Vapour Products/E-Cigarettes: Claims and Evidence

by

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Abstract

Vapour products (e-cigarettes) have rapidly grown in sales. While competing claims about the effects of vaping are fiercely debated within the public health community, no studies have examined the claims accepted in the regulatory arena. In the first article of this manuscript-based dissertation, my co-authors and I utilized narrative policy framework to identify the claims about vapour devices in legislation recommendation reports from Queensland Australia, Canada, and the European Union, and the United States. The vast majority of claims represented vapour devices as a threat, while the potential benefits were very rarely presented, resulting in bans and strict regulations.

Evidence on two claims, youth vaping as a risk for nicotine dependence, and vapour products as a cessation aid, was evaluated with systematic reviews. For the youth claim, we retrieved population surveys on (1) the first product used, (2) non-nicotine vaping, (3) the prevalence of infrequent users among past-30-day users, and (4) cannabis vaping. Surveys indicated that a near majority of students who were past-30-day users vaped only once or twice a month, and an appreciable number, 25% and more, reported consuming non-nicotine liquids. Furthermore, 80% to 90% of ever-users tried cigarettes first. Far fewer youth are at a risk for nicotine addiction than indicated by any past-30-day use. On the other hand, vaping as a mode of administration of other drugs has received little attention, and presents an unknown risk to youth.

We evaluated the claims about cessation with a review of systematic reviews (umbrella review). Three reviews, Hartmann-Boyce et al. (2016), Malas et al. (2016) and El-Dib et al. (2017) received the better quality ratings. They were unable to reach a definitive conclusion due

to the limited number of randomized controlled trials and the low quality of most of the studies. We considered the reviewers' tentative statements on their findings, the findings of the quality cohort studies, the potential underestimation of effectiveness in the studies, and the improved nicotine delivery of newer models. The weight of the evidence allowed us to state our optimism that vapour products have potential as a cessation aid.

In the jurisdictions studied in this dissertation, vapour products have been claimed to be a threat by leading youth to smoking and impeding cessation. Does the evidence support the claims? The possible risk of youth becoming dependent on nicotine from vaping is substantially lower than indicated by the metric of any past-30-day use. There is reasonable evidence that vapour products may be an effective cessation aid. With a better understanding of these two claims, we in public health should revisit the regulations, policies, and interventions for vapour products so that they are in line with the evidence, not unsupported claims.

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Acknowledgments

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Foreword

The electronic cigarette (e-cigarette) was invented in China in 2003, and the product was introduced to the international market around 2006 (Euromonitor International, 2016a), exported primarily to Europe and the US (Consumer Advocates for Smoke-Free Alternatives Association, n.d.). Sales estimates for 2005 were USD $50.9 million, and in 2016 the figures for worldwide sales had risen 240-fold to USD $12.29 billion (Euromonitor International, 2017b), increasing by 34% from 2015 to 2016 (Euromonitor International, 2017a). The term "e-cigarettes" encompasses a range of products with evolving designs such as: tank systems, mods, vape pens, e-hookahs, pods, drip tips, and thousands of liquids with nicotine, non-nicotine, and other formulations and flavours. Nearly all vapourizers no longer resemble cigarettes, and not all liquids contain nicotine, so the broader term *vapour products* is a better descriptor. It is also the current commercial term for e-cigarettes (Euromonitor International, 2016b).

The uptake of vaping caught the public health community off guard (Hasselbalch, 2016; McKee, 2013). A number of those working in tobacco control have observed that their community of practice has fractured into two camps over the product's potential risks and possible benefits (Bell & Keane, 2012; Kmietowicz, 2014; Royal College of Physicians, 2016; Sim & Mackie, 2015; Wagener, Meier, Tackett, Matheny, & Pechacek, 2016). Some authors such as Polosa (2015), have described it as an ideological battle between those supporting harm reduction and those supporting the precautionary principle.

Harm reduction is premised on the belief that drug use is part of society, and cannot be eliminated (Hatsukami & Parascandola, 2005; Ritter & Cameron, 2006). Nutt, King, and Phillips (2010) identify potential harms from drug use in three areas: physical harms to the user, the potential for dependence, and the effects on others. In the broadest definition, harm

reduction is “a set of compassionate and pragmatic approaches for reducing harm associated with high-risk behaviors and improving quality of life" (Collins et al., 2012, p. 5). Historically, harm reduction strategies took shape with a report by Dr. John Rolleston in 1926 that set up a system for physicians in Great Britain to prescribe opium and cocaine for patients who had become addicted through self-injection (Collins et al., 2012).

The most comprehensive definition for tobacco harm reduction is the reduction of morbidity and mortality without eliminating nicotine or tobacco use (McNeill & Munafo, 2013; Parascandola, 2011). In practice, tobacco harm reduction involves offering smokers products deemed safer than cigarettes (Polosa et al., 2013; Royal College of Physicians, 2007; Saitta et al., 2014). Before 2009, the tobacco harm reduction products available were nicotine replacement therapies and snus, along with a few short-lived reduced exposure products from multinational tobacco companies (for example, Ellipse) which were market failures. Today, “e-cigs might be the most promising product for tobacco harm reduction to date” (Polosa et al., 2013 p. 7). Cigarettes are rated at 99.6 out of a 100 point maximum relative harm scale, and in comparison, e-cigarettes score 4 in the widely cited study by Nutt et al. (2014).

While the debate can be framed as the clash of the precautionary principle and harm reduction, I have come to see the debate as a dispute about the impact of vapour products on the tobacco epidemic. Many in tobacco control see vapour products as a threat sustaining or increasing nicotine dependence, and others hope that the products offer new opportunities for cessation or harm reduction via a disruptive technology (Abrams, 2014; Bullen, 2016; Correa, Ariel, Menzie, & Brandon, 2017; Fagerström, Etter, & Unger, 2015; Farsalinos & Le Houezec, 2015; Hajek, 2014; Pechacek, Nayak, Gregory, Weaver, & Eriksen, 2016; Weaver et al., 2016).

The larger faction in the debate, many from the US, includes public health officials, medical societies, and health organizations who foresee threats to individual and population health from vapour products. They invoke the precautionary principle in support of immediate restrictions or bans on the manufacturing, importation, sales, and/or advertising of the products (Caponnetto, Saitta, Sweanor, & Polosa, 2015; Chapman, 2014; Cobb & Cobb, 2013; Pisinger & Døssing, 2014). The other faction, those who see potential benefits from vapour products, is a smaller group, many from the UK, and those who support efforts initiated in the UK. Public Health England (McNeill et al., 2015) and the Royal College of Physicians (Royal College of Physicians, 2016) have issued reports about the opportunity for vapour products as a new cessation aid, or as a substitute for cigarettes for harm reduction. Today the tobacco control community's highest priority topic is vapour products, catalyzing into often rancorous debates over two issues: the products' roles as a potential "gateway" to tobacco use, and their efficacy, or lack thereof, as a cessation aid (Lindson-Hawley, Heath, & Hartmann-Boyce, 2016).

While the "ferocious row" (Gornall, 2015) over vapour products continues in the public health community of practice, what is going on in the regulatory arena, where legislation has a tremendous impact on the availability of vapour products? Whether vapour products are perceived as a threat or as an opportunity will shape how politicians regulate them. "The sorts of policies that are implemented will depend on… whoever dominates the debate" (Green, Bayer, & Fairchild, 2016, p. 1303). What claims about vapour products have had traction in the regulatory process? While dozens of academic journal articles have detailed the positions taken in the healthcare community, no studies, except the one reported in my first article, have examined the claims about vapour products put forward in the halls of government as they formulate their regulations. In *Claims in Vapour Device (E-Cigarette) Regulation: A Narrative*

Policy Framework Analysis (2017) (short title, *Claims Study*), I identified the claims in four legislative recommendation reports to understand how the policy problem of vapour products has been defined, and then my co-authors and I observed how these claims potentially influenced the resulting legislation in Queensland, Australia, Canada, the European Union (EU), and the United States (US).

How vapour products are regulated is no small matter because the stakes for public health are potentially huge. In 2015, smoking accounted for 6.4 million deaths globally (95% confidence interval (CI) [5.7, 7.0]), and smoking was one of the top five causes for the loss of disability-adjusted life years in 109 countries (Global Burden of Disease 2015 Tobacco Collaborators, 2017). How will vaping impact the tobacco epidemic? Will more youth become addicted to nicotine or become smokers by vaping? Can more smokers quit with vapour products? Answers to these questions are critical for how vapour products are regulated, and how public health policies deal with this consumer product that may or may not deliver nicotine.

Two of the most frequently made claims in the regulatory reports concern the same two issues that dominate the tobacco control community. One claim is that vaping will cause an increase in youth smoking, a policy narrative presented in all four reports. The other claim, offered in the EU and US reports, is the potential for vapour products as a cessation aid. What evidence is available about these claims? How many youth who vape are at risk for nicotine addiction and smoking? What do the findings of clinical studies demonstrate about the effectiveness of vapour products for tobacco cessation? These questions are key issues for vapour product regulations and public health policies.

Obtaining evidence for answering these questions about youth use and cessation is not as straightforward as conducting a couple of standard literature reviews. There are problems with

the literature. As my co-authors and I demonstrate in my second article *Youth Vaping: Evaluating Risks* (short title, *Youth Review*), the current research on the risk for youth of nicotine dependence from vaping is biased because the research rarely reports on non-nicotine vaping, and the metric of past-30-day use captures the large numbers of youth who vape only once or twice a month. Other problems with the literature have limited the evaluation of vapour products for cessation. In the third article *Vapour Products (E-Cigarettes) and Tobacco Cessation Outcomes: A Review of Systematic Reviews* (short title, *Cessation Review*), none of the systematic review teams were able to reach a definitive conclusion on the effectiveness of vapour products for cessation. These problems in the literature required me to extend my analyses beyond the simple reporting of data.

In summary, I ask in *Vapour Products/E-Cigarettes: Claims and Evidence* what claims have been made about vapour products in the regulatory arena, and their potential influence on legislation. Then I examine the evidence for two of the claims: vapour products as a risk for youth nicotine dependence, and vapour products as a cessation aid. Do the claims match up with the evidence? Before presenting my articles, in the Foreword I provide background information on vapour products and prevalence data, an overview of the literature and research on youth vaping and cessation studies, and more details on the methods than could be included in the articles.

Vapour Products

The invention of the electronic cigarette is credited to Chinese pharmacist Hon Lik in 2003, but other inventors had designed vapourizers much earlier. Vapourizer designs were patented in the 1930s (Farsalinos, 2017), and in 1963 Gilbert's patent was registered, but the product was never commercialized (Euromonitor International, 2016a). The inventors of a 1979

nicotine evaporation product appear to be the first to use the term *vape* (Consumer Advocates for Smoke-Free Alternatives Association, n.d.). A nicotine inhaler product, Favor, was tested for nicotine uptake in 1987 (Russell, Jarvis, Sutherland, & Feyerabend, 1987). The Ruyan e-cigarette was bench tested in 2009 with industry funding (Laugesen, 2009). The first vaper conferences, or vapefests, started to appear from 2010 (Consumer Advocates for Smoke-Free Alternatives Association, n.d.)

The early market was supplied entirely by independent companies, and the trans-national tobacco companies, like the tobacco control community, were late to the party. The first acquisition of an e-cigarette company by a trans-national tobacco corporation did not occur until 2012, with Lorillard purchasing blu (Euromonitor International, 2016a). In 2013 Imperial Tobacco bought out Hon Lik's company and patent, and also that year British American Tobacco launched its Vype e-cigarette. The following year Altria purchased Green Smoke and developed their own product; Mark Ten, and Japan Tobacco International purchased the E-lites company (Consumer Advocates for Smoke-Free Alternatives Association, n.d.; Tobacco Tactics, n.d.). Unfortunately, no data have been published on the market-share of trans-national tobacco corporations as compared to independent companies.

The first contemporary models are known as cig-a-likes, a pre-filled disposable product. Cig-a-likes are rapidly falling out of popularity as refillable "open tank" systems and "closed tank" pre-filled pods appear to comprise the great majority of sales (Euromonitor International, 2016a). Second generation vapourizers (sometimes referred to as eGo, a popular model) have a rechargeable battery and a refillable tank, and came out in 2009 (Grey, 2016). Third generation vapourizers (mods) are user-modified vapourizers and were first developed in Germany in 2010, and in 2014, fourth generation devices (advanced personal vapourizers) came on the market

featuring a user-adjustable temperature control (Grey, 2016). What matters most for cessation is that the newer devices provide better nicotine delivery, "very close" to cigarettes (Farsalinos, 2017).

The biggest market is the US with an estimated 44% of worldwide sales (Euromonitor International, 2016a). The US National Health Interview Survey 2015 (N=33,672, ≥ 18 years old) prevalence rate for every day/some days use was 3.5% (95% CI [3.2, 3.8]) (Phillips et al., 2017), and in the 2014 Survey it was 3.3% (95% CI [3.1, 3.5]) (Hu et al., 2016). The 2014 National Health Interview prevalence rate for every day/some days use was 3.7% (Schoenborn & Gindi, 2015). Youth prevalence of any use in the past-30-days is 11.3% recorded in the 2016 National Youth Tobacco Survey (Jamal et al., 2017). The regulation of vapour products in the US with the FDA Deeming Rule is detailed in *Claims Study*.

Western Europe is considered the second largest market for vapour products accounting for an estimated one third of worldwide sales (Euromonitor International, 2016a). The European Union regulation of vapour products with the Tobacco Products Directive is described in *Claims Study*. The European Union adult population prevalence of "current users" (self-defined) is 2% in 2017, with 4% in France and Belgium, and 5% in the UK (European Commission, 2017). The prevalence in 2016 for any past-30-day use by youth in Great Britain aged 11-18 was 2.6% (95% CI [1.9, 3.6]) (Eastwood et al., 2017). More youth prevalence data are presented in *Youth Review*.

By 2013, when I began my research, many governments had already enacted bans and regulations on vapour products, brought into effect through a decree or notification, or by classifying them under existing or amended legislation (Institute for Global Tobacco Control, 2017). Yet at that time, four English-speaking jurisdictions were in the process of crafting their

regulations: the major markets of the US and the European Union, plus Canada, and Queensland, Australia. This juncture in their regulatory processes gave me the opportunity to read the recommendation reports prepared for the legislators in these jurisdictions, and to observe the regulatory outcomes, the primary data for *Claims Study*.

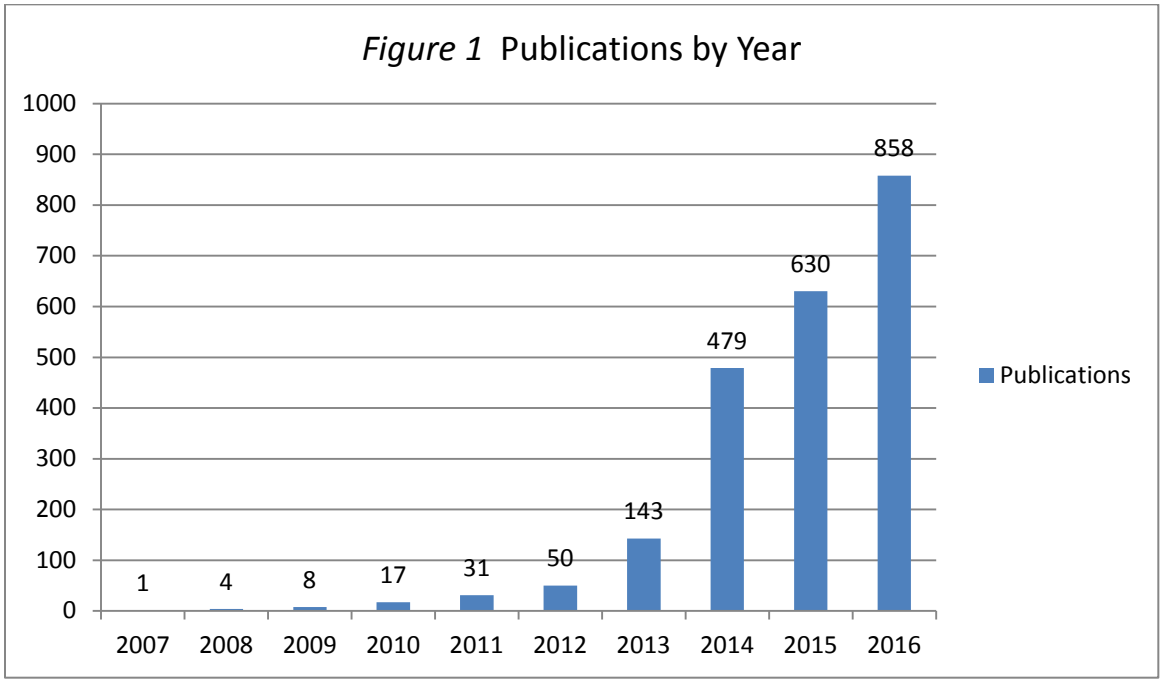
By way of an update on regulations since *Claims Study* was published, by June, 2017, 27 countries have banned vapour products altogether, 9 have banned nicotine-containing vapour products, and 79 countries had laws regulating vapour products: 42 regulating them as tobacco products; 22 as medicines, drugs, or medical devices; 16 as consumer products; and three as hazardous substances (nicotine) (Institute for Global Tobacco Control, 2017). The World Health Organization issued a provisional agenda item in August 2016 for the Framework Convention for Tobacco Control, Conference of the Parties (World Health Organization, 2016, August) supporting the regulation of non-nicotine vapour devices in the same manner as nicotine devices, all the while suggesting a complete ban on vapour products as the preferred policy.

Vapour Product Literature and Research

The first notice of the current generation of vapour products (post Hon Lik) in a peer-reviewed journal was a letter in *Tobacco Control* in 2007 by Pauly, Li, and Barry (2007) commenting with alarm about the e-cigar they had purchased at an airport in China. The next journal publication about vapour devices is a 2008 news item in *Chemical and Engineering News* (Everts, 2008). The first peer-reviewed research studies on vapour devices were not published in academic journals until 2010.

The number of new publications began to increase in 2013, and rose rapidly from 2014 – see Figure 1. These counts come from a library of 2,323 articles in peer-reviewed journals published from 2007 to February 8, 2017. The library was produced for the *Clearing the Air*

knowledge synthesis project (MacDonald, O'Leary, Stockwell, Reist, & Clearing the Air project team, 2016; O'Leary, MacDonald, Stockwell, & Reist, 2017), a meta-narrative review on the harms and benefits of vapour products funded by the Canadian Institutes for Health Research. (The library search strategy and retrievals are reported in the Appendix). For 2017 publications, my systematic search on November 8, 2017 retrieved 638 articles, but this is a raw count without a title/abstract check. Currently, it is quite the task to keep up with the 60+ new journal articles published every month, plus industry surveillance and grey literature too.



Half or more of the publications are not empirical research. Glasser et al. (2017) conducted a systematic review with a search through May 31, 2016, and 42% of the articles were empirical studies. Correa et al. (2017) reviewed all vapour product articles published through 2014 and found an even split between research reports and opinions/editorials. Correa et al. observe that this state of affairs "suggests a potentially maladaptive situation in which opinion is outpacing the science that should provide the basis for informed opinion" (p. 181). In addition,

Pisinger and Døssing (2014) assert that over a third of the research studies exhibit a conflict of interest. The debate over vapour products is reflected in the composition of the literature, fueling the dominance of claims over evidence.

Claims in the debate.

The differing positions on vapour products, as a threat or an opportunity, were solidified with the first editorials, commentaries, and review articles. Other frequently referenced publications reinforce these positions. This discussion of claims highlights the highly-cited early literature as per citations counts of articles in Google Scholar as of August 2016.

One of the first editorials on vapour products by Cobb, Byron, Abrams, and Shields (2010) contains the claims that vapour products will both increase the number of youth addicted to nicotine, and delay cessation by smokers. Established tobacco control researchers Simon Chapman (2014) and Neal Benowitz (2014) published widely cited commentaries coming to opposite conclusions about the likely risks to youth. (Benowitz has recently evaluated harm reduction with vapour product substitution, see Benowitz and Fraiman (2017) and Goniewicz et al. (2017), suggesting there is less cardiovascular risk with vapour product use than from cigarette smoking, and a substantial reduction in carcinogen and toxicant exposure.) Other researchers, including Jessica Barrington-Trimis, have argued that youth are at risk from vaping (Barrington-Trimis, Samet, & McConnell, 2014), and a number of researchers have claimed that vapour products will lead youth to nicotine dependence and cigarette or tobacco use (Dutra & Glantz, 2014; Klein, 2015; Stanbrook, 2016; Stanwick, 2015). Grana, Benowitz, and Glantz (2014) currently have the most highly cited vapour product review in the literature, and they conclude that vapour products increase the rates of youth smoking initiation, and that vapour products are ineffective for cessation. Two other review teams, Pisinger and Døssing (2014) and

Harrell, Simmons, Correa, Padhya, and Brandon (2014) also claim in their highly cited reviews that vapour products are not effective cessation aids. In addition to peer-reviewed articles, The World Health Organization in July, 2014 published a report in advance of the sixth Conference of the Parties recommending that vapour products be subject to the same provisions as tobacco products.

In reports by prominent health organizations, The American Heart Association policy statement on vapour products (Bhatnagar et al., 2014) is frequently referenced, and states that vapour products will lead to youth nicotine addiction, that they are ineffective for cessation, and their use will delay cessation. In contrast, Public Health England published a report in May 2014 stating that vapour products "clearly have potential to reduce the prevalence of smoking in the UK" (p. 13). The Royal College of Physicians UK issued a statement on e-cigarettes in June 2014 endorsing the potential for vapour products to reduce smoking prevalence, prevent morbidity and mortality, and reduce the social inequalities from tobacco use.

Other researchers have contested claims of risk. The authors of two early commentaries, Cahn and Siegel (2011) and Borland (2011), dispute the claim that youth vaping will increase the prevalence of nicotine dependence. In one of the most frequently cited systematic reviews, vapour product researchers Farsalinos and Polosa (2014) contest the claim that vapour products act as a gateway. Other research teams in early systematic reviews state that vapour products aid cessation; the highly cited ones are Caponnetto, Campagna, Papale, Russo, and Polosa (2012), Polosa, Rodu, Caponnetto, Maglia, and Raciti (2013), and Caponnetto, Russo, et al. (2013). Two frequently cited commentaries by Wagener, Siegel, and Borrelli (2012) and Fagerström and Bridgman (2014) are endorsements of vapour products as a potential cessation aid.

In *Claims Study* I observe the claims that have been put forward in another arena: government. Which claims are supported by sound evidence, and which are not? I examined two of the most common claims with a systematic review on the risks of youth vaping in *Youth Review*, and a review of systematic reviews on vapour products and cessation in *Cessation Review*.

Evidence.

What evidence is available on these two central claims in the debate over vapour products? In *Youth Review*, my co-authors and I found that very few studies on youth vaping were based on valid measurements of the risk for nicotine dependence. In *Cessation Review*, we observed that there were an insufficient number of RCTs to resolve the debate over the effectiveness of vapour products for cessation. This section provides a discussion of the research on youth vaping, and an overview of the RCTs and clinical trials on vaping and cessation.

So how many youth who report vaping in the past-30-days, the most common metric, have a pattern of problematic use, incurring substantial risk for nicotine dependence? A problem with the research, explored in *Youth Review*, is how almost all researchers have assumed that vaping invariably involves nicotine – only nine surveys inquired about non-nicotine vaping. In the systematic search, only 10 of 99 studies had measured the frequency of use more detailed than any past-30-day use, and many of the studies applied ever-use as their variable. These problems in the literature prompted our re-estimation of the number of youth at risk for becoming nicotine dependent through vaping.

So how effective are vapour products for cessation? Only three RCTs have been published to date. Bullen et al. (2013) conducted an RCT (ASCEND) for cessation with 657 participants in three arms: nicotine device, placebo device, and NRT patch, and all participants

received telephone counseling. Caponnetto, Campagna, et al. (2013) provided vapour devices (one placebo, two with different nicotine levels) for an RCT (ECLAT) to 300 smokers without a quit intention, and instructed the smokers to vape as desired. Adriaens, Van Gucht, Declerck, and Baeyens (2014) carried out an RCT of 48 smokers without a quit intention to examine the effects of vaping on cravings after a short period of abstinence. The findings and conclusions of these RCTs are reported in *Cessation Review*. The Cochrane review of vapour products and cessation (Hartmann-Boyce et al., 2016) lists 15 RCTs and clinical trials in progress, but as of November 8, 2017, none have been published.

The systematic reviews in *Cessation Review* encompass four clinical trials. In one, Caponnetto, Auditore, Russo, Cappello, and Polosa (2013) offered 14 smokers with schizophrenia free vapour products, and directed them to vape as desired. In a second trial, Polosa, Caponnetto, Maglia, Morjaria, and Russo (2014) provided 50 non-quitting smokers with 24 weeks of free vapour products. In another trial, Nides, Leischow, Bhatter, and Simmons (2014) trained 29 smokers who were vaping novices how to vape, and biochemically verified one week abstinence. In the fourth clinical trial, Hajek, Corbin, Ladmore, and Spearing (2015) followed 69 treatment-seeking smokers who opted for vapour products for their quit attempt. These trials were included in one or more of the systematic reviews evaluated in *Cessation Review*.

Two clinical trials were published in 2016 after the systematic reviews. James et al. (2016) provided a cessation intervention for 28 women smokers with cervical cancer, and Nolan et al. (2016) offered vapour products as a temporary abstinence intervention for 75 pre- and post-operative patients who smoked. These trials are included in the cessation evidence review in the *Clearing the Air* monograph (O'Leary et al., 2017) along with study tables for all the RCTs and

clinical trials. No further clinical trials have been published as of November 8, 2017, based on the Clearing the Air library and my 2017 literature search, although at least 15 other trials are underway (Hartmann-Boyce et al., 2016).

Looking beyond the peer-reviewed studies, market research demonstrates how popular vapour products have become in the past 10 years, and commercial news items announce the product's frequent design changes. Editorials, commentaries, and blogs show that the healthcare community is split over vapour products. Many of these authors claim that vaping will increase youth smoking rates, and that vapour products are ineffective, even detrimental, for cessation, while others dispute the risks to youth and endorse vapour products as a possible cessation aid.

Putting aside the heated debate in public health, what claims are being presented in the regulatory process? We appear to be the first to have analyzed the claims promoted in legislation recommendation reports. What is the evidence for the claims about youth vaping and cessation? As this discussion of the literature reveals, data are sparse, and even flawed. As a consequence, the available data had to be further analyzed to uncover the evidence. In *Youth Review*, my co-authors and I applied the available statistics on the frequency of use and non-nicotine vaping to population prevalence survey findings. In *Cessation Review*, we reached a conclusion on vaping and cessation by considering potential confounders in the primary studies in addition to the findings of the higher quality systematic reviews. The methods for conducting these analyses are explored next.

Methods

Identifying claims and locating evidence required different methodologies. Identifying claims in government reports necessitated a technique of content analysis. A systematic review was the best method for finding and synthesizing evidence on youth vaping. A review of

reviews facilitated an evaluation of multiple systematic reviews and a summary of evidence on the effectiveness of vapour products as a cessation aid. This section provides a fuller discussion of the methods than what is published in the articles.

Narrative policy framework.

Coming across narrative policy framework (NPF) was a very fortunate find. An edited volume on NPF, *The Science of Stories*, had been published a few months before I started my research. NPF was the perfect tool for identifying and analyzing the claims in the legislation recommendation reports.

Narrative policy framework (NPF) was developed in 2005 (Pierce, Smith-Walter, & Peterson, 2014), although the role of narrative in policy has been studied since at least 1989 (Jones, McBeth, & Shanahan, 2014). The term *narrative policy framework* was coined in 2010 (Jones et al., 2014). Before the introduction of NPF, the study of policy narratives had been dominated by the postpositive theoretical perspective that narratives are value-laden and social constructions of facts, and that text cannot be understood independently from how it is interpreted by individuals (Jones & McBeth, 2010). In contrast, Jones and McBeth, two of the developers of NPF, classify their methodology as a "quantitative, structuralist, and positivistic approach to policy narratives" (2010, p. 330). NPF is grounded in the philosophical paradigm of positivism, and applies a structuralist approach based on the assertion that narratives contain "consistent and identifiable components from which generalizations can be formed" (Jones & McBeth, 2010, pp. 331-332). Policy narrative studies continue to be almost completely dominated by postpositive theories, resulting in tensions between the post-positivists and the proponents of NPF (Jones & McBeth, 2010).

With its positivist orientation, NPF is a quantitative methodology that conceptualizes policy narratives as a specialized category of powerfully persuasive communication. Policy narratives are defined as the messages of policy stakeholders (interest groups, media, politicians), which represent their interpretations of policy problems and solutions (McBeth, Jones, & Shanahan, 2014; Pierce et al., 2014). The method constructs variables of generalizable content structures and narrative strategies that can be applied in multiple policy arenas (Jones et al., 2014; McBeth et al., 2014). The broad goal of NPF is to understand "to what extent do policy narratives influence policy outputs?" (Jones et al., 2014, p. 18; see also Jones & McBeth, 2010).

As described in *Claims Study*, the categories of analysis in NPF are taken from the construct of the *story*, comprising the setting, characters, plot, and moral of the story (Jones & McBeth, 2010; Jones et al., 2014; Pierce et al., 2014). Jones, McBeth, and Shanahan developed the brilliant innovation of applying the constructs of the story for analyzing policy narratives. First and foremost, humans think with stories, "[a] fondness for stories is just one of the many artifacts, side effects of the way our brains work" (Levitin, 2014, p. xiv).

NPF researchers use content analysis to identify policy narratives. Content analysis is an empirically grounded method that examines texts (among other materials) to understand their messages and meanings in context through their semantics (language content), patterns (message structures), differences, and attributions (categories of meaning) (based on Krippendorf, 2013). A simpler definition is "the systematic, objective, quantitative analysis of message characteristics" (Neuendorf, 2002, p. 1). Content analysis is highly recommended by NPF researchers as the analytic approach of choice: "to understand what narratives are being used, the collection and content analysis of documents remains a superior approach," (Pierce et al., 2014,

p. 35). Content analysis is the primary method to locate narrative elements in meso level studies (Jones et al., 2014), and this is the level of analysis for our article, as explained shortly. The content analysis of *Claims Study* was conducted with multiple readings of the text for familiarization, and then claims were coded manually due to the small number of categories, only 13 in total. Content analysis can provide the data to demonstrate how narratives actually influence decision-makers (Jones & McBeth, 2010).NPF is scalable because research studies can be conducted at the micro level of individual action, the meso level of the group, or the macro level of institutions and culture. While multi-level studies would be possible in theory, it appears that no researchers have yet done so. *Claims Study* is research at the meso level of groups, for example legislative committees or commissions. The paradigm that informs the meso level is the *agora narrans*, the ancient Greek institution in which speeches (narratives) were presented to champion a preferred course of action (McBeth et al., 2014). Meso-level NPF research focuses on the construction and communication of policy narratives of competing groups for their effectiveness in achieving their policy goals (Jones et al., 2014).

Finally, the structure of NPF narrative analysis had a particular strength for *Claims Study* as a highly contested field. The objective of NPF is not to judge which policies are right, but to analyze narratives systematically (Jones et al., 2014). This meant that claims could be identified without having to classify them as "pro" or "con." With the NPF methodology, the claims were not classified as right or wrong – identifying evidence on the claims is the purpose of the next part of my research program, the systematic literature reviews.

Systematic literature reviews.

The *Youth Review* is a systematic literature review. Systematic reviews appeared with the first few research summaries written in the 1800s, but modern statistical synthesis techniques

for research synthesis started in 1904 with Pearson's analysis of typhoid vaccines published in the *British Medical Journal* (Chalmers & Wilson, 2002). Additional statistical techniques were created in the 1930's and post-World War II (Chalmers & Wilson, 2002). Further development of systematic reviews took place in the late 1970s in response to the demand for evidence-based medicine (Shea et al., 2009). During the early 1990s interest in reviews increased within the healthcare disciplines due to the adoption of evidence-based practice (Grant & Booth, 2009), and the work of the Cochrane Collaboration founded in 1993 (Lefebvre, Glanville, Wieland, Coles, & Weightman, 2013). Systematic reviews are a primary input for evidence-informed health policy (Oxman, Lavis, Lewin, & Fretheim, 2009).

The goals of a systematic review are twofold. The first is to retrieve and describe all of the available robust studies pertaining to a research question (Mullen & Ramírez, 2006). The traditional systematic review is particularly strong for cataloguing all available research (Mullen & Ramírez, 2006) with many systematic reviews conducting search strategies focused on obtaining a perfect recall of all relevant literature (Tsafnat et al., 2014). A quality assessment is performed to exclude weak studies (Harden & Thomas, 2005). The second goal of a systematic review is to interpret or synthesize the findings of the individual primary studies (Kastner et al., 2012) through "further exploration and manipulation" (Sandelowski, Voils, Leeman, & Crandlee, 2012, p. 319). This can be in the form of a narrative synthesis or a meta-analysis. *Youth Review* is a narrative synthesis.

There are numerous supports for conducting a systematic review. One of the most widely used guides is the Preferred Reporting Items of Systematic Reviews (PRISMA) (Moher, Liberati, Tetzlaff, & Altman, 2009), an update of the Quality of Reporting of Meta-Analyses (QUOROM) statement (Moher et al., 1999). The Cochrane Library (Becker & Oxman, 2011)

and Joanna Briggs Institute (Aromataris et al., 2014) have created checklists for preparing systematic reviews. All these guides were consulted in the preparation of *Youth Review*. The RAMESES checklists (Realist and Meta-Narrative Evidence Synthesis Evolving Standards) (Wong, Greenhalgh, Westhrop, Buckingham, & Pawson, 2013a, 2013b) are guides for those specialized review methods.

In this digital age, several software programs are available for conducting reviews. RevMan5 was designed by the Cochrane team and was used in the Cochrane review on vapour products (Hartmann-Boyce et al., 2016). DistillerSR is another widely known program; the Malas et al. (2016) systematic review team used it. QUOSA is published by Elsevier. Three other software programs are EPPI-Reviewer 4, EROS (Early Review Organizing Software), and Covidence, and additionally one open source wiki, the Toolkit for Mixed Studies Reviews. The popularity of systematic reviews is reflected in the large number of commercial software packages available. Due to the small number of studies in *Youth Review*, the data extractions were performed manually.

A key component of a systematic review is a quality assessment of the studies, and many tools are available for the process. For *Youth Review*, I used the UK National Institute for Health and Care Excellence (NICE) quality assessment checklists in the 3rd edition of their Methods handbook (2012), developed with seven years of experience with the production of hundreds of healthcare guidance documents. The checklists are structured for public health reviews, so are appropriate for this topic. The checklists systematically assess the areas of study participant selection, study design, outcomes, and methods of analysis. NICE quality assessments are conducted with one of three checklists: one for quantitative interventions with 25 questions, a second for quantitative studies of correlations and associations with 17 questions, and the third

for qualitative studies with 14 questions. The quantitative checklists rate internal and external validity separately. The extensive use of sub-questions forms a transparent audit trail. The electronic format checklists are easy-to-use with pop-up windows with question prompts, plus the handbook has an extensive guidance section and references to additional resources.

With the NICE checklists, the final study assessment is scored as

"++" all or most criteria fulfilled and conclusions very unlikely to alter.

"+" some criteria unfulfilled but conclusions unlikely to alter.

"-" few or no checklist criteria fulfilled and conclusions are likely or very likely to alter.

NICE reviews cite each study's quality rating in their discussions and reports, a convention utilized in *Youth Review*.

In *Cessation Review*, the systematic review teams utilized other quality assessment tools. The Cochrane Risk of Bias tool was used by Hartmann-Boyce et al. (2016) and El Dib et al. (2017), and Malas et al. (2016) customized the QualSyst tool (Kmet, Lee, & Cook, 2004) for their quality assessment. The Cochrane Risk of Bias tool is defined in Table 8.5.a in the Cochrane Handbook (The Cochrane Collaboration, 2011). It has five defined domains: selection bias, performance bias, detection bias, attrition bias, and reporting bias, plus a category for other bias. The risk of bias for items in each domain is rated as high, low, or unclear, but the tool does not produce a composite score. The Cochrane Risk of Bias tool is well known and frequently used.

Not nearly so well-known is QualSyst, developed by the Health Technology Assessment Unit of the Alberta Heritage Foundation for Medical Research, although it has been applied to over 100 articles (per my search on October 30, 2017). QualSyst has separate checklists for quantitative and qualitative studies, and calculates a summary score that is applied as an

inclusion/exclusion criterion. The Malas et al. team customized the tool by combining its checklists, and modifying some questions for non-clinical studies, producing 16 indicators, and they classified the summary scores into specific ranges for *strong*, *moderate*, and *weak* quality assessments. With the QualSyst tool, a study's score can be downgraded when any flaw compromises the validity of the study's findings. The Malas review team followed the standard systematic review practice of excluding weak or low quality studies, while the Hartmann-Boyce and El Dib teams did not, as discussed in *Cessation Review*.

All of the top-rated reviews in the *Cessation Review* assessed their confidence in their findings with the GRADE system. GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) rates a body of evidence for an outcome, not the individual studies. GRADE was developed by a working group of health professionals and researchers in 2000 (Guyatt, Oxman, Schunemann, Tugwell, & Knottnerus, 2011), and published in 2008 in six articles in the *BMJ* (Guyatt et al., 2008). The *Journal of Clinical Epidemiology* published a series of 20 articles on GRADE in 2011 (Guyatt et al., 2011). The most significant change was an update of the definition of the quality of evidence to "confidence in the true effect" (Balshem et al., 2011). GRADE has its own software, GRADEpro. As well as rating the quality of evidence, the GRADE system can assess the strength of recommendations, evaluated on the quality of evidence, trade-offs of desirable and undesirable effects, patient preferences and values, and resource costs. GRADE is used in most systematic reviews (Papageogiou & Biondi-Zoccai, 2016), but I did not use GRADE in *Youth Review* because all the data were drawn from surveys, and survey data are automatically classified as LOW or VERY LOW confidence in the GRADE system.

Systematic reviews are a well-known and well-established methodology for assessing and synthesizing the evidence of primary studies, particularly in healthcare. A quality assessment of the primary studies is a key component of a systematic review, and in *Youth Review*, I used the NICE checklists. Primary studies are the unit of analysis for systematic reviews, and systematic reviews themselves are the data for umbrella reviews, the methodology of *Cessation Review,* discussed next.

Umbrella reviews.

Although a systematic review on cessation was part of my research plan, when I started work, the literature on cessation already had ten systematic reviews published in 2016, so the contribution of yet another systematic review would be minimal at best. Instead I investigated the quality and findings of the systematic reviews themselves with an umbrella review, a tertiary methodology, to point out the best systematic reviews for the benefit of researchers and policy decision-makers. The advantage of the umbrella review methodology is that it provided my co-authors and I sufficient evidence to be optimistic that vapour products have potential as a cessation aid, while the systematic review teams could not reach a conclusion.

There are more variations in the terminology for umbrella reviews than space permitted in *Cessation Review*. Biondi-Zoccai, the editor of the edited volume *Umbrella Reviews*, defines the terms more narrowly: a *review of systematic reviews* assesses the quality of systematic reviews while an umbrella review synthesizes evidence (2016). Biondi-Zoccai, Tsagris and Fragkos (2016) and Papageogiou and Biondi-Zoccai (2016) (the latter changing his definition) propose the term *overview of reviews* as the general term, and umbrella review for compilations of evidence on clinical topics. The Cochrane team (Becker & Oxman, 2011) and the editors of *Systematic Reviews* have adopted the term *overview of reviews*, as have other review teams

(Ballard & Montgomery, 2017; Cooper & Koenka, 2012; Pieper, Buechter, Jerinic, & Eikermann, 2012; Pussegoda et al., 2017). For the sake of simplicity, *Cessation Review* is titled a review of systematic reviews because it is an assessment of review quality and a summary of evidence.

As discussed in *Cessation Review*, umbrella reviews serve multiple functions: an assessment of the quality of systematic reviews, an evaluation of the state of the literature, and a presentation of the findings of the reviews. Umbrella reviews can focus on a specific clinical condition or treatment (Becker & Oxman, 2011; Biondi-Zoccai, 2016; Tsagris & Fragkos, 2016), and the "treatment" examined in our review is vapour product use. Umbrella reviews have been conducted for the primary purpose of providing evidence-based recommendations for practice and future research (Ortega, Lopez-Briz, & Fraga-Fuentes, 2016; Papageogiou & Biondi-Zoccai, 2016). A meta-epidemiologic study is a specialized umbrella review that synthesizes the meta-analyses of systematic reviews (Biondi-Zoccai, 2016). Because umbrella reviews have so much functionality, and with the large number of systematic reviews published, overviews of reviews deserve to be more frequently utilized.

Publications are available to assist reviewers in conducting an umbrella review. A new textbook for conducting umbrella reviews is *Umbrella Reviews* (2017). Guidance documents for conducting overviews have been produced by 19 research groups, although not all of the materials have been published (M. Pollock, Fernandes, Becker, Featherstone, & Hartling, 2016). A. Pollock, Campbell, Brunton, Hunt, and Estcourt (2017) offer detailed advice for umbrella reviewers, and provide examples from five high quality umbrella reviews. Very recently, Bougioukas, Liakos, Tspas, Ntzani, and Haidich (2018) have published a checklist for

conducting umbrella reviews of healthcare interventions. These publications should spur the production of more umbrella reviews.

A critical component of every umbrella review is the assessment of the quality of systematic reviews. As discussed in *Cessation Review*, AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) was the tool we selected. The initial version of AMSTAR was developed in 2007 by Shea et al. It was developed from earlier tools, including Sack et al.'s checklist of 23 items in six categories (Sacks, Berrier, Reitman, Ancona-Berk, & Chalmers, 1987), and the Overview Quality Assessment Questionnaire (OQAQ) with ten questions and a seven point rating scale (Oxman & Guyall, 1991). These earlier tools became obsolete because they did not cover the more modern statistical tests, such as for heterogeneity or publication bias (Baker, Bennetts, Coleman, & Cappelleri, 2016). Now AMSTAR 2 has been published (Shea et al., 2017). AMSTAR 2 has an extended description in *Cessation Review*, so that information is not repeated here.

Two other quality assessment tools for examining systematic reviews have been published. The most recent is ROBIS. It assesses risks of bias in study eligibility criteria, study selection, data collection, and synthesis of findings and calculates an overall risk of bias (Whiting et al., 2016). Perry et al. (2017) conducted a side by side evaluation of AMSTAR and ROBIS, and they found ROBIS difficult to use for systematic reviews without a meta-analysis, and its inter-rater reliability was rated only as "fair" at 60%. Another tool, R-AMSTAR, was developed by Kung et al. (2010), not the AMSTAR Group; it assigns a score of 0-4 for each question. Researchers who evaluated R-AMSTAR recommended that it be further tested (Pieper, Buechter, Li, Prediger, & Eikermann, 2015), but with the revised tool now published, that project may be moot.

In addition to published tools, umbrella review teams have created their own criteria for the evaluation of systematic reviews. In a study of 76 overviews of reviews of healthcare literature, Pussegoda et al. (2017) observed that 24% of the authors constructed their own quality criteria. Two examples are Cooper's 20 question checklist for reviews in the behavioural sciences (published in Cooper & Koenka, 2012), and Thorne's (2017) five critical questions on exclusion, data, context, theory, and contribution.

Unfortunately, there is no tool for evaluating the quality of an umbrella review. The GRADE tool is "not directly transferable" to umbrella reviews (Ortega et al., 2016, p. 70; Papageogiou & Biondi-Zoccai, 2016). Meta-epidemiologic studies, synthesizing the findings of multiple systematic reviews, run into bias problems when primary studies are included in more than one systematic review (McKenzie & Brennan, 2017, see also Pieper et al., 2014). Because double or multiple counting overstates a study's findings, Pieper, Antoine, Mathes, Neugebauer, and Eikermann (2014) developed and validated a statistical test, the *corrected covered area* (CCA) that calculates the degree of overlap in the primary studies in the systematic reviews included in an umbrella review. The CCA is a sensitivity analysis (Squires, Sullivan, Eccles, Worswick, & Grimshaw, 2014). The formula is CCA=(N-r)/(rc-r) where N is the total number of publications, r is the number of index studies, and c is the number of reviews. The CCA score is classified as *slight* (0%-5%), *moderate* (6%-10%), *high* (11%-15%), and *very high* (>15%) (Pieper et al., 2014).

The CCA is being increasingly employed in umbrella reviews, as evidenced by its use in 16 umbrella reviews over the past two years (see Appendix A). Seven reviews had slight overlaps, one moderate, three high, three very high, and two were protocols specifying the CCA. The CCA test is a required item in a recently published checklist for overviews of healthcare

interventions by Bougioukas et al. (2018). In *Cessation Review*, the overlap of reviews was 23%, so it was not feasible to conduct a synthesis of the findings of the systematic reviews.

An interesting, but unintended feature of my dissertation is that it encompasses three levels of research. *Claims Study* consists of primary research with content data from legislative research reports. *Youth Review* is a secondary study of survey data. *Cessation Review* is an umbrella review at the tertiary level of analysis, examining systematic reviews. The three articles fit together in that *Claims Study* identifies the claims, and the two systematic reviews retrieve and interpret the data on two of the most frequently cited claims. As the debate over vapour products in the public health community continues, which claims are having traction in the regulatory process? Are more youth at risk for nicotine dependence from vaping? Are vapour products an effective cessation aid? These three questions are explored in the three articles presented next. The articles are followed by the Afterward with further discussions and my final conclusions on *Vapour Products/E-Cigarettes: Claims and Evidence*.

Claims in Vapour Device (E-cigarette) Regulation: A Narrative Policy Framework Analysis

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Abstract

Background

The electronic cigarette or e-cigarette (vapour device) is a consumer product undergoing rapid growth, and governments have been adopting regulations on the sale of the devices and their nicotine liquids. Competing claims about vapour devices have ignited a contentious debate in the public health community. What claims have been taken up in the state arena, and how have they possibly influenced regulatory outcomes?

Methods

This study utilized Narrative Policy Framework to analyze the claims made about vapour devices in legislation recommendation reports from Queensland Australia, Canada, and the European Union, and the 2016 deeming rule legislation from the United States, and examined the claims and the regulatory outcomes in these jurisdictions.

Results

The vast majority of claims in the policy documents represented vapour devices as a threat: an unsafe product harming the health of vapour device users, a gateway product promoting youth tobacco uptake, and a quasi-tobacco product impeding tobacco control. The opportunity for

vapour devices to promote cessation or reduce exposure to toxins was very rarely presented, and these positive claims were not discussed at all in two of the four documents studied.

Conclusion

The dominant claims of vapour devices as a public health threat have supported regulations that have limited their potential as a harm reduction strategy. Future policy debates should evaluate the opportunities for vapour devices to decrease the health and social burdens of the tobacco epidemic.

From its invention in 2003, the electronic cigarette and its evolving product designs (for example, tank systems) have become a US$ 7.99 billion worldwide market in 2015, with sales projected to more than double by 2020 (Euromonitor International, 2016). Governments have been faced with the policy problem of how to regulate these new consumer products which can (but do not necessarily) deliver nicotine. All these products are termed *vapour devices* in this study. As of 2016, vapour devices have been regulated as medicinal products (18 countries), as tobacco products (26 countries), or as a controlled substance (nicotine) (4 countries), while 26 countries have banned their sale (Institute for Global Tobacco Control, 2016).

In prior policy processes on tobacco, the public health community has presented a virtually united front, but when it comes to vapour devices, there is no agreement (Costa, Gilmore, Peeters, McKee, & Stuckler, 2014). A vitriolic debate rages (Sim & Mackie, 2014) as public health officials and researchers espouse radically divergent viewpoints on the health and population level effects of vapour devices. Claims have been dominating the debate. As Stimson, Thom, and Costall (2014) observed, “claims are made and contested by manufacturers,

distributors, retailers, consumers, social movements, the state, and professional organisations. How this will play out with respect to electronic cigarettes is uncertain…" (p. 655).

In this study, we examined claims about vapour devices that have been taken up in the state arena. To date, no research has been conducted to examine what claims about vapour devices have been accepted in the legislative process. Understanding these claims reveals how the policy problem of vapour devices has been defined in government legislation. In our research questions we asked: What claims about vapour devices have been put forward in the documents recommending or justifying vapour device regulation? How have these claims potentially influenced the resulting legislation?

To identify these claims, we analyzed four government documents: three legislation recommendation reports and one regulatory ruling. These documents are from Queensland, Australia (2014) *Health Legislation Amendment Bill 2014, Report No. 59*; from Canada (2015) *Vaping: Towards a Regulatory Framework for E-Cigarettes*; from the European Union (2013) *Report A7-0276/2013, 24.7.2013*; and from the United States (2016) *Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act.* For Queensland, the European Union, and the United States, these documents are the recommendation reports on draft legislation written to inform the regulation of vapour devices and other tobacco products. The Canada report is a preliminary report initiated to prepare for drafting legislation for vapour devices. These four documents were selected, first and foremost, because they contained the claims about vapour devices that were not written in the regulations but provided the rationale for them. They also were chosen to provide examples of claims about vapour devices in the differing contexts of regional, national, and trans-national governments to observe the possible differences in their policy narratives.

Finally, these documents were picked because they were written in the same language, facilitating the comparison between documents with their common English narrative text structures.

To examine these claims about vapour devices, we applied the Narrative Policy Framework (NPF), a methodology developed in 2004 (Shanahan, Jones, & McBeth, 2011) premised on the hypothesis that "narrative stories are the principal means for defining and contesting policy problems" (Stone, 2012, p. 158). NPF posits narratives as a key mechanism in the policy process because humans, by their very nature, are storytellers (McBeth, Jones, & Shanahan, 2014). Policy narratives are socially constructed stories produced within belief systems (Jones, McBeth, & Shanahan, 2014) that narrate the "reality" of the policy problem, and assign blame (McBeth et al., 2014). The purpose of policy narratives is persuasion (Weible & Schlager, 2014) to influence the framing of a policy problem and shape policy beliefs (Pierce, Smith-Walter, & Peterson, 2014).

NPF has been described as both a research platform (Weible & Schlager, 2014) and as a rubric (Shanahan et al., 2011). As a research platform, NPF provides a "structuralist interpretation of narrative" (McBeth et al., 2014, p. 228) which asserts that policy narratives can be empirically studied across different policy contexts by examining their strategies and policy beliefs, as opposed to the post-positivist view that every narrative is unique and therefore not generalizable (narrative relativism). As a rubric, NPF offers generalizable content structures (or structural elements) for analyzing policy narratives. These content structures are based on the construct of the *story*, and NPF approaches policy narratives as stories constructed through the elements of the setting, characters, plot, and moral of the story (Jones & McBeth, 2010; Jones et al., 2014). These variables can be applied across different contexts, and at micro (individual),

meso (group), and macro (culture) levels (Jones et al., 2014). This study applies NPF at the meso-level of policy making and policy outputs, which is symbolized in NPF by the *agora narrans*, the ancient Greek public space where citizens made their speeches (McBeth et al., 2014).

The broad goal of NPF is to understand "to what extent do policy narratives influence policy outputs?" (Jones et al., 2014, p. 18). The primary goal of this study is to identify claims about vapour devices that may have had traction in the regulatory process, and to show how these claims may have, in turn, influenced policy outcomes. A secondary purpose of this research is to inform interested parties on how vapour device regulation has been crafted in four jurisdictions, including the major markets of the European Union and the United States. In addition, this study contributes to the further development of the relatively new NPF methodology through the transparent reporting of this study's techniques for the identification of characters and the classification of plots. Finally, it enriches the scope of NPF by utilizing the framework with a public health policy issue, as NPF research has to date focused almost exclusively on environmental policy (Pierce et al., 2014).

Methods: Narrative Policy Framework Analysis

The unit of analysis for this study is the claim, which for this research is a statement of fact about the potential or actual effects of vapour devices made in the documents of Queensland, Canada, the European Union (EU), and the United States (US). Claims act as a form of evidence, a truth claim. Claims about vapour devices purport to be a true evaluation of the product or a trustworthy prediction of its impacts on health.

This study is based on three sets of textual data: (1) contextual information about vapour device prevalence, prior regulations, and the processes that produced the policy document; (2)

the claims presented in the document; and (3) the regulatory outcome. These data sets facilitate an understanding of the contexts of the policy processes, identify the claims for NPF analysis, and provide details of the regulations to examine how specific claims in the documents may have influenced the resulting policy outputs.

The datasets were constructed from multiple sources. For the context data, vapour device prevalence was located in national health surveys, and prior regulations were found in scholarly journals and reports from non-profit organizations. The policy processes that produced the documents were identified through reviewing the respective governments' websites with additional historical details provided by journal articles and grey literature. This contextual information acts as the NPF's setting of the story, and it has been presented as a narrative summary for each jurisdiction in the Results section. The selected policy documents were downloaded from the governments' websites, and the process of identifying the claims is described in the Methods section below. The final legislation is, in effect, the moral of the story, and the legislation was summarized from the final published regulations.

The identification of claims was carried out through multiple close readings of the documents. Semantic content analysis was conducted to retrieved declarative sentences and phrases about vapour devices which constitute the claims, and all further analysis was performed with the NPF content structures described below. The documents reported the testimony and claims of numerous witnesses, but not all of their claims were accepted in the recommendations. For example, the US document reported but dismissed a research study demonstrating that bans on vapour device sales to youth resulted in *higher* smoking rates compared to states without a ban, and instead the US report endorsed bans on sales to youth. Therefore, only the claims about

vapour devices that were endorsed in the Queensland, Canada, and EU recommendation reports and only the claims validated in the US regulatory document were included in the analysis.

Once identified, the full claim text was then extracted, and listed in a table for each document. Some texts, particularly those in the Queensland report, contained multiple claims in one sentence, so for purposes of analysis, these were segmented into single claims. These segmented texts are indicated by shading in the claims text tables. Each claim text was assigned an identification number (ID). The tables of the claim texts were edited into a truncated text to support our readers in following the analysis. (The full texts of the claims are reported in the Appendix.)

For the analysis of the claims, the first author defined each claim's content with the NPF content structures of characters and plots. In this framework, the *characters* are classified as the heroes who purport to solve the policy problem, the villains who cause the problem, and the victims who are/will be harmed. These characters need not be human, and can be abstract objects (Pierce et al., 2014; Weible & Schlager, 2014). As well as identifying characters, NPF uses the variable of the *plot.* NPF defines a plot as the relationships between the story's characters and their actions. These plots and characters can be understood as the variables within a claim.

The NPF's content structure of characters and plots was applied to the four policy documents under study using the following steps. An example of the framing process is presented in Table 1 below. The plot framing was constructed first. To begin the process, the plots were composed by centering vapour devices as the pivot point (subject) of the claim with this template: "vapour devices [action/verb] on [character]." Mutually exclusive plots were composed from the texts so that all claims were represented with a plot about vapour devices.

Next, the first author composed standardized scripts based on these plots, and assigned a standardized plot to each claim. The last step in framing the plot analysis involved categorizing each plot as a *threat plot* or an *opportunity plot*, a classification derived from the SWOT (strengths, weaknesses, threats, and opportunities) analysis (Nason, 2010). We have not conducted a SWOT analysis here, but have appropriated the terms as means of identifying the narrative thrust of the plots.

After the plots were framed, the characters were identified in the plots. Names were recorded for the characters and then assigned a generic character name. Following this, the characters were classified according to their role in the plot as victim, villain, or hero. In the final step of the NPF analysis, the framing of the plot and characters was checked for fit against the full claim text. The entire process of framing a claim with a plot and characters follows in Table 1.

Table 1

Worked Example of Framing a Claim with Plot and Characters

NPF Text Framing	Process Step
the potential of e-cigarette use to impair the process of de-normalizing smoking behaviour which has played such a key role in reducing tobacco use, and that they could undermine smoke-free legislation and controls across the country	Identify declarative statements (from Canada report, page 9 – claim 14)
E-cigarettes could impair the de-normalizing of smoking	Apply plot template
Vapour devices could impede tobacco control	Assign to standardized plot
E-cigarettes, de-normalization	Identify characters in plot
Vapour devices, tobacco control	Standardize character names
Vapour devices – villain Tobacco control - victim	Classify character role
the potential of e-cigarette use [vapour devices] to impair [impede] the process of de-normalizing smoking [tobacco control]	Check for fit

A special procedure for identifying characters was created because some characters, for example, vapour device manufacturers, were not directly presented in the claim texts. Unnamed characters, or shadow characters as we have termed them, though not directly referred to in the narrative, became visible through their actions in the plots. Two examples of shadow characters identified in claim texts are provided in Table 2.

Table 2

Examples of Shadow (Unnamed) Characters in Claim Texts

Claim Text (ID)	Shadow Character	Indication of Plot Actions
bystanders are exposed to exhaled nicotine and particles from e-cigarettes (QLD 10)	Vapour device user	Vapour device user vapes [smokes] near others.
some devices available in Canada that are advertised as not containing nicotine do, in fact, contain nicotine (CAN 2)	Vapour device manufacturer	Manufacturer produces mislabeled or tainted products.

The framing of the claims was conducted by the first author. The framing (coding) was independently verified by the third author (TS) for the complete Queensland and Canada documents, reviewing 44% of all claims. The inter-coder agreement was 93%. Disagreements were resolved through discussion, and all were resolved without referral to a third author. In addition, the coding of every claim was carefully reviewed by all the study authors.

These processes of searching for contextual information, applying NPF variables to the policy documents, and reporting the legislative outcomes produced three data sets for each document: the contextual data supplying the setting of the story, a list of claims, and a summary of the final legislation that acts as the moral of the story. The NPF framing of the claims with the variables of plot and characters generated the primary analysis. These results are presented in the following section.

Results

In this section, the results are displayed for each document, starting with the contextual data (setting), followed by a table of the claims in the document, and concluding with a summary of the final legislation or policy outcome. After presenting the documents' results, this section

displays a table of the plots and characters for each of the documents, and provides a summary of the analysis.

Queensland

An Australia-wide survey of 14+ year olds conducted in 2013 estimated vapour device use (any use in the past year) at 14.8% (Australia Institute of Health and Welfare, 2014).

Australia at the federal level prohibited the sale of liquid nicotine before the advent of vapour devices (Krawitz, 2014), and several states, including Queensland, had banned the sale of goods that look like a tobacco product (Douglas, Hall, & Gartner, 2015). Nevertheless, the *Personal Importation Scheme* allows limited importation of nicotine as an unapproved therapeutic good by individuals with a physician's prescription (Douglas et al., 2015). Yet with or without a prescription, an estimated 89% of vapour device users purchase their liquids online (Yong et al., 2015). In this strict regulatory environment, there is a substantial and growing black market for nicotine liquids (Gartner & Hall, 2015; Hall & Gartner, 2014; Krawitz, 2014; Yong et al., 2015).

The Queensland government proposed regulating vapour devices through *The Health Legislation Amendment Bill 2014*, an omnibus Bill that amended eight health acts, with vapour devices to be placed under the *Tobacco and Other Smoking Products Act 1998*. The bill was introduced on September 9, 2014, and referred to the Health and Community Services Committee. The Committee held two hearings, one with the Queensland Department of Health, and the second which included four invited witnesses who testified on vapour devices. Additional testimony on vapour devices was accepted from 14 written submissions, and two correspondences from the Queensland Department of Health. The expedited recommendation

report (usually a six month process) was published November 17, 2014. The claim texts from this document are listed in Table 3 below.

Table 3

Truncated Queensland Claims Texts

ID	Truncated Claim Text
1	no benefit in the devices to assist people to stop smoking
2	used as an introductory process for people, and particularly children, into the very bad and life-limiting habit of smoking
3	children, into the very bad and life-limiting habit of smoking.
4	Their unregulated availability to children, retail advertising and display, and use in smoke-free public places risks a return to smoking becoming popular and desirable especially to youth.
5	retail advertising and display…risks a return to smoking becoming popular and desirable
6	use in smoke-free public places risks a return to smoking becoming popular and desirable
7	years of campaigning by governments and communities to 'denormalise' smoking and reduce smoking rates could be undermined
8	may be exposed to the second-hand…'smoke'
9	different devices deliver different amounts, user puffing behaviour may lead to overdose through unreliable dosage delivered by devices
10	user puffing behaviour may lead to overdose
11	Possible nicotine poisoning (mainly to children) due to leakage from devices
12	leakage from devices
13	health risks to non-users from inhalation of second hand e-cigarette aerosol
14	a possibility that children and non-smokers will start to use e-cigarettes and develop a nicotine addiction that may lead them to switch to cigarette smoking
15	a possibility that…non-smokers will start to use e-cigarettes and develop a nicotine addiction that may lead them to switch to cigarette smoking
16	vaporisers may also contain unknown, possibly toxic chemicals and have incorrect or inconsistent labelling and unsafe packaging
17	may… have incorrect or inconsistent labelling and unsafe packaging

Claim text within full text

The bill placing vapour devices under tobacco regulation was ratified on November 26, 2014 as *Act No 65 of 2014*, a few weeks ahead of the Queensland election when the ruling party

lost its majority in a landslide election. The *Act* went into effect on January 1, 2015. It exempted vapour devices from the "look-alike" ban, and subjected them to the same regulations as tobacco, including smoking bans, retail advertising restrictions, vending machine bans, and age restriction for sales to 18+ years old. Liquid nicotine remains illegal.

Canada

A 2013 survey of Canadians 15+ years old found that 8.5% had ever used a vapour device, and 1.8% had used one in the past 30 days (Czoli, Reid, Rynard, & Hammond, 2015).

Vapour devices with nicotine are regulated as drugs/drug delivery devices under the *Food and Drugs Act* as specified by the 2009 Health Canada Notice 09-108446-55. No nicotine-containing devices have been approved for sale, nevertheless they are "widely available" (Hammond et al., 2015). Vapour devices that do not contain nicotine and do not make health claims are legal, and are sold in many retail stores (ibid.).

The Health Minister referred the issue of vapour devices to the Standing Committee on Health on September 29, 2014. The Committee held eight meetings with 33 witnesses: federal and provincial government officials, vapour device manufacturers, users, non-governmental organizations, and medical experts. The Committee issued its recommendation report on March 10, 2015. The texts of the claims in this document are listed in Table 4 below.

Table 4
Truncated Canada Claims Texts

ID	Truncated Claim Text
1	may pose health risks
2	advertised as not containing nicotine do, in fact, contain nicotine
3	use of e-cigarettes in places where smoking is banned
4	an undermining effort to helping kids stop or not to start [tobacco use]
5	the addictive nature of nicotine
6	the trigger for calls to poison control centres
7	possible health risks
8	flaws in the manufacture of the device
9	possible or probable negative impacts [on bystanders]
10	a gateway effect for youth in particular
11	candy flavoured electronic cigarettes as being particularly appealing to youth
12	undermining the gains made by tobacco control efforts… the "renormalizing effect"
13	a risk to the efforts and successes in tobacco control
14	impair the process of de-normalizing smoking behaviour… undermine smoke-free legislation and controls
15	use by the tobacco industry to re-engage in tobacco policy
16	used in smoke-free environments as a way to break the enforcement of smoke-free policies
17	the co-branding of e-cigarettes with tobacco industry logos or brands…would only help to renormalize tobacco smoking
18	to help prevent renormalization of smoking, electronic cigarettes should be visually distinct from other tobacco products
19	the lack of safety and quality assurance…including both their liquids and their components, such as batteries
20	concerns about "renormalization" of smoking
21	potential health risks to bystanders
22	free product offers, celebrity endorsements, overt lifestyle advertising, and attractive product packaging and flavours. This type of promotion influences the perceived acceptability of e-cigarette use and smoking
23	attractive product packaging and flavours… influences the perceived acceptability of e-cigarette use and smoking
24	non-smokers who start using electronic cigarettes may start using tobacco products (the "gateway effect")
25	cross-branding could contribute to the renormalization of smoking and increased take-up of tobacco products

26	cross-branding could contribute to…increased take-up of tobacco products
27	a possible “gateway” to tobacco use

The House of Commons’ rules require the government to table a response to a recommendation report within 120 calendar days, but the response to the vapour device report was delayed pending the upcoming federal election (Vogel, 2015). The report lapsed with the dissolution of the Canadian Parliament on August 2, 2015, and it was not re-tabled as the ruling party lost its majority in the election. Under the current status quo, vapour devices, both legal non-nicotine and prohibited nicotine devices, remain widely available. A number of regional and local jurisdictions have gone forward with regulating vapour devices on their own. As this study goes to press, Bill S-5, *An Act to Amend the Tobacco Act*, “to regulate the manufacture, sale, labelling and promotion of vaping products” (p. ii, Summary) was introduced with a first reading on November 22, 2016. Its provisions have not been finalized.

European Union

Vapour device prevalence in the EU in 2012 for ages 15+ was 7.2% for ever use, and 0.7% for regular use (survey question, frequency not defined) (Ooms, Bosdriesz, Portrait, & Kunst, 2016).

Prior to EU-wide regulations, different Member States had regulated vapour devices as a consumer product, a medicine, a poison, or a tobacco product; Greece and Lithuania had banned their sale (Institute for Global Tobacco Control, 2016). Regulations among various Member States included smoking bans in public spaces and on transportation, minimum age for purchase, market restrictions, and advertising bans or limitations (ibid).

In what has been described as a tortuous five-year process (Maurice, 2014), which commenced in 2009, vapour device regulation in the EU was debated as one part of the revision

of the 2001 *Tobacco Products Directive*. Vapour device regulation escalated into a contentious issue during Parliamentary negotiations in 2013 when the Council and Commission's proposed medicinal regulation of vapour devices was rewritten, and the product was included in the revised tobacco regulation (Hasselbalch, 2016). The 2013 *Report* on the proposed legislation was written by the Committee on the Environment, Public Safety and Food Safety, and it included opinions from six other committees, three of which also made recommendations on vapour devices (see Table 5 legend). Few claims were offered in the Report, and they are listed in Table 5 below.

Table 5

Truncated EU Claims Texts

ID	Truncated Claim Text
1	the harmless nature of which is not yet scientifically proven
2	clearly produced to be appealing to young and underage consumers
3	the habits created by young consumers and minors
4	different regulatory approaches to address health and safety concerns
5	safety concerns
6	aid with smoking cessation
7	potential health risks
8	can damage your health
9	allowed on the market with health warnings
10	could renormalize smoking
11	cardiovascular toxicity of nicotine
12	can help consumers to quit smoking
13	an appropriate health warning
14	contain toxic chemicals and tobacco specific components suspected of being dangerous to consumers
15	labelled as containing no nicotine in many cases do in fact contain low levels of nicotine
16	consumers… mainly use e-cigarettes to quit smoking
17	much less harmful than tobacco products

Claims 1-7, 9-10 Committee on the Environment, Public Health, and Food Safety

Claim 8 Legislation proposed text

Claims 11-13 Committee on Industry, Research and Energy

Claims 14-16 Committee on the Internal Market and Consumer Protection

Claim 17 Committee on Legal Affairs

The *Tobacco Products Directive 2014/40/EU* (TPD) was approved on February 26, 2014; the legislation entered into force on May 19, 2014. It was scheduled to be implemented by May 20, 2016, but by that date, only 11 of the EU Member States had complied with the TPD, and those Member States not in compliance were granted a two month extension (Associated Press, 2016, May 20). Article 20, *Electronic Cigarettes*, limits the nicotine content of vapour devices, with those above the limit regulated as pharmaceuticals. Vapour devices are also subject to purity standards, and must include a leaflet with health warnings and an ingredient list, with liquids required to be sold in child-proof containers. Manufacturers and Member States have specific duties under the TDP. Manufacturers must submit pre-market notifications, maintain an adverse effects registry, and report their sales to the Member States where they do business. On top of this, advertising and promotional sponsorship are prohibited. Member States are mandated to monitor the uptake of vapour devices by youth and non-smokers. Member States can enact provisional bans on specific devices or refills with reports of serious health risks, and the EU Commission is authorized to ban any products if three or more Member States have done so. Article 20 was challenged in the EU Court of Justice by the vapour device manufacturer Totally Wicked (application C-477/14, 12 Dec 2014), but the Court dismissed the suit (Court of Justice of the European Union, 2016, May 4).

United States

In 2014, 12.6% of US adults (aged 18+ years old) had ever tried a vapour device, and 3.7% used a vapour device every day or some days (Schoenborn & Gindi, 2015). A 2015 national survey of students reported that 16.0% of high school and 5.3% of middle school students had used a vapour device in the past 30 days (Singh et al., 2016).

It appears that no vapour devices were marketed in the US prior to February 15, 2007 (Freiberg, 2012). From 2008 to 2010, the Food and Drug Administration (FDA) attempted to regulate vapour devices as an unapproved medical drug/device (US Food and Drug Aministration, 2011, April 25) and took steps to interdict their importation and distribution (Washington Legal Foundation, 2010, July 21). Smoking Everywhere (NJOY) filed suit against the FDA, and on January 14, 2010 was granted a preliminary injunction. On July 8, 2010 Smoking Everywhere, Sottera Inc. filed suit against the FDA (627 F.3d 891, DC Cir 2010), and on December 7, 2010 the US Court of Appeals struck down the FDA ruling that electronic cigarettes were medical devices. The FDA issued a stakeholder letter on April 25, 2011 indicating its intention to regulate vapour devices as tobacco products.

The proposed "deeming rule" by the FDA was circulated on April 25, 2014; it contained regulations for cigars, pipe tobacco, and hookahs, and placed vapour devices under the jurisdiction of the *Tobacco Act*. The comment period on the proposed regulation was originally scheduled to close on July 9, 2014, but was extended 30 days. Three public workshops were held between December 2014 and June 2015. The FDA stated it received over 135,000 comments (FDA Deeming Rule, 2016). Nicotine exposure warning labels and child proof cap requirements were proposed by the FDA in a separate docket on July 1, 2015. Before the

publication of the final regulations, the ruling was reviewed by the Executive Branch, and a news source reported that the Office of Management and Budget had deleted a flavour ban for vapour devices (Clarke, 2016). The finalized deeming rule was published on May 5, 2016. The claims presented in this policy document are listed in Table 6 below.

Table 6

Truncated US Claims Texts

ID	Truncated Claim Text
1	concerns about dual use of e-cigarettes and combusted tobacco products
2	leading children to initiate tobacco use
3	alarming rise in e-cigarette use by middle school and high school students
4	rise in use…by youth
5	rise in use [by]…young adults
6	dramatic rise in ENDS use among youth
7	rise in ENDS use among youth
8	rise in ENDS use among…young adults
9	dual use of ENDS and combusted products in…youth
10	dual use of ENDS and combusted products in…adults
11	the toxicants in e-liquid
12	concerns regarding…the exhaled aerosol
13	concerns regarding…the nicotine delivery
14	the potential to addict users
15	diethylene glycol is a toxicant
16	concerns with ENDS aerosol
17	risk of nicotine poisoning
18	rise in nicotine poisoning
19	poisoning concerns
20	toxicological concerns of chemical ingredients
21	quality control concerns
22	concerns about the safety
23	adverse events…overheating and exploding batteries
24	accidental nicotine poisoning
25	concerns remain regarding quality control
26	concerns regarding…the safety
27	consumer misperceptions…believed e-cigarettes to be safe tobacco products
28	could lead to the re-normalization of cigarette smoking
29	rapid increase in use among adolescents
30	risk of accidental nicotine poisoning
31	could serve as alternatives to combusted tobacco products
32	use…in conjunction with cigarettes or other tobacco products
33	dual users of ENDS and cigarettes may be transitioning away from combustible tobacco use

34	potential impact of [dual use]…on nicotine addiction
35	potential impact of [dual use] on…cessation
36	youth may…become addicted
37	youth may initiate tobacco use with ENDS
38	youth may use…ENDS…and dual use with other tobacco products in the future

Deeming Tobacco Products was written into law on May 10, 2016. In addition to vapour devices, it issued regulations for cigars, disolvables, gels, pipe tobacco, and waterpipe tobacco. It appears that vapour device liquids without nicotine or tobacco components are not covered by the deeming rule, but the devices and their component parts (batteries, digital displays, tanks, vials, and software) are clearly subject to regulation. Provisions for warnings about nicotine poisoning and child proof caps were proposed in separate legislation, yet as of this writing, such regulations had not been announced. Under the deeming rule, vapour devices have age requirements for sales of 18 plus years old, and restrictions on vending machine sales, both of which took effect 90 days after the regulation was published. Specified health warnings on product packaging and advertisements are to be in place by May 2018. As for marketing, free samples are prohibited, but vapour device products are exempt from the bans placed on other tobacco products for minimum pack size, self-service displays, non-tobacco (promotional) items, and event sponsorship. The most stringent regulation is the pre-market authorization required for all deemed products, a procedure that entails manufacturer registration, ingredient listings, harmful or potentially harmful product testing, clinical studies, and reporting standards. The pre-market authorization requirement will be phased in over a three year initial compliance period. Finally, any business that mixes or prepares vapour liquids (as do many vape shops), or modifies vapour devices, is subject to regulation as a manufacturer.

Lawsuits contesting vapour device regulation were swiftly filed by three individual companies (Tobacco Control Legal Consortium, 2016, June 24), and a joint filing was made by 11 trade associations (manufacturers, distributors, and retailers) (case 1:16-cv-01210, DC). U.S. Senator Ron Johnson questioned the regulations for vapour devices in a formal request for information on public health data and projections of the ruling's impacts on small businesses (Johnson, 2016, May 17).

NPF Content Structures

Table 7 below lists the number of claims in each document (N), and identifies the plots and the frequency (n) in which they appeared in the documents, followed by the claim identification numbers from the texts in Tables 3-6. Table 8 lists the characters by jurisdiction and frequency (supplemental Tables S5-S8 identify the claims in which the characters appeared).

Table 7

Plots by Report, Frequency, and Claim ID

Plots with Plot Category	QLD N=17		CAN N=27		EU N=17		US N=38	
	n	ID	n	ID	n	ID	n	ID
Vapour devices may expose users to health risks. Threat.	1	10	3	1, 5, 7	8	1, 4, 7, 8, 9,11, 13,14	6	11, 14, 15, 20, 34, 36
Vapour devices could impede tobacco control. Threat.	3	5, 6, 7	12	3, 12, 13 14, 15, 16 17, 18, 20 22, 23, 25	1	10	1	28
Vapour devices are unsafe/untrustworthy products. Threat.	4	9, 12, 16 17	3	2, 8, 19	2	5, 15	7	13, 21, 22, 23, 25, 26, 27
Vapour devices put youth at risk to start smoking. Threat.	3	3, 4, 14	2	4, 10	1	3	2	2, 37
Vapour devices are appealing to youth. Threat.	-		1	11	1	2	5	3, 4, 6, 7, 29
Vapour devices may produce second hand health risks. Threat.	2	8, 13	2	9, 21	-		2	12, 16
Vapour devices are a risk for poisoning. Threat.	1	11	1	6	-		5	17, 18, 19, 24, 30
Vapour devices put adults at risk to start smoking. Threat.	2	2, 15	3	24, 26, 27	-		-	
Vapour devices are not useful for cessation. Threat.	1	1	-		-		1	35
Vapour devices may lead to dual use with other combustible tobacco products. Threat.	-		-		-		5	1, 9, 10, 32, 38
Vapour devices are appealing to young adults. Threat.	-		-		-		2	5, 8
Vapour devices could aid cessation. Opportunity.	-		-		3	6, 12 16	1	33

Vapour devices are less harmful than tobacco products. Opportunity.	-		-		1	17	1	31

The documents presented 99 total claims that were framed with 13 plots, two of which were unique to the US document. The plots consisted of two overarching narratives of 11 threat plots and two opportunity plots. Nine threat plots were presented in at least two documents, and the US document narrated two unique threat plots. Opportunity claims made up only six of the 99 total claims.

The threat plots were dominant by both claim frequency and the number of plots. Overall, threat plots were narrated in 93 of the 99 claims: in13 of 17 EU claims, 36 of 38 US claims, and all of the claims in the Queensland and Canada reports. Four specific threat plots appeared in all four documents, and they comprise 60% of the total claims: exposing users to potential health risks, impeding tobacco control, functioning as innately unsafe products, and putting youth at risk to start smoking.

Five of the same characters were present in all four documents: the vapour device users, youth, tobacco control, vapour devices and the manufacturers. All four documents consistently presented vapour device users, youth, and tobacco control as victims, and vapour devices and manufacturers as villains. Only the US document positioned young adults as a specific victim. Vapour device users were presented as the predominant victims in the EU and US documents, while tobacco control was by far the most frequently mentioned victim in the Canada report. On the other hand, no single victim was the central focus of the Queensland report.

Claims in all four documents identified vapour devices as villains. They caused harm by being innately risky to the health of users and bystanders, and by impeding tobacco control. These threats were intrinsic to the vapour devices themselves.

Claims about the lack of safety and quality of vapour devices pointed to, but did not name, another villain: the vapour device manufacturers. Only the tobacco manufacturers were directly named as a villain, and only in the Canada report. The independent vapour device manufacturers were unnamed villains, shadow villains, who caused harm by their shoddy manufacturing of unsafe and untrustworthy products.

The independent vapour device manufacturers were one of three shadow villains. A second shadow villain who appeared in the Queensland and Canada reports was the vapour device user who exposed bystanders to second-hand vapour and impeded tobacco control by modeling smoking. The third shadow villain popped up in the Queensland report, the retailers who promoted smoking through their vapour device sales tactics. The NPF storyline analysis identified these unnamed shadow villains through their actions in the plots.

The vapour device made an appearance as a hero just four times in the EU report, only two times in the US document, and never acted positively as a hero in the Queensland and Canada reports.

Table 8

Characters and Roles by Report and Frequency

Character by Role	QLD	CAN	EU	US
Victim – vapour device user	5	9	10	20
Victim - youth	3	5	2	10
Victim – tobacco control	3	13	1	1
Victim - adults	2	3	-	2
Victim - bystanders	2	2	-	2
Victim - children	1	1	-	4
Victim - smokers	1	-	-	1
Villain – vapour devices	8	15	11	31
Villain - manufacturers	4	6	3	4
Villain – vapour device users	3	4	-	1
Villain – tobacco industry	-	4	-	-
Villain – retailers	2	-	-	-
Hero – vapour devices	-	-	4	2

Discussion

The following discussion seeks to answer these pertinent questions: What do the NPF content structures of plot and character reveal about the claims adopted by the regulatory bodies? What kinds of claims appear to have had the greatest traction in influencing the legislative outcomes? After discussing these questions, this section covers the strengths and limitations of the study.

NPF Content Structures

The homogeneity of the plots in the four documents is amazing. Four plots dominated the narratives, showing that the same claims of threat were being taken up, regardless of the level of government. Even though the four documents each contained a substantially different

quantity of text, whether 17 sentences (EU) or 29 pages (Canada), 11 plots encompassed 92 of the 99 total claims. This was an unexpected level of homogeneity of claims among such a diverse set of government structures.

The characters too demonstrated a large degree of homogeneity among the claims with five characters appearing in all the reports. Nevertheless, there were some notable divergences between the reports in their treatment of characters. For example, only the US specifically noted young adults in their policy discussions. Why it is unique to the US is unclear. Perhaps it is due to the number of tobacco prevalence studies conducted on this age group in the US, or perhaps it reflects a policy belief that young adults are as susceptible as youth to tobacco uptake. Another difference between the reports is that although they encompassed the same three victims (vapour device users, youth, and tobacco control), the characters received a differing amount of emphasis in each document, with the result that different victims received more attention in one report over another.

As for villains, vapour devices were far and away the dominant character in the claims. Yet there were three other villains who were not named, although they were visible by their actions in the risk plots. Why were vapour device manufacturers, retailers, and vapour device users (as villains) not directly named in the reports? Only the Canada report explicitly identified big tobacco as a source of threat, perhaps due to the anti-tobacco industry sentiments held by many advocates and politicians active in Canada's longstanding engagement in tobacco control. Otherwise, the documents' authors fail to directly name the independent vapour device manufacturers as the villains who, in actuality, created threats with their unsafe products and mislabeled liquids. We can only speculate that the Queensland, Canada, and EU committees were unfamiliar with the myriad of vapour device manufacturers, and so failed to name them. A

second shadow villain found only in the Queensland report was the tobacco retailers whose sales activities for vapour devices were identified as a source of threat to normalize and increase smoking. We conjecture that the retailers may have been shielded from being named as a villain through the legitimacy they hold as regulated tobacco sellers. The third unnamed villain was the vapour device user who exposed others to toxic second hand "smoke." Users were not identified as the agent of second hand exposure even though second hand vapour was identified as a policy problem. We have no guesses to offer as to why the users were not directly blamed for causing these exposures. Although these three shadow villain characters created policy problems with their activities, they escaped being named and identified as a source of threat.

Claims and Policy Outcomes

Queensland, Canada, the EU, and the US adopted different regulations for vapour devices. Having identified the claims as policy narratives, we now turn to our research question: how have these claims potentially influenced the resulting legislation?

The claims in the Queensland recommendation report, with eight threat plots and seven victims, narrated such a catastrophic story of threat from any vapour device that it seems it required swift regulation. The large number of victims in the narratives in the report likely transformed the claims into a persuasive set of stories, as victims show the extent of threat (Shanahan et al., 2011). As the government was facing the prospect of being unseated, it acted to protect the public against the threats posed by this novel, non-nicotine product by applying the current tobacco regulations.

The Canadian government, like the Queensland government, was preparing for an election that would potentially end their majority. However, unlike the Queensland government, it did not move forward with vapour device regulation. The claims in the Canada report focused

primarily on threats to tobacco control, an impersonal, abstract victim, rather than on threats to actual persons (users or youth). An impersonal victim may not have been compelling enough to legislators to warrant action.

Unlike the Canada report, the main threat plot in the EU report, harms to users, centered on actual persons. This threat was addressed with legislative provisions that regulated the content and packaging of vapour devices, and required the centralized reporting of adverse effects. Yet, despite the dominant stories of the threats from vapour devices, nicotine devices were not banned outright, but were limited with a cap on nicotine content. Perhaps the countervailing opportunity plot of reducing the harms of tobacco use, although narrated in only a handful of claims, helped persuade policy makers that it was reasonable to continue to permit nicotine devices, albeit as highly regulated. Perhaps the opportunity claims in the EU report may have helped nicotine vapour devices to escape the ban imposed on them by Queensland, Canada, and many other countries.

As in the EU, the US has opted to permit the sale of nicotine vapour devices, and this may likewise may have been supported by the opportunity plots (as few as they are) presented in the deeming rule document. On the other hand, the US adoption of a complicated (and costly) pre-market inspection and certification policy speaks to the most frequently narrated plot in the deeming rule, the claim that vapour devices were unsafe/untrustworthy products. With pre-marketing authorization allowing the sale of only approved (i.e., safe) products, the threat of vapour devices as an unsafe/untrustworthy product is averted.

In this study, we have identified the claims about vapour devices endorsed in four recommendation reports, and have examined how these claims may have influenced legislation in four jurisdictions. The opportunity plots of vapour devices as a cessation aid or a less harmful

product than tobacco, presented only in the EU and US documents, may have supported the regulated sale of nicotine vapour devices in those jurisdictions, whereas the claims of threat plots without opportunity plots in the Queensland and Canada documents may have helped to justify their ongoing bans on nicotine. In Queensland, the policy narratives containing a plethora of victims may have amplified the perceived threat of vapour devices. In Canada, the threat to tobacco control from vapour devices may not have been sufficiently persuasive to support regulation after the tabling of its recommendation report. Vapour devices in the EU recommendation report were represented primarily as a policy problem of harms to the users, and legislation contained provisions to limit risks to users. The US document most often presented vapour devices as unsafe/untrustworthy products, and it established an extensive pre-market testing and authorization process unique to the US. Thus, in every jurisdiction, the presence or absence of opportunity plots, and the emphasis on specific victims in the policy documents appear to have influenced the policy outcomes. Regardless of the level of influence exerted by the claims, it is clear that claims of threat have completely or almost completely dominated the political narratives around vapour devices in all four jurisdictions,

Strengths and Limitations

This study provides the first research that identifies the claims made about vapour devices taken up in the legislative process as they appeared in three recommendation reports and one regulatory ruling. One particular strength of this study is its examination of documents from regional, national, and trans-national governments. The homogeneity of the threat claims about vapour devices across the documents is all the more remarkable considering the diversity of the institutions where the claims were made.

NPF demonstrated particular efficacy for structuring this research and analyzing the data. First of all, it has a special utility for comparing documents with unequal quantities of text. Although the documents had substantially differing quantities of text material, the NPF framework was able to tease out plots and characters from the minimal amount of text in the EU report while compressing the much longer text in the Canada and US documents.

Another value of NPF is its more complex representation of the claims through plots and characters, as compared to the more commonly utilized method of word count content analysis. Furthermore, content analysis would not have revealed the shadow characters made visible through the NPF plot analysis, and, as a consequence, content analysis would have missed how some policy narratives obscured the actual sources of the policy problem.

Our study contributes two new forms of analysis to NPF: shadow characters and the threat/opportunity plot classifications. One addition to NPF is the concept of shadow characters, who are unnamed in the narrative text but are revealed as policy actors through their actions in the plot. The inclusion of shadow characters improves the ability of NPF to identify policy actors. Second, this study adds to the utilization of plots in NPF analysis. The development of plot analysis is sorely needed as only a few NPF studies have conducted one (Weible & Schlager, 2014). Plots as variables have been characterized as difficult to operationalize (Pierce et al., 2014), so we have illustrated the mechanics for how texts can be configured into standardized plot scripts. We think our strongest contribution to NPF is our introduction of the threat/opportunity plot categories. These categories provide a higher order classification for the comparison of plots and for the identification of the narrative thrust of policy documents. For NPF, the SWOT classification adds, we believe, to the generalizability of plot analysis, and the

identification of shadow characters has the potential to improve NPF's research gaze on policy actors.

This study has been conducted within three limitations. First, NPF is a relatively new methodology, so specific guidance on using the methodology is scarce. Another limitation of this study is that only English sources were analyzed. A cross-case analysis of plots and characters between countries with different languages could be hampered or even rendered impossible given irreconcilable linguistic or cultural content. Finally, this study was limited to the analysis of the policy narratives found in only one document for each jurisdiction, albeit the major referent of a recommendation report. Other documents, witness testimonies, the policy beliefs of the legislators, and/or narratives presented in other sources may have had an equal or even greater influence on the resulting legislation.

Conclusion

In the policy documents of Queensland, Canada, the EU, and the US, the dominant stories claimed that vapour devices were rife with potential threats, putting vapour device users, tobacco control, and youth at risk. The EU and US documents presented a few opportunities around the potential role of vapour devices in promoting cessation and reducing toxic exposures for smokers, but they were vastly outnumbered by the threat plots. The opportunities for vapour devices to function as a harm reduction strategy have been neglected in the legislative reports, and threats have been over-represented.

In reporting these results, we seek to alert those contesting or defending vapour device legislation as to what claims appear to have had traction in the regulatory arena. Claims about the perceived threats from vapour devices have almost completely subsumed any mention of vapour devices as a potential strategy for harm reduction. It seems unlikely that governments

would be inclined to consider the opportunity for vapour devices to provide public benefit when their recommendation reports focus so strongly on the claims of threats from the products. Although we have identified claims made about vapour devices, NPF analysis does not establish the truth or falsity of a story (Jones et al., 2014) – or a claim, and policy narratives may not in be in accord with the evidence (Shanahan, McBeth, & Jones, 2014). NPF authors have observed that "the power of a good story is likely to shape subsystem policy learning and outcomes, regardless of the available scientific information" (Shanahan et al., 2011, p. 549). Therefore, those seeking to influence the fractious debate around vapour devices should consider how to craft their evidence into more compelling stories.

Our study has demonstrated the potential of NPF to get to the heart of policy debates. To date, the debate over vapour devices in the regulatory arena has been heavily slanted to claims of risk and harm, as shown in the four jurisdictions examined here. Those who seek policies to facilitate vapour devices as a harm reduction strategy or as an alternative cessation treatment will need to more effectively present their evidence in the *agora narrans* if they are to change the current direction of regulation. The public health community and government bodies have a responsibility to carefully analyze the both the potential costs and benefits of this new class of nicotine products. So long as the narratives in the state arena about vapour devices are only stories of threats, any potential opportunity vapour devices may offer for tobacco harm reduction is automatically lost.

Youth Vaping: Evaluating Risks

R. O'Leary, T. Stockwell, M. MacDonald – in submission to *Journal of Adolescent Health*

The introduction of the e-cigarette has raised fears among healthcare providers and researchers concerning youth use of vapour products (vapourizers and liquids). First and foremost, vaping is deemed as a "gateway" to tobacco use by many clinicians and policy-makers (Dutra & Glantz, 2014; Klein, 2015; O'Leary, Borland, Stockwell, & MacDonald, 2017; Stanbrook, 2016; Stanwick, 2015), and it is one of the most popular theoretical models in the literature (Bullen, 2016). Another perceived risk is vaping leading to nicotine dependence (Gilreath et al., 2016; Rennie, Bazillier-Bruneau, & Rouëssé, 2016). There is another potential source of risk that has received little attention to date: vapourizers as a mode of administration of cannabis and other drugs. While these risks will continue to be debated, what data are available to evaluate them?

To start with, what is the sequence of initiation of vaping and smoking? Many in public health consider vapour devices a "starter product" for tobacco use (Bell & Keane, 2014). Some versions of the gateway theory predict that many youth who report using cigarettes or other tobacco products will also report having first used nicotine-based vapour products (Schneider & Diehl, 2016). Among youth dual-users, those who use both vapour and tobacco products, what product have they reported using first?

Nicotine consumption is generally considered the primary mechanism for youth vapour product use leading to cigarette or other tobacco use (Cahn & Berg, 2018; Echevarria & Sinha, 2017). Yet how common is non-nicotine vaping? Questions about non-nicotine vaping have rarely been included in youth surveys (Echevarria & Sinha, 2017; Greenhill, Dawkins, Notley, Finn, & Turner, 2016). Almost all researchers assume that youth are consuming nicotine when

vaping (Miech, Patrick, O'Malley, & Johnson, 2017). A more accurate assessment of the prevalence of youth at risk requires the identification of those who are actually using nicotine.

Another factor for the development of nicotine dependence is the frequency of use. This is a key question because any harms to the user may differ by the frequency of use: experimental, occasional, heavy sessional use, chronic use, and problematic (or compulsive) use (Riley & Pates, 2012). Delnevo, Gundersen, Manderski, Giovenco, and Giovino (2017) observe "there is a paucity of data on the validity of e-cigarette and hookah measures [for youth]" (p. 409). Very few studies on youth vaping measure regular use (Greenhill et al., 2016).

The most commonly used metric for defining a current user, including among youth, is any past-30-day use (Delnevo et al., 2017; Echevarria & Sinha, 2017). In North American and European countries, the youth population prevalence for past-30-day use have been surveyed at around 10%, plus or minus one point, for the United States (Jamal et al., 2017), Canada (Montreuil et al., 2017), and Wales (de Lacy, Fletcher, Hewitt, Murphy, & Moore, 2017); over 5% in France (Paris) (Dautzenberg, Berlin, Tanguy, Rieu, & Birkui, 2015); and around 3% in Great Britain (Eastwood et al., 2017) and Ireland (Babineau, Taylor, & Clancy, 2015). Yet studies measuring past-30-day use do not capture the differing frequencies of use in this population. How many youth reporting past-30-day use are vaping with a frequency of use that would signal a potential risk for nicotine dependence?

Finally, nicotine is not the only substance that can be vaped, and vaping as a mode of drug delivery is another potential source of risk for youth. Few surveys have been conducted on the prevalence of cannabis vaping (Fischer, Russell, & Tyndall, 2015), and cannabis researchers often ignore the mode of vaping (Mammen, Rehm, & Rueda, 2016). What about youth vaping other substances? Vapourizers can be a used for any number of heat-stable substances (Blundell,

Dargan, & Wood, 2017b). What data are available about the prevalence of youth vaping cannabis or other substances?

This systematic review reports data on youth vaping from peer-reviewed publications to assess these patterns of use:

(1) How often vaping precedes cigarette smoking among youth who have used both products;

(2) Whether non-nicotine vaping is a common mode of use;

(3) What proportions of infrequent users (1-2 days/ past 30 days) are included in prevalence data of past-30-day users;

(4) Whether some youth reporting vaping may be consuming cannabis or other drugs.

The precise answers to these questions will, of course, vary by country, year of the survey, and precise age and gender composition of samples. The dual purpose of this systematic review, however, is first to test the general validity of assumptions about the extent to which youth who vape are at risk for smoking uptake and nicotine dependence. The second goal is to alert healthcare providers and researchers to the potential risks of vaping as a mode of administration of cannabis and other drugs.

Method

The majority of the articles in this systematic review were retrieved from the library produced for the *Clearing the Air* project (MacDonald, O'Leary, Stockwell, Reist, & Clearing the Air project team, 2016), a meta-narrative review on the debate over vapour products for harm reduction. The library contains 2,323 publications on vapour products in peer-reviewed journals retrieved from 15 databases through February 8, 2017.

The initial literature search retrieved 417 articles on youth from the CTA Library with the keywords in the title or abstract of *youth, student (-university, –college), teen, young, child,* and *adolescent*. Articles not in English or French were reviewed with the English abstract (all non-English articles included an English abstract). Articles that were not empirical research were excluded.

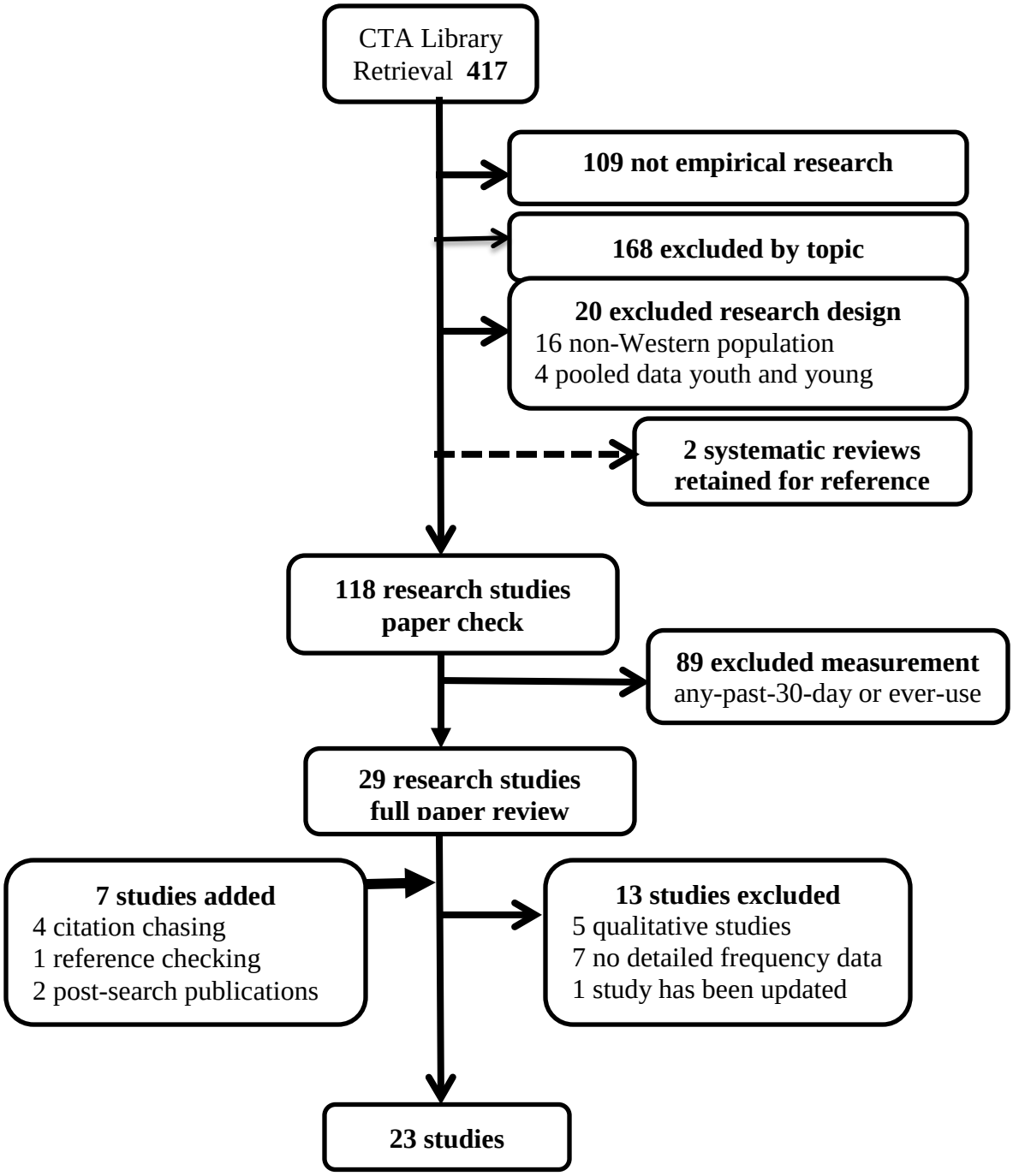
The empirical studies were reviewed by title and abstract to include those with findings on (1) sequence of initiation of vaping and smoking OR (2) non-nicotine use OR (3) frequency of vaping OR (4) vaping cannabis or other drugs. Studies with pooled data on youth and other age groups were excluded. Studies in non-Western locations were excluded to bracket out Asian cultural differences such as homosocial (male bonding) smoking (Kohrman, 2007) and the heavy stigmatization of female smoking (Xun, 2004). Cultural differences most likely influence youth patterns of vapour product use (Greenhill et al., 2016).

Next a paper check excluded studies that did not report a more detailed frequency than any past-30-day use or ever-use, and retained studies on non-nicotine or cannabis vaping. Twenty-nine studies were included. They were reference checked and citation chased in Google Scholar for both peer-reviewed and grey literature through June 25, 2017, adding five studies and one grey literature survey. Five qualitative studies were excluded because they did not report patterns of use data.

In the final selection, eight studies were excluded during data extraction, seven because the data was an average frequency of use, and one because the research project had been updated; the update was included. While conducting the review, two additional studies were identified during the first author's monthly surveillance of publications on vapour products

through October, 2017, and they were added to the review. The final count of included studies is 23. The inclusion/exclusion steps of the search process are presented in Figure 1.

Figure 1 Study selection flow diagram



The data extraction categories for the study tables were pre-defined as (1) the sequence of initiation of use, (2) non-nicotine prevalence, (3) the frequency of use, and (4) the prevalence of vaping cannabis or other substances. Research design, study year, prevalence data, and sub-group data for age and sex are included in the tables. Significance calculations and 95% confidence intervals (CI), when reported, are noted in the study tables.

The 23 studies identified, all surveys, were assessed for quality by the first author with the National Institute for Health and Care Excellence (NICE) 2012 Quality Appraisal Checklist. The tool rates studies as *higher quality* which are noted as [++], *acceptable quality* noted as [+], and weak studies noted as [-]. The final ratings were reviewed by the co-authors. Background articles were not assessed for quality. So that all available studies are included, no studies were excluded by their quality assessments, but the quality ratings are noted in the citations and should be considered when judging the evidence.

Literature Review

This section details the studies with data on the sequence of initiation, the prevalence of non-nicotine use, detailed frequency data, and cannabis vaping. The studies are summarized for each pattern of use, and the study table displays additional data. The evaluation of the data follows in the Discussion.

Sequence of initiation.

In eight surveys, two each from the US, Great Britain, and France, and one each from Wales and Poland (Table 1), a substantial majority of youth self-reported trying a tobacco product, primarily cigarettes, before vapour products.

The US surveys were conducted nearly two years before the other surveys, and each surveyed different age groups. One internet survey had nearly zero tobacco ever-users who

reported the vapour product as their first tobacco product (Soneji, Sargent, & Tanski, 2016 [-]). By defining a vapour product as a tobacco product, Morean, Kong, Camenga, Cavallo, and Krishnan-Sarin (2015 [+]) determined that 18.5% of vapour product ever-users had tried a vapour product first, but the researchers do not report on subsequent use of tobacco in this group.

Surveys in Great Britain and France reported that the great majority of students who have used both cigarettes and vapour products tried cigarettes first. In Great Britain, a small survey of 11-18 year olds reporting both vapour product and cigarette ever-use found that 10% tried a vapour product first (ASH UK, 2016, October [-]). In another survey in Great Britain, 8.2% of all students aged 11-18 had tried a vapour product before trying cigarettes (Eastwood et al., 2015 [+]). Researchers in France surveyed 12-19 year old students, and among those student who had tried both cigarettes and vapour products, 88.4% had tried tobacco first (Stenger & Chailleux, 2016 [+]), and conversely, 3.1% of tobacco ever-triers had tried a vapour product first (Dautzenberg, de Souza Moura, Rieu, Dautzenberg, & Birkui, 2016 [+]).

Two surveys present data on the sequence of use for youth who are current tobacco users. Among Welsh youth who were weekly smokers, 17.1% had tried a vapour device before tobacco (de Lacy et al., 2017 [+]). In Poland, 15.7% of past-30-day dual-users had used a vapour product first (Goniewicz et al., 2016 [-]).

Table 1

Sequence of Use of Vapour Products and Cigarettes/Tobacco

First Author, Year, Title	Study Design	Findings
ASH (2016) Use of electronic cigarettes among children in Great Britain. [-]	Smokefree GB Youth Survey 2016 online, aged 11-18. n=318 ever users	10% report trying EC before smoking a cigarette
Dautzenberg (2016) [The e-cigarette disrupts other consumptions in Parisian teenagers (2012-2014)] [+]	Cross-sectional survey, N=3279 students aged 12-19, comparing rates in 2012 with 2014. n=383 youth reporting first experimentation	Of those using tobacco, 3.1% used EC first.
de Lacy (2017) Cross-sectional study examining the prevalence, correlates and sequencing of electronic cigarette and tobacco use among 11-16-year olds in schools in Wales. [+]	2015 survey, students aged 11-16 (N=32,479), aged 15-16 (n=5353). Past-30-day use: 4.4% aged 11-16 9.0% aged 15-16.	For n=877 weekly smokers, 17.1% used EC first.
Eastwood (2015) Electronic cigarette use in young people in Great Britain 2013-2014. [+]	2013-2014 two wave cross-sectional online study, N=1952, aged 11-18. 8.2% ever try EC.	Of EC ever triers, 69.8% (95% CI [62.2,77.3]) smoked cigarette first, 8.2% [4.1,12.2] smoked EC first, and 18.3% [11.7, 24.8] have never smoked a cigarette.
Goniewicz (2016) Dual use of electronic and tobacco cigarettes among adolescents: a cross-sectional study in Poland. [-]	Survey of N=1785 students aged 16-18 conducted Dec. 2013 – Feb. 2014. Past 30 day EC use 29.6%.	15.7% of dual-users tried EC first.
Krishnan-Sarin (2015) E-cigarette use among high school and middle school adolescents in Connecticut. [+]	2013 survey n=3,614 high school students and n=1,166 middle school students. 1.5% middle school and 12.0% high school past-30-day use	n=912 EC ever users high school 18.5% EC first "tobacco" product tried, but no data on subsequent products used.
Soneji (2016) Multiple tobacco product use among US adolescents and young adults. [-]	2012-2013 web-based survey, N=927 ever tobacco user, n=32 aged 10-14, and n=201 aged 15-17.	EC as first tobacco product used, 0% for ages 10-14, and 0.5% for ages 15-17.
Stenger (2015) [Survey on the use of electronic cigarettes and tobacco among children in middle and high school.] France [+]	2014 survey of N=3319 middle and high school students. 56% ever tried EC; 3.4% daily EC use.	For students trying both cigarettes and vapour products, 88.4% used tobacco before trying EC.

Non-nicotine use.

Researchers address the use of non-nicotine containing liquids in nine surveys (Table 2), four from the US, and one each from Sweden, Canada, Finland, France, and Switzerland. The measurements differ widely, with some findings based on ever-users, and one study reporting the last substance vaped. The data should not be construed to mean that non-nicotine use precludes nicotine use, as an individual could be using some products that contain nicotine and others that do not (see Morean et al., 2015 [+]; Pepper et al., 2017 [-] in Table 3). In addition, other research has determined that some vapour products labeled as not containing nicotine do, in fact, contain trace amounts (Goniewicz et al., 2015).

In the US, before the federal prohibition in August 2016 on the sale of vapour products to minors under 18, two surveys of high school past-30-day users indicated that 22% (Morean et al., 2015 [+]) and 28.5% (Morean, Kong, Cavallo, Camenga, & Krishnan-Sarin, 2016 [+]) were consuming non-nicotine products. A convenience sample of US 15-17 year old past-30-day users reported their "usual" liquid, and 29.2% endorsed non-nicotine and another 38.6% said "both" (Pepper et al., 2017 [-]). Rates of non-nicotine liquid as the last substance vaped are even higher: 44% for more frequent users and 66% for less frequent users in US grade 12 (Miech et al., 2017 [+]).

In addition to the US rates of non-nicotine use, in two countries with legal nicotine vapour products, the rates of youth vaping of non-nicotine products is 38% of Swedish ever-users, (Geidne, Beckman, Edvardsson, & Hulldin, 2016 [-]), and 42.2% of French smokers who are ever-users (Stenger & Chailleux, 2016 [-]). In Switzerland and Canada non-nicotine containing devices are legal and nicotine containing vapour products are illegal, and youth in these two countries reported nearly equivalent and high rates of non-nicotine use, 70.2% (Surís,

Berchtold, & Akre, 2015 [-]) and 72% (Hamilton et al., 2015 [-]) respectively. These high rates are for ever-users who are more likely to try non-nicotine products, and for youth whose access to nicotine products is restricted by regulations.

Cigarette smoking status appears to exert a strong influence on whether youth use vapour products that contain nicotine. In France, 92.9% of ever-users who were non-smokers consumed non-nicotine containing products, compared to 42.2% of dual-users (Stenger & Chailleux, 2016 [-]). In Finland, 52.4% of never-smoking ever-VP-users used non-nicotine liquids compared to 25.2% of ever-cigarette-triers (Kinnunen, Ollila, Lindfors, & Rimpela, 2016 [-]).

Table 2

Prevalence of Non-Nicotine Use

First author, year, title	Study design, population	Prevalence of non-nicotine use
Geidne (2016) Prevalence and risk factors of electronic cigarette use among adolescents: Data from four Swedish municipalities. [-]	2014 survey N=665 students grade 9, aged 15-16. 26% ever-use VP, 22.4% female, 29.2% male ($p<.05$).	50% ever-users used nicotine 38% ever-users used non-nicotine
Hamilton (2015) Ever use of nicotine and non-nicotine electronic cigarettes among high school students in Ontario, Canada. [-]	2013 **Ontario Student Drug Use and Health Survey**, random half sample of N=2,892 high school students, aged ≤ 19. 14.6% (95% CI [12.3, 17.3]) ever-use, 10.3% [8.0-13.1] female, 18.6% [14.9, 23.1] male ($p<.001$)	72% of ever-users vaped without nicotine.
Kinnunen (2016) Changes in electronic cigarette use from 2013 to 2015 and reasons for use among Finnish adolescents. [-]	2015 **Adolescent Health and Lifestyle Survey,** mailed surveys, N=6698, (response rate 41%) students aged 12-18. Females 24.8% ever-use, Males 32.8% ever-use ($p<.05$).	Cig triers: 25.2% Never cig triers: 52.4% Ever VP users: 29.7 Non-nicotine use.
Krishnan-Sarin (2015) E-cigarette use among high school and middle school adolescents in Connecticut. [+]	2013 survey n=3,614 high school students and n=1,166 middle school students. 1.5% middle school and 12.0% high school past-30-day use	"Typical use" by past-30-day user 22.0% non-nicotine 17.1% both nicotine and non-nicotine.
Meich (2016) What are kids vaping? Results from a national survey of US adolescents. [+]	2015 **Monitoring the Future** survey, 12th (n=4591), 10th (n=5379), and 8th (n=5013) grade students. Prevalence is for last substance vaped. For ever-users, 69.85% (SE 2.40) females used non-nicotine, 61.00% (2.23) males used non-nicotine ($p<.05$).	Grade 12: 1-5 use past-30-days, non- nicotine 66.26% (SE 2.57); 6+ use past-30-days, non-nicotine 44.55% (4.28)* Grade 10: 65.57% (2.71); 49.98% (4.16)* Grade 8: 64.26% (3.75); 59.61% (5.37) *$p<.05$ 1-5 users compared to 6+ users
Morean (2016) Nicotine concentration of e-cigarettes used by adolescents. CT US [+]	2014 survey (N=513 past-30-day-users) 4 high schools and 2 middle schools in Connecticut.	28.5% non-nicotine use among past-30-day users.
Pepper (2017) Risk factors for youth e-cigarette 'vape trick" behavior. US [-]	Online survey (date not reported) N=1,729, aged 15-17, English-speaking, past-30-day use	"usual" liquid 27.3% nicotine 29.2% without nicotine 38.6% both 4.8% not sure
Stenger (2016) [Survey on the use of electronic cigarettes and tobacco among children in middle	2014 survey of N=3319 middle and high school students. Ever-use 59.9% males, 49.3% females	Non-nicotine rates: 92.9% of non-smoker ever-user 42.2% of smoker ever-user

and high school] France [-]	[significance not reported]	
Suris (2015) Reasons to use e-cigarettes and associations with other substances among adolescents in Switzerland. [-]	2014 internet survey, N=621, aged 16, French-speaking. Used several times, n=136, and "regular users" (undefined) n=12 (2%),	70.2% used non-nicotine.

Frequency of use.

In 10 surveys (Table 3) researchers measured the frequency of vaping in greater detail than past-30-day use, six from the United States (US), and one each from Finland, France, Poland, and Wales. Researchers examining two US surveys (three studies) of high school students report the same figure for occasional use: 44% of past-30-day users were vaping only once or twice a month (Neff et al., 2015 [++]; Patrick et al., 2016 [+]; Warner, 2016 [++]). In another US survey combining middle and high school students, 47% of past-30-day users reported use on one or two days (Villanti et al., 2017 [++]).

Fewer dual-users had a 1-2 days a month frequency of use compared to vapour-product-only users (Demissie, Everett Jones, Clayton, & King, 2017 [++]; Goniewicz et al., 2016 [-]), while another study found equal frequency (Villanti et al., 2017 [++]). In one US study, 29.2% of high school dual-users with past-30-day use were vaping once or twice a month (Demissie et al., 2017 [++]) compared to 44% all past-30-day users. In Poland, where prevalence rates are the highest, among past-30-day users, 51.9% of dual-users and 71.9% of vapour-product-only users reported less than weekly use (Goniewicz et al., 2016 [-]).

Table 3

Detailed Frequency of Past-30-Day Use

<table>
<tr><th>First author, year, title, quality rating</th><th>Study design, population</th><th>Frequency among past-30-day-users or total population</th></tr>
<tr><td>de Lacy (2017) Cross-sectional study examining the prevalence, correlates and sequencing of electronic cigarette and tobacco use among 11-16-year olds in schools in Wales. [+]</td><td>2015 survey, students aged 11-16 (N=32,479), aged 15-16 (n=5353).
Past-30-day use:
4.4% aged 11-16
9.0% aged 15-16.</td><td><table><tr><th>Days of VP use</th><th>Total pop. 11-16</th><th>Total pop. 15-16</th></tr><tr><td>< Weekly</td><td>1.8</td><td>3.3</td></tr><tr><td>Weekly</td><td>1.3</td><td>2.4</td></tr><tr><td>Daily</td><td>1.4</td><td>3.3</td></tr></table></td></tr>
<tr><td>Demissie (2017) Adolescent risk behaviors and use of electronic vapor products and cigarettes. US. [++]</td><td>2015 US Youth Risk Behavior Survey, N=15,624, high school students.
15.8% (95% CI [14.2, 17.5]) past-30-dayVP-users,
15.4% [13.8-17.1] female,
16.3% male [14.1-18.7].

7.5% [6.5, 8.8] past-30-day dual –users, 6.7% [5.6-8.1] female,
8.3% [7.1-9.6] male . (p=.04)</td><td><table><tr><th>Days of VP use</th><th>VP only users</th><th>Cig+VP dual-users</th></tr><tr><td>1-2</td><td>55.6%</td><td>29.2%</td></tr><tr><td>3-5</td><td>19.4%</td><td>22.0%</td></tr><tr><td>6-9</td><td>9.1%</td><td>14.7%</td></tr><tr><td>10-19</td><td>7.5%</td><td>15.3%</td></tr><tr><td>20-30</td><td>3.1%</td><td>5.8%</td></tr><tr><td>Daily</td><td>5.3%</td><td>13.0%</td></tr></table></td></tr>
<tr><td>Goniewicz (2016) Dual use of electronic and tobacco cigarettes among adolescents: A cross-sectional study in Poland. [-]</td><td>Dec 2013/Feb 2014 survey of N=1785 students aged 16-18.
29.6% (n=528) past-30-day-user.</td><td><table><tr><th>Days of VP use</th><th>VP only users</th><th>Cig+VP dual-users</th></tr><tr><td>< Weekly</td><td>71.9%</td><td>51.9%</td></tr><tr><td>Few /week</td><td>11.5%</td><td>21.3%</td></tr><tr><td>Daily</td><td>12.2%</td><td>26.2%</td></tr></table></td></tr>
<tr><td>Kinnunen (2016) Changes in electronic cigarette use from 2013 to 2015 and reasons for use among Finnish adolescents. [-]</td><td>2015 Adolescent Health and Lifestyle Survey, mailed surveys (N=6698, response rate 41%) students aged 12-18.</td><td><table><tr><th>Age</th><th>Male pop.</th><th>Female pop.</th></tr><tr><td>14</td><td>2.6 < weekly
0.6 weekly+
0.6 daily</td><td>2.4 < weekly
0.8 weekly+
0.1 daily</td></tr><tr><td>16</td><td>7.1 < weekly
1.9 weekly+
1.3 daily</td><td>4.9 < weekly
1.0 weekly+
0.1 daily</td></tr><tr><td>18</td><td>5.4 < weekly
0.9 weekly+
3.9 daily</td><td>4.0 < weekly
1.1 weekly+
0.5 daily</td></tr></table></td></tr>
<tr><td>Neff (2015) Frequency of tobacco use among middle and high school students—United States, 2014. [++]</td><td>2014 US National Youth Tobacco Survey N=22,007 [Overall prevalence of past-30-day-use not reported.]</td><td><table><tr><th>Days of VP use</th><th>Middle school [95% CI]</th><th>High school [95% CI]</th></tr><tr><td>1-2</td><td>54.5% [49.4, 59.3]</td><td>45.4% [41.9, 49.0]</td></tr><tr><td>3-5</td><td>17.3% [13.7, 21.6]</td><td>16.2% [14.0, 18.5]</td></tr><tr><td>6-9</td><td>9.2% [7.0, 12.0]</td><td>12.0% [10.0, 14.3]</td></tr></table></td></tr>
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<tr><td></td><td></td><td>
<table>
<tr><td>10-19</td><td>7.3%
[5.2, 10.1]</td><td>10.9%
[9.1, 13.0]</td></tr>
<tr><td>20-30</td><td>3.9%
[unreliable]</td><td>5.8%
[4.5, 7.5]</td></tr>
<tr><td>daily</td><td>7.9%
[5.4, 11.4]</td><td>9.7%
[7.5, 12.5]</td></tr>
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<tr><td>Patrick (2016) Self-reported reasons for vaping among 8th, 10th, and 12th graders in the US: Nationally-representative results. [+]</td><td>2015 Monitoring the Future survey N=4,066, 8th, 10th, and 12th graders. 14.1% (n=574) past-30-day use.</td><td>45.5% (n=261) use 1-2 days a month [other measure 3+ days/month]</td></tr>
<tr><td>Pepper (2017) Risk factors for youth e-cigarette ‘vape trick” behavior. US [-]</td><td>Online survey (date not reported) N=1,729, aged 15-17, English-speaking, past-30-day use</td><td>19.0% “rarely” (not defined)
48.7% “some days” (not defined)
32.3% every day</td></tr>
<tr><td>Stenger (2016) [Survey on the use of electronic cigarettes and tobacco among children in middle and high school] France [+]</td><td>2014 survey of N=3319 middle and high school students. Ever-use 59.9% males, 49.3% females [significance not reported]</td><td>3.4% of ever-users are daily users</td></tr>
<tr><td>Villanti (2017) Frequency of youth e-cigarette and tobacco use patterns in the United States: Measurement precision is critical to inform public health. [++]</td><td>2014 National Youth Tobacco Survey N=22,007 middle and high school students. 9.3% [CI 8.0, 10.9] any past-30-day use.</td><td>Total population prevalence
<table>
<tr><td>Days of use</td><td>All VP users</td><td>Exclusive VP</td></tr>
<tr><td>1-2</td><td>4.4%</td><td>2.2%</td></tr>
<tr><td>3-5</td><td>1.5%</td><td>0.5%</td></tr>
<tr><td>6-9</td><td>1.1%</td><td>0.3%</td></tr>
<tr><td>10-19</td><td>1.1%</td><td>0.2%</td></tr>
<tr><td>20-29</td><td>0.5%</td><td>0.1%</td></tr>
<tr><td>All 30</td><td>0.9%</td><td>0.1%</td></tr>
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</td></tr>
<tr><td>Warner (2015) Frequency of e-cigarette use and cigarette smoking by American students in 2014. [++]</td><td>2014 Monitoring the Future survey N=7,915 US high school 12th grade students. 17% (n=1358) past-30-day-use. [percentage calculated from Table 1]</td><td>
<table>
<tr><td>Days of use</td><td>n</td><td>% of past-30-day-users</td></tr>
<tr><td>1-2</td><td>601</td><td>44%</td></tr>
<tr><td>3-5</td><td>234</td><td>17%</td></tr>
<tr><td>6-9</td><td>163</td><td>12%</td></tr>
<tr><td>10-19</td><td>140</td><td>10%</td></tr>
<tr><td>20-30</td><td>220</td><td>16%</td></tr>
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Cannabis vaping.

Five studies (Table 4) contain data on youth cannabis vaping, four from the US, and one from Canada. The measures differ between the studies. In US state surveys, researchers have estimated the population prevalence of high schoolers ever-vaping cannabis at 5.4% in Connecticut (Morean et al., 2015 [-]) and 11.5% in Florida (Eggers et al., 2017 [-]). Among US

12th grade students with past-30-day-cannabis use, 9.6% (95% CI [6.1, 13.1]) stated that they usually used vapourizers for cannabis (Johnson et al., 2016 [++]). In the Monitoring the Future Survey, between 5%-6% of US 12th graders, past-30-day vapourizer users, indicated that last substance they vaped was cannabis (Miech et al., 2017 [+]). For Canadian high school students, 8.2% reported vaping cannabis in the past year (Mammen et al., 2016 [-]). The design of these surveys does not capture how many youth were solely vaping cannabis, or vaping cannabis and other liquids, nicotine or non-nicotine.

Table 4

Prevalence of Cannabis Vaping

<table>
<tr><th>First author, year, title, country</th><th>Study design, population</th><th>Prevalence of cannabis vaping</th></tr>
<tr><td>Eggers (2017) Youth use of electronic vapor products and blunts for administering cannabis. US [-]</td><td>2015 Florida Youth Tobacco Survey N=12,320 middle and high school students. Question on the use of marijuana oil/hash oil.</td><td>3.4% ever-vape middle school,
3.1% female (95% CI [2.5, 3.8])
3.8% male [3.1,4.6] (NS)
11.5% ever-vape high school
10.0% female [8.9, 11.2]
13.1% male [11.8, 14.5] (NS)</td></tr>
<tr><td>Johnson (2016) Usual modes of marijuana consumption among high school students in Colorado. US [++]</td><td>2013 Healthy Kids Colorado Survey (pre-legalization) high school students N=25,197, 19.7% (95% CI [18.7, 20.6], n=2,637) past-30-day cannabis use
17.7% [16..6, 18.8] female
21.5% [20.2, 22.9] male (p<.0001)</td><td>“usual mode of use”
past-30-day cannabis users
9th grade 3.7% (95% CI [2.0, 5.4])
10th grade 5.2% [2.5, 8.0]
11th grade 5.8% [3.7, 7.9]
12th grade 9.6% [6.1, 13.1]
Total 6.2% [4.2, 8.2]
3.1% [2.0, 4.1] female
8.8% [5.9, 11.6] male
(OR 3.1 [2.2, 4.5])</td></tr>
<tr><td>Mammen (2017) Vaporizing cannabis through e-cigarettes: Prevalence and socio-demographic correlates among Ontario high school students. Canada [-]</td><td>2015 Ontario Student Drug Use and Health Survey, Random half sample n=3,171 grades 9-12. Question on vaping cannabis, hash oil, liquid, and wax.</td><td>8.2% past-year use.
6.0% female
9.6% male (p< .05)</td></tr>
<tr><td>Meich (2016) What are kids vaping? Results from a national survey of US adolescents. [+]</td><td>2015 Monitoring the Future survey, 12th (n=4591), 10th (n=5379), and 8th (n=5013) grade students. <u>Prevalence is for cannabis (plant or oil) as the last substance vaped</u>. For ever-VP-users, 6.12% (SE 0.82) last vaped cannabis, 5.03% (1.01) female, 6.76% (1.03) males (NS)</td><td><table><tr><th>Grade</th><th>1-5 VP use in past-30-days, last use cannabis</th><th>6+ VP use in past-30- days, last use cannabis</th></tr><tr><td>12</td><td>5.01% (SE 2.57)</td><td>5.69% (1.86)</td></tr><tr><td>10</td><td>9.87% (2.39)</td><td>6.98% (1.70)</td></tr><tr><td>8</td><td>9.71% (2.62)</td><td>12.26% (3.61)</td></tr></table></td></tr>
<tr><td>Morean (2015) High school students' use of electronic cigarettes to vaporize cannabis. US [-]</td><td>2014 survey, N=3847 CT high school students. 5.4% of all students had ever-vaped cannabis as hash oil, wax, or dried leaves.</td><td>18.4% of ever-cannabis-users had vaped cannabis.
26.5% of ever-VP-users had vaped cannabis.</td></tr>
</table>

Discussion

In this section the patterns of use are evaluated to understand the risks for youth vaping to lead to tobacco use and nicotine dependence, and the risks for other drug use. The section closes with a discussion of the strengths and limitations of this review.

Risks for tobacco use and nicotine dependence.

What portion of youth initiate tobacco use after first trying vapour products? The sequence of initiation was cigarettes or tobacco first for 80% to 90% and more of youth vapour product ever-users. The handful of studies available indicates that for the great majority of youth, tobacco experimentation preceded vapour device use, and not the other way around.

Contrary to current assumptions, youth are commonly vaping non-nicotine liquids. Miech et al. (2017 [+]) observe that "nicotine came in a distant second place among youth who had used a vaporiser" (p. 4). Two surveys indicate a lower but appreciable prevalence of non-nicotine vaping: 22.0% (Morean et al., 2015 [+]) and 28.5% (Morean et al., 2016 [+]) for exclusive non-nicotine use among US students with past-30-day use.

Therefore, the assumption that all youth vaping involves nicotine over-inflates the number of youth actually consuming nicotine. Using the prevalence rates from the two studies above, based on the 2016 NYTS prevalence of 11.3% past-30-day use (Jamal et al., 2017), the over-estimation of nicotine exposure for US high school students with past-30-day use is 28% to 41%. The past-30-day metric over-represents the prevalence of youth nicotine use in other countries as well (see Table 2).

Non-nicotine vaping, in and of itself, may have few risks. A transition to smoking is not impossible, but unlikely (Etter, 2017). Problematic use is probably rare. "If adolescents are ever using flavored non-nicotine e-cigarettes, then this behavior is not necessarily problematic, aside

from any potential risks posed by other constituents in the vapor" (Greenhill et al., 2016, p. 618). The toxicological profile of vapour products is not risk free, but it is substantially lower than the toxicological risks from cigarettes (Drope et al., 2017; O'Leary, MacDonald, Stockwell, & Reist, 2017).

Having shown that the main trajectory of use is from smoking to vaping, and that an appreciable number of youth are not consuming nicotine, how can these data be reconciled with studies demonstrating a high association between vaping and smoking (Soneji et al., 2016)? Dr. Etter, an established tobacco researcher, argues that "even if there was a gateway effect, it may explain only a small part of smoking, compared to common vulnerabilities" (Etter, 2017, p. 5). The common liabilities model proposes that youth at risk for cigarette smoking are also at risk for vaping. The assumption is that "cigarette and e-cigarette use co-occur" (Pentz et al., 2015, p. 77). Some of these risks are psycho-social factors such as perceived stress (Leventhal et al., 2017), risk-taking propensity (Owotomo, Maslowsky, & Loukas, 2017), and family members and peers who smoke (Pentz et al., 2015). Hammond et al. (2017), examining their findings of a strong association between vaping and smoking, state that "it is highly plausible that 'common factors' account for a substantial proportion of increased cigarette-smoking initiation among e-cigarette users" (p. E1135).

Nevertheless, the common liabilities hypothesis is hard to test because youth personality traits are difficult to measure, and can change over time (Drope et al., 2017; Etter, 2017). The constellations of risk behaviours are complex as dual-users and single-product users have similar odds of risk for some behaviours (for example, truancy), but not for many others (for example, substance use) (Kristjansson, Mann, Smith, & Sigfusdottir, 2017; McCabe, West, Veliz, & Boyd, 2017). In one study, cigarette-only users and dual-users appear to be at much greater risk for

alcohol or substance use than vapour-product-only users (McCabe et al., 2017). The patterns of use data in this review are not the right variables to examine the common liabilities hypothesis.

One last observation on the fears that vaping nicotine can be a "gateway" to smoking cigarettes. Such fears would be supported if the prevalence of tobacco users increased as the prevalence of vaping nicotine has increased, or if the rate of decline in tobacco use were to decrease (Etter, 2017). Fortunately, this has not occurred. The great news is that youth tobacco use has dropped dramatically in the US. The prevalence rate of youth who have used 100 cigarettes lifetime and reporting any-past-month smoking has fallen from 11.9% in 2000 to 2.6% in 2015, and daily smokers have dropped from 6.0% in 2000 to 1.0% in 2015 (Drope et al., 2017). Were US youth tobacco use rates in rapid decline before 2010 when vapour products were introduced? No. The US Centers for Disease Control found little overall decline in tobacco use among middle and high school students from 2006 to 2009, stating "the current rate of decline in tobacco use is relatively low" (Arrazola, Dube, Kaufmann, Caraballo, & Pechacek, 2010, p. 1066). The gateway hypothesis has shown little predictive power for the steep decline in US youth smoking prevalence subsequent to the introduction of vapour products, and the hypothesis is at odds with the data showing that smoking preceded vaping for the great majority of dual-users.

What are the possible risks of nicotine dependence for youth vaping nicotine? Recent evidence indicates that vaping carries no additional risk for future nicotine dependence or smoking. Seyla et al. (2018) followed the smoking trajectories of 1007 Chicago US 9th and 10th grade students (79.7% retention, n=299 any past-30-day vapour product users) for eight years, and found that any past-30-day vapour product use was not significantly correlated with future smoking or nicotine dependence. The researchers conclude that "e-cigarette use did not predict

later conventional smoking and nicotine dependence [and] raises doubts about their hypothesized effects on tobacco use" (p. 330). More research is necessary to confirm these preliminary indications that vaping carries little or possibly no risk of nicotine dependence.

For further consideration of what frequencies of nicotine vaping may pose a risk for nicotine dependence, the trajectories of youth vapour product use may be similar to the trajectories of youth cigarette smoking. In three multi-year longitudinal studies, youth smoking at low frequencies very rarely escalated their use over time. Dutra et al. (2017) tracked 8,791 smokers from ages 12 to 16 at baseline for 15 years, and divided them into five trajectory groups. The lowest frequency group, the Experimenter group, smoked an average of 1.2 days per month, and they did not increase frequency over the 15 year study period, and only 2.0% ever progressed to daily smoking. The next higher frequency group smoked 9 days a month, and 48.4% progressed to daily smoking. Another study did not find any escalation of smoking by youth who smoked under 10 cigarettes a month (N=998), following them from 12 to 23 years old (Nelson, Van Ryzin, & Dishion, 2014). A study by Riggs et al. (2007) tracked 1,017 smokers from age 12 to 28, and identified the risk for nicotine dependence at a frequency of two to four cigarettes a week. Vaping nicotine once or twice a month may have similarly negligible risks for progression to more frequent use and nicotine dependence.

The patterns of use shed light on the risks of vaping leading to tobacco use and nicotine dependence. The dominant sequence of initiation is from tobacco to vaping. Non-nicotine vaping is common, and youth rates of tobacco use are dropping. All these indicators challenge the claim that vaping leads to smoking. As for nicotine dependence, half or more are youth who report vaping in the past-30-days are doing it once or twice a month, a pattern of use that most likely has a very low risk for nicotine dependence.

Risks for other drug use.

As the data display, nicotine is not the only substance that youth can be vaping. There is little robust evidence on the prevalence of youth cannabis vaping. The one strong Colorado (US) survey (Johnson et al., 2016 [++]) posts a high school population prevalence of 19.7% past-30-day cannabis use, of which 6.2% (95% CI [4.2, 8.2]) endorsed vaping as their "usual mode of use." This would place the population prevalence of youth cannabis vaping at just over 1% in a state that at the time of the survey was about to legalize recreational cannabis.

Cannabis vaping has potentially mixed influences on health risks for youth. Vaping cannabis may reduce exposure to combustion toxicants (Borodovsky, Crosier, Lee, Sargent, & Budney, 2016), and could possibly displace tobacco-based modes of cannabis consumption, such as blunts or mulling (Gartner, 2015; Giroud et al., 2015; Hindocha, Freeman, Winstock, & Lynskey, 2016). On the other hand, some researchers are voicing concerns about vaping increasing youth cannabis use (Blundell et al., 2017b; Budney, Sargent, & Lee, 2015; Giroud et al., 2015). No figures are available on the number of youth using vapourizers exclusively for cannabis. Certainly some vaping by youth involves consuming cannabis, not nicotine.

No youth studies have checked for vaping other drugs. This is a serious shortcoming. Commercial manufacturers are producing cartridges pre-filled with synthetic cannabinoids (Castellanos & Gralnik, 2016), and synthetic cannabinoids can be consumed in vape pens (Giroud et al., 2015). Prescription opioids (Gasior, Bond, & Malamut, 2016) including fentanyl (Blundell et al., 2017b), methamphetamine, cocaine, heroin, dimethyltryptamine (DMT), and bath salts (cathinones) all can be vaped, and numerous websites show how to modify vapourizers for consuming them (Giroud et al., 2015).

Two studies of adults have inquired about vaping other substances. In an online survey of 2,501 adults (mean age 46 ± 17) in the UK, 9.4% reported vaping recreational drugs, notably synthetic cannabinoids ("spice") (Blundell, Dargan, & Wood, 2017a). A survey of college students who were vapour product ever-users (n=1,542) found 6.94% (n=107) reporting vaping other drugs, primarily cannabis, although a number of students declined to identify which substances they had vaped (Kenne, Fischbein, Tan, & Banks, 2017). It is likely that some youth are vaping other drugs, but the prevalence of this practice is unknown (Blundell et al., 2017b).

Strengths and weaknesses.

This systematic review retrieved and evaluated data on four patterns of vapour product use: sequence of initiation, non-nicotine use, frequency of use, and cannabis vaping. On the positive side, this review is tightly focused on youth, without any admixture of data from young adults. No studies were excluded so that all available data were reported, an important consideration in this fraught field of inquiry. Finally, the research design produced an exhaustive search, kept up-to-date through citation chasing and ongoing surveillance of the literature.

Some limitations for this review arise from the state of the research. Data are scarce for detailed frequencies of vapourizer use and prevalence rates of non-nicotine or cannabis use. As for the studies themselves, 12 of 23 were rated as weak, and 13 are US studies with only five surveys from non-English speaking countries. In addition, due to the mismatch of measures in the various studies, comparing and synthesizing data across studies was not always feasible.

Another limitation is the confounding impact of vapour product regulations on patterns of use. Different countries and localities have different regulations for vapour products, and they can change over time. Jurisdictional regulations such as a ban on nicotine, age restrictions for purchase, and recreational cannabis laws would be expected to influence the prevalence of

vaping and the substances that youth consume. This makes it difficult to generalize findings, so often the discussion has been limited to one country, mainly the US.

Finally, other sources of risk have not have been covered here, such as the effects of nicotine on adolescent development. Other potential risks may not have been identified, for example, the quantity of use. The focus of this review is limited to providing evidence from data on four patterns of vapour product use – they do not cover all possible risks.

For future research, better measurements would improve public health population surveillance of vaping (Amato, Boyle, & Levy, 2016). Villanti et al. (2017) call for improved frequency and intensity measurements. Pearson et al. (2017) have created a set of items for measurement of adult vapour product use, and recommend that youth surveys apply some of the same metrics. Echevarria and Sinha (2017) propose that a collaboration of stakeholders develop a set of core variables for research on youth vapour product use. Questions about substance use and a detailed measurement of the frequency of use should be standard.

Summary and Implications

The goal of this review is to "move forward in understanding the extent to which e-cigarettes pose…a risk to adolescent public health" (Greenhill et al., 2016, p. 618). Some risks appear to have been overstated, while others have not been sufficiently studied. The image of tobacco-naïve youth lured to smoking by vaping is contradicted by the data showing the great majority of dual-users started with tobacco, not vapour products. The estimates of the number of youth consuming nicotine are greatly exaggerated because researchers either assume nicotine is always used, or fail to ask about non-nicotine use. Approximately half or more of youth who report past-30-day use are vaping only once or twice a month, a pattern of use unlikely to lead to

nicotine dependence. This means that far fewer youth are at risk for smoking or nicotine dependence than indicated by the prevalence of past-30-day users.

On the other hand, the risks to youth from vaping as a mode of administration of other drugs have received little attention. Some youth are vaping cannabis, but the risks are not understood, and vaping might possibly have a harm reduction potential for displacing tobacco-based consumption. A few youth may be vaping other substances, but researchers to date have failed to investigate this potentially risky mode of use among youth.

Be aware that youth vaping may be in decline. The rates of any past-30-day vaping for US high school seniors dropped from 16.3% in 2015 to 12.5% in 2016 (Drope et al., 2017). Time and future surveys will tell if this drop in prevalence continues, and if a decline is occurring in other countries as well.

While risks of non-nicotine use are probably very low, the risks of other drug use are unknown and require surveillance. Over-estimating some risks while overlooking others may be negatively influencing healthcare delivery and public health policy. It may be fueling unnecessary worry among parents, teachers, and others while failing to alert them to the possibility of other drug use. Instead of assuming that all youth with any past-30-day use of vapour products are at risk for smoking, we in public health should offer a more nuanced understanding of the actual risks of vaping. One simple question could elicit vital information on the risks of youth vaping: “What are you vaping?” Then we would better know what questions to ask next.

Vapour products (e-cigarettes) and tobacco cessation outcomes: A review of systematic reviews

R. O'Leary, T. Stockwell, M. MacDonald

In revision for *Nicotine & Tobacco Research* (Supplemental Materials in Appendix C)

Since the introduction of the electronic cigarette over a decade ago, newer models of vapour products (tanks, mods, vape pens, e-hookahs, pods) have reached worldwide sales of US $12.29 billion in 2016 (Euromonitor International, 2017). A number of healthcare practitioners and researchers have investigated vapour products to determine if they could function as a tobacco cessation aid. Vapour products provide more than nicotine – they mimic the smoker's hand-to-mouth behaviour habits, and vaping generates familiar sensory experiences, such as the visible smoke and "throat hit." Several surveys (e.g. Adkison et al., 2013; Dawkins, Turner, Roberts, & Soar, 2013; Goniewicz, Lingas, & Hajek, 2013; Tackett et al., 2015) demonstrate that an appreciable number of smokers have turned to vapour products in an attempt to quit cigarettes.

To date dozens of studies have been published investigating the effects of vapour product use on tobacco cessation, and 21 systematic reviews have been conducted on this topic to date. The initial systematic reviews on vapour product use for cessation were published in 2014, the first Cochrane review (McRobbie, Bullen, Hartmann-Boyce, & Hajek, 2014) and six others (Franck, Budlovsky, Windle, Filion, & Eisenberg, 2014; Grana, Benowitz, & Glantz, 2014; Gualano et al., 2015; Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014; Harrell, Simmons, Correa, Padhya, & Brandon, 2014; Orr & Asal, 2014). Three systematic reviews were published in 2015 (Lam & West, 2015; Rahman, Hann, Wilson, Mnatzaganian, & Worrall-Carter, 2015; Waghel, Battise, & Ducker, 2015) and a report by Public Health England (McNeill et al., 2015).

All of these reviews were conducted on a much smaller pool of studies because by the end of 2014, the number of primary studies published had increased dramatically. From 2016 to September, 2017, ten systematic reviews have been published on vapour product use and tobacco cessation. Which of the current systematic reviews are the best quality, and what are their findings?

To answer these questions, we conducted a review of systematic reviews, a tertiary review method that examines systematic reviews, primarily or exclusively, also known as an umbrella review. Umbrella reviews can serve multiple functions: an assessment of the quality of systematic reviews, an evaluation of the state of the literature, and an examination of the multiple reviews' findings and conclusions (Aromataris et al., 2015; Baker, Bennetts, Coleman, & Cappelleri, 2016; Ballard & Montgomery, 2017; Papageogiou & Biondi-Zoccai, 2016; Pieper, Buechter, Jerinic, & Eikermann, 2012). We evaluated the methodological quality of the current systematic reviews on vapour products and tobacco cessation with AMSTAR 2 to identify the highest quality reviews, and present their findings and conclusions (Hartling, Vandermeer, & Fernandes, 2014; Papageogiou & Biondi-Zoccai, 2016). Our goal is to provide what Hartling et al. (2014) and Ortega et al. (2016) call a "one-stop-shop" for policy-makers and researchers.

Methods

This review of reviews is based on a systematic retrieval of all published systematic reviews since 2016 on vapour products and tobacco cessation outcomes. This search date was selected because 13 cohort studies were published in 2015, a major addition to the available research. In this section we describe the literature search, the AMSTAR 2 assessment, the data extraction, and how we evaluated the state of the literature.

Search for Systematic Reviews

The search for the systematic reviews was conducted in two sets of resources, one a reference library from a meta-narrative review project, and the other a selection of systematic review databases. The library comes from the *Clearing the Air* project, a Canadian Institutes of Health Research funded knowledge synthesis project on the harms and benefits of vapour products (MacDonald, O'Leary, Stockwell, Reist, & the Clearing the Air project team, 2016). The library (CTA library) comprises 2,323 publications in peer-reviewed journals from 2007 to February 8, 2017 (search strategy in supplemental materials). The first author searched the CTA library with the keyword "systematic review" in the title or abstract of publications dated 2016 or later. The search retrieved seven systematic reviews. One systematic review is in French; it was assessed with a full reading of the text.

The second search was conducted on March 8, 2017 in 10 systematic review databases from Golder and Wright (2016): Cochrane Database of Systematic Reviews, Health Technology Assessment Database, Database of Promoting Health Effectiveness, JBI Database of Systematic Reviews and Implementation Reports, 3ie Systematic Review Database, PROSPERO, Epistemonikos, TRIP, National Institute for Health and Care Excellence, and McMaster's Health Evidence Website. The keywords were "electronic" OR "e-cigarette," published in 2016 or later, including grey literature, and in any language. The retrievals from the searches were reviewed by title and abstract for inclusion by the topics of vapour products and tobacco cessation. No grey literature or non-English reviews were found. The second search retrieved three additional systematic reviews, for a total of 10.

An updated search for new systematic reviews was conducted with the CTA Library search strategy on September 8, 2017. No new publications or grey literature were located.

Final study selection was made by two authors (RO, TS) and two outside reviewers. Three systematic reviews have been excluded. Khoudigian et al. (2016) is excluded because its search dates, through May 26, 2014, are a full year older than any of the other systematic reviews, and an up-to-date search is an important criterion for including systematic reviews in an umbrella review (Hartling et al., 2014; Papageogiou & Biondi-Zoccai, 2016). Glasser et al. (2017) is excluded because the authors pooled cessation rates and smoking reduction data in the findings and conclusions, and it was not possible to extract the cessation studies separately. Nevertheless, this is an excellent resource for empirical studies on vapour products with an extensive bibliography. Ioakeimidis et al. (2016) is excluded because the cessation section presents the meta-analyses from two other systematic reviews, and the authors do not examine any additional studies.

The search is illustrated in Figure 1 (in Appendix C). The final selection is seven systematic reviews, listed in Table 1. Several of the reviews cover other topics, such as smoking reduction, and they are noted in Table 1. Where a review covers other outcomes, the count of studies is for the cessation studies only. For ease of reference, the systematic reviews are identified in text by the last name of the first author. Study tables of the reviews' search strategies, meta-analysis data, and the narrative findings of the systematic reviews are provided in Appendix C.

Table 1
Systematic Reviews Evaluated

Citation	Funder(s)	Cessation studies	Closing search date	Other topics
El Dib et al. 2017	Commissioned by the World Health Organization	12	29 Dec 2015	risk assessment smoking reduction adverse effects
Hartman-Boyce et al. 2016	Commissioned by the Cochrane Library	17	Jan 2016	adverse effects
Kalkhoran & Glantz 2016	Grants from US Ntl. Institutes of Health, Ntl. Cancer Institute, Food and Drug Administration	20 in meta-analysis, 38 total	17 Jun 2015	none
Knight-West & Buller 2016	Not reported	21	Sep 2015	safety health risks clinical practice
Malas et al. 2016	Grant from Ontario, Canada Ministry of Health and Long-Term Care	15	1 Feb 2016	smoking reduction withdrawal symptoms urges to smoke
Orellana-Barrios et al. 2016	Not reported	8	18 Jan 2016	none
Vanderkam et al. 2016 [French language]	Not reported	13	14 Jun 2015	smoking reduction toxicology safety

Assessing Systematic Review Quality

AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) (Shea et al., 2017) is the quality evaluation tool used in this review. It has been developed primarily for evaluating systematic reviews of healthcare interventions. AMSTAR 2 has 16 questions, called domains. In brief, these domains or criteria require: (1) a PICO-based (population, intervention, comparator, outcome) research question, (2) a written protocol, (3) a justification of inclusion

criteria, (4) a comprehensive literature search, (5) duplicate reviewer study selection, (6) duplicate reviewer data extraction, (7) a list with justification for excluded studies, (8) adequate description of primary studies, (9) a risk of bias assessment, (10) identification of conflicts of interest (COI) statements for primary studies, (11) appropriate meta-analysis calculations, (12) risk of bias applied to the meta-analysis, (13) risk of bias referenced in the conclusions, (14) explanation of any heterogeneity, (15) assessment of publication bias, and (16) COI for review authors. The questions can be answered as *Yes*, *Partial Yes*, *No*, and *No Meta-Analysis*. A *No* is described as a weakness in the review.

Some of these questions are classified as *critical domains* that, if not satisfied, "undermine confidence in the results of a systematic review" (p. 6). We selected three of them: Q4 search, Q9 risk of bias assessment, and Q11appppropriate meta-analysis calculations. Q4 checks for the adequate retrieval of primary studies, Q9 evaluates the validity of the data of the primary studies, and Q11 tests the validity of the meta-analyses of the reviews. Our goal is to capture the critical domains relevant to the cohort and observational studies analyzed in the reviews along with the RCTs and clinical trials.

The AMSTAR 2 rating is an expression of the "overall confidence in the results of the review" (p. 6). A review with one or no non-critical weaknesses is rated as *High*, and a review with more than one is rated as *Moderate*. Reviews with one critical weakness are rated as *Low*, and those with more than one are rated as *Critically Low*. Multiple non-critical weaknesses may justify reducing a rating.

The AMSTAR 2 quality assessment was conducted by the first author (RO). For this review, both the published review and its supplemental materials and appendices are included in the assessment. An independent outside reviewer checked the scoring of 25% of the questions,

and the inter-rater agreement was 89%. For a comprehensive evaluation of the quality of the reviews, the AMSTAR 2 rating is paired with a narrative evaluation (Aromataris et al., 2014).

Reporting the Best Information

In some cases, a meta-epidemiologic review will synthesize the findings of the systematic reviews, in much the same fashion as a meta-analysis combines the findings of primary studies (Ballard & Montgomery, 2017). The major consideration for conducting such an analysis is the number of overlapping primary studies among the systematic reviews (McKenzie & Brennan, 2017). Double counting, in effect, overstates a study's findings (Pieper, Antoine, Mathes, Neugebauer, & Eikermann, 2014). A statistical test, the *corrected covered area* (CCA), calculates the degree of overlap (Pieper et al., 2014). Our review of systematic reviews scores "very high" on the CCA (calculation in Supplemental Materials). Therefore, although we are able to compare the findings and conclusions of the reviews, we cannot synthesize their findings without a high risk of bias.

Evaluating the State of the Literature

The analysis of the state of the literature has two components. One is a cross-index table of the primary studies included in at least one review, and their quality assessments. The second is a narrative summary of the reviewers' comments on the limitations of the studies published in their review.

The methods employed for this review of systematic reviews are all pointed to one purpose: to provide the best information available on vapour product use and tobacco cessation. Next we present the results of this review.

Assessments

The outputs of this umbrella review are the quality assessments of the systematic reviews, the findings and conclusions of the top-rated reviews, and the overview of the state of the literature.

Systematic Review Quality Assessment

The evaluation of the systematic reviews is composed of their AMSTAR 2 rating, a narrative evaluation of the rating, and comments on the review's strengths and contributions. The scoring of the AMSTAR 2 questions is presented in Supplemental Materials. The reviews are discussed in order from the highest to the lowest ratings.

Hartmann-Boyce – AMSTAR 2 rating High. This is a high-quality Cochrane review, but its only shortcoming in AMSTAR 2 is that the Cochrane method does not require authors to extract data on the studies' funding and conflicts of interest. The review's study inclusion criteria include a minimum of six months follow-up for cessation. The authors provide extensive background information, a full narrative description of the studies, a detailed reporting of bias risks, a list of excluded studies with the reason for exclusion, a table of research studies in progress, and a summary table of prior systematic reviews.

Malas – AMSTAR 2 rating High. The only missing domain is an assessment of publication bias. This is a very robust review with 62 studies assessed in total, and the analysis and conclusions are based on the higher quality studies. Study tables in the supplemental materials include the vapour product model and the study's limitations. This is the sole review in our study that reports the financial conflicts of interest for the primary studies (AMSTAR 2 Q10).

El Dib – AMSTAR 2 rating Moderate. The only weaknesses of this review are the omission of a list of excluded studies, and the lack of conflict of interest information on the included studies.

The missing case calculation applies a specialized technique, not the standard intention-to-treat analysis where drop-outs are computed as treatment failures. The study tables are excellent and informative, and include a PICO categorization (population, intervention, context, outcome). The supplemental tables provide the studies' full search strategy and data on the devices.

Orellana-Barrios – AMSTAR 2 rating Low. The critical weakness is the calculation of an average combined abstinence rate from studies with a duration of abstinence ranging from 6 to 24 months. A partial critical weakness is that the individual scores for the Cochrane Risk of Bias are not reported. The review has errors in the list of excluded studies, and does not provide the exclusion reasons. On the plus side, the review's inclusion criteria are stringent, requiring biochemical verification of abstinence, one arm or group using vapour products exclusively, and a follow-up of six or more months. As a consequence, the primary studies in this review have the most rigorous study designs.

Vanderkam – AMSTAR 2 rating Low. The critical weakness is a partial literature search, and multiple non-critical weaknesses including the lack of a list of excluded studies. This review is in French and has an English abstract. Its primary goal is to evaluate smoking reduction, and cessation is a secondary topic. In line with its secondary purpose, the narrative descriptions of the cessation studies are brief. The cessation study tables include the vapour product model and the recruitment strategy. This systematic review makes a unique contribution to knowledge translation by providing access in French to the findings of thirteen English language research studies.

Kalkhoran – AMSTAR 2 rating Critically Low. One critical weakness of this review is its meta-analysis of heterogeneous study types with wide variations in cessation outcomes. The second critical weakness is the limited search conducted only with databases. The review scored

No for Q5 and Q6 because the primary author performed the study selection and data extraction, and the second author "reviewed" them, but did not perform an inter-rater reliability test. The studies not included in the meta-analysis are given a full paragraph of description in the appendix, but no quality assessment or study tables, and they make a very limited contribution to the review's discussions. The study table for the meta-analysis studies includes information on dependency, confounders, and the study's definition of cessation. This review is given further evaluation in the Discussion section following.

Knight-West – AMSTAR 2 rating Critically Low. One critical weakness of this review is the lack of a quality assessment of the studies, although the reviewers do comment on the limitations of some of them. The second critical weakness is its limited literature search conducted only with databases. Other weaknesses occur because the authors fail to report their study selection and data extraction procedures. Finally, the lack of study tables limits its usefulness for reviewers. This publication is structured for the concerns of clinicians. It provides a helpful background section on the development of vapour products, and a description of product generations. The reviewers note the additional support for cessation with vapour products from YouTube self-help videos and vaping discussion forums.

Based on the AMSTAR 2 ratings, we have high confidence in the Hartmann-Boyce and Malas reviews, and moderate confidence in the El Dib review. We have low confidence in the findings of Orellana-Barrios and Vanderkam reviews, and critically low confidence in the Kalkhoran and Knight-West reviews. We next present an overview of the studies included in the three top-rated reviews, and what the reviewers indicate about the state of the literature on vapour product use and tobacco cessation.

The State of the Literature

The evaluation of the state of the literature is based on the quality assessments of the primary studies on cessation in the three top-rated reviews, and a summary of the reviewers' published comments on the literature.

Primary studies.

Table 2 displays every study evaluated in at least one of the three reviews, stratified by the number of reviews including the study. The study is coded with the reviews' quality assessment(s).

Table 2 *Included Primary Studies with their Quality Assessments*

Study first author (year)	Hartmann	Malas	El Dib
Included by 3			
Adriaens (2014)	+	+	●
Borderud (2014)	●	+	●
Bullen (2013)	+	+	●
Included by 2			
Al-Delaimy (2015)	●	ex	●
Biener (2015)	ex	+	●
Brose (2015)	●	ex	●
Caponnetto (2013) ECLAT	+	ex	●
Caponnetto (2013) schizophrenia	●	+	
Grana (2014)	●	+	
Hajek (2015)	●		●
Manzoli (2015)	●	ex	●
Polosa (2014) success	●	+	
Prochaska (2014) mental illness	●	ex	●
Unique El Dib			
Harrington (2015)		ex	●
Vickerman (2013)	ex	ex	●

Study first author (year)	Hartmann	Malas	El Dib
Unique Hartmann			
Choi (2014)	●		
Ely (2013)	●		
Etter (2014) longitudinal	●	ex	
Humair (2014)	●	ex	
McRobbie (2015)	●		
Nides (2014)	●	ex	
Pacifici (2015)	●		
Polosa (2011) 6 month	●	ex	
Polosa (2014) 24 month	●	ex	
Polosa (2014) asthmatic	●	ex	
Polosa (2015) vape shop	●	ex	
Unique Malas			
Adkison (2013)	ex	+	
Brown (2014)	ex	+	
Christensen (2014)		+	
Dawkins (2013)	ex	+	
Goniewicz (2013)		+	
Lechner (2015)		+	
Pearson (2015)		+	
Tackett (2015)		+	

● weak quality rating

+ positive quality rating

ex - study excluded

Blank cell - study not evaluated

The reviews cover 34 primary studies on cessation in total (reference list in Supplemental Materials). Three randomized controlled trials (RCT) have been conducted: Bullens et al (2013), Caponnetto et al. (2013), and Adriaens et al. (2014). The three review teams differ greatly in their quality assessment of the RCTs. The El Dib and Hartmann-Boyce review teams both apply the Cochrane Risk of Bias assessment, but El Dib et al. assess all the RCTs as at high risk of bias while Hartmann-Boyce et al. score the RCTs at low risk. Malas et al., using a modified Qual Syst tool from the Alberta Heritage Foundation for Medical Research (Kmet, Lee, & Cook, 2004), rate the RCTs by Bullen and Adriaens as moderate quality studies, but exclude Caponnetto as a weak study.

Of the 34 studies, 26 garner at least one negative quality rating. El Dib et al. rate all of their included studies at high risk of bias, and Hartmann-Boyce et al. score all non-RCTs at high risk. The Malas review team rated and excluded 14 studies as weak that were included in one or both of the other reviews, and all but one of these studies were also rated as weak in Hartmann-Boyce and/or El Dib. Negative quality ratings are not universal: Malas et al. assessed four studies as moderate quality that were rated at high risk of bias by Hartmann-Boyce et al. The Malas review team rates 15 cessation studies as moderate or strong quality.

Review authors' comments on literature quality.

The review authors' comments on the studies point to many problems with the primary studies. They discuss issues with participant selection, methodology, and confounders. Their strongest criticisms concern participant selection as a major source of bias in the literature. It is worth quoting Hartmann-Boyce et al. in full on this point:

> Those studies which analyze results in smokers based on EC use
>
> at baseline have by the nature of their design already excluded people

> who have successfully quit using EC, and therefore only retain participants
> who, at entrance to the study, would be classed as 'treatment failures'
> or are in the midst of a cessation attempt (p. 22).

El Dib et al. and Hartmann-Boyce et al. state that a study population composed of treatment failures (persons unable to quit on their own) would underestimate the effectiveness of vapour products for cessation. This critical issue of bias from the selection of the study participants is further explored in the Discussion section.

Other problems in the literature are noted by the reviewers. Malas et al. are concerned about convenience sampling, and both Hartmann-Boyce et al. and Malas et al. find difficulties arising from small sample sizes. Harman-Boyce et al. point out the hurdles facing reviewers when studies have differing definitions of a current user or what constitutes cessation. Hartmann-Boyce et al. and Malas et al. observe that many studies fail to specify outcomes in advance, resulting in a high risk for reporting bias. El Dib et al. encounter problems with missing data. Malas et al. state that the researchers of many primary studies failed to conduct routine statistical tests, and based their conclusions on data with wide confidence intervals or without statistical significance. Study population bias plus these issues constitute a significant concern for the quality of studies in the literature.

Systematic Review Results

The review teams of Hartmann-Boyce, Malas, and El Dib applied the GRADE system to their findings. GRADE is Grades of Recommendation, Assessment, Development, and Evaluation which was developed in 2000 (Guyatt, Oxman, Schunemann, Tugwell, & Knottnerus, 2011), and it is used in most systematic reviews (Papageogiou & Biondi-Zoccai, 2016). GRADE rates a body of evidence for an outcome, not individual studies. The GRADE definition of

quality is “confidence in the true effect” (Schunemann, Brozek, Guyatt, & Oxman, 2013). The quality of evidence for randomized trials is rated at High (very confident) or Moderate (moderately confident), and observational studies are rated as Low (limited confidence) or Very Low (very little confidence). Ratings may be downgraded through a risk of bias, inconsistency, indirectness, imprecision, and publication bias, or the rating upgraded by large effect, dose response, plausible confounding, or large sample sizes. The GRADE ratings are presented with the findings.

The three reviews use a different set of the three RCTs for their syntheses. El Dib includes all three. The Hartmann-Boyce synthesizes Bullen and Caponnetto, and calculates Adriaens with the cohort studies (due to the research design). Malas includes Bullen, includes Adriaens with cohort studies, and excludes Caponnetto (due to its low quality assessment).

Hartmann-Boyce: “There is evidence from the pooled results of two trials that electronic cigarettes (ECs) with nicotine, compared with placebo ECs, helped smokers to stop smoking long-term” (p. 23) (RR 2.29, 95% CI [1.05, 4.96], 5% effect size, GRADE low). “There is evidence from one trial that ECs may lead to six-month quit rates similar to those achieved with NRT, but the confidence interval is wide” (p. 23) (RR 1.26, 95% CI [0.68, 2.34], GRADE very low).

Malas: Bullen RCT analysis: vapour product compared to placebo, non-significant. GRADE low. Vapour product compared to NRT, non-significant, GRADE low. In conjunction with findings from Brown et al. “e-cigarettes with nicotine may be more effective than NRTs for smoking cessation…[evidence] weak and inconclusive” (p. 4).

El Dib: "Results from two RCTs suggest a possible increase in smoking cessation with ENDS [electronic nicotine delivery systems] in comparison with ENNDS [electronic non-nicotine delivery systems]" (p. 12) **(**RR 2.03, 95% CI [0.94, 4.38], p=0.07, GRADE low).

Cohort studies.

Each review team selected a different set of studies. Typically some differences in study selection can be explained as an artifact of the reviews' search date ranges, but not in this case because all three reviews searched date ranges within one month of each other. The largest factor in their differing selection of studies is that Malas et al. used quality rating as an exclusion criterion, but the other reviewers did not. Differing inclusion/exclusion criteria for the duration of cessation also impacted study selection, with Hartmann-Boyce and El Dib specifying six months or more, but Malas requiring 30 days. The result is that each review team evaluates a different combination of cohort studies.

Looking at Table 2, Hartmann-Boyce included 11 studies not in the other reviews, Malas included eight unique studies, and El Dib included two studies excluded in the other reviews. As noted earlier, Malas excluded 14 studies included in the other reviews, and Hartmann-Boyce excluded five studies included in one of the other reviews. Notably, Malas excluded 11 of the 20 Hartmann-Boyce cohort studies, and six of the nine cohort studies in El Dib. The differences in cohort study selection are substantial.

Hartmann-Boyce: "[Of] seven longitudinal surveys which analyzed cessation at follow-up based on EC use at baseline, five detected no significant difference based on baseline EC use, and two found that EC use at baseline was significantly associated with decreased rates of abstinence at follow-up" (p. 21). Abstinence rates in cohort studies (both intending and not intending to quit) range from 5% - 53%, and 8% - 46% for intention-to-treat figures (Table 1).

Malas: One cross-sectional study, duration of abstinence not reported, compared to NRT AOR 1.63 (95% CI [1.17, 2.27], p<.001). One cross-sectional study, duration of abstinence not reported, compared to no aid AOR 1.61 (95% CI [1.19, 2.18], p<.01)**.** Five studies, abstinence duration not reported: no control, 11%-75% abstinence, GRADE very low. Six studies abstinence 6+ months: no control, 13.1% - 36% abstinence, GRADE low. "11 of the 14 studies individually rated as moderate or strong provide some evidence suggesting e-cigarettes' effectiveness for smoking abstinence…[but] it is not possible to draw reliable conclusions" (p. 4).

El Dib: Eight cohort studies comparing nicotine and non-nicotine devices "failed to show a benefit in smoking cessation" (p. 14) OR 0.74 (95% CI [0.55, 1.00], p=0.051, GRADE very low). Eight cohort studies suggest "a possible reduction in quit rates with use of ENDS compared with no use of ENDS" (p. 16) OR 0.74 (95% CI [0.55, 1.001], p=.051).

Despite their different findings from cohort studies, the conclusions of the three review teams are the same. In their own words... El Dib et al. state, "owing to the limitations in the studies…it is impossible to make strong inferences regarding whether e-cigarette use promotes, has no effect or hinders smoking cessation" (p. 18). Hartmann-Boyce et al. detail the findings from the RCTs, but have low confidence in the results, "evidence from two trials that ECs help smokers to stop smoking… However the small number of trials, low event rates and wide confidence intervals… mean that our confidence in the result is rated "low" by GRADE standards" (p. 2). Malas et al. say flatly, "the evidence for the effectiveness of e-cigarettes as a cessation aid is inconclusive…there are simply too few well-designed studies" (p. 9). All three research teams decline to make a definitive conclusion on vaping and cessation.

Discussion

The discussions evaluate the conclusions of the lower-rated reviews, and consider the possible underestimation of effectiveness of vapour products for cessation. We go on to present a weighting of the evidence and our conclusion. We finish the discussions by considering the limitations of our review and offering suggestions for future research.

Conclusions of the Lower-Rated Reviews

In accord with the top-rated reviews, Orellana-Barrios et al. and Vanderkam et al. decline to present a definitive conclusion on the effectiveness of vapour products due to the lack of RCTs and clinical trials. Yet Kalkhoran and Glantz state "e-cigarette use is associated with reduced smoking cessation in the real world" (p. 126), and, in contrast, Knight-West and Bullen conclude that vapour products have "modest potential for helping smokers to quit" (p. 116).

Study selection appears to account in large part for the differing conclusions in the two lowest-rated reviews. Knight-West and Bullen differ in their study selection from the other reviews by including four case studies and six user surveys, study designs of interest to clinicians. Based on individual descriptions of 21 studies with no formal quality assessment and no meta-analysis, the authors conclude that vapour products have the potential to be an effective cessation aid.

On the other hand, Kalkhoran and Glantz conduct a meta-analysis, and conclude that vapour product use is detrimental to cessation. They include four studies in the meta-analysis that are not included in any of the other reviews in this study; they account for 19.86% of the weighting of their meta-analysis, and none favour vapour product use for cessation. These reviewers exclude the Capponnetto and Adriens RCTs due to the lack of a non-user control group. Furthermore, they compute the Bullen RCT as one of 15 cohort studies in the meta-

analysis, giving it a weight of less than 5%, so the meta-estimate is over-weighted towards the observational study findings (Shea et al., 2017). Another issue with the meta-analysis is its synthesis of multiple study designs: 15 cohort studies, three cross-sectional studies, and two clinical trials. A further major source of bias is how the meta-analysis synthesizes studies with widely different durations of abstinence, resulting in unbalanced comparison groups. Overall, therefore, the meta-analysis was not conducted with the appropriate methods for synthesizing the studies.

We are not the first reviewers to observe these drawbacks. Hajek et al. (2016) argue that the Kalkhoran review has "serious selection bias," and describe the meta-analysis as "lumping incongruous studies together…makes no scientific sense in the first place" (p. e23). Orellana-Barrios et al. (2016) too are "concerned about the variable and heterogeneous group comparisons made in the meta-analysis" (p. e24). Notwithstanding, Kalkhoran is the most highly cited of all the systematic reviews with 185 citations, as compared to 86 for Hartmann-Boyce, 50 for Malas, and eight for El Dib (as per Google Scholar, Sep 29, 2017). Shea et al (2017) warn that "uncritically accepting the results of a single systematic review has risks" (p. 1). Our AMSTAR 2 evaluation indicates that the Hartmann-Boyce, Malas, and El Dib reviews are far more reliable sources of evidence.

Underestimating Potential

As noted in the Review Authors' Comments section, many studies are biased from their inclusion of treatment failures in the study population - i.e. the dual users of tobacco and vapour products who have failed to quit or are in the midst of a quit attempt. Hartmann-Boyce et al. identify dual users as a "heavy confounder" in cessation studies. The reviewers state that "following up 'treatment failures' is likely to show a low treatment effect, even for treatments

that are highly effective" (p. 19). El Dib et al. agree that dual users "may already be failing in their attempts to stop smoking…these participants will underestimate ENDS beneficial effects" (p. 16). The findings of many of the primary studies may have been skewed towards lower success rates by the inclusion of dual-users.

In the meta-analyses, nicotine products were more effective for cessation than non-nicotine (placebo) products, indicating the importance of nicotine in achieving abstinence. Newer vapourizers provide better nicotine delivery than early generation models (Chen, Zhuang, & Zhu, 2016; Farsalinos et al., 2015; Hajek, Przulj, Phillips, Anderson, & McRobbie, 2017; Hitchman, Brose, Brown, Robson, & McNeill, 2015; Meier et al., 2017; Tackett et al., 2015; Wagener et al., 2016). Five of the review teams propose that the newer models may be more effective for cessation. "If these poorly performing EC products can assist smokers, products with better nicotine delivery may have better effects" (Hartman-Boyce, p. 21). "Second-generation e-cigarettes may be more effective than first-generation devices in helping smokers to quit" (Malas, p. 9). El Dib et al. mention that "it is possible that later generations of e-cigarettes would have greater benefit" (p. 17). Vanderkam et al. and Knight-West and Bullen suggest that newer devices could be more effective.

In addition to the expert opinions, two studies demonstrate that newer models are more effective for cessation than the first models of vapourizers. In a survey by Tackett et al. (Tackett et al., 2015) included in the Malas review, among 215 adult vapor store customers, those using newer generation devices were almost three times more like to have quit (biochemically verified) than those using earlier models. In a one year cross-sectional study of 348 dual users, daily users of tank models were significantly more likely to have quit than cig-a-like users and non-vaping

smokers (Hitchman et al., 2015). Newer model vapourizers are expected to have increased effectiveness for cessation due to their improved nicotine delivery.

The consumer appeal of vapour products may also provide benefits for cessation. Two studies from England demonstrate that smokers frequently choose vapour products for making a quit attempt. In the 2017 Smoking Toolkit survey (N=12,859), 35% of adult smokers making a quit attempt used a vapour product, while less than 20% used over-the-counter NRT, the next most popular option (West, Beard, & Brown, 2017, Jul 7). One hundred clients of the City of London Specialist Stop Smoking Service were offered four weeks of free vapour products - 69% accepted them (Hajek, Corbin, Ladmore, & Spearing, 2015). In qualitative studies and surveys, users have said that vapour products were better for them for quitting than other methods (Barbeau, Burda, & Siegel, 2013; Etter, 2015; Harrell et al., 2015; Nelson et al., 2015). The appeal of vapour products to consumers could attract more smokers to make a quit attempt, and provide a pleasurable product that could make it easier to stay with the process of cessation.

The Weight of the Evidence

The three review teams have been unable to state a conclusion on the effectiveness of vapour products for cessation. Are we at an impasse in reaching a conclusion? We argue that by weighing the observations of the reviewers along with their tentative assessments of their findings, that the potential for vapour devices as a cessation aid is, nonetheless, supported.

To begin with, the tentative comments on the findings of the RCT are positive. Hartmann-Boyce et al. state that vaping “may lead to” six-month quit rates similar to NRT. Malas et al. go a further and say vapour products “may be more effective than NRTs.”

Next, the cohort studies in Malas passed a quality review, while Hartmann-Boyce and El Dib reviews conducted their analyses on studies that they assessed as at a high risk of bias. Malas excluded as weak studies 11 of the 20 Hartmann-Boyce cohort studies, and six of the nine El Dib cohort studies. Malas et al. found that 11 of the 14 studies quality studies "provide some evidence" that vapour products have effectiveness for cessation.

Turning to the reviewer observations, they criticize the primary studies for population bias that would result in an underestimation of effectiveness. Almost all the cohort studies include dual-users, so the syntheses of the systematic reviews likely carry forward lower rates of cessation.

Finally, five review teams propose that newer models provide better nicotine delivery and thereby are more effective for cessation. Two research studies have demonstrated that newer models were more effective for cessation than older ones. Future studies would be expected to show better rates of cessation with the newer models than those obtained in the current studies with the first, frequently poorly functioning models. In addition, the consumer appeal of vapour products may add to their contribution as a cessation aid.

We suggest that the weight of the evidence shows that vapour products have promise as a cessation aid. The top-rated systematic reviews present preliminary positive assessments of the findings from the RCTs and the quality cohort studies in Malas show a positive effect for vapour products for cessation. Add to these findings the probable under-estimation of cessation rates in most of the studies, the expected improvement in effectiveness of newer vapourizers, and the consumer appeal of vapour products. While further research on the potential value of vapour

products as cessation aids is urgently needed, we suggest that the weight of the evidence provides grounds for optimism for their use as a cessation aid.

Limitations of the Review

A few limitations must be noted. The first limitation is at the level of the primary studies, where low quality predominates. All the studies in the El Dib review and all the cohort studies in Hartmann-Boyce are rated at a high risk of bias. Malas excluded 14 of 29 studies as weak quality. Furthermore, the strength of the evidence is rated as GRADE low to very low in the top-rated reviews.

Another limitation of the studies and for this review is the generalizability of the findings of the primary studies. As we discussed earlier, many of the studies in the reviews were conducted with early generation vapour products, and now newer models with better nicotine delivery have taken their place. As well as the numerous models of vapourizers, the presence of thousands of available e-liquid flavours may also be an issue for generalizing findings as Tackett et al. (2015) found better quit rates (biochemically verified) among those who vaped non-tobacco and non-menthol flavours. Knight-West and Bullen observe, “only a fraction of the available devices and liquids have been tested” (p. 112), and it is a very small fraction indeed looking at the variety of vapour products for sale online. Hartmann-Boyce et al. counsel that systematic review teams must exercise caution in generalizing their findings across divergent products.

Future Research

Two components are key to improving the quality and usability of future studies of vapour products and tobacco cessation. First, it is imperative that vapour product researchers design their studies with safeguards against population bias, particularly with participants who

are dual users. Shea et al. (Shea et al., 2017) advise that for health intervention studies "it is good practice to recruit new users of a technology or drug into studies to avoid prevalence bias" (p. 5), and Hartmann-Boyce et al. concur. The second critical item is the selection of vapour products for the research. As Knight-West and Bullen remark, "it would be unfortunate to conclude in a few years' time that data from these new RCTs have little bearing on what vapers might then be using" (p. 116). However, this recommendation may be difficult to implement in practice due to the time lag between study design and participant recruitment and publication, particularly for RCTs.

We have three recommendations for systematic review teams evaluating the topic of vapour products and cessation. First and foremost, the quality assessment of studies should specifically probe for the risk of bias from the study population because several review teams have observed the inclusion of dual users who are "treatment failures." Furthermore, if quality assessment is an exclusion criterion, then studies with a high risk of bias in this category should be considered for exclusion. Second, reviewers could reasonably justify excluding studies on early vapour product models from their review, given the improvements in the products. Another option would be a sub-group analysis of vapourizers by the model type (generation) or product features (for example, user-adjustable voltage). Finally, data extraction should include conflicts of interest information, regardless of what quality tool is used.

Summary

In our review of systematic reviews, we have used AMSTAR 2 to identify the best reviews for policy-makers and healthcare researchers as Malas et al. (2016) and Hartmann-Boyce et al. (2016), the Cochrane review. For now, the most highly cited systematic review on

vapour products and cessation is Kalkhoran and Glantz (2016), but based on its AMSTAR 2 assessment, there should be very little confidence in its findings.

We have provided a list of the primary studies, and find that the state of the literature is poor. Many studies were rated as weak or at high risk of bias, and the reviewers observed numerous problems with the research design of the studies.

Due to the small number of RCTs and the low GRADE ratings for the findings, the review teams were unable to reach a definitive conclusion on the effectiveness of vapour products for cessation. We are optimistic that vapour products have the potential to be effective cessation aids. We base our optimism on (1) the review team comments on the findings, (2) the Malas cohort studies, (3) the possible underestimation of effectiveness in current studies, (4) the projection of improved effectiveness of newer models, and (5) the consumer appeal of the products. Further research on vapour products as cessation aids is urgently needed to confirm their potential value.

Afterword

This closing chapter serves as a summary of my research project on the claims made about vapour products in four legislative reports, and the reviews conducted on youth vaping, and vaping and cessation. The summary starts with a synthesis of the three articles. Next, I consider the implications of my research for tobacco control, and offer recommendations for public health policies. I then present my recommendations for research, commenting in particular on the potential of narrative policy framework and umbrella reviews to increase understanding in contested areas of scientific inquiry. I close my dissertation with a brief concluding statement.

Synthesis of the Articles

The legislative recommendation reports of Queensland, Canada, and the EU, and the US deeming rule convey many of the claims about vapour products debated in the wider healthcare community. The dominance of threat claims across all the reports is an astounding 11 of 13 claims, and 93 of 99 claim statements. The Queensland and Canada reports presented only threat claims, and they continued their bans on nicotine products. The US and the EU reports contained two opportunity claims, yet nonetheless based their legislation on threat claims, with the US establishing a pre-market authorization process, and the EU placing low limits on nicotine content.

One of the claimed threats is that vapour products lead youth to smoking, a claim presented in all four reports. It represents one of our greatest fears, harm to youth. Only two claims were opportunities offered by vapour products: as a cessation aid or as a less harmful substitute for tobacco. A new, effective and popular treatment for tobacco dependence would be the greatest hope of healthcare professionals who see the toll of tobacco on their patients. Yet

finding evidence on vaping and youth smoking and the effect of vaping on cessation was not at all straightforward.

First of all, many researchers studying youth vaping routinely applied past-30-day use as an indicator of problematic use, and moreover almost every researcher assumed that nicotine was being consumed. The findings from my systematic search of survey data showed that many youth were vaping infrequently, and an appreciable number reported that they were not vaping nicotine. My co-authors and I had to question the metric of past-30-day use and the assumption of nicotine vaping to get a more accurate assessment of risk for youth nicotine dependence from vaping. Because past-30-day use includes a large number of low frequency users, the metric over-estimates the number of youth with a problematic pattern of use by 78% to 119%. The metric over-estimates nicotine use by 28% to 41% because surveys have not inquired about non-nicotine consumption. Moreover, 80% to 90% of youth who had ever, even once, used a vapour product, had tried cigarettes first, findings that further contradict the claim that vaping will cause youth to initiate smoking.

On evidence for cessation and vaping, there were more systematic reviews than RCTs, and many of the primary studies were low quality. The review teams of the better quality systematic reviews were unable to state a definitive conclusion. Supplementing their findings with other information – tentative comments on the findings, the probability that current studies underestimate effectiveness, and the improvements in newer model vapourizers – allowed us to support our optimism that vapour products are likely to be effective for cessation after considering the weight of the evidence overall.

Thus we have demonstrated that two of the claims made about vapour products are largely inaccurate. The problem is that current regulations and public health policies are based in

large part on these two questionable claims. Despite the evidence, the debate in public health continues to be dominated by the 'gateway theory' and an unwillingness on the part of most clinicians to recommend vaping for cessation.

Implications for Tobacco Control

As evidenced in *Claims Study* and from the state of the current regulations on vapour products, to date the precautionary principle appears to have has won the debate, and protectionist legislation dominates the regulation of vapour products. The precautionary principle is based on the assumption that no harm will occur from exercising precaution (Offit, 2017), but on the contrary, "the precautionary principle is costly, and when interpreted strictly, it can be paralyzing" (Kahneman, 2011, p. 351). Loud calls for the precautionary principle by many in the tobacco control community may well squelch the opportunity for vapour products to contribute to the tobacco control "endgame" - a world where combustible tobacco use is negligible. Wagener, Meier, Tackett, Matheny, and Pechacek (2016) dismiss the precautionary principle for vapour products because the products offer cleaner nicotine delivery, while highly toxic cigarettes remain widely available, and current cessation treatments have limited effectiveness. Unfortunately, this reasonable argument is not dislodging the stranglehold of the precautionary principle in many countries in the debate over vapour products.

The World Health Organization, citing the precautionary principle, has recommended extending the regulatory ambit of the Framework Convention for Tobacco Control (FCTC) to non-nicotine vapour products (World Health Organization, 2016, August). So the question becomes, when does a mode of administration (vapourizers) become a tobacco product? The very terms e-cigarette and ENDS (electronic nicotine delivery system) contribute to the classification of the devices as a tobacco product. Yet non-nicotine vaping is not tobacco

consumption in any form, and, as reported in *Youth Review*, non-nicotine vaping is fairly common among youth. Arguably, the FCTC may have fallen into the trap of mission creep as "e-cigarettes have turned into a distraction from the goal of reducing combustible tobacco" (Wagener et al., 2016, p. 731).

Another issue for tobacco control is the tenacity of the gateway theory as a key claim for the strict regulation or ban on vapour products. The central premise of the gateway theory is that the use of a less harmful substance primes the user for consumption of a more harmful substance (Lee, 2015), yet with vaping, the transition would be from one mode of nicotine administration to another. The gateway theory continues to be invoked regarding vapour products despite the fact that "evidence that e-cigarettes lead one inexorably down a path towards smoking is very limited" (Bell & Keane, 2014, p. 49). In *Youth Review*, we presented evidence that any potential gateway effect would be restricted to the very small number of youth who vape with a regular frequency of use and also consume nicotine. Nevertheless, I do not expect the claim of vapour products as a gateway to smoking to disappear anytime soon. Trying to undermine a core belief is exceptionally difficult, and any evidence to the contrary is not expected to be well received (Alvesson & Sandberg, 2011). Nobel prize winner Kahneman (2011) labels this type of entrenched belief "theory-induced blindness" (p. 277), and "theories can survive for a long time after conclusive evidence falsifies them" (p. 374).

With the ongoing and ugly debate over vapour products, the tobacco control community is creating problems for themselves. As discussed in the Foreword, the public health community has largely fractured into two camps over vapour products. First and foremost, this divide threatens to bias the production of research and reviews, as experts with strong opinions push their positions, and researcher alliances with one faction or the other influences who is hired for

research projects (Uttley & Montgomery, 2017). Another consequence of the debate is that public health has lost face and credibility with vapers (Wagener et al., 2016), and public confidence in public health has been eroded (Sim & Mackie, 2014). Sim and Mackie (2014) plead, "as a matter of urgency, we need to resolve this situation to avoid perpetuation of the damage done to public trust and confidence in public health practice" (p. 870), yet almost a year later, they observed that the debate had "become even more vituperative" (2015, p. 1135). The tobacco control community needs to clean up the personal attacks and eliminate fiat claims before more harm is done to its reputation. As public health researchers, our ability to present credible evidence and advice depends on it.

Recommendations for Public Health Policy

If, as concluded in *Cessation Review*, vapour products may well be effective cessation aids, then those public health policies based on the current precautionary approach should be revisited. As evidence accumulates for the benefits of vapour products, restrictive regulations will need to be revised, or the opportunity for decreasing the harms of the tobacco epidemic will be forfeited. Public health policies for vapour products should shift from a threat-focused response to one that maximizes the opportunities to increase cessation and reduce the harms from smoking. To accomplish these changes, as recommended in *Claims Study*, advocates should not present evidence exclusively - they must craft their evidence into compelling stories for maximum persuasive impact on policy-makers. The blogosphere is full of quit stories by vapers.

The promise of vapour products for cessation is gradually being acknowledged in a small number of countries, including the UK where researchers have argued:

> Taking the totality of evidence including controlled trials,
> observational studies, changes in population smoking and ENDS

> use, the experience of nicotine replacement therapy, and widely reported user experience, there is confidence that ENDS are helping many smokers to quit smoking and not having negative effects like renormalising smoking, reducing quit rates or creating gateway effects (Britton, Bogdanovica, McNeill, & Bauld, 2016, p.3).

This one statement challenges several of the claims of threat, and endorses the opportunity to increase treatment options for smokers. Our findings in *Cessation Review* support this statement. How many healthcare providers and researchers worldwide are aligned with this evidence-based position is an open question.

Recommendations for Research

Our recommendations for research are offered in *Youth Review* and *Cessation Review*. In short, for those researching youth vaping, research should be conducted with a measurement of the frequency of use that is a valid indicator of problematic use, perhaps six times per month as per the guideline for adult problematic use by Amato, Boyle, and Levy (2016). Research instruments include open-ended questions on the substances being consumed. Cessation review teams must examine primary studies for population bias from treatment failures, and account for differences in the effectiveness of different generations (models) of vapour products.

The published research on cessation with vapour products is in a lull as we in the tobacco control community of practice wait for further studies to be completed. As noted in the Foreword, as of November 8, 2017, no new RCTs on cessation have been published since 2014, although many are underway. As a consequence, there is no need for reviewers to conduct another systematic review until the findings of new RCTs are published. As my co-authors and I

suggest in *Cessation Review*, many of the studies with first generation products could be excluded in future reviews, or their findings bracketed in a sub-group analysis. More RCTs and clinical trials are required so that review teams can confidently present conclusions on the effectiveness of vapour products for cessation.

In addition to clinical studies, evidence from newly published and future population level studies may help refute the claims that vapour products have negative effects on cessation. By way of example, in England, Beard, West, Michie, and Brown (2016) computed quarterly data on approximately 1200 smokers from the Smoking Toolkit Study between 2006 and 2015, and contrary to the claim that vaping decreases cessation, the researchers found that the success rate of quit attempts increased by 0.098% (95% CI [0.064, 0.132]; $p<.001$) for every 1% increase in the prevalence of vapour product use by smokers.

In the US, data from the US Current Population Survey-Tobacco Use Supplement (TUS-CPS) "provides a strong case that e-cigarette use was associated with an increase in smoking cessation at the population level" (Zhu, Zhuang, Wong, Cummins, & Tedeschi, 2017, p. 6) as vapour product users had a 8.2% cessation success rate compared to 4.8% for smokers not using vapour products, a 73% relative increase ($p<.001$). The overall US population cessation rate increased from 4.5% in 2010/2011 to 5.6% in 2014/2015, the first significant increase in smoking cessation for US adults in 15 years (Zhu et al., 2017), and the quit attempt rate in the US is at its highest recorded level since 1997 (Gitchell, Shiffman, & Sembower, 2017). Furthermore, the 2014/2015 TUS-CPS indicated a positive association of more frequent vapour product use with more quit attempts and improved quit success (3 months abstinence, self-report) (Levy, Yuan, Luo, & Abrams, 2017). The findings of these studies support our optimism in *Cessation Review* that vapour products have potential as a cessation aid, and may suggest that

approaches other than RCTs and clinical trials may be better for evaluating the role of vapour products in cessation.

For future studies of vapour product regulation, as well as many other areas, the narrative policy framework (NPF) has a bright future in policy research. The number of NPF studies has increased sharply since the publication in 2014 of *The Science of Stories*, growing from 19 studies to 52 in less than three years (studies listed in the Appendix D). As my co-authors and I stated in *Claims Study*, NPF is an excellent tool for analyzing policy narratives. The majority of NPF research continues to be on environmental topics, but researchers in other diverse fields are now conducting NPF studies. Some examples are gun policy (Merry, 2016, 2017; Smith-Walter, Peterson, Jones, & Nicole Reynolds Marshall, 2016), campaign finance reform (Gray & Jones, 2016; Jorgensen, Song, & Jones, 2017), education (Bragg & Soler, 2017; Ertas, 2015), and terrorism (Paliwal, 2017). *Claims Study* used NPF for examining public health legislation on vapour products, and researchers have applied the methodology to other areas of healthcare: elder care policies (Jacobsen, 2015), foster care policies (Mosley & Gibson, 2017), epigenetics (Robison, 2016), obesity (Husmann, 2015), and the anti-vaccination movement (Veselková, 2014). I most heartily recommend NPF for future research in tobacco control and public health policy.

Umbrella reviews have much to offer to future research on healthcare, particularly for evaluating the quality of systematic reviews. Researchers have conducted at least 86 umbrella reviews for the sole or primary purpose of assessing the methodological quality of systematic reviews in their healthcare field (see Appendix D). Pussegoda et al. (2017) propose the simple term *reports* for umbrella reviews which assess the methodological and/or reporting quality of a group of systematic reviews. In healthcare, dentistry researchers have produced the most reports

(18), followed by surgery (11). Systematic reviews in burn care have been subject to sharp criticism in two reports (Campbell, Kavanagh, Kurmis, & Munn, 2017; Wasiak, Tyack, Ware, Goodwin, & Faggion, 2016). Reports have been published in a wide range of other healthcare fields, including anesthesiology (Hall, Lee, & Zurakowski, 2017; Hedin, Umberham, Detweiler, Kollmorgen, & Vassar, 2016); pain management (Minguez et al., 2017); urology (Corbyons, Han, Neuberger, & Dahm, 2015; Han, Gandhi, Bockoven, Narayan, & Dahm, 2017); sports medicine (Weir, Rabia, & Ardern, 2016); and animal research (Mueller et al., 2014). I believe that in the next few years more healthcare researchers will be conducting umbrella reviews, and reports in particular, in the quest for the best evidence.

Contributions

The goal of doctoral students is to create a contribution to their field. I have included in each article recommendations for future research, a second set of contributions in addition to the findings of the studies. The following are the contributions I have strived for with the articles for my dissertation.

In *Claims Study* we demonstrated that vapour products are represented in the political arena as a threat to individual and public health. The article also supplies the reader with information on the legislation regulating vapour products, including the two largest markets, the US and the EU. Furthermore, our study makes contributions to the NPF methodology with two new categories: the threat/opportunity classification of plots, and shadow characters. Dr. Ron Borland had remarked after reading an early draft of the study that the plots resembled a SWOT analysis, and I was able to apply *threats* and *opportunities* as categories of plots. This classification should prove generalizable to other NPF research. For another contribution, I created the concept of shadow characters, actors not directly named in text. These characters

cannot be identified with machine language or keywords, but require the close reading of the researchers to find them. I am certain that these two additions will improve NPF. Already Dr. Mark McBeth, one of the developers, is aware of these innovations, and he has included *Claims Study* in his Public Policy Analysis class at Idaho State University (personal communication May 19, 2017). I also note in passing that my Co-Supervisor Dr. MacDonald has added NPF to her graduate Nursing methods class.

With *Youth Review*, we have sought to "clear the air" in the debate over the gateway theory with a more accurate picture of population level risk of nicotine dependence among youth who vape. Yet as discussed earlier, the gateway theory is firmly entrenched in the debate on vapour products, an appeal to fear. Perhaps hard numbers for the over-estimation of risk will quell these fears. Another contribution of the review is that we raised the question of youth vaping as a mode of administration of drugs other than nicotine or cannabis – the first time this subject has been broached in the literature on youth to the best of my knowledge.

The contribution of *Cessation Review* is the quality assessment of the systematic reviews, and the overview of the research studies. Our review will remain up to date for some time with the lag in the publication of RCTs and clinical studies on cessation with vapour products. Our review will be among the first (maybe even the first) to conduct and publish the quality assessment of systematic reviews with the newly released AMSTAR 2. For the ongoing debate in tobacco control, it is important to challenge the confidence in the critically low quality Kalkhoran and Glantz review that is cited far more often than other, more robust reviews. My goal with our review is to point researchers and policy-makers instead to the high quality Malas et al. and Cochrane (Hartmann-Boyce et al.) reviews.

At the end of the day, I hope that my articles will make a difference in the debate on vapour products, and remove the perceptions of vapour products as a terrible threat requiring bans or restrictive regulations. I have alerted vapour product advocates to the dominance of threat claims in the regulatory arena with our NPF study. With the youth article, I have challenged the gateway theory and critiqued research designs based on past-30-day use and assumptions of nicotine vaping. The findings of the cessation umbrella review support our optimism that vapour products have potential as a cessation aid.

Concluding Statement

My research project has identified the claims about vapour products in the regulatory arena, and has examined the evidence on two of the most common claims: vaping causing youth nicotine dependence, and vapour products as cessation aids. I have shown that the regulatory processes have been nearly or completely dominated by vapour products as threat, resulting in bans on nicotine products and other highly restrictive regulations. My co-authors and I have pointed out that the claim of youth becoming nicotine dependent from vaping is a risk that is highly over-estimated because the research metrics include large numbers of youth who vape only once or twice a month, and questions about non-nicotine use have rarely been included in studies. We have added support to the claim that vapour products can be a cessation aid by considering the weight of the evidence, even as most other review teams have declined to state a definitive conclusion on their effectiveness.

In short, the fear of vapour products as a gateway to youth nicotine dependence is overblown, and the hope that vapour products can be an effective cessation aid is understated. Will the evidence from our articles prompt revisions in current regulations and public health

policies? It is very likely that many more researchers will need to speak up and present their evidence before unfounded claims about vapour products are silenced at last.

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Appendix B

Supplemental Files – Claims in Vapour Device (E-Cigarette) Regulation

Table S1 - Queensland Claims Texts

ID	Section	Claim
1	9.2.3	There is no benefit in the devices to assist people to stop smoking.
2	9.4	There is no doubt that many of these personal vaporisers are certainly being used as an introductory process for people, and particularly children, into the very bad and life-limiting habit of smoking.
3	9.4	Their unregulated availability to children, retail advertising and display, and use in smoke-free public places risks a return to smoking becoming popular and desirable especially to youth.
4	9.4	Their unregulated availability to children, retail advertising and display, and use in smoke-free public places risks a return to smoking becoming popular and desirable especially to youth.
5	9.4	Their unregulated availability to children, retail advertising and display, and use in smoke-free public places risks a return to smoking becoming popular and desirable especially to youth.
6	9.4	Years of campaigning by governments and communities to 'denormalise' smoking and reduce smoking rates could be undermined by the sale and use of electronic cigarettes and other personal vaporisers.
7	9.4	People, and in particular children, may be exposed to the second-hand-and I use the word in inverted commas-'smoke' from the e-cigarettes.
8	9.4.1	Risks from nicotine inhalation: different devices deliver different amounts, user puffing behaviour may lead to overdose through unreliable dosage delivered by devices.
9	9.4.1	Possible nicotine poisoning (mainly to children) due to leakage from devices or nicotine containers that are not childproof.
10	9.4.1	Health risks to non-users from inhalation of second hand e-cigarette aerosol – bystanders are exposed to exhaled nicotine and particles from e-cigarettes.
11	9.4.1	There is considered to be a possibility that children and non-smokers will start to use e-cigarettes and develop a nicotine addiction that may lead them to switch to cigarette smoking.
12	9.4.1	Queensland Health website states that vaporisers may also contain unknown, possibly toxic chemicals and have incorrect or inconsistent labelling and unsafe packaging.
13	9.4.1	Queensland Health website states that vaporisers may also contain unknown, possibly toxic chemicals and have incorrect or inconsistent labelling and unsafe packaging.

Table S2 – Canada Claims Texts

ID	Page	Claims Texts
1	3	Health Canada issued a notice cautioning consumers that electronic cigarettes may pose health risks…
2	3	some devices available in Canada that are advertised as not containing nicotine do, in fact, contain nicotine
3	4	"[t]here is lots of U.S. advertising that encourages use of e-cigarettes in places where smoking is banned."
4	4	advertising of e-cigarettes in the US is "certainly becoming an undermining effort to helping kids stop or not to start [tobacco use]"
5	5	there was widespread agreement as to the addictive nature of nicotine
6	5	Risks associated with liquid nicotine itself, identifying it as a poison that has been increasingly the trigger for calls to poison control centres in the U.S.
7	6	possible health risks associated with the use of the devices
8	6	flaws in the manufacture of the device
9	6	possible or probable negative impacts [on bystanders]
10	8	research suggests that there is a gateway effect for youth in particular.
11	8	candy flavoured electronic cigarettes as being particularly appealing to youth
12	9	the role that electronic cigarette use could have in undermining the gains made by tobacco control efforts, both in Canada and internationally. This phenomenon is referred to as the "renormalizing effect"
13	9	electronic cigarettes "pose a risk to the efforts and successes in tobacco control"
14	9	"the potential of e-cigarette use to impair the process of de-normalizing smoking behaviour which has played such a key role in reducing tobacco use, and that they could undermine smoke-free legislation and controls across the country"
15	10	the possible risks of electronic cigarettes as including "use by the tobacco industry to re-engage in tobacco policy"
16	10	"aggressive marketing of ENDS by some tobacco companies to be used in smoke-free environments as a way to break the enforcement of smoke-free policies."
17	10-11	"the co-branding of e-cigarettes with tobacco industry logos or brands. We don't want e-cigarettes being labelled as Rothmans, du Maurier, or Export A. That would only help to renormalize tobacco smoking."
18	18	to help prevent renormalization of smoking, electronic cigarettes should be visually distinct from other tobacco products.
19	19	concern over the lack of safety and quality assurance relating to electronic cigarettes, including both their liquids and their components, such as batteries
20	22	concerns about "renormalization" of smoking were expressed by several witnesses
21	22	concerns about potential health risks to bystanders

22	23	“free product offers, celebrity endorsements, overt lifestyle advertising, and attractive product packaging and flavours. This type of promotion influences the perceived acceptability of e-cigarette use and smoking, and I'm particularly concerned about its impact on youth”
23	23	“flavours. This type of promotion influences the perceived acceptability of e-cigarette use and smoking, and I'm particularly concerned about its impact on youth”
24	24	non-smokers who start using electronic cigarettes may start using tobacco products (the “gateway effect”)
25	24	cross-branding could contribute to the renormalization of smoking
26	24	cross-branding could contribute to the renormalization of smoking and increased take-up of tobacco products
27	25	the use of electronic cigarettes as a possible “gateway” to tobacco use...

Table S3 - EU Claims Texts

ID	Page	Claim
1	16	Do not contain nicotine but have the form of cigarettes and try to imitate the smoking process through vaporizing substances, the harmless nature of which is not yet scientifically proven
2	16	Such [non-nicotine] products are clearly produced to be appealing to young and underage consumers
3	16	the habits created by young consumers and minors by the use of such [non-nicotine] imitation cigarettes
4	24	different regulatory approaches to address health and safety concerns
5	24	different regulatory approaches to address health and safety concerns
6	24	the potential of such products to aid with smoking cessation
7	25	Labeling provisions…drawing the attention of consumers to potential health risks.
8	67	This product contains nicotine and can damage your health
9	79	Those below the [nicotine content] threshold would be allowed on the market with health warnings
10	80	ecigarettes could renormalize smoking
11	115	The cardiovascular toxicity of nicotine is established.
12	123	lower-risk nicotine containing products which can help consumers to quit smoking
13	123	lower-risk nicotine containing products…provided they feature an appropriate health warning
14	160	Nicotine-containing products as for example e-cigarettes contain toxic chemicals and tobacco specific components suspected of being dangerous to consumers.
15	160	e-cigarette cartridges labelled as containing no nicotine in many cases do in fact contain low levels of nicotine
16	160	Consumers indicate as well, that they mainly use e-cigarettes to quit smoking
17	261	These products (which are much less harmful than tobacco products)

Table S4 – US Claims Texts

ID	Page	Claim Text
1	29028	concerns about dual use of e-cigarettes and combusted tobacco products
2	29028	the possibility that flavored e-liquids are leading children to initiate tobacco use with e- cigarettes
3	29028	the alarming rise in e-cigarette use by middle school and high school students
4	29028	concerned about the rise in use of newly deemed products by youth and young adults, particularly the increase in use of ENDS
5	29028	concerned about the rise in use of newly deemed products by…young adults, particularly the increase in use of ENDS
6	29028	concerned about the dramatic rise in ENDS use among youth
7	29029	FDA remains concerned about the rise in ENDS use among youth and young adults
8	29029	FDA remains concerned about the rise in ENDS use among…young adults
9	29029	FDA remains concerned about… dual use of ENDS and combusted products in both youth and adults
10	29029	FDA remains concerned about… dual use of ENDS and combusted products in…adults
11	29029	we identified concerns regarding the toxicants in e-liquid and the exhaled aerosol and the nicotine delivery from e- cigarettes
12	29029	we identified concerns regarding… the exhaled aerosol
13	29029	we identified concerns regarding… the nicotine delivery from e-cigarettes
14	29031	Even if ENDS products have lower levels of nicotine, they still have the potential to addict users
15	29031	FDA agrees that the amount found was low, but reiterates that diethylene glycol is a toxicant and, therefore, is a cause for concern
16	29032	FDA's concerns with ENDS aerosol
17	29032	FDA is concerned about the risk of nicotine poisoning in both users and nonusers
18	29033	the dramatic rise in nicotine poisoning from e-liquid exposures is very concerning
19	29033	also noted poisoning concerns
20	29033	toxicological concern of chemical ingredients, such as diacetyl and acetyl propionyl, in e-liquids

21	29034	quality control concerns
22	29034	FDA understands the comments' concerns about the safety of e-liquids
23	29035	FDA remains concerned about adverse events associated with ENDS use, including overheating and exploding batteries as reported in the news
24	29035	the vast evidence that accidental nicotine poisoning is increasing in the wake of growing e-cigarette use
25	29035	concerns remain regarding quality control, which could impact the functionality of these products
26	29035	FDA agrees with comments' concerns regarding quality control and the safety of ENDS manufactured both domestically and in other countries.
27	29035	FDA noted its concerns regarding consumer misperceptions of currently unregulated products, particularly e-cigarettes…the believed e-cigarettes to be safe tobacco products.
28	29036	FDA is concerned that the growth in ENDS use, particularly among youth and young adults, could lead to the re-normalization of cigarette smoking.
29	29039	the rapid increase in use among adolescents is concerning
30	29039	FDA also remains concerned that ARPVs [advanced refillable personal vaporizers] present the risk of accidental nicotine poisoning
31	29040	FDA believes that ENDS could serve as alternatives to combusted tobacco products.
32	29040	FDA noted its concerns that adult consumers may use one or more of the proposed deemed products in conjunction with cigarettes or other tobacco products
33	29040	It is also recognized that some dual users of ENDS and cigarettes may be transitioning away from combustible tobacco use and that such transient periods of dual use may not present greater health risks than that observed during sole use of combustible tobacco.
34	29040	FDA is aware of dual use of ENDS and combusted tobacco products and is concerned about the potential impact of this practice on nicotine addiction and cessation.
35	29040	FDA is aware of dual use of ENDS and combusted tobacco products and is concerned about the potential impact of this practice on…cessation
36	29040	FDA shares similar concerns that youth may initiate tobacco use with ENDS, become addicted, and then dual use or move on to traditional tobacco products

37	29040	FDA shares similar concerns that youth may initiate tobacco use with ENDS… then dual use or move on to traditional tobacco products
38	29041	FDA remains concerned that youth may use one of the newly deemed products, whether it be an ENDS or any other tobacco product, and dual use with other tobacco products in the future

Table S5 Queensland Characters

Character	**Actor**	**Claim Texts**
Victim	Vapour device users	8, 9, 11, 12, 13
Victim	Youth	2, 3, 4, 5, 7
Victim	Tobacco control	3/4/5, 6
Victim	Adults	2, 11
Victim	Bystanders	7, 10
Victim	Smokers	1
Victim	Children	9
Villain	Manufacturers	8, 9, 12, 13
Villain	Vapour devices	1, 2, 6, 11
Villain	Vapour device users	5, 7, 10
Villain	Retailers	3, 4

Table S6 Canada Characters

Character	**Actor**	**Claim Texts**
Victim	Tobacco control	3, 12, 13, 14, 15, 16, 17, 18, 20, 22, 23, 25, 26
Victim	Vapour device users	1, 2, 5, 7, 8, 10, 19, 24, 27
Victim	Youth	4, 10, 11, 22, 23
Victim	Bystanders	9, 21
Victim	Children	6
Villain	Vapour devices	1, 5, 6, 7, 10, 11, 12, 13, 14, 18, 20, 22, 23, 24, 27
Villain	Manufacturers	2, 3, 4, 8, 19, 22
Villain	Vapour Device Users	3, 9, 16, 21
Villain	Tobacco industry	15, 17, 25, 26

Table S7 EU Characters

Character	**Actor**	**Claim Texts**
Victim	Vapour device users	1, 4, 5, 7, 8, 9, 11, 13, 14, 15
Victim	Youth	2, 3
Victim	Tobacco control	10
Villain	Vapour devices	1, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14
Villain	Manufacturers	2, 5, 15
Hero	Vapour devices	6, 12, 16, 17

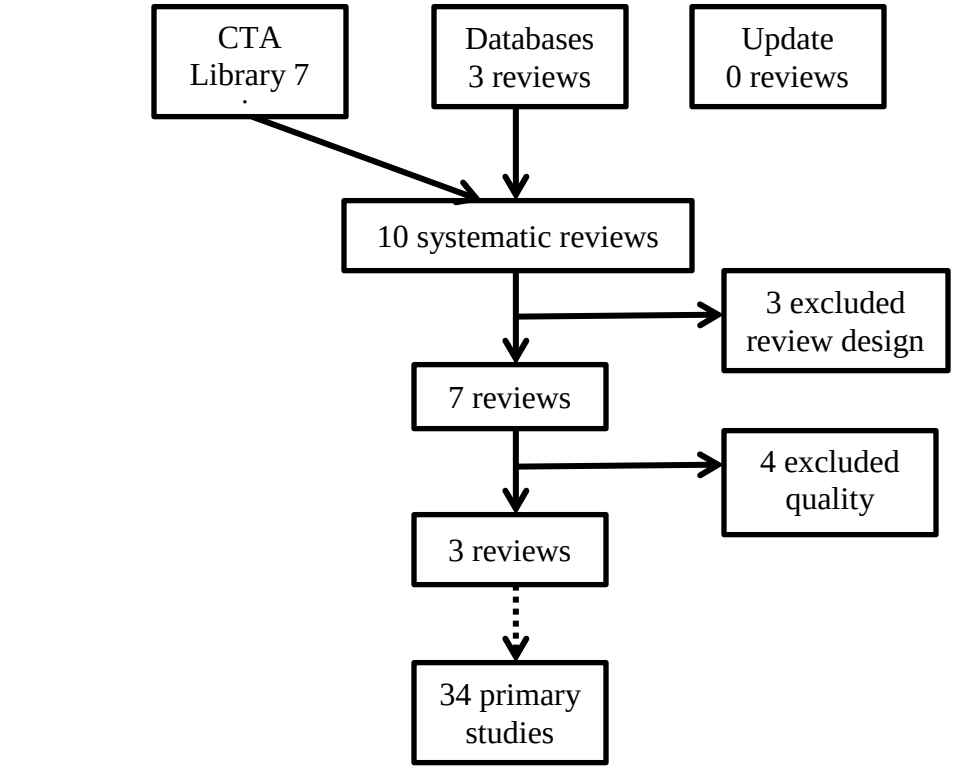
Table S8 US Characters

Character	**Actor**	**Claim Texts**
victim	user	1, 10, 11, 13, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 30, 32, 34
victim	youth	2, 3, 4, 6, 7, 9, 29, 36, 37, 38
victim	young adults	5, 8
victim	bystanders	12, 16
victim	children	17(a), 18, 19, 24
victim	tobacco control	28
victim	smokers	35
villain	vapour devices	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22, 24, 28, 29, 30, 32, 34, 35, 36, 37, 38
villain	manufacturers	21, 23, 25, 26
villain	user	27
hero	vapour devices	31, 33

Appendix C

Supplemental Materials for Vapour products (e-cigarettes) and tobacco cessation outcomes: A review of systematic reviews

Figure 1 Search Funnel



CTA Library inclusions:
Systematic review
published 2016 or later
Any language
Peer-reviewed and grey reports

Database Searches
Inclusion: review on vapour devices
published 2016 or later
Any language
Peer-reviewed and grey reports
Exclusion: no findings on cessation

Research design exclusions
Searches before 2016
Pooled data
No original analysis

Supplemental Table 1

CTA Library Search Strategy

Database	Search fields	Keywords
Academic Search Complete (EBSCO) CINAHL with full text (EBSCO) Cochrane Central Register of Controlled Trials (CENTRAL) (EBSCO) LGBT Life (EBSCO) MEDLINE (EBSCO) PsycArticles (EBSCO) PsycINFO (EBSCO) Social Sciences Citation Index (H.W. Wilson) Women's Studies International (EBSCO)	abstract OR title	[electronic cigarettes OR (e-cigarettes AND multiple topics) OR e-cigs OR vapor cigarettes] OR [electronic nicotine AND (delivery systems OR delivery device OR devices)]
Business Source Complete (EBSCO), limited to scholarly (peer reviewed) journals	subject terms	electronic cigarettes
LILACS (Latin American and Caribbean Literature on Health Sciences)	abstract words	vaporizer
MEDLINE 1996 – on (OVID)	keyword	electronic cigarette*
PubMed	title/abstract	electronic cigarette* (AND sub headings) OR electronic nicotine delivery (AND sub headings OR e-liquid* OR vaping)
ScienceDirect (Elsevier)	abstract, title, keywords	electronic cigarette* OR "electronic nicotine" OR vaping
Web of Science (Thomson Reuters)	topic	"electronic cigarette*" OR e-cigarette* OR "electronic nicotine" OR vaping

Supplemental Table 2

Systematic Review Search Strategies

Review ID # of studies	Study types	Databases	Additional searches	Inclusion criteria (exclusions)	Quality tool
El Dib 12 studies	RCT Prospective cohort	Medline EMBASE PsycINFO CINAHL Cochrane CENTRAL Web of Science	CDC Smoking and Health alerts, web news items from Gene Borio	Studies with comparators to no aid, other cessation aid, or alternative VP	Ottawa-Newcastle, Cochrane Risk of Bias, GRADE
Hartmann-Boyce 17 studies	RCT Cohort follow-up	Cochrane Tobacco CENTRAL. MEDLINE EMBASE PsychINFO	Reference checking, metaRegister database	6+ months f/u	Cochrane Risk of Bias
Kalkhoran 38 studies	RCT Clinical trials Cohort Cross-sectional	3 meta-analyses PubMed Web of Science	None reported	Cessation as the primary outcome. (excluded adolescents populations)	ACROBAT-NRSI, Cochrane Risk of Bias
Knight-West 21 studies	RCT User surveys Case reports Cohort	Google Scholar PubMed	None reported	Not reported	No systematic assessment.
Malas 15 studies	Empirical qualitative Empirical quantitative	PubMed MEDLINE PsychINFO CINAHL ISI Web of Science + 5 others + 12 grey lit	None reported	English Original data 30+ day f/u (excluded public awareness, weak quality studies)	Modified QualSyst, GRADE
Orellana-Barrios 8 studies	RCT Prospective observation.	MEDLINE Web of Science	Reference checking, Expert consultation	English. Biochemical verification. One arm only VP. 6+ months f/u.	Cochrane Risk of Bias
Vanderkam 13 studies	RCT Longitudinal cohort	MEDLINE Cochrane CENTRAL	Contacted researchers	English. 10+ cig/ day, ages 18-60, 3+ month f/u. (excluded participants w/ comorbidities)	Cochrane Risk of Bias

Supplemental Table 3

Summary of Meta-Analyses Findings

Review ID	Meta-Analysis
El Dib	2 RCTs nicotine vs non-nicotine EC RR 2.03, 95% CI [0.94, 4.38], p=0.07 possible increase in cessation - low certainty. 8 cohort OR 0.74, 95% CI [0.55, 1.00], p=0.051 for EC vs. no EC, no benefit for cessation – low certainty.
Hartmann-Boyce	2 RCT nicotine EC vs placebo RR 2.29, 95% CI [1.05, 4.96], 5% effect size, GRADE low. 1 RCT nicotine EC vs. NRT RR 1.26, 95% CI [0.68, 2.34] GRADE very low. Research based on first generation devices.
Kalkhoran	20 studies – 28% less likely to quit, 95% CI [0.57, 0.91]. Smokers with quit intentions 14% less likely to quit, 95% CI [0.60, 1.23], not significant.
Knight-West	N/A
Malas	5 studies, abstinence duration not reported: no control 11%-75% abstinence EC compared to NRT, AOR 1.63, 95% CI [1.17, 2.27] EC compared to no aid, AOR 1.61, 95% CI [1.19, 2.18]. 6 studies abstinence 6+ months: no control 13.1% - 36% abstinence; EC compared to NRT and placebo, both non-significant. GRADE low.
Orellana-Barrios	4 prospective studies average combined abstinence rate (at 6-18 months) 29.1%.
Vanderkam	2 studies, excluding subjects with psychiatric diseases, nicotine vs non-nicotine RR 2.55, 95% CI [1.31, 4.98].

Supplemental Table 4

Summary of Narrative Findings

Review ID	Findings
El Dib	N/A
Hartmann-Boyce	All non-RCT studies at high risk of bias. Longitudinal studies have serious limitations due to study population, with 7 studies finding no significant difference in abstinence rates and 2 determining a decreased in rates. Abstinence rates in cohort studies (both intending and not intending to quit) range from 5% - 53%, and 8% - 46% with ITT. Definitions of EC use, level of quit support, and other confounders vary considerably. Abstinence outcomes not always defined, and frequently based on self- report, lowering confidence in the findings.
Kalkhoran	Description of each individual study, no summary.
Knight-West	Self-selection bias in cross-sectional studies. Studies differ in their conclusions. Quality and generalizability of data are low. Specific devices in trials no longer commercially available. 2nd and 3rd generation devices have greater cessation efficacy. Vaping topology improves with practice. Greater frequency and intensity of use appears to improve cessation rates. Online user groups and videos offer a unique source of cessation support.
Malas	11 of 14 moderate/strong studies show effectiveness, but GRADE low to very low. Limited evidence that EC potentially useful for some smokers. 2nd generation devices may be more effective than 1st generation.
Orellana-Barrios	Studies described individually. When devices used in trials are no longer available, it diminishes the applicability of the findings. Some evidence that EC may have better cessation rates than other methods.
Vanderkam	RCT cessation rates with nicotine devices compared to patch or placebo not significant at 6 months. Other studies indicate cessation rates of 20% - 30% at 6 months, but rates decrease over time. Intensive use and 2nd generation devices increase quit rates.

Supplemental Figure 1

Corrected Coverage Area Calculation

The formula is CCA=(N-r)/(rc-r) where N is the total number of publications, r is the number of index studies, and c is the number of reviews. The CCA score is classified as *slight* (0%-5%), *moderate* (6%-10%), *high* (11%-15%), and *very high* (>15%).

CCA very high at 23%
N = 50 total publications (cells)
r = 34
c = 3

(50-34)/(102-34) = 16/68 = 0.23

Supplemental Table 5

AMSTAR 2 Quality Assessments

Systematic Review	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Rating
Hartmann-Boyce	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Malas	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	High
El Dib	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Orellana-Barrios	Y	P	Y	P	Y	Y	P	Y	P	N	N	X	Y	Y	X	Y	Low
Vanderkam	Y	P	Y	P	Y	Y	N	Y	Y	N	Y	Y	Y	N	N	Y	Low
Kalkhoran	Y	Y	Y	P	N	N	Y	Y	Y	N	N	N	Y	Y	Y	Y	Critically Low
Knight-West	Y	N	Y	P	N	N	N	P	N	N	X	X	N	Y	X	Y	Critically Low

Y = Yes N = No P = Partial Yes X = no meta-analysis

Critical domains: Q4, Q9, Q11

Rating

High = no or one non-critical weakness

Moderate = more than one non-critical weakness

Low = one critical flaw with or without non-critical weaknesses

Critically low – more than one critical flaw with or without critical weaknesses

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