understanding of the influence of contextual factors in the decision-making process and discuss how these impact resulting policies and recommendations. Concerning e-cigarettes, using multi-methods allowed me to explore the potential reasons as to why different policies are being pursued across jurisdictions.

In addition, employing multi-methods allowed for the comparison of two data sources (Chapter 7) and for the triangulation across all data sources (Chapter 8). First, I was able to compare data from the development documents (including COI policies) and expert interviews to examine the processes by which public health bodies collect and manage COI during the development of policies and recommendations. In doing so, I identified the varying processes used for collecting and managing COI, highlighting that the current processes are insufficient and that on one occasion the process stated in COI policy was not carried out in practice. Second, I was able to triangulate across the four data sources to examine how context influences the role and use of evidence. This resulted in the discovery that, in this case study, there is an interplay between external and internal contextual factors, which without employing multiple methods may not have been feasible.

There are criticisms of using multi-methods that are important to consider. One criticism is that it is not enough to simply compare different data from different methodological sources, without understanding the data collection process of each (Fielding and Fielding, 1986; Flick, 2004). Silverman (1985) states "what goes on in one setting is not simple corrective to what happened elsewhere" (p.21). Selected methods should be used in conjunction carefully and purposefully. In order to avoid only comparing the different data sources, I analysed each data source individually, paying attention to the data collection process of each. I then synthesised the data sets to analyse issues from these varying perspectives with reference to these different settings (see Chapter 4 for more details). In doing so, it allowed for the different sources and types of data to be analysed in conjunction with one another, resulting in both a broader and more in-depth understanding of the relationship between evidence in policy.

9.3.2 Document analysis of public health bodies' e-cigarette recommendation documents and development documents

The analysis of recommendation documents has been particularly helpful for this research in several ways. The review of published recommendation documents allowed me to have an overview of the key e-cigarette policy recommendations being produced both within and across the four jurisdictions. This allowed me to be aware of the policy background prior to conducting the expert interviews and thereby allowed me to create an interview schedule that would utilise the time spent with participants. In addition, this meant that I was better prepared for the interviews, and I was able to position myself to the participant as a credible researcher which in turn helped increase the chance of recruitment and quality of interview data obtained.

The development documents (including the COI policies) produced by the included public health bodies provided an important resource for analysis. In particular, they provided insight into how public health bodies search for and review the evidence, how evidence is transferred into recommendations and how COI are collected, assessed, and managed during the development of public health recommendations. This in combination with the information contained in the recommendation documents was helpful in planning the expert interviews and informed the development of the interview schedules.

There are several methodological strengths of the approach I adopted to identify the recommendation and development documents. I purposively identified different jurisdictions for investigation and systematically identified recommendation documents for consideration. To ensure I had not missed or excluded any recommendation documents, positions, or policy statements, relevant experts within each jurisdiction were contacted and asked to provide details of other documents or statements they believed to be influential but were not included in the original sample. A similar process was adopted for identifying the development documents (including COI policies). If a development document was not publicly available, I contacted the public health body by email and asked if they could provide any details on the process used to develop recommendation documents. Although I employed multiple approaches to identify and include all relevant recommendation and development documents, it is possible that I may have missed some recommendation documents, position, or policy statements, and/or development documents that were not made publicly available. That said, the documents that I analysed have provided valuable insight into understanding e-cigarette policies and recommendations and the process by which they are developed.

An important strength of this research is the use of existing coding frameworks combined with inductive coding. The coding of the recommendation documents was based on an adapted version of the WHO MPOWER framework for tobacco control (World Health Organisation, 2013). The MPOWER framework is well-suited to the types of regulation my thesis explores (as discussed in Chapter 5). The focus of my thesis is on policymaking at the level of public health bodies, therefore I have not addressed some of the broader aspects of e-cigarette policymaking (i.e., supply-side regulation) that occur at other levels of governance and which might have yielded different findings in terms of the relationship between evidence and public health policy. The development documents were coded using two existing frameworks (supplemented by inductive coding). When exploring reasons for the ways in which evidence influenced guideline development (which contributed to answering research question 5), I drew upon the GRADE EtD (Alonso-Coello et al., 2016b). When exploring the ways which COI were collected and managed (which contributed to answering research question 4), I drew upon the standards and recommendations proposed by IOM (Institute of Medicine, 2009; Institute of Medicine, 2011) and ICMJE (International Committee of Medical Journal Editors, 2021). The use of existing coding frameworks, supplemented by inductive coding, allowed a structured approach for assessing different theoretically important aspects (including the absences of data).

Despite the advantages of studying public health bodies' recommendation and development documents, their analysis was not unproblematic. The recommendation documents included in the sample were produced at a certain time (the year of publication ranged from 2014-2019) and addressed slightly different remits and this influences the recommendations made. I attempted to consider the likely implications of these factors in my analysis, but I note that doing so is difficult, particularly since the policy background may have evolved during the time period covered by the documents and new e-cigarette products may have been introduced to the market.

9.3.3 Citation network analysis of evidence cited in e-cigarette recommendation documents

The use of citation network analysis to investigate and illustrate the sources of evidence drawn upon by public health bodies when making recommendations is a relatively novel method that highlights the inter-relationships between the evidence used by different public health bodies. The method of citation analysis has several strengths including its unobtrusiveness. Unlike data obtained from interviews or questionnaires, citations are unobtrusive as they do not require the cooperation of a participant/respondent and they are unreactive (Bornmann and Daniel, 2008).

Citation analysis allows for the examination of how frequently a citation is used in the citing article; however, this was not the focus of my study. It is possible that in some cases citations may reflect critiques of presented evidence rather than the use of evidence to justify a position or recommendation. However, when conducting further analysis of the 53 most influential citations I found no examples of this. Although I found no examples of this in the 53 influential citations, it is possible that other, less cited, citations may critique the presented evidence. Similarly, the method does not allow for examination of the type of impact a citation has on a resulting policy. For example, an evidence source may have been cited an equal number of times across two recommendation documents. However, one document cited it positively (e.g., agreed with the study findings and supported their recommendations) and the other negatively (e.g., they disagreed with the study findings and used this in support as to why their opposing recommendations). Each of the recommendation documents included in the sample were produced at a specific time and to address slightly different remits. This is likely to lead to some divergence in the type and number of citations included, making comparison more challenging.

9.3.4 Expert interviews on e-cigarettes and policy development

Recruitment took place between June 2019 and June 2020. Overall recruitment was largely successful; however, some difficulties did occur. There were instances where a potential participant was not able to participate and recommended an additional respondent but on examination, the additional respondent was not involved in the development of the recommendation document. Recruitment proved to be difficult after March 2020 as a result of the global COVID-19 pandemic. Due to the pandemic, numerous academics and policymakers returned to clinical work and were juggling other commitments (such as childcare). Thus, I found it more difficult to recruit participants as they were not able to set aside time for the interview. As a result, some individuals who are likely to have unique insights into the decision-making process were not interviewed (for example I was only able to interview two methodologists). It is unfortunate that this incident occurred, and it is unlikely that any alternative methodological approach could have been undertaken to further assist recruitment.

As with any research method, there are limitations to expert interviews. One limitation is that experts are individuals who can be extremely busy, therefore, difficult to access (Smith, 2006; Harvey, 2011; Littig, 2013). Potential participants were largely positive about the study. However, I did experience a few difficulties in relation to access as discussed. Another limitation is that experts may provide rehearsed answers. These individuals may have prepared for the interviews and may answer questions according to their organisation's views rather than their personal views. To avoid receiving answers that were already within the documents or publicly available, I asked questions that probed about the development process and how evidence is transferred to recommendations. Also, I asked questions on topics that emerged during the interview. Furthermore, participants might not recall accurately the processes used to develop recommendations and also, might not be aware of all aspects of the process (i.e., their information can only ever be partial). A final limitation is that experts often have limited time to speak, therefore, asking for too much time might lead to the participant refusing to be interviewed. However, asking for too little time could lead to limitations in the quality and quantity of data provided by the participants (Harvey, 2011; Littig, 2013). To avoid this, I prepared well beforehand by learning about the participant as this would ensure I asked the most useful questions and did not waste time asking questions about information already detailed in the selected recommendation documents.

Some factors appear to have been successful in assisting recruitment. First, the initial emails that I sent to potential participants asking if they would be willing to take part in an informal discussion about e-cigarettes proved to be successful, as seven experts agreed to take part in the research. Unfortunately, not everyone I spoke to was able to be interviewed. However, when this was the case, the individual provided me with other potential participants and allowed me to use their name as a way of gaining access. By sending the initial emails I was able to build a relationship with the potential participant, meaning when asked if they would be able to participate in the study, they knew who I was and my professional background. Second, a small number of participants valued the confidentiality provided and mentioned this during our discussions about the interview. It is possible that this method for achieving confidentiality may have resulted in some participants refusing permission for the use of quotations. However, the openness of some participants suggests that this is unlikely to have compromised the findings to any great extent. Third, during the initial discussions with potential participants, I stated where I was undertaking my research and who my supervisors were. A few participants commented on the work of my supervisors and that they had crossed paths professionally. It, therefore, appears likely that the SPHSU's reputation and the professional background of my supervisors allowed participants to be comfortable that the research would be worthwhile and carried out to a high standard.

Finally, the use of interview data always requires consideration of issues of reflexivity which may have influenced both data collection and analysis. The implications of the researcher's position on the findings have been considered in Section 4.10.

9.4 Original contributions of study: public health policy and academic implications

9.4.1 Public health policy contributions and implications

The findings presented in this thesis raise a number of potential lessons for those seeking to improve the use of evidence within public health policy. This thesis has illustrated the need to understand the role and use of evidence in public health decision-making. My research accentuates the importance for decision-makers to understand the various contextual factors that influence decision-making and how evidence is contextualised.

Decision-makers and public health researchers should consider evaluating contextual factors throughout the development process as this gives them an opportunity to evaluate the impact of a more context-sensitive approach (including how contextual factors may facilitate or hinder this approach) on the production and application of policies and recommendations.

In relation to the case study of e-cigarettes, evidence appears to have played an important role in the development of policies and recommendations. Epidemiological features were important in demonstrating the need for a policy and the remit of that policy. Furthermore, my research suggests that e-cigarettes provide an example where external contextual factors (such as multi-level governance) can drive policy innovation to result in potentially more impactful policies.

In addition, this thesis has also demonstrated, using the novel method of citation network analysis, the prevalence of COI in the sources of evidence drawn upon by public health bodies during the development of public health recommendations. It is alarming that reputable public health bodies are drawing upon evidence with industry COI. Decision-makers and public health researchers need to consider the implications of drawing upon studies with COI, including decreasing the trustworthiness of their recommendations. As such, public health bodies, decision-makers, and public health researchers should consider implementing mechanisms (such as guidelines) on how to identify, assess and manage COI within the evidence base which they intend to draw upon. Similarly, they should consider discussing how to protect against the undue influence of COI when making recommendations about novel topics where the evidence base may be limited (e.g., e-cigarettes). For example, this could include mentioning the evidence drawn upon has COI, but the source and authors have been examined and they believe the declared COI are not influencing the study results.

Furthermore, this thesis has shown that the processes to collect and manage COI among those involved in the development process to be insufficient. Public health bodies and organisations (including medical organisations) should have robust policies or processes for collecting and managing COI when developing policies and recommendations. Although I found half of the public health bodies in my sample to have a publicly available COI policy, it is alarming that not all public health bodies were able to disclose the processes. Managing COI is more complex as there are a variety of approaches that can be adopted, as shown in this thesis. Decision-makers should consider how to balance the competing goals of incorporating diverse knowledge and

expertise into policies and recommendations while minimising the potential influence of COI.

This thesis draws on data from four jurisdictions and investigates the case study of e-cigarettes which is a priority for public health policy. Therefore, it is likely to be of interest to both policymakers and researchers internationally. As discussed in the literature and demonstrated by this thesis, e-cigarette regulatory policies vary by jurisdiction and the classification of e-cigarette products (e.g., tobacco product vs. medicinal product) appears to shape the type of regulations that are made. As such, policymakers might want to consider developing policy approaches and recommendations that facilitate harm reduction for certain population groups (e.g., smokers), while simultaneously protecting the health of other population groups (e.g., non-smoking adults and youths). Therefore, a balance of e-cigarette policies in each jurisdiction is required to allow for the achievement of policy goals and objectives that may be in tension. However, it is difficult to achieve a balance, due to the fact that the long-term health effects are currently unknown (Henkler and Luch, 2014; Sapru et al., 2020; Smith et al., 2021b) and it will take several years to generate this evidence (Merrill et al., 2017). Policymakers need to determine which goals and objectives to prioritise, and which ones cannot be optimally achieved. What has been learned from other jurisdictions may assist in the development of e-cigarette policy recommendations that are adapted to their jurisdiction.

9.4.2 Academic contributions and implications

As far as I am aware, this research is the first of its kind to employ a variety of data collection methods in relation to the policy debate regarding the regulation of e-cigarettes across four jurisdictions. By employing multi-methods, I have been able to conduct an in-depth investigation of the relationship between evidence and public health policy. In addition, through triangulation of four data sources I have been able to investigate how context influences the role and use of evidence in the development of public health recommendations. Within my research, the cross-jurisdiction comparison has allowed me to compare and contrast e-cigarette public health recommendations and the process by which public health recommendations are developed.

The relationship between evidence and public health policy has been widely researched and debated. As discussed in Chapter 1, the emergence of EBM has resulted in an increasing interest among policymakers and public health researchers to pursue EBPM

and more rigorous approaches to policy development (Norris et al., 2011; Parkhurst, 2017). Using e-cigarettes as a case study, I have explored the relationship between evidence and public health policy. I highlight how evidence is an important factor in decision-making; however contextual factors (such as epidemiological features and the remit of decision-makers) need to be considered, particularly when the evidence base is limited or contested. As discussed in Section 2.3.5.1, there are a lack of frameworks and guidance for assessing the applicability of public health interventions in other settings which appropriately address the contextual factors in decision-making. Therefore, I suggest that the EBPM community draws upon existing developed frameworks and guidance (e.g., Cambon et al., 2013; Moore et al., 2021) and develops these in a way which addresses and incorporates contextual factors into the decision-making process. In doing so, we move beyond debates which have historically ignored the philosophical and political nature of decision-making to a process which addresses a variety of contextual factors, this argument has been raised by various researchers (such as Smith, 2013a; Cairney, 2016; Cairney and Oliver, 2017; Parkhurst, 2017).

My research is the first to employ network citation analysis of the evidence sources drawn upon when developing e-cigarette recommendations. It is also one of the first to examine the presence of COI in these cited sources of evidence. The findings demonstrated that there is considerable overlap in the sources of evidence drawn upon by public health bodies when making e-cigarette recommendations. However, this evidence was used to articulate different policy approaches; the UK adopted a 'harm reduction' approach, and WHO, Australia, and USA adopted a 'precautionary' approach. In addition, the findings demonstrate that evidence influencing public health policies and recommendations may stem from research where COI are not declared or where there are direct conflicts. By using e-cigarettes as a case study, I have demonstrated the need for robust methods to manage evidence derived from industry funding or incorporating industry COI within public health recommendations. These COI extend to even the most concerning industries, such as tobacco and an urgent debate is needed about whether such evidence should inform public health policy.

Previous research has examined contextual factors influencing the role of evidence in public health policy and the role of evidence in e-cigarette policies. However, this thesis is the first that qualitatively examines the contextual factors influencing the role and use of evidence in international e-cigarette policy recommendations. Further, based on my analysis, I refined Dobrow et al.'s (2004) conceptual framework on evidence-based decision-making to acknowledge the interplay between external and

internal contextual factors. The findings from this part of the research are important as it helps our understanding of the potential reasons why different jurisdictions are pursuing different regulatory and public health approaches towards e-cigarettes. In terms of practical implications, this framework could be readily employed, by local or national public health professionals, policymakers, and academics across other public health topics seeking to analyse the contextual factors that influence decision-making.

9.5 Recommendations for research

This thesis has highlighted several future research directions that would be beneficial to pursue, both in relation to the selected case study and the evidence-policy relationship in general.

The e-cigarette debate is continuously evolving as a result of new evidence, and this thesis is only a snapshot of the debate, given that public health bodies' recommendation documents were published between 2014 and 2019. Future research could examine how policy positions have changed over time in response to emerging evidence and whether any public health bodies had moved from a 'precautionary' approach towards a 'harm reduction' approach or vice versa. In line with this, future research could also examine how policy positions have changed to incorporate HNB products (such as IQOS), and, particularly in the USA, how policy positions changed in response to the EVALI incident.

My research has focused on e-cigarette recommendations produced by public health bodies across four selected jurisdictions. I did not include government documents in the sample as government departments would be expected to be subject to greater political influences, are less transparent, and less easy to interrogate. Therefore, future research could examine compare and contrast government e-cigarette policies. In addition, research investigating other jurisdictions' e-cigarette recommendations and/or government documents would be worthy.

As mentioned within Chapter 4 and limitations (Section 9.3) of the research, the sample size of expert interviews and there was a limited number of each expert type. Firstly, the recruitment of additional experts would allow for a greater understanding of how different experts use evidence when developing recommendations. Secondly, future research should attempt to engage with different experts involved in the decision-making process, for example, stakeholders (such as civil servants and politicians). In

doing so, this would provide insights into how different types of experts are involved in the decision-making process and their level of involvement.

The findings of this research suggested that there is a lack of transparency in the development process, particularly how COI are managed. As such, future research could focus on a larger sample of public health bodies, possibly including medical organisations, and examine the associated development documents and COI policies. Future research could build on the findings from Chapter 7, to examine how both financial and non-financial COI declared by those involved in the development process impacts on their decision-making, their assessment of the certainty of evidence, the inclusion of specific studies (such as those that declare COI or industry funding/sponsorship), and the translation of evidence into recommendations.

The findings of this thesis could be adapted and built upon in other areas of public health, including in a recent public health crisis, the global COVID-19 pandemic. In the absence of long-term evidence on COVID-19, global policies and recommendations have focused on behavioural changes (e.g., social distancing) and uptake of vaccines to help to reduce the number of cases and spread of the virus. There are some transferable ideas (e.g., contextual factors and use of industry funded data) from this thesis that could be worth investigating further, such as contextualising the evidence from the pandemic when developing policies and recommendations. Similar to e-cigarettes, countries around the world adopted different strategies and policies to help prevent the transmission of COIVD-19, with some countries enforcing mandatory lockdowns (such as the UK) while other countries relied upon voluntary population adherence to recommendations (e.g., Sweden) (Mishra et al., 2021). This thesis used e-cigarettes as a case study and future research could replicate the multi-methods approach using COVID-19 as the case study. Adopting the multi-methods approach would provide an in-depth insight into the role and use of evidence in COVID-19 policies and recommendations. However, future research could also draw upon one of the methods used (for example, the citation network analysis).

9.6 Conclusions

In the four years that I have been researching e-cigarettes, there has been a wealth of academic studies produced in this topic area. As I write the concluding chapter of this thesis the landscape is different from when I started. For instance, tobacco control policies have been amended to include e-cigarettes and regulations have been

introduced to protect youths and young people. In addition, the debate has evolved, and research has shown there to be a 'middle ground' regarding the regulation of e-cigarettes. There has been a response to emerging evidence, with some altering their position on e-cigarette regulations in response to new evidence (Smith et al., 2021b).

Public health policies and recommendations should be informed by the best available evidence. E-cigarette policies vary across jurisdictions, but it is unclear why there is divergence among the previously coordinated tobacco control communities. In an attempt to explain this divergence, this thesis examined the relationship between evidence and public health policy. COI and study funding associated with the tobacco industry is still present within the evidence base and this evidence has been drawn upon by public health bodies' when developing e-cigarette recommendations. This is important to understand as it raises questions about why this evidence is drawn upon and calls for an urgent debate about the inclusion of industry associated data.

The processes for collecting and managing COI are insufficient and this can result in the underreporting of COI. Public health bodies should have a well-defined and robust process to assess and manage COI. Also, decision-makers should consider how to balance the competing goals of incorporating diverse knowledge and expertise into the development process while minimising the potential influence of COI.

My research has shown that there are a variety of both external and internal contextual factors that are considered during the development of e-cigarette policies and recommendations. By refining Dobrow et al's (2004) conceptual framework, I was able to highlight a key finding from my study, the interaction between internal and external contextual factors. This is important as it demonstrates that despite public health policies and recommendations aspiring to be evidence-based however, other factors are influencing the process. My study highlighted that in some instances policies could be transferable to another jurisdiction, while in others it may be more efficient to develop new policies. Thus, the application of interventions often depends on contextual factors within a jurisdiction (Moore et al., 2021).

Overall, this thesis seeks to make an important contribution to understanding the topic of e-cigarettes and the relationship between evidence and public health policy more broadly. In addition, I have highlighted various e-cigarette regulatory approaches, 'harm reduction' and 'precautionary'. Context is crucial in understanding divergence in e-cigarette policy across jurisdictions, with similar evidence used by public health bodies

internationally. COI are common in the evidence base and a lack of standardisation in managing COI might threaten evidence-informed decision-making. Through an examination of contextual factors, this thesis highlights an interplay between the decision-making process and broader context, and this may be why different jurisdictions are pursuing varying e-cigarette policies.

Appendices

Appendix A: Detailed search strategy for the sampling of documents

Steps in search

1. **Identified key public health bodies (n=19)**

UK

1. Public Health England
2. NHS England
3. National Institute for Health and Care Excellence
4. NHS Health Scotland
5. Public Health Scotland
6. Scottish Intercollegiate Guidelines Network
7. Public Health Wales
8. Public Health Agency (Northern Ireland)

Australia

9. National Health and Medical Research Council
10. Public Health Association Australia

USA

11. U.S. Department of Health and Human Services
12. Centres for Disease Control and Prevention
13. U.S. Food and Drug Administration
14. Health Resources and Services Administration
15. National Institutes of Health
16. Alcohol, Drug abuse, and Mental Health Administration
17. Agency of Toxic Substances and Disease Registry
18. American Public Health Organisation

WHO

19. World Health Organisation

2. Records identified via keyword search of public health bodies websites (n=27)

UK

1. Public Health England: E-cigarettes: an evidence update (2015)
2. Public Health England: Use of e-cigarettes in public places and workplaces (2016)
3. Public Health England: Evidence review of e-cigarettes and heated tobacco products (2018)
4. Public Health England Vaping in England: an evidence update (2019)
5. The National Institute for Health and Care Excellence: Stop smoking intervention and services [NG92] (2018)
6. NHS Health Scotland: Smoke-free prisons and e-cigarettes (2016)
7. NHS Health Scotland: Consensus statement on e-cigarettes (2017)
8. Scottish Intercollegiate Guidelines Network: Risk Estimation and the prevention of cardiovascular disease: A national clinical guideline (2017)
9. Public Health Wales: E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)
10. Public Health Agency (Northern Ireland): Tobacco Control Northern Ireland (2015)

Australia

11. National Health and Medical Research Council NHMRC CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)
12. Public Health Association Australia: E-cigarettes policy position statement (2018)

USA

13. U.S. Department of Health and Human Services: E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)
14. U.S. Department of Health and Human Services: Surgeon General's Statement on FDA's E-cigarette Prevention Campaign (2018)
15. U.S. Centre for Disease Control and Prevention: About Electronic Cigarettes (E-cigarettes) (ND)
16. U.S. Centre for Disease Control and Prevention: What's the Bottom Line on the Risks of E-cigarettes for Kids, Teens, and Young Adults? (ND)
17. U.S. Centre for Disease Control and Prevention: E-cigarettes Talk to Youth about Risks (ND)

18. U.S. Centre for Disease Control and Prevention: E-cigarette, or vaping, products visual directory (ND)
19. U.S. Centre for Disease Control and Prevention: E-cigarettes shaped like USB flash drives (ND)
20. U.S. Food and Drug Administration: 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 (2016)
21. U.S. Food and Drug Administration: How are Non-Combusted Cigarettes, Sometimes Called Heat-Not-Burn Products, Different from E-Cigarettes and Cigarettes? (ND)
22. National Institutes of Health: E-cigarettes summary (ND)
23. National Institutes of Health: Vaping Devices (Electronic Cigarettes) Drug Facts (ND)
24. National Institutes of Health: Tobacco, Nicotine, & Vaping (E-Cigarettes) (2020)
25. American Public Health Association: Supporting Regulation of Electronic Nicotine Delivery Systems (2018)

<u>WHO</u>

26. WHO: Electronic nicotine delivery systems (2014)
27. WHO: Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)

3. Full-text records assessed for eligibility (n=27)

4. Records excluded and why (n=12)

1. Scottish Intercollegiate Guidelines Network: Risk Estimation and the prevention of cardiovascular disease: A national clinical guideline (2017) - No recommendations on policy, only research recommendations
2. Public Health Agency (Northern Ireland): Tobacco Control Northern Ireland (2015) - No recommendations on policy
3. U.S. Department of Health and Human Services: Surgeon General's Statement on FDA's E-cigarette Prevention Campaign (2018) - webpage/media release
4. U.S. Centre for Disease Control and Prevention: About Electronic Cigarettes (E-cigarettes) (ND) - webpage
5. U.S. Centre for Disease Control and Prevention: What's the Bottom Line on the Risks of E-cigarettes for Kids, Teens, and Young Adults? (ND) - factsheet

6. U.S. Centre for Disease Control and Prevention: E-cigarettes Talk to Youth about Risks (ND) - factsheet
7. U.S. Centre for Disease Control and Prevention: E-cigarette, or vaping, products visual directory (ND) - factsheet
8. U.S. Centre for Disease Control and Prevention: E-cigarettes shaped like USB flash drives (ND) - factsheet
9. U.S. Food and Drug Administration: How are Non-Combusted Cigarettes, Sometimes Called Heat-Not-Burn Products, Different from E-Cigarettes and Cigarettes? (ND) - webpage
10. National Institutes of Health: E-cigarettes summary (ND) - webpage
11. National Institutes of Health: Vaping Devices (Electronic Cigarettes) Drug Facts (ND) - webpage
12. National Institutes of Health: Tobacco, Nicotine, & Vaping (E-Cigarettes) (2020) - webpage

5. Additional documents identified through contacting relevant experts (n=2)

1. National Academy of Sciences, Engineering, and Medicine: Public Health Consequences of E-cigarettes (2018)
2. U.S. Preventative Services Taskforce: Behavioural and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement (2015)

6. Record excluded and why (n=2)

1. National Academy of Sciences, Engineering and Medicine: Public Health Consequences of E-cigarettes (2018) - No public health recommendations, only research recommendations
2. U.S. Preventative Services Taskforce: Behavioural and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement (2015) – No public health recommendations

7. Additional documents identified via citation lists within each selected document (n=0)

8. Records included in the analysis (n=15)

UK (n=8)

1. Public Health England: E-cigarettes: an evidence update (2015)
2. Public Health England: Use of e-cigarettes in public places and workplaces (2016)
3. Public Health England: Evidence review of e-cigarettes and heated tobacco products (2018)
4. Public Health England: Vaping in England: an evidence update (2019)
5. National Institute for Health and Care Excellence: Stop smoking intervention and services [NG92] (2018)
6. NHS Health Scotland: Smoke-free prisons and e-cigarettes (2016)
7. NHS Health Scotland: Consensus statement on e-cigarettes (2017)
8. Public Health Wales: E-cigarettes (Electronic Nicotine Delivery Systems (ENDS)) (2017)

Australia (n=2)

9. National Health and Medical Research Council NHMRC CEO Statement: Electronic Cigarettes (E-Cigarettes) (2017)
10. Public Health Association Australia: E-cigarettes policy position statement (2018)

USA (n=3)

11. U.S. Department of Health and Human Services: E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (2016)
12. U.S. Food and Drug Administration: 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 (2016)
13. American Public Health Association: Supporting Regulation of Electronic Nicotine Delivery Systems (2018)

WHO (n=2)

14. WHO: Electronic nicotine delivery systems (2014)
15. WHO: Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS) (2016)

Appendix B: Coding framework for the analysis of public health bodies' recommendation documents

A framework was created to summarise the coding of the e-cigarette recommendation documents in Excel. As this framework was large and therefore difficult to reproduce here, the codes used for the framework are reproduced in Table B.1 below, alongside an example quotation. Each of these codes formed a vertical column in the framework, with a separate row for each recommendation document. The coding of the framework was checked by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington.

Name of code	Description	Illustrative example quotation
Monitoring e-cigarette use and prevention policies	Where e-cigarette use among smokers, non-smokers, and young people should be monitored and how policies should be tailored to address the needs of different population groups.	"Trends in smoking and vaping should continue to be monitored, particularly in the light of concerns in North America about youth smoking and vaping." (Public Health England, 2019, p.12)
Protecting people from passive vaping	Where restrictions should be placed on the use of e-cigarettes indoors and the inclusion of e-cigarettes in smoke-free legislation.	"Prohibiting by law the use of ENDS/ENNDS in indoor spaces or at least where smoking is not permitted." (World Health Organisation, 2016, p.7)
Offering to help quit tobacco use and use of e-cigarettes as a smoking cessation tool	Where smokers should be offered advice and guidance to help overcome their dependence.	"Offer advice on using nicotine-containing products on general sale, including NRT and nicotine-containing e-cigarettes." (National Institute for Health and Care Excellence, 2018, p.9)
Warning about the danger of tobacco and e-cigarette use	Where the general population should be warned about the dangers of tobacco and e-cigarette use	"There is a need to publicise the current best estimate that using EC is around 95% safer than smoking." (Public Health England, 2015, p.80)

	including the potential health effects	
Enforcing bans on e-cigarette advertising, promotions, and sponsorship	Where restrictions should be placed on e-cigarette advertising promotions and sponsorship	"Advertising and promotion of e-cigarettes should be prohibited and consistent with tobacco advertising prohibitions." (Public Health Association Australia, 2018, p.1)
Raising taxes on e-cigarette products	Where taxes should be imposed on e-cigarette products	"A tax on the nicotine liquid used in e-cigarettes should be imposed, as evidence from the existing literature indicates that increased ENDS prices are associated with reduced selection and sales of ENDS." (American Public Health Association, 2018b, p.12)
Minors	Where minors were the target population for the recommendation and their protection was key.	"Access to e-cigarettes needs to be controlled carefully; they are not products for children or non-smokers." (NHS Health Scotland, 2017, p.1)
Other	Where recommendations did not fall within one of the other predefined codes	"Requiring premarket review of new or changed tobacco products and authorization by FDA before they can be introduced into the marketplace." (U.S. Department of Health and Human Services, 2016, p.242)

Table B.1: Coding framework for the analysis of public health bodies' recommendation documents, with an example illustrative quotation

Appendix C: Coding framework for the analysis of public health bodies' development documents

A framework was created to summarise the coding of the development documents in Excel. As this framework was large and therefore difficult to reproduce here, the codes used for the framework are reproduced in Table C.1 below, alongside an example quotation. Each of these codes formed a vertical column in the framework, with a separate row for each development document. The coding of the framework was checked by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington.

Name of high-level code	**Name of middle-level code**	**Description**	**Illustrative example**
Acceptability		What regulations are acceptable or unacceptable to a range of key stakeholders	"Acceptability is affected by several factors, such as who benefits from an intervention and who is harmed by it; who pays for it or saves money on account of it; and when the benefits, harms, and costs occur." (World Health Organisation, 2014b, p.127)
Conflicts of interest	In evidence drawn upon	Perceptions and experiences of conflicts of interest in the sources of evidence drawn upon when developing recommendations	"There are robust processes in place to manage conflict of interest [in the evidence base] and to use the best available scientific methods for making recommendations such as the use of GRADE." (National Health and Medical Research Council, 2016)
	In development process	Perceptions and experiences of conflicts of interest of individuals	"To ensure a guideline's recommendations are objective and unbiased all members must declare their interests and careful steps must be taken to manage any conflicts." (National Health and Medical Research Council, 2016)

		involved in the development process	
Development of recommendations	Stages in the development process	What is the process of going from evidence to recommendations	"The evidence-to-recommendation tables depict not only the evidence and judgements leading to a recommendation, but also the justifications for the recommendation's direction and strength. They also describe the subgroups considered, the process used to formulate recommendations (e.g., if voting took place) and key issues surrounding implementation, evaluation, and monitoring (see Chapter 13) as well as research gaps." (World Health Organisation, 2014b, p.128)
	Stakeholder engagement	Stakeholder engagement in the development process	"Stakeholders potentially affected by the statement will need to be consulted at the earliest opportunity and be included in considerations regarding publication of the statement." (Public Health Wales, 2016, p.5)
Evidence	Certainty of evidence	Assessment of the quality and level of certainty of the evidence	"Assessing the quality of the evidence for a review question is critical. It requires a systematic process of assessing potential biases through considering both the appropriateness of the study design and the methods of the study (critical appraisal) as well as the certainty of the findings (using an approach, such as GRADE)." (National Institute for Health and Care Excellence, 2022, p.111)
	Reservations of evidence	Concerns about the quality and lack of certain evidence (e.g., long-term health effects)	"When there is a lack of evidence on issues important to people affected by the guideline (including families and carers, where appropriate), the developer should consider seeking information via a call for evidence, or approaching experts who may have access to additional data sources, such as surveys of user

			views and experiences, to present as expert testimony." (National Institute for Health and Care Excellence, 2022, p.83)
	Role of evidence	What should the role of evidence be when making public health recommendations	"PHE will strive to ensure all public health decisions, be they policy or operational, are based on the best available evidence." (Public Health England, 2013, p.19)
	Types of evidence	Mention of different types of studies and forms of evidence from anecdotal through to RCTs	"Not all reviews are systematic and not all systematic reviews are of high quality. So-called "narrative" or non-systematic reviews are missing one or more of the essential characteristics noted above. Non-systematic reviews and low-quality systematic reviews should not inform WHO guidelines and WHO staff must be able to recognize these and understand their limitations." (World Health Organisation, 2014b, p.93)
Equity		How health inequalities are considered during the development process and which groups are identified as being at risk	"The planned achievements should focus not only on the average level of health, but also on how health is distributed within populations and across groups. The idea is to ensure that those of lower social position and with greater needs can benefit more than more advantaged persons." (World Health Organisation, 2014b, p.51)
Outcome importance		How is the outcome importance determined	"The steering group should list relevant outcomes, including both the potential benefits and harms of the intervention or exposure. The steering group should then ask the GDG to identify any other outcomes that have not been listed. Once a workable list of outcomes has been collected, they need to be ranked in order of priority." (World Health Organisation, 2014b. p.87)

Other		Information I feel that is important but does not fit within other codes	“This is important because guidelines have to be easily located and accessible if they are to be used. Guideline developers write guidelines with the expectation that they will be used, but too often they publish them in ways that make them inaccessible to their intended users. For example, developers may set financial barriers by choosing to publish their guidelines in journals where they sit behind expensive paywalls, or on the websites of organisations which are only accessible to members, or by selling them directly to users.” (National Health and Medical Research Council, 2016)
Politics	Political influence	How does politics or institutions influence the development of public health recommendations	“Based on current evidence and in line with recommendations from the WHO, the World Federation of Public Health Associations, the Cancer Council, Heart Foundation, Cancer Australia and other leading evidence-based organisations, the PHAA strongly supports a precautionary approach to the use, promotion and availability of e-cigarettes in Australia.” (Public Health Association Australia, 2018, p.3)
	Previous and current tobacco control policies	How are previous and current tobacco control policies considered during the development of public health recommendations	“The position statement must pay due regard to current legislation and policy, outlining how the organisation’s proposed position aligns with the existing policy context.” (Public Health Wales, 2016, p.4)
Vested interests		How are vested interests considered and handled during the	“Tobacco companies and those who speak for them or are funded by them (collectively referred to as 'tobacco organisations') cannot register as stakeholders. This is in line with NICE's obligation under Article 5.3 of the WHO

	development of public health recommendations	Framework Convention on Tobacco Control (FCTC) to protect public health policies from the commercial and other vested interests of the tobacco industry." (National Institute for Health and Care Excellence, 2022, p.194)

Table C.1: Coding framework for the analysis of public health bodies' development documents, with an example illustrative quotation

Appendix D: Coding framework for the analysis of public health bodies' COI policies

A framework was created to summarise the coding of the COI policies in Excel. As this framework was large and therefore difficult to reproduce here, the codes used for the framework are reproduced in Table D.1 below, alongside an example quotation. Each of these codes formed a vertical column in the framework, with a separate row for each COI policy. The coding of the framework was checked by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington.

Name of high-level code	**Name of middle-level code**	**Illustrative quotation from COI policy**
Definition of COI		"A conflict of interest arises when the judgement of someone involved in the work of NICE may be compromised, by the financial or other considerations set out in this policy." (National Institute for Health and Care Excellence, 2019, p.4)
Disclosure of COI	Types of financial COI	"Any other relevant direct or pecuniary interest (for instance, having provided expert testimony for a fee on behalf of an entity with a commercial or other interest in the issues being considered by the Committee)." (National Health and Medical Research Council, 2019, p.5)
	Types of non-financial COI	"Prior publication of a study or systematic review that is part of the evidence base under consideration in the guideline." (World Health Organisation, 2014b, p.63)
	Time period considered	"The period of relevance for all declarations made by members of a NICE advisory committee is 12 months before joining and during the membership of the committee." (National Institute for Health and Care Excellence, 2019, p.12)
	About whom are COI collected	"All committee members, executive board members, governing councillors and Special Primary Interest Group members." (American Public Health Association, 2018a, p.1)

	Information on financial and non-financial COI of individuals' personal relationships	"Individual's immediate family members (defined as the pose or partner with whom one a close personal relationship and the children)." (World Health Organisation, 2014b, p.63)
Collection of COI	How COI are disclosed	"Declarations of interests are collected using the standard WHO form for experts." (World Health Organisation, 2014b, p.63)
	Disclosure required prior to involvement	"The obligation for members to disclose interests starts during the appointment process and continues throughout the period of committee membership." (National Health and Medical Research Council, 2019, p.7)
	Who reviews disclosure of COI	"The Board's/Committee's/Council's decision as to whether a conflict of interest in fact existed." (American Public Health Association, 2018a, p.3)
Management of COI	Exclusion procedure	"For disclosed interests, the NHMRC and PGPA Acts require that the member is not present when matters that relate to the interest are considered and does not take part in any decision of the Committee in relation to those matters unless the members of the Committee determine otherwise (as set out below in 6.1)." (National Health and Medical Research Council, 2019, p.7)
	Prohibited relationships	"Hospitality is where there is an offer of food, drinks, accommodation, entertainment or entry into an event or function by a third party, regardless of whether provided during or outside normal working hours e.g., attendance at an industry awards ceremony." (Public Health Wales, 2019, p.20)
	Penalty for non-disclosure	"A failure to disclose an interest without a reasonable excuse will result in the termination of the member's appointment." (National Health and Medical Research Council, 2019, p.8)

Table D.1: Coding framework for coding of the COI policies, with an example illustrative quotation

Appendix E: Coding framework for the interpretation of highly cited sources of evidence used in recommendation documents

- Concerns
    - Dual-use
    - Gateway effect
    - Renormalising smoking
- Context
    - Epidemiology
    - Market
    - Nicotine toxicity and delivery
    - Overview of the literature
    - Regulations
- E-cigarettes as a smoking cessation tool
- Health risks of e-cigarettes
    - Comparison to tobacco products
    - Passive exposure
    - Risks associated with specific population groups
- Safety of e-cigarettes
    - Comparison to tobacco products
    - Chemical compositions

A framework was created to summarise the coding of the highly cited sources of evidence used in recommendation documents in Excel. As this framework was large and therefore difficult to reproduce here, an example of the coding is reproduced in Table E.1 below. Each of recommendation documents formed a vertical column in the framework, with a separate row for each of the 53 highly cited sources of evidence. The coding of the framework was checked by Dr Kathryn Skivington.

Citation	Recommendation document[1]						Comparison
	WHO 2016	PHE 2016	PHE 2018	PHE 2019	PHW 2017	SGR 2016	
McNeill A, Brose L, Calder R, Hitchman S, Hajek P, McRobbie H. 2015. E-cigarettes: an evidence update A report commissioned by Public Health England. Public Health England [2]	"The magnitude of these risks is likely to be smaller than from tobacco smoke [34,35,36,] although there is not enough research to quantify the relative risk of ENDS/ENNDS over combustible products." p.3 **Health risks associated with e-cigarettes- lower than that of tobacco.**	"An independent review of the latest evidence published by PHE in 2015 found that, based on the international peer-reviewed evidence, vaping is around 95% safer for users than smoking" p.4 **Safety of e-cigarettes (e-cigarettes 95% safer than tobacco).**	"The literature search was based on the search developed and used in the 2015 PHE report (5) to ensure consistency between the two reports." p.25 **Context- reference literature** "The 2015 PHE report on EC[5] stated that since 2013, EC had been the most common quitting aid for smokers in England." p.106 **E-cigarettes as a smoking cessation tool- useful.** "Among adults in Great Britain, the previously observed trend of increased perceived relative harm of EC has continued [(5, 21)]." p.176 **Context- prevalence of perceived harm**	"Previous evidence reviews reported data about vaping in stop smoking services during the periods April 2014-March 2015 [3] and April 2015-March 2017 [21]." p.93 **Context- previous literature on smoking cessation** "However, like previous years the highest quit rates were observed when the quit attempt involved the use of a licensed medicine and an EC consecutively (73%), a licensed medicine and EC concurrently (60%) or an EC on its own (60%)." p.93 **E-cigarettes a smoking cessation tool- harm reduction (high quit rates)**	"The 'evidence suggests that the health risks posed by e-cigarettes are relatively small by comparison [to tobacco]' but the long-term effects should be continued to be studied." p.5 **Health effects associated with e-cigarette use (lower than that of tobacco) and lack of evidence**	"Current knowledge of the characteristics of the inhaled aerosol from e-cigarettes suggests that if a current adult smoker of conventional cigarettes or other combustible tobacco products would use e-cigarettes exclusively instead of combustibles as a substitute nicotine delivery system, either en route to quitting tobacco completely or even as a long-term alternative, the risks of tobacco-related diseases would be reduced substantially compared with the risk imparted by continued smoking of conventional cigarettes." p.185 **Health risks associated with e-cigarettes (lower than that of tobacco)**	Different interpretations and conclusions of the reference Safety WHO- cannot quality risk associated with e-cigarettes PHE 2016- 95% safer PHW 2017- lack of evidence on safety SGR- reduced risk compared to tobacco Cessation PHE 2018-smoking cessation -useful and lack of evidence in relation to cessation and vulnerable groups PHE 2019- Smoking cessation-useful

[1] PHE=Public Health England; PHW=Public Health Wales; SGR=U.S. Department of Health and Human Services: A Report of the Surgeon General; WHO=World Health Organisation

[2] Only six of the recommendation documents cited McNeill et al. (2015), therefore, the rest of the recommendation documents (n=9) were coded as NA. For illustrative purposes only the recommendation documents that cite the reference are shown. It should be noted that McNeill et al. (2015) is the PHE (2015) recommendation document but has been cited differently to allow differentiation.

Figure E.1: Coding framework for the interpretation of the highly cited sources of evidence used in the recommendations documents

Appendix F: Ethics approval letter for expert interviews

Appendix G: Participant information sheet for expert interviews

MRC/CSO Social and Public Health Sciences Unit

PARTICIPANT INFORMATION SHEET

Title: Understanding the role of evidence in e-cigarette regulation and policy development

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please ask if there is anything that is not clear or if you would like more information. If you decide to take part in this study, you will be given a copy of this Participant Information Sheet and the signed consent form to keep.

What is the Project About?

E-cigarettes are gaining increasing scientific and policy recognition globally. There is perceived to be considerable variation in recommendations related to e-cigarettes. Some public health bodies have adopted a strategy of actively encouraging e-cigarette use as a quit aid whereas others have emphasised their potential role in re-normalising the use of conventional cigarettes.

What is the purpose of the study?

The purpose of this research is to understand how public health bodies prioritise and use evidence in developing recommendations for e-cigarette policy. Specifically, it will seek to explore the differences and similarities in e-cigarette policy approaches and the role of different types of evidence in contributing to e-cigarette recommendations.

Why have I been invited to participate?

You have been invited to take part in this study because the organisation where you work is involved in the planning and development of e-cigarette recommendations. You have been identified as someone who may be interested in participating.

What would I have to do?

If you decide to take part, you will be asked to provide an informed consent. We will arrange a meeting or Zoom (video conferencing software)/ telephone interview. The interview will take place at your preferred location and in your convenient time. The interview will be recorded and transcribed verbatim. You will be given the opportunity to read and approve the transcript after the interview. Firstly, I will ask some questions about your professional background and current role within your organisation. Next you will be asked a series of questions relating to e-cigarettes, the role of evidence in recommendations and the relationship between evidence and policy development.
The interview will last between 45-60 minutes.

Do I have to take part?

Taking part in this project is voluntary. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time during the data collection and without giving a reason.

What are the possible benefits of taking part?

The information that is collected during this study will give us a better understanding of how public health bodies prioritise and use evidence in developing recommendations for e-cigarette policy.

What are the possible disadvantages and risks of taking part?
We are not anticipating any risks associated with taking part in this study.

Will my taking part in this study be kept confidential?
All information which is collected about you, or responses that you provide, during the course of the research will be kept strictly confidential. To do this, your name and other personal identifiers will be separated from the interview recording and any future transcripts. The interviewer will then anonymise the transcript by removing any information that clearly identifies you and any text that is not to be quoted as it make may make you identifiable will be highlighted. A copy of the transcript will be sent for you to review to ensure that you anonymity is maintained. The transcripts will be analysed by the researcher and will not be made publically available. Selected quotations that do not disclose your identity may be used to illustrate the findings of the research.

In order to make the best use of the data you have contributed, it is possible that future research may make use of these transcripts. Any such use would be directly overseen by either Marissa Smith or Professor Shona Hilton who would be responsible for ensuring your ongoing anonymity.

Any data in paper form will be stored in locked cabinets in rooms with restricted access at the University of Glasgow. All data in electronic format will be stored on secure password–protected computers linked to secured servers within University of Glasgow.

What will happen to my data?

We may be collecting and storing identifiable information from you in order to undertake this study. This means that the University is responsible for looking after your information and using it properly. We may keep identifiable information about you for the duration of the study and will not pass this information to a third party without your express permission. Your rights to access, change or move the information we store may be limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum information possible.

Researchers from the University of Glasgow collect, store and process all personal information in accordance with the General Data Protection Regulation (2018). All study data will be held in accordance with The General Data Protection Regulation (2018). When the project ends, the data will be stored in archiving facilities in line with the University of Glasgow retention policy of up to 10 years. After this period, further retention may be agreed or your data will be securely destroyed in accordance with the relevant standard procedures.

What will happen to the results of the research study?
The results of this research will be used within my PhD thesis and in the publication of journal articles. The anonymised direct quotes from the interview might be used in any resulting publications and reports. You will be given the opportunity to indicate if there is any information that you provided during interview that you wish not to be quoted.

Who has reviewed the study?

The project has been reviewed by the College of Medical, Veterinary & Life Sciences Ethics Committee.

Contact for Further Information

If you would like to discuss any details in this participant information sheet or have any questions please contact lead researcher Marissa Smith on m.smith.8@research.gla.ac.uk or Professor Shona Hilton on Shona.hilton@glasgow.ac.uk

If you want to talk to someone that isn't related to the study, you could email Dr Jesse Dawson who is the University College Ethics Officer: Jesse.Dawson@glasgow.ac.uk

Thank you for taking the time to read this Participant Information Sheet

Appendix H: Participant consent form for expert interviews

Participant Identification Number for this project:

Title of Project: Understanding the role of evidence in e-cigarette regulation and policy development

Name of Researcher(s): Marissa Smith

CONSENT FORM

	Please initial box
I confirm that I have read and understood the Participant Information Sheet Version 1.1 dated 10/07/2019	☐
I have had the opportunity to think about the information and ask questions and understand the answers I have been given.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	☐
I agree to my interview being audio-recorded.	☐
I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	☐
I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐

I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project. ☐

I understand that if I withdraw from the study, my data collected up to that point will be retained and used for the remainder of the study. ☐

I understand that my information and things that I say in an interview will be used in reports and academic papers that are published about the study, but my name or anything else that could tell people who I am will not be revealed. ☐

I agree to take part in the study. ☐

I agree to take part in a follow up interview. This should last between 10-15 minutes. ☐

Name of participant	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher)

Appendix I: Academic interview schedule

Checklist

1. Introduce self and thank them for agreeing to participate
2. Check that the consent form has been signed and confirm the date of signing
3. Check they have received and read the participant information sheet
4. Restate
    a. Length of the interview (approximately 1 hour)
    b. Interview was being recorded
    c. Confidentiality- emphasise confidentiality rules
    d. Anonymity- pseudonyms will be used in any extracts used in publication etc.
5. Check for questions or concerns
6. Switch on recorder
7. Use the interview schedule to guide discussion

Section 1- Introductory questions

1. Could we start with you telling me a bit about your job and professional background?

Section 2- Tobacco control

1. What do you see are the major goals and what you want to achieve through tobacco control policy?
    - PROBE: within the interviewee's jurisdiction

Section 3- E-cigarettes

1. How has tobacco use changed as a consequence of e-cigarettes?
    - PROBE: Did you envisage this change?

2. Is there a role for e-cigarette policy in wider tobacco control policies?
    - PROBE: Please describe the role? What difference will that make to policy?

Section 4- E-cigarette guidelines

1. What do you think are the main guidelines and policy documents influencing e-cigarette policy in your jurisdiction?

2. What are the key recommendations within these documents?

3. What do you see are the most consistent e-cigarette recommendations across different parts of the world?

4. What are the main differences in e-cigarette recommendations across different parts of the world?

Section 5- Evidence to decision framework

1. Have you been involved in the development of e-cigarette guidelines or policies?

2. What process was used to develop these recommendations?
    - PROBE: What was their role in the process?

3. Why were guidelines created on e-cigarette policy?
    - PROBE: Do you agree with this approach?

4. How was the evidence selected for the guideline?
    - PROBE: Systematic reviews

5. How was the evidence assessed?
    - PROBE: risk of bias, critical appraisal

6. How do you go from the evidence to making recommendations?

7. How did you decide what was the most important outcomes for consideration?
    - E.g., smoking cessation

8. How were health inequalities considered when making recommendations?

9. When creating recommendations how did you consider the acceptability to key stakeholders?

10. What was the process for managing conflicts of interest?
    - PROMPT: How was this process developed?

Section 6- E-cigarettes

1. Why do you think different stances towards e-cigarettes have been adopted?
    - PROMPT: Was this expected?

2. What do you think the role of evidence should be when developing e-cigarette recommendations?
    - PROMPT: Does that happen in practice?

- PROMPT: What are the facilitators and barriers to this happening?

Section 7- Concluding Questions

1. We're almost at the end of the interview is there anything important we haven't spoken about yet? Is there anything you would like to say?

2. Is there anyone you think I ought to contact in relation to this research?

Thank you very much for participating in this research.

Appendix J: Policymaker and methodologist interview schedule

Checklist

1. Introduce self and thank them for agreeing to participate
2. Check that the consent form has been signed and confirm the date of signing
3. Check they have received and read the participant information sheet
4. Restate
    a. Length of the interview (approximately 1 hour)
    b. Interview was being recorded
    c. Confidentiality- emphasise confidentiality rules
    d. Anonymity- pseudonyms will be used in any extracts used in publication etc.
5. Check for questions or concerns
6. Switch on recorder
7. Use the interview schedule to guide discussion

Section 1- Introductory questions

1. Could we start with you telling me a bit about your job and professional background?

Section 2- E-cigarette guidelines

1. What do you think are the main guidelines and policy documents influencing e-cigarette policy in your jurisdiction?

2. What do you see are the most consistent e-cigarette recommendations across different parts of the world?

3. What are the main differences in e-cigarette recommendations across different parts of the world?

Section 3- Evidence to decision framework

1. Have you been involved in the development of e-cigarette guidelines or policies?

2. What process was used to develop these recommendations?
    - PROBE: What was their role in the process?

3. Why were guidelines created on e-cigarette policy?

- PROBE: Do you agree with this approach?

4. How was the evidence selected for the guideline?
    - PROBE: Systematic reviews

5. How was the evidence assessed?
    - PROBE: risk of bias, critical appraisal

6. How do you go from the evidence to making recommendations?

7. How did you decide what was the most important outcomes for consideration?
    - E.g., smoking cessation

8. How were health inequalities considered when making recommendations?

9. When creating recommendations how did you consider the acceptability to key stakeholders?

10. What was the process for managing conflicts of interest?
    - PROMPT: How was this process developed?

Section 4- Tobacco control

1. What do you see are the major goals and what you want to achieve through tobacco control policy?
    - PROBE: within the interviewee's jurisdiction

Section 5- E-cigarettes

1. How has tobacco use changed as a consequence of e-cigarettes?

2. Is there a role for e-cigarette policy in wider tobacco control policies?

3. Why do you think different stances towards e-cigarettes have been adopted?

4. What do you think the role of evidence should be when developing e-cigarette recommendations?
    - PROMPT: Does that happen in practice?
    - PROMPT: What are the facilitators and barriers to this happening?

Section 6- Concluding Questions

1. We’re almost at the end of the interview is there anything important we haven’t spoken about yet? Is there anything you would like to say?

2. Is there anyone you think I ought to contact in relation to this research?

Thank you very much for participating in this research.

Appendix K: Coding framework for the analysis of expert interviews

A framework was created to summarise the coding of the development documents in Excel. As this framework was large and therefore difficult to reproduce here, the codes used for the framework are reproduced in Table K.1 below, alongside an example quotation. Each of these codes formed a vertical column in the framework, with a separate row for each development document. The coding of the framework was checked by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington.

Name of high-level code	Name of middle-level code	Description	Illustrative example quotation
Acceptability		What regulations are acceptable or unacceptable to a range of key stakeholders	"They're also part of this process you need information acceptability of the intervention, is this specific intervention acceptable." (Methodologist, International)
Conflicts of interest	In evidence drawn upon	Perceptions and experiences of conflicts of interest in the sources of evidence drawn upon when developing recommendations	"We do the searches, systematic searches of PubMed and MedLine we will automatically exclude anything funded by industry." (Academic, UK)
	In development process	Perceptions and experiences of conflicts of interest of individuals involved in the development process	"All the members [of the development group] had to declare whether they had any conflicts of interest." (Academic, Australia)
Development of recommendations	Stages in the development process	What is the process of going from evidence to recommendations	"We just try to take a logical approach, we look through the research, through the evidence and then translating it into policy positions that would seek to address what we've found there. For example, we had the research that we did involving e-cigarettes and the scientific survey research, we look at a great deal beyond that and we understand what

			the prevalence is like among these different populations." (Policymaker, USA)
	Stakeholder engagement	Stakeholder engagement in the development process	"It wasn't a formal Delphi process or anything like that, but it was a series of stakeholder meetings and refinements of the documentation with a conscious effort to bring in diverse perspectives." (Policymaker, UK)
	Using recommendations for health policy	Why recommendations documents are important and how they are used to improve health	"You have to look at what's best for public health, what's the most important to public health. It's a matter of being able to present a consistent evidence-based position and to protect the health of the community." (Academic, USA)
Equity		How are health inequalities considered during the development process and which groups are identified as being at risk	"I think in the context of tobacco control it [equity] is important and it should be addressed. Smoking affects different populations to a different extent and the alternative products like that may actually be increasing inequalities or close the gap." (Academic, USA)
Evidence	Certainty of evidence	Assessment of the quality and level of certainty of the evidence	"We put everything through GRADE, to look at the confidence or the certainty and we take into account the other domains within GRADE, as well." (Methodologist, UK)
	Challenges of e-cigarette evidence	What are the challenges of gathering and synthesising evidence	"We're not going to be able to run a 35-year clinical trial to see if people who use e-cigarettes developed illnesses versus people who don't versus smokers, versus…you know, we just ethically can't do that." (Academic, Australia)
	Reservations of evidence	Concerns about the quality and lack of certain evidence (e.g., long-term health effects)	"There is a lack of evidence which to guide policymaking and it's tricky to know when there isn't enough evidence and how cautious one should be with statements." (Academic, Australia)
	Role of evidence	What should the role of evidence be when making public health recommendations	"Well, I think it should be the driving factor in guidelines." (Academic, USA)
	Types of evidence	Mention of different types of studies and forms of evidence from anecdotal through to RCTs	"We look at SRs of RCTs if available. In case RCTs are not available, they would then the default is to then look for observation studies" (Methodologist, International)

Goals of tobacco control policy		What the goals of public health bodies and tobacco control	"The main goals of tobacco control in the UK are to reduce the numbers of people smoking so that's to encourage people to quit smoking and to deter young people from starting smoking. And now I think there is the harm reduction and approaches to kind of minimise the harm that smoking can have on the population level and to and to help people to make those choices and to quit smoking." (Academic, UK)
Outcome importance		How is the outcome importance determined	"When you prioritise outcomes, you have to make sure that you are starting with a comprehensive list of outcomes, so you are not missing any potentially relevant outcomes. And there must be an approach about how to prioritise. So mainly before that make sure whoever is involved in that exercise really understands what each outcome means. And then having a process of prioritisation of the most important outcomes to consider." (Methodologist, International)
Other		Information I feel that is important but does not fit within other codes	"There is absolutely no common ground between people who share the same objective." (Policymaker, USA)
Politics	Political influence	How does politics or institutions influence the development of public health recommendations	"A lot of people are concerned that the UK relies way too much on that original Public Health England report, about 95%. I don't think that that conclusion was worth all of the reliance it received at the time and has continued to receive." (Policymaker, USA)
	Previous and current tobacco control policies	How are previous and current tobacco control policies considered during the development of public health recommendations	"In Australia, our response has been a little bit ego-driven, wanting to recognise the success of previous tobacco control measures. There's a real sense of responsibility to not undermine those successes, like plain packaging, like the excise increases." (Policymaker, Australia)
Vested interest		How are vested interests considered and handled during the development of public health recommendations	"Nobody can claim that they weren't allowed to participate in the debate, apart from the tobacco industry because they were systematically excluded from the whole process from start to finish." (Policymaker, UK)

Table K.1: Coding framework for coding of the expert interviews, with an example illustrative quotation

Appendix L: Coding framework for the comparison of public health bodies' COI policies and expert interviews

A framework was created to summarise the coding of the COI policies and expert interviews in Excel. As this framework was large and therefore difficult to reproduce here, the codes used for the framework are reproduced in Table L.1 below, alongside an example quotation. Each of the COI policies and interview transcripts formed a vertical column in the framework, with a separate row for each code. The coding of the framework was checked by Dr Kathryn Skivington.

Name of high-level code	**Name of middle-level code**	**Illustrative quotation from COI policy**	**Illustrative quotation from interview transcript**
Definition of COI		"A conflict of interest arises when the judgement of someone involved in the work of NICE may be compromised, by the financial or other considerations set out in this policy." (National Institute for Health and Care Excellence, 2019, p.4)	
Disclosure of COI	Types of financial COI	"Any other relevant direct or pecuniary interest (for instance, having provided expert testimony for a fee on behalf of an entity with a commercial or other interest in the issues being considered by the Committee)." (National Health and Medical Research Council, 2019, p.5)	"There are partial declarations of interest, so you'll get people saying, I've done work for the [vaping company], but they won't say the [vaping company] is actually a tobacco industry body." (Academic, Australia)
	Types of non- financial COI	"Prior publication of a study or systematic review that is part of the evidence base under consideration	"To limit the scope for introducing bias to simply to where you have a connection, financial connection to tobacco industry or vaping industry or whatever, is pretty

		in the guideline." (World Health Organisation, 2014b, p.63)	reductive. Actually, there are lots of influences on people's lives that would influence how they view research or how they wish to see the world and they are all kinds of conflicts of interest." (Academic, UK)
	Time period considered	"The period of relevance for all declarations made by members of a NICE advisory committee is 12 months before joining and during the membership of the committee." (National Institute for Health and Care Excellence, 2019, p.12)	"There are potential pitfalls with declaration and that depends on what is expected in terms of the time frame, and this can result in underreporting conflicts of interest." (Methodologist, International)
	About whom is the COI collected	"All committee members, executive board members, governing councillors and Special Primary Interest Group members." (American Public Health Association, 2018a, p.1)	"Declaration is a must there is no question that everyone must declare." (Methodologist, International)
	Information on financial and non-financial COI of individuals' personal relationships	"Individual's immediate family members (defined as the pose or partner with whom one a close personal relationship and the children)." (World Health Organisation, 2014b, p.63)	
Collection of COI	How COI are disclosed	"Declarations of interests are collected using the standard WHO form for experts." (World Health Organisation, 2014b, p.63)	"For the [UK recommendation document] there is a verbal declaration at the beginning of every meeting about conflicts of interest." (Academic, UK)
	Disclosure required prior to involvement	"The obligation for members to disclose interests starts during the appointment process and continues throughout the period of committee membership." (National Health and Medical Research Council, 2019, p.7)	"There was a process of signing disclosures and conflicts of interest disclosures and once I completed it, I was able to start working." (Academic, USA)
Management of COI	Exclusion procedure	"For disclosed interests, the NHMRC and PGPA Acts require that the member is not present when matters that relate to the interest are considered and does	"Abstain [conflicted individuals] from voting on the recommendations." (Policymaker, Australia)

		not take part in any decision of the Committee in relation to those matters unless the members of the Committee determine otherwise (as set out below in 6.1).” (National Health and Medical Research Council, 2019, p.7)	
	Prohibited relationships	“Hospitality is where there is an offer of food, drinks, accommodation, entertainment or entry into an event or function by a third party, regardless of whether provided during or outside normal working hours e.g., attendance at an industry awards ceremony.” (Public Health Wales, 2019, p.20)	“[Public health bodies and organisations] are banning anybody who has spoken at forums on vaping, or nicotine because they think that these have a slant in favour of vaping” (Academic, USA).
	Penalty for non-disclosure	“A failure to disclose an interest without a reasonable excuse will result in the termination of the member’s appointment.” (National Health and Medical Research Council, 2019, p.8)	

Table L.1: Coding framework for the comparison of COI policies and expert interviews

Appendix M: Coding framework for the triangulation of the four data sources

Three large data frameworks were created in Excel, one from each stage of evidence utilisation. As these frameworks were large and therefore difficult to reproduce here, the codes used for the frameworks are reproduced in the table below, alongside an example quotation from one stage of evidence utilisation. In each of the three frameworks, the data source formed a vertical column in the framework, with a separate row for each code. The coding of the framework was checked by Professor Srinivasa Vittal Katikireddi and Dr Kathryn Skivington.

Descriptive Code	**Illustrative quotation from recommendation document**	**Illustrative quotation from development document**	**Illustrative quotation from expert interview**
Prevalence of smoking and vaping	"The increasing trend of ENDS use has the potential to create a new generation of youths addicted to nicotine, which threatens to undermine the public health gains of the past half-century by renormalizing smoking." (American Public Health Association, 2018b, p.4)	"The problem's priority is determined by its importance and frequency (i.e., burden of disease, disease prevalence or baseline risk)." (World Health Organisation, 2014b, p.124)	"In the US context, it is really increasing the prevalence among young people. This is something that we see here and the data (on youth prevalence) is really strong, it is increasing. It is increasing, the vaping among young people is increasing, we see not only increase in experimentation, but we see that the daily use pattern among the young people, many of those never smoked tobacco cigarettes." (Academic, USA)
Previous and current tobacco control policies	"PHE's ambition is to secure a tobacco-free generation by 2025. We believe e-cigarettes have the potential to make a significant contribution to its achievement." (Public Health England, 2016, p.4)	"The position statement must pay due regard to current legislation and policy, outlining how the organisation's proposed position aligns with the existing policy context." (Public Health Wales, 2016, p.4)	"I think in Australia, our response has been a little bit ego-driven, wanting to recognise the success of previous tobacco control measures. There's a real sense of responsibility to not undermine those successes, like plain

			packaging, like the excise increases." (Policymaker, Australia)
Politics and institutions	"In revising the Position Statement the team has taken account of the available scientific evidence and the views of national and international public health bodies." (Public Health Wales, 2017, p.3)	"The committee should also judge to what extent it will be feasible to put the recommendations into practice." (National Institute for Health and Care Excellence, 2022, p.179)	"We had a pre-existing statement, it wasn't a position statement, it was just a very brief statement. Because we had the pre-existing statement that was about the precautionary approach typically when we go to do these things unless there's really strong evidence of a need to change that position… we didn't necessarily go into it with a clean slate, I'll be honest about that. We went into that having developed a very brief statement on e-cigarettes the year before with that overarching group of 40. We had a sense check for the position that they supported and felt comfortable with. So, when that other group was going away and looking at the evidence around that, there wasn't necessarily a discussion about, let's only support precautionary approaches, but there was a general sense that that was the position that had been supported by the overarching and that they would need to come up with a very strong and robust argument for changing that position." (Policymaker, Australia)
Social norms and public acceptability	"Smoke-free policies are designed not only to protect non-smokers from second-hand smoke, but also to provide incentives to quit	"Context-sensitive scientific evidence looks at what works and how well in real-life situations. It includes information on	"Restrictions on advertising or banning of advertising is another policy that seems to have an impact. None of these have huge

	smoking and to denormalise smoking as adolescents are particularly vulnerable to visual cues and social norms." (World Health Organisation, 2014a, p.8)	attitudes, implementation, organisational capacity, forecasting, economics, and ethics. It is mainly derived using social science and behavioural research methods, including quantitative and qualitative research studies, surveys, theories, cost-effectiveness analyses, and mapping reviews." (National Institute for Health and Care Excellence, 2022, p.86)	impacts individually, but collectively when they change the culture, they change the norms." (Academic, USA)
Vested 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." (World Health Organisation, 2014a, p.12)	"Tobacco companies and those who speak for them or are funded by them (collectively referred to as 'tobacco organisations') cannot register as stakeholders. This is in line with NICE's obligation under Article 5.3 of the WHO Framework Convention on Tobacco Control (FCTC) to protect public health policies from the commercial and other vested interests of the tobacco industry." (National Institute for Health and Care Excellence, 2022, p.194)	"That evidence [tobacco industry evidence] isn't just excluded automatically, we include it, but we make it very, very clear, when we're presenting to the committee and when we're writing things up, which bits of evidence are related to tobacco organisation." (Methodologist, UK)
Decision-making process	"The searches were undertaken in two steps; firstly, resources were searched for systematic reviews, guidance, and other high-level evidence only. Secondly, as numbers of high-level evidence found were low the search was broadened to include all primary research studies, poster presentations,	"The evidence-to-recommendation tables depict not only the evidence and judgements leading to a recommendation, but also the justifications for the recommendation's direction and strength. They also describe the subgroups considered, the process used to formulate recommendations (e.g., if voting	"But usually, the evidence is presented to the committee and they have a chance to interrogate it and make sure everything looks good and make sure that they're aware of what the limitations are and what they think of the evidence." (Methodologist, UK)

	protocols, conference abstracts, and other types of grey literature such as reports published on organisational websites." (Public Health Wales, 2017, p.22)	took place), and key issues surrounding implementation, evaluation, and monitoring (see Chapter 13) as well as research gaps." (World Health Organisation, 2014b, p.128)	
Participants involved in the decision-making process		"Registered stakeholders comment on the draft scope and draft guideline and they may be invited to provide evidence during guideline development." (National Institute for Health and Care Excellence, 2022, p.19)	"Nobody can claim they weren't allowed to participate in the debate, apart from the tobacco industry because they were systematically excluded from the whole process from start to finish." (Policymaker, UK)
Remit of the document	"This paper outlines a proposed revised position statement on Electronic Nicotine Delivery Systems (ENDS) and supporting Background Paper. The revised position statement takes account of changes in legislation and increasing research evidence in relation to the population health impact of ENDS and proposes a more complete position statement more appropriately tailored to different population groups. The proposed changes also incorporate the position adopted by Public Health Wales in responding to the Public Health Bill." (Public Health Wales, 2017, p.1)	"NICE guidelines are a key source for the development of NICE quality standards and therefore new guidelines developed by NICE are usually chosen from a library of topics for quality standards and then agreed with the relevant commissioning body (NHS England or the Department of Health and Social Care)." (National Institute for Health and Care Excellence, 2022, p.15).	"This [the remit] is determined by the [UK organisation] and they fund us. In the tender, they outlined the areas they wanted us to cover for example vulnerable populations, pregnancy, mental health etc." (Academic, UK)
Certainty of the evidence		"Assessing the quality of the evidence for a review question is critical. It requires a systematic process of assessing potential biases through considering both the	"We assess the quality, the risk of bias, the strength of the evidence (Methodologist, UK)

		appropriateness of the study design and the methods of the study (critical appraisal) as well as the certainty of the findings (using an approach, such as GRADE)." (National Institute for Health and Care Excellence, 2022, p.111)	
Conflicts of interest in the evidence base		"There are robust processes in place to manage conflict of interest [in the evidence base] and to use the best available scientific methods for making recommendations such as the use of GRADE." (National Health and Medical Research Council, 2016)	"Industry data should not be part of the formal literature." (Academic, Australia)
Role of evidence		"PHE will strive to ensure all public health decisions, be they policy or operational, are based on the best available evidence." (Public Health England, 2013, p.19)	"Evidence should be absolutely central in policymaking." (Policymaker, UK)
Types of evidence	"Peer-reviewed journal articles, reviews that integrate findings from numerous studies and books. This report also refers, on occasion, to unpublished research, such as presentations at a professional meeting, personal communications from a researcher, or information available in various media. These references are employed when acknowledged by the editors and reviewers as being from reliable sources, which add to the emerging literature on a topic." (U.S. Department of Health and Human Services, 2016, p.5)	"Not all reviews are systematic and not all systematic reviews are of high quality. So-called "narrative" or non-systematic reviews are missing one or more of the essential characteristics noted above. Non-systematic reviews and low-quality systematic reviews should not inform WHO guidelines and WHO staff must be able to recognize these and understand their limitations." (World Health Organisation, 2014b, p.93)	"Another body of evidence that is relevant is those are done in cells, cell line studies, or studies that are done with rodent models, with mice and rats. However, translating those to the human population is highly problematic." (Academic, UK)

What constitutes evidence	"Peer-reviewed journal articles, reviews that integrate findings from numerous studies and books. This report also refers, on occasion, to unpublished research, such as presentations at a professional meeting, personal communications from a researcher, or information available in various media. These references are employed when acknowledged by the editors and reviewers as being from reliable sources, which add to the emerging literature on a topic." (U.S. Department of Health and Human Services, 2016, p.5)	The evidence base for a position statement should include available Welsh data and literature where relevant; however, the position statement should also look beyond Wales for evidence, as well as positions from organisations from the UK and internationally." (Public Health Wales, 2016, p.5)	"The standard for developing guidelines these days is to use systematic reviews." (Methodologist, International)

Table M.1: Coding framework for the triangulation of the four data sources

Appendix N: What is considered evidence by public health bodies

Table N.1 below details what is considered evidence by the seven public health bodies who had a publically available development document.

Public health body	What is considered evidence according to development documents
World Health Organisation (World Health Organisation, 2014b)	"Recommendations in WHO guidelines should be based on a systematic review of the scientific literature guided by specific key questions about the intervention, exposure or approach under consideration." (p.93) "Non-systematic reviews and low-quality systematic reviews should not inform WHO guidelines and WHO staff must be able to recognise these and understand their limitations." (p.93)
National Health and Medical Research Council (AUS) (National Health and Medical Research Council, 2016)	"Published data: There are a wide range of published and unpublished information sources that can inform a systematic review. The primary published sources are bibliographic databases of peer-reviewed journal articles such as MEDLINE, CINAHL, PsycINFO, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Global Health (via Ovid)." (National Health and Medical Research Council, 2016)
National Institute for Health and Care Excellence (UK) (National Institute for Health and Care Excellence, 2022)	"We use a wide range of different types of evidence and other information – from scientific research using a variety of methods to testimony from practitioners and people using services. Review questions guide the search for evidence and the type of evidence used depends on the type of question. For example, a randomised controlled trial is often the most appropriate type of study to assess the efficacy or effectiveness (including cost-effectiveness) of an intervention. However, a range of other non-randomised evidence, such as observational evidence (including that derived from the analysis of primary data sources such as patient registries), experimental and qualitative evidence, may also be used to inform assessments of effectiveness, or aspects of effectiveness. This evidence may include ways of delivering services or the experience of people using services and how this contributes to outcomes. For some topics, there is little evidence from scientific studies, or the evidence is weak or contradictory. In these cases, we look for

	evidence from other sources to see if it agrees or differs ('triangulation'). When there is little or no evidence, the committee may also use expert testimony, make consensus recommendations using their knowledge and experience, or make recommendations for further research. Whatever evidence is used, it is selected and quality assessed using clear and appropriate methods (such as GRADE)." (p.16)
Public Health England (Public Health England, 2013)	"In this context "information" is anything we gather, for instance, patient record data, stakeholder surveys, outcomes measures, lifestyle trends or medication use, with the intention of adding to the evidence base for public health" (p.8)
Public Health Wales (Public Health Wales, 2016)	"A strong position statement needs to be shaped by relevant, timely and quality-assured evidence. Advice and guidance will be sought from the Observatory Evidence Service (OES) prior to the development of position statements." (p.4) The evidence base for a position statement should include available Welsh data and literature where relevant; however, the position statement should also look beyond Wales for evidence, as well as positions from organisations from the UK and internationally." (p.5)
American Public Health Association (American Public Health Association, 2019)	Unavailable
U.S. Department of Health and Human Services: A Report of the Surgeon General (U.S. Department of Health and Human Services, 2016)	"Peer-reviewed journal articles, reviews that integrate findings from numerous studies and books. This report also refers, on occasion, to unpublished research, such as presentations at a professional meeting, personal communications from a researcher, or information available in various media. These references are employed when acknowledged by the editors and reviewers as being from reliable sources, which add to the emerging literature on a topic." (p.5)

Table N.1: What is considered evidence by the seven public health bodies who had a publically available development document

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