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Informing E-cigarette Policy: Population Effects and Tobacco Industry Incentives

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Informing E-cigarette Policy: Population Effects and Tobacco Industry Incentives

By

Zachary Cahn, MA

Advisor: Richard Saltman

An abstract of a dissertation submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Health Services Research and Health Policy, 2016.

Abstract

Informing E-cigarette Policy: Population Effects and Tobacco Industry Incentives
By **Zachary Cahn**

This dissertation consists of a set of papers intended to inform practitioners and scholars of nicotine policy in general and e-cigarettes specifically. The first chapter frames the subsequent chapters and introduces some key concepts that are necessary to understand this framing. The second chapter synthesizes the research on past obstacles to cigarette innovation in order to 1) determine why cigarette innovation did not yield substantially reduced hazard for decades, and 2) gain insight into how tobacco companies are likely to behave today and in the future. Special attention will be paid to the emergence of e-cigarettes and why the industry did not enter this market sooner. The third chapter focuses on the potential for e-cigarettes to "renormalize" cigarette smoking. Looking at one specific pathway – social renormalization – this chapter seeks to estimate whether peer vaping affects the perception of peer smoking among youths. The fourth chapter **e**xamines predictors of initiation of e-cigarette use among consistent smokers and analyzes the impact of e-cigarette use on cessation among smokers in a national U.S. consumer panel. The fifth chapter puts the findings from the previous chapters into context and develops core lessons for scholars that seek to study e-cigarettes and policymakers that seek to regulate them.

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Chapter 1. Approaching e-cigarette policy: Harm reduction and population effects

Introduction

The emergence of alternative nicotine products, particularly electronic cigarettes (e-cigarettes), presents a number of vexing questions for health policymakers. E-cigarettes can potentially represent a "harm reduction" approach to smoking policy. Unlike abstinence-oriented policies that aim to eliminate harmful behaviors, harm reduction policies seek to reduce the hazards associated with those activities. However, many scholars argue that e-cigarettes are at least as likely to *increase* the harm associated with nicotine use by either prolonging the use of nicotine among people who would otherwise quit nicotine altogether, lowering the odds of smoking cessation, or creating a causal gateway from vaping to smoking.

Harm reduction debates in tobacco control policy can be categorized as *static* or *dynamic*. The static debates focus on the potential for products already in existence to improve or worsen tobacco-related disease. Dynamic harm reduction debates focus on how policies can impact products likely to be developed and marketed in the future, rather than the costs and benefits to population health associated with products already in existence.

Dynamic Harm Reduction

The next chapter will address the dynamic harm reduction debate as it applies to the role of tobacco companies in cigarette innovation. Most scholarly attention to the tobacco industry since the late 1980s has focused on the deceptive practices of the

industry (*1–3*). This history raises two core issues for dynamic harm reduction policy. First, can the tobacco industry be expected to make a genuine effort to reduce the harm that their products when, historically, they have not done so? Second, and closer to the main purpose of this article, what factors can explain their prior lack of effort in this regard, and how many of the factors that hindered meaningful health innovation in the past are still operative in tobacco companies today? Answers to these questions can help us predict how the industry will behave today and should inform how policymakers approach modern tobacco companies and other nicotine sellers in order to avoid the disasters of the past and lower tobacco-related disease in the future.

The next chapter itself will be focused on describing the story of less hazardous cigarette innovation and considering how it applies to current policy toward novel nicotine products. The word "dynamic" is meant to echo the Schumpeterian concept of "dynamic efficiency", which he coined to direct focus on the innovative output of an economy apart from its productive output at any one moment in time (*4*). This concept is at the heart of academic debates over intellectual property and patents (*5*, *6*) or anticompetitive market structures (*7*). These debates concern a more abstract notion of innovative output. Often, scholars will point to the amount of resources that appear to be devoted to innovative activities as a primary good rather than focusing on downstream innovative output.

In the case of cigarettes, looking at the amount of resources devoted to innovation would be particularly misleading as a measure of societal welfare. The reason for this is that, for cigarettes, there is one particular dimension of the product – hazardousness to health – that is of far more societal importance than any other. Thus, the most important,

socially optimal innovations are those that reduce the unparalleled hazards of the product. Altering the cigarette in other ways, either those that do not address the health issue at all or in ways that only pretend to do so, are so much less socially significant that it would be preferable to ignore them altogether than to include them in a measure of innovative output. This is what separates dynamic harm reduction from dynamic innovation more generally. In industries where negative externalities – or internalities (*8*) – are of overwhelmingly greater societal importance than their consumer and producer surpluses (*9*), we should focus particularly on innovations which mitigate the harms of the product to the exclusion of more traditional considerations. Thus, this dissertation will not focus on the general barriers to innovative output in the tobacco industry, but instead on the barriers that specifically hinder the innovation of truly *safer* products. Readers outside of tobacco control may recognize that these lessons apply to innovation in the context of dirty or dangerous status quo states where an industry is attempting to innovate amidst substantial political controversy. Producers of products that are inherently hazardous to health, create substantial environmental waste, or are otherwise damaging to public welfare can be analyzed in similar fashion.

Static Harm Reduction

The core issue in determining the appropriate policy response to any given potential alternative product is whether this product will increase or reduce total population harm (*10*)(*11*)(*12*). In order for total population harm reduction to be achieved, there must be both a substantially increased probability of quitting and/or reducing cigarette consumption among users and a substantial reduction in harm to the user for vaping compared with smoking (*10*). Simultaneously, whatever harm reduction

gains are realized must not be offset by either increased smoking initiation among nonsmokers due to gateway effects or increases in the prevalence of overall nicotine use due to non-gateway e-cigarette proliferation. An increase in overall nicotine use, even if smoking is reduced, would entail increases in harm for users who would be completely abstinent from nicotine without the availability of alternative nicotine products. Thus, the net effect on cigarette and alternative product use in the population, as well as the harmfulness of the alternative products themselves, will together determine the effect on total population harm (*12*).

Population effects of e-cigarettes on traditional tobacco cigarette use are arguably the primary driver of total population harm. They are also an important component of the criteria necessary for "reduced harm" or "reduced-exposure" designation under the 2009 Family Smoking Prevention and Tobacco Control Act (FSPTCA) (*13*). Shedding light on the true population *effects* – causal mechanisms by which use of e-cigarettes affects subsequent tobacco smoking behavior – can provide policymakers with estimates of the most critical parameters in the population harm function presented in Figure 1.

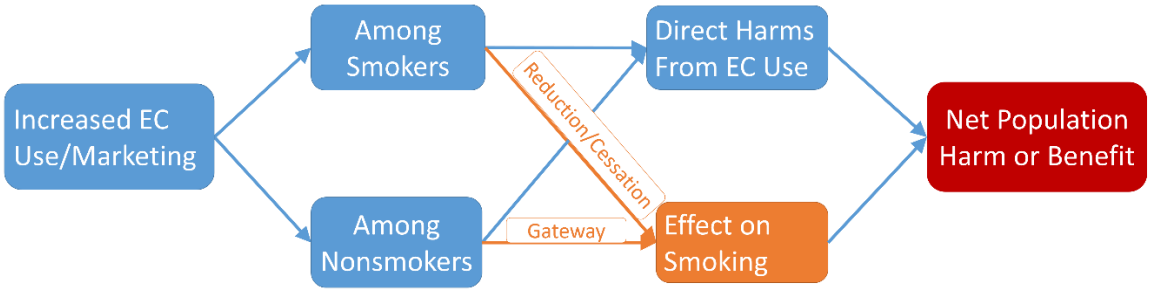

Figure 1: population harm function

A critical set of questions relate to the effects of e-cigarette use on traditional tobacco cigarette use among both nonsmokers ("gateway" effects) and smokers ("cessation" or "reduction" effects). Together, these can be considered the "population

effects" of e-cigarettes. Chapter three of this dissertation will focus on gateway effects, while chapter four will look at the potential for e-cigarettes to contribute to cessation or reduction of smoking. Population effects are extremely important but difficult to quantify, making them particularly susceptible to studies that provide flawed reasoning and erroneous conclusions. In fact, MacNeill et al., after addressing the difficulty of isolating the true gateway *effect* of e-cigarette use, wrote that "we strongly suggest that use of the gateway terminology be abandoned until it is clear how the theory can be tested in this field" (*14*). This would be an improvement over much of the current discourse on these issues. However, this phenomenon is likely to continue to be central to the argument about population impact, as will the impact of e-cigarettes on harm reduction and cessation, as they all have significant implications for policy. However, it is certainly necessary to be more specific about precisely what causal mechanisms population effects research should aim to quantify.

Gateway Mechanisms

The vast majority of studies that examine associations between vaping and smoking either make no clear gateway claims, or allude to a gateway effect without explicitly detailing the mechanism by which it is meant to occur. However, several possible causal gateway mechanisms have been highlighted in the existing literature, to which we can add others. The first group of mechanisms relates to the psychopharmacological properties of nicotine. If nonsmoking youths develop an addiction to nicotine, then this addiction may make them more susceptible to tobacco smoking as a means to deliver nicotine more efficiently (*15*). Or addiction to nicotine will alter their brain chemistry leading them to be more susceptible to addiction in general

(*16*). A similar pathway that does not assume addiction to nicotine could be called the "positive affinity" pathway. E-cigarettes are designed to both deliver nicotine and mimic the act of smoking (*17*), and so early use of an e-cigarette may increase positive affinity toward the act of smoking and reduce psychological barriers to tobacco smoking. This would be relevant to users of non-nicotine e-cigarettes as well.

A second group of mechanisms centers on the behavior of e-cigarette sellers and marketers. These mechanisms are particularly relevant in light of the recent entry of major tobacco cigarette makers into the e-cigarette market. While we should be concerned about marketing to nonsmokers from all e-cigarette sellers, only those that also produce tobacco cigarettes will have an interest in "graduating" their e-cigarette consumers on to combustible cigarettes. A mechanism that applies broadly to all e-cigarette sellers is the "nicotine/vaping image" pathway, where marketing for e-cigarettes enhances the image of nicotine and smoking-like behavior, potentially spilling over into increased interest in smoking (*18*). More ominously, the "tobacco company malfeasance" pathway concerns the possibility that makers are creating branding that is specifically designed to facilitate gateway or dual use (*19*). This is highly plausible on its face, especially as more and more tobacco companies enter the e-cigarette space (*20*) (*19*). Past tobacco company behavior shows that they are willing to prioritize cigarette sales even when they are ostensibly marketing an alternative (*21*).

Lastly, the main focus of this dissertation will be on the "renormalization hypothesis," which holds that increases in public vaping will stymie efforts to *denormalize* the smoking act (*22*). This hypothesis holds that public vaping subjects bystanders and youths to witnessing a smoking-like tableaux when they might otherwise

not see such imagery that reflects a smoking culture. The increased prevalence of smoking-like behavior will make smoking itself appear more "normal" and tolerable. The mechanisms underlying this hypothesis are more difficult to identify and would seem to require some key assumptions. If vaping truly represents the *renormalization* of smoking as opposed to the *normalization* of vaping alongside the continued *denormalization* of smoking, then bystanders must be either unable to distinguish between vaping and smoking or are consciously or subconsciously conflating their views on the acceptability of vaping and smoking. This confusion or conflation is understandable. E-cigarettes are often designed to look like tobacco cigarettes and both their own messaging and public health messaging often emphasize the similarities between vaping and smoking rather than the differences. As familiarity with e-cigarettes increases, the public may become better at distinguishing between the two products, but there is substantial confusion presently. Chapter three of this dissertation will take a closer look at the denormalization, attempting to measure the degree to which peer vaping affects the perception of peer smoking in the United States.

It is also possible that the presence of e-cigarettes will lead to less tobacco smoking initiation rather than more. Increased likelihood of progression to traditional tobacco smoking is often assumed to be the only possibility, when in fact it is possible that e-cigarette availability, use, or marketing may actually reduce smoking initiation. This could be because would-be smokers may instead prefer e-cigarettes or because e-cigarette marketing contains implicit or explicit antismoking messaging. Econometric evidence presented by Friedman (2015) supports this possibility (*23*).

Cessation Mechanisms

There are several plausible effects that e-cigarettes may have on the smoker community, either increasing or decreasing the odds of smoking cessation. The most obvious is the substitution effect, where smokers reduce or cease tobacco cigarette smoking by using e-cigarettes as a replacement. This is a particularly valuable role if e-cigarettes are used in this way, as smokers unmotivated to quit might quit simply because they prefer e-cigarettes (*11*). Another possibility is that smokers intending to quit may use e-cigarettes as a cessation device even though they may not marketed for this purpose (*24*). E-cigarettes would represent an improvement in cessation device technology if they are either more efficacious or more appealing (i.e., more smokers are willing to attempt quitting using e-cigarettes) than existing nicotine pharmacotherapy options.

In addition, if e-cigarette marketing continues to contain explicit anti-smoking messages (e.g., NJOY's messaging), there may be an effect on quit intention that leads to increased cessation, even in the absence of e-cigarette use. Creating and marketing an e-cigarette product risks reducing cigarette sales. Tobacco companies are increasingly willing to take this risk. Nevertheless, compare the branding for Blu Cigs (a tobacco company subsidiary) with NJOY (a standalone company). Blu Cigs proclaims "We're all adults here" and "It's time to take our freedom back" (*25*), while NJOY suggests "Friends don't let friends smoke" (*26*). Standalone e-cigarette providers are much more likely to directly challenge tobacco cigarettes and use explicit anti-smoking marketing strategies.

As in the case of the gateway effect, it is possible that e-cigarette marketing and use might decrease the odds of cessation. Many are concerned that smokers will have

more trouble quitting tobacco cigarettes if they maintain their addiction through e-cigarettes (*19, 20*). In particular, the effect of smoking bans on cessation might be lessened if smokers are able to vape where smoking is not allowed. Additionally, e-cigarette users who continue smoke may be increasing their overall nicotine intake, potentially leading to greater nicotine addiction and a reduced likelihood of cessation. We should be particularly concerned with the involvement of tobacco cigarette companies. McNeill and Sweanor (2009) reported that Philip Morris designed a snus product (a noncombustible tobacco product which has provoked a similar debate to e-cigarettes) with reduced nicotine for the likely purpose of facilitating dual use rather than substitution for tobacco cigarettes (*21*). Pesko et al. (2015) found that the overly elaborate MarkTen (an Altria e-cigarette) warning label made consumers more likely to want to continue purchasing tobacco cigarettes (*27*). It is also possible that e-cigarette ads will have smoking "cues" that will lead ex-smokers back to cigarettes or nicotine (*18*). The Fin "Welcome back" ad campaign is a notably brazen attempt to lure back ex-smokers to nicotine use (*28*). Chapter four of this dissertation will attempt to assess the degree to which e-cigarettes are increasing or decreasing the likelihood of cessation among a population of American smokers.

Policymaking Amidst Uncertainty

Lastly, chapter five will summarize the lessons of the previous chapters, add additional evidence on e-cigarette population effects gleaned from other authors, describe how e-cigarette policy differs from other policy areas and previous tobacco control debates, and give a set of policy guidelines and prescriptions for handling e-cigarette policy. One major factor that makes e-cigarette policy unique is the enormous level of

uncertainty about the true effects of e-cigarettes to individuals and the population at large. This final chapter will describe this uncertainty and why it is likely to continue, concluding with a discussion of how this uncertainty should impact our policy approach to e-cigarettes.

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Chapter 2. Barriers to hazard-reducing innovation: Understanding why e-cigarettes did not emerge sooner

Introduction

Ever since scientific papers began to definitively uncover the link between smoking and disease (*1–5*), policymakers seeking to reduce tobacco-related illness through the proliferation of less hazardous products have faced one key obstacle: the tobacco industry could not be trusted (*5–7*). Why were tobacco industry efforts so lacking?

The main goal of this chapter is to synthesize the research on past obstacles to cigarette innovation in order to gain insight into how tobacco companies are likely to behave today and in the future. Reviewing the factors that have historically aided or hindered cigarette innovation can both improve our understanding of why tobacco industry research "efforts" were so lacking for so long and help tailor our modern policy approach to optimize the prospects of successful harm reduction and minimize the prospects of further deception.

This synthesis is particularly timely now that e-cigarettes have emerged as the preeminent policy debate within tobacco control. E-cigarettes, while not harmless (*8*), appear to reduce harm to their users who had been using traditional cigarettes (*9*). If it turns out that the net effect of e-cigarettes reduces total population harm, then it will logically follow that smoking rates and disease would be reduced today if e-cigarettes had entered the marketplace earlier. This review will pay special attention to why e-cigarettes did not emerge sooner and why they were not introduced by tobacco companies. Specifically, we will highlight 1) types of incentives at play, specifically

indirect disincentives, direct disincentives, and bottom-up disincentives; and 2) some modifying factors that affect the strength of these disincentives across firms and time and that may help explain the sequencing of events leading to the current status of the e-cigarette market.

Incentives, Disincentives, and Innovative Effort

The net incentive to engage in innovative effort at the firm level – the expected net effect on the firm's profits from a prospective new product – can be disaggregated into a set of individual incentives and disincentives. We will focus on the disincentives, since they dominate tobacco industry thinking over the years. It is useful to dichotomize these disincentives in 2 ways: direct v. indirect and bottom-up v. top-down. *Direct* incentives or disincentives are the factors that affect the perceived revenues or costs that a prospective new product is expected to generate (incentives either raise expected revenues or reduce expected costs, while disincentives either raise expected costs or lower expected revenues). *Indirect* incentives and disincentives are any other factors associated with a prospective new product that affect the overall firm's expected profit. A potential new product that is expected to be individually profitable might nevertheless be perceived as net costly to the firm due to indirect disincentives to innovate. Similarly, many "charitable" activities are not revenue-positive but are engaged in for their indirect effects on company profitability (*10, 11*). Distinguishing between *direct* or *indirect* disincentives can highlight ways that industrial organization can impact research effort that are not usually considered in debates about industrial organization and technological progress (*12*).

Distinguishing between *bottom-up* and *general* disincentives can help understand why products like e-cigarettes were so slow to come to market, even after technological barriers were lowered. *Bottom-up* disincentives apply specifically to products that attempt to build up from nicotine rather than down from tobacco (*13*). *General* disincentives apply to any new health-oriented innovation, whether bottom-up or top-down. We do not similarly separate out top-down incentives because there does not turn out to be many specific barriers to top-down innovation aside from the eventual perception that this approach was infeasible.

There are also several modifying factors that altered the strength of these disincentives (Table 1). Many of these factors are dependent on a firm's market position. Other factors depend on order of entry. We will elaborate on these modifying factors after our discussion of the disincentives themselves.

While some disincentives are essentially constant across time, others have waxed and waned depending on contingent and contextual factors that have varied over the years. Figure 1 gives a rough summation of how the impact of each disincentive has shifted over time, with red indicating a strong impact, green a weak or non-existent one, and yellow something in between. This chart broadly conveys the story of cigarette innovation over the past few decades.

Indirect Disincentives: Threats to the Existing Business

Indirect disincentives affect a firm's willingness to innovate new products due to concerns about how this innovative effort will redound on the existing business of the firm.

Knowledge and Admissions of Harm

The threat of crippling legal liability was probably the single most important factor hindering innovative effort for much of the past 60 years (*6*, *14*, *15*). "Subsequent repair" doctrine, encapsulated in Federal Rule of Evidence 407, is meant to "allay the concern that liability rules may encourage unsafe behavior"(*16*). Rule 407 is intended to encourage companies to make safety improvements by deeming such improvements inadmissible as evidence that the original product was unreasonably dangerous. However, Rule 407 is "riddled with exceptions so that it provides uncertain protection to those who repair unsafe conditions" (*16*). Beyond that, it does not automatically privilege health-oriented research that might lead to a safety improvement, which severely undermines the ability of the rule to shield juries from making adverse inferences about corporate negligence (*17*). As such, tobacco defense litigators recognized that ignorance was their best defense (*18*).

Public Relation (PR): Public Perception of Harm

In addition to concerns about what juries and judges might think, tobacco companies had reasons to be concerned about what other citizens – smokers, potential smokers, voters, representatives, policymakers, etc. – thought about the harmfulness of their product. As such, tobacco companies recognized a strong public relations benefit to sowing doubt about any causal connection between smoking and disease (*19–21*). The difficulty of truly solving the problem of cigarettes and harm (*1*, *22*), in combination with the ease with which the industry and their outside partners were able to create uncertainty over key causal questions, favored the strategy of denial. Once the tobacco industry had adopted a public position that cigarettes were not proven to be unsafe, then even attempting to innovate safer products would undermine their position that there is no

cause for concern in the first place. Put differently, shielding jurors from knowledge of reparative efforts does not prevent views of regulators, voters, and consumers from receiving this knowledge and interpreting it unfavorably.

Marketing: Inherent Disparagement of Other Products

Leaving aside the legal and PR concerns associated with reduced-hazard innovation, how can a cigarette manufacturer *market* a new reduced-hazard innovation in a way that does not inherently disparage the rest of their cigarette business? While tobacco companies can subtly suggest a health benefit without emphasizing it, there is less to be gained from developing a safer product if it is not going to be explicitly marketed as such. And, if a new product *is* marketed as healthier, this cannot but reflect poorly on the remaining products that are less healthy by implication.

Cannibalization of Existing Product Lines and Market Destabilization

New products introduced to the market might cannibalize existing sales of other products. This is a well-known phenomenon that is widely applicable to other industries, especially in technology. Cannibalization mutes the incentive for a firm to develop a new product (*23*, *24*) or introduce it upon development (*25*). This disincentive is proportionate to the expected market share absent that new product, applying more to larger and growing companies than to small and declining ones (and not at all to new entrants). Although it is not specific to tobacco, this has been a lingering concern among tobacco control advocates who have argued that Philip Morris in particular is unwilling to introduce products that might compete with cigarettes (*26*).

Beyond first-order cannibalization, a major innovation might lead to a flurry of destabilizing competition where competing firms are induced into releasing hazard-

reducing features of their own. Such a response is particularly likely for a radical innovation from a large firm (*27*). Not only will the rate of product introduction into the marketplace go up, but the rate of brand-product switching may accelerate as consumers perceive a reduction in hazard associated with a new product type and value this reduction.

Collusive Cooperation and Retaliatory Behavior

Tobacco companies had collaborative discussions about the collective damage being wrought by health-oriented innovations. Langenfeld and Noffster point out that "there should be limited or no economic motivation to conspire when the industry members know it is in each individual's interest to act in a certain way" (*28*), although they do not specifically apply this logic to safety innovation. The strong disincentives present at the company level meant that there was not necessarily a need for strong collusion at the industry level.

Consider Solow's analysis showing a steep decline in "fear advertising" – ads that drew attention to the cigarette health issue in order to sell purported harm-reducing innovations – after a famous meeting among five of six industry members in 1953 (*29*). "Fear advertising" created a classic prisoner's dilemma, similar to the issue of less hazardous products in general, where increasingly brazen health claims by manufactures were succeeding in selling new brands but having the collective effect of raising alarm about the dangers of cigarettes and harming overall cigarette sales. Almost immediately, most members who were party to that meeting ceased fear advertising, while Liggett, who was not at the meeting, did not change its behavior (*29*). Solow and others consider this to be an example of collusive behavior on the part of the industry. However,

Reynolds, at the time one of the biggest companies with the brightest future, chose to unilaterally cease fear advertising years earlier, which could not have been due to a collusive agreement. Thus, while seemingly collusive behavior occurred, the degree to which this behavior was explicitly or implicitly coordinated, or would have occurred without such coordination anyway, is unclear.

There have been several documented instances of retaliation from large tobacco companies toward outside companies, but this does not necessarily mean that a collusive agreement is being enforced. The most severe instances of retaliation appear to have occurred outside of any "cartel" system. Harris lists the examples of Philip Morris boycotting Dow Chemical in response to aggressive Nicorette Ads, but Nicorette was not a party to any collusive agreement. Nor was Liggett, who faced retaliation for their XA project in the late 1970s (*30*). In other words, Philip Morris and R. J. Reynolds (RJR) were willing and able to pressure other companies not to compete on health whether or not any explicit or implicit agreement was in place.

Chronology

Figure 1 shows how the strength of these factors have changed over time. In the years immediately following the 1953 health scare, PR concerns were central, and liability concerns more secondary. The PR effect of the reader's digest article of 1952 (*4*), on top of accumulating evidence in medical journals (*2*, *3*), led to a stunning sales decline in 1952 that spurred the tobacco industry into a PR strategy that sought to emphasize that the dangers of cigarettes were overstated and unproven (*5*, *21*). However, liability concerns were not far behind. Within a couple of years, the "first wave" of liability lawsuits emerged (*31*). Soon, all research efforts were put under "lawyer control" (*15*).

By the "third wave" of tobacco litigation in the mid-1990s (*31*), it had become less clear that refusal to engage in safer product development was the most favorable course or action to take from a liability or public relations perspective (*32*), due to the advent of warning labels and the increasingly overwhelming consensus on harms. Tobacco makers could argue that they were simply responding to consumer beliefs about harm (*32*). Indeed, the industry's position completely reversed on this point, employing expert historians to make the argument that the harms of smoking were not only known but *common knowledge* when the plaintiffs took first took up smoking (*33*, *34*). By 1999, cigarette manufacturers were willing to explicitly concede that the scientific consensus linking smoking to disease was "overwhelming" (*35*). Today, since tobacco companies have admitted the dangers of using their products (*35*), e-cigarettes have gained a foothold in the market, and the Tobacco Act has been passed creating regulatory categories devoted to less hazardous nicotine products (*36*); there is relatively little possibility that current innovative activity will redound to weaken industry defenses regarding previously sold products.

The other indirect disincentives to innovate have been more stable over time. While it may be less costly to emphasize the dangers of cigarettes today than it was in the 1940s and 1950s when a much higher share of the population was persuadable on this issue (*19*), this is still a message that cigarette manufacturers would prefer to avoid. Fear of destabilization and cannibalization have remained relatively constant, since these business factors are not the product of specific contextual strategies but more general factors associated with the industrial structure in the tobacco industry.

As for collusion, it is very unclear whether there was ever any real fear of the consequences of violating an agreement, such that we do not assign much weight to this factor even if such an agreement did exist. In any case, it could not have exerted much influence since the late 1980s, when RJR went to market with a major reduced-harm innovation in the late 1980s, followed by Philip Morris in the mid-1990s. Today, small players beyond the reach of tobacco giants will continue to push innovation forward anyway, such that collusion on this issue is essentially fruitless. Retaliation remains something to watch out for. Tobacco companies have shown an ability to reach outside of their own industry to influence behavior in the NRT industry. Will they be able to exert pressure on standalones, through patent lawsuits for example? (*37*, *38*).

Direct Disincentives: Substance and Substantiation

Direct disincentives affect the profitability a potential new product regardless of how it might impact on other products.

Information Environment: Ease of Deception

The business incentive to create a safer product derives from consumer desire for safer products. However, what primarily matters for profits is that consumers *believe* the product to be safer. As the difficulties associated with reducing the hazards of cigarettes became clear, the tenor of research efforts shifted toward "health-image" products that consumers might simply perceive to be less harmful (*39*, *40*). When independent experts and health authorities, let alone consumers, cannot easily distinguish which seemingly harm-reducing innovations are likely to be meaningful, then health-image innovations represented a cheaper way of competing on the health issue. This approach yielded similar sales benefits at a much lower innovation cost.

Marketing Restrictions and Claim Substantiation

In the environment created by constant dubious health claims and insinuations, the FTC had a natural regulatory role in policing these deceptive claims. Imposing a standard of substantiation does not necessarily hinder innovation. Such regulations are only problematic if that standard is too weak (facilitating aforementioned deceptive health-image innovations) or too strong (hindering actual health-oriented innovation). Lanzilotti forcefully argues that FTC actions in 1960 banning reporting of tar and nicotine numbers led to higher tar and nicotine yields (*41*) during a time when many public health organizations remained optimistic that reduced tar would lead to reduced disease. Only in retrospect can we say that lowered tar did not substantially reduce disease (*42*), such that the true damage of this action was minimal.

Third Party Support for Less Hazardous Products

With barriers to making health claims themselves, tobacco companies were increasingly reliant on third parties and public health figures to supply information about relative hazards. Third party endorsement from public health authorities and independent experts always drove sales of supposedly less hazardous products more than direct industry messaging, as the industry was widely viewed suspiciously (*28*). However, once the public health community lost patience with the entire "safer cigarette" endeavor (*43*), a "zero-tolerance" approach to harm reduction took hold in the public health community (*43, 44*). The initially optimistic public health view that less hazardous cigarettes could represent the "Fourth Pillar" of tobacco control (*45*) was replaced by such deep cynicism that even liberal outlets like the New York Times – hardly a tobacco industry sympathizer – were publishing editorials wondering why the response to Premier, an RJR heated cigarette product introduced in the late 1980s, was so one-sided (*46*, *47*). Low

prospects for third party endorsement correspondingly lowered the revenue expectations for health-oriented innovation, especially when the industry's own credibility had reached rock bottom.

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The direct disincentives to innovate over time have changed over time as the credibility of the industry's efforts have shifted (Figure 1). The industry never seemed particularly credible (*4*), but for a time it at least seemed logical that the tobacco industry was *trying* to reduce the hazards of cigarettes. Indeed, the initial response by the tobacco industry was a weak but genuine effort to remedy the problem (*22*). This effort was short-lived. However, the industry was able to abuse the initial benefit of the doubt that they were attempting to address the health issue by releasing health-image products. The ability for tobacco companies to mislead consumers about the health benefits of health-image products was particularly high during the tar derby and the emergence of filters in the 1950s and 1960s and persisted into the 1980s.

The regulators stepped into this void in 1960, when FTC decided upon a policy of banning the reporting of tar and nicotine levels, reasoning that smokers would likely draw overly strong inferences about the health implications of these numbers. Tar and nicotine levels, which had been declining steadily in the late 1950s, appeared to level off concurrent with the 1960 FTC decision to ban reporting of tar and nicotine levels (*41*). The FTC's own ambivalence about this move is clear in their subsequent ruling on the issue, not only reversing the 1960 ruling in 1966, but actually *mandating* that tar and nicotine levels be reported.

By the mid-1980s, the failure of light and low-tar cigarettes to reduce risk had undermined public health support for harm reduction efforts of any kind. Then, in the late 1980s, thousands of damaging documents were obtained from legal discovery proceedings, many of which leaked into the public sphere (*6*, *48*), reducing tobacco industry credibility to rock bottom and sowing further mistrust among independent voices that might otherwise have been willing to support harm reduction products (*43*, *49*). In recent years, there has been a rebound of sorts in the sway of harm reduction arguments (*42*), in part because a new product, e-cigarettes, emerged from outside of the established tobacco industry (*50*).

Perceived Feasibility: Do the Scientists Foresee Success?

In tobacco, as in tobacco control generally, the perceived feasibility of a project feeds directly into the revenue expectations associated with that product. There is copious literature showing that "perceived feasibility" is a factor in determining entrepreneurial behavior (*51*, *52*). The essential logic – profit-seeking actors are more likely to put forth innovative effort when they have a more favorable subjective assessment of success – applies to any potential innovator.

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Figure 1 shows how beliefs about the feasibility of cigarette innovation have affected innovative effort. Although industry scientists and executives had initially believed that they would be able to identify and remove harmful agents from cigarette smoke (*22*), it did not take long for them to realize that it was nearly impossible to turn tobacco smoke into something that was not extremely hazardous to the user (*6*, *22*). As faith in top-down innovation waned, bottom-up innovation emerged as a possible way

forward in the mid-1980s (*53*). Although Battelle viewed the feasibility of e-cigarettes lower than that of other possible reduced-hazard designs (*54*), Philip Morris was actively at work creating just such a product (*55*, *56*). However, just as bottom-up innovation began to gain adherents among industry researchers, tobacco companies began to face a raft of additional disincentives that applied specifically to these products.

Bottom-up Disincentives

There are a number of disincentives that applied specifically to "bottom-up" innovation. These are additive, in that all previous disincentives might may also apply, in addition to these that are specific to bottom-up products.

New Drug-Device Classification

FDA statutory authority applies to products that are "intended to affect the structure or function of the body," which would seem to apply to nicotine delivery devices (*53*). The FDA maintained that tobacco cigarettes were grandfathered into the market and not subject to their jurisdiction until the early 1990s, but the industry was concerned that a novel bottom-up product would not receive such lenient treatment (*57*) This tension came into focus in the 1980s with the emergence of Favor Smokeless Cigarette, a smokefree tube that attempted to deliver nicotine via inhalation (without generating any visible aerosol). The FDA ruled that Favor was a new "drug delivery device" requiring years of costly study before coming to market. The substantial costs associated with pre-market approval represented a direct disincentive to developing this sort of product. What "cleaner" devices did emerge always contained at least some tobacco, making them simultaneously less effective at reducing hazard and more able to evade FDA jurisdiction.

Battling FDA Jurisdiction of *All* Cigarettes

Beginning in the early 1990s, FDA took a markedly different tack to *all* tobacco products. The torrent of damaging documents both weakened the political position of the industry and revealed how essential the drug nicotine was to the cigarette product. Tobacco companies were clearly aware of the centrality of nicotine in cigarettes and manipulated their product in various ways to adjust nicotine levels (*58*). Thus, the essential rationale that took Favor off of the market in the 1980s could seemingly also be applied to tobacco cigarettes – that cigarettes are essentially drug-delivery device for nicotine

The tobacco industry response was to attempt to argue that nicotine was incidental to the smoking experience, and that smokers smoked for "smoking pleasure" rather than to obtain nicotine. It would have been difficult to develop a non-tobacco nicotine product while at the same time maintaining that nicotine was not the key ingredient in tobacco cigarettes. As a result, bottom-up innovation faced a prohibitive indirect disincentive, where any efforts to build up from nicotine placed all other tobacco products under greater threat of regulation.

PR and Legal Redux: Addictiveness

The scientific battle in the 1990s shifted from harm to addictiveness on a number of fronts. Civil liability suits were increasingly relying on the argument that smokers were addicted and thus less culpable for their own consumption of cigarettes. A nation of potential jurors might find it strange that the companies denying the centrality of nicotine in their products were also producing a substitute that was nicotine-*only*. The aforementioned political battle with the FDA made these concerns even more acute. As a

result, the tobacco industry perceived a strong incentive to take a denialist tack on addictiveness that mirrored their denial of the link between smoking and disease decades before. The development of non-tobacco nicotine cigarettes would undermine and contradict their PR position, their legal defenses in class action suits, and their fight against FDA jurisdiction.

Alliance with Tobacco Farmers

Tobacco farmers provided an important backbone to the political efforts of the tobacco industry, providing a number of highly sympathetic legislators who were highly motivated to do the industry's bidding. The alliance between tobacco manufacturers and growers in tobacco states formed a classic "iron triangle" that greatly furthered the legislative agenda of tobacco manufacturers (*59*). To the degree that a new innovation might reduce tobacco demand, it could potentially damage this relationship (*60*).

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Figure 1 shows when each bottom-up disincentive was operable, and to what degree. The longest running bottom-up concern is the prospect, evident from at least 1962, that a nontobacco cigarette might come under the guise of FDA drug regulations, and that this would be undesirable from a business perspective (*57*, *60*). After Favor was taken off the market, other tobacco companies adjusted their expectations of FDA behavior accordingly (*54*, *61*). Other nicotine only products, such as nicotine water and lollipops, were similarly taken off of the market in the 2000s, demonstrating that the FDA v. Brown and Williamson decision, reference below, had not altered the FDA approach to non-tobacco nicotine products. The first direct challenge to the FDA's assertion of drug jurisdiction for non-tobacco nicotine products occurred in 2009 with Soettera vs. FDA.

This case happened to coincide with new legislation, the Family Smoking Prevention and Tobacco Control Act (hereafter Tobacco Act), that created modified-risk and reduced-exposure regulatory categories that are more obviously suited to non-tobacco aerosol cigarettes. While it is clear that drug regulations will not be applied to all non-tobacco products going forward, the nature and scope of the FDA regulations of this category is still to be determined.

While concern for new non-tobacco products was a fairly constant factor from the 1960s through to 2009, the white-hot regulatory battle with the FDA over the regulation of *all* cigarettes took placed over a relatively brief period from 1994 to 2000. On February 25th 1994, Commissioner David Kessler unexpectedly announced his intention to bring tobacco cigarettes under FDA jurisdiction (*58*). The notion that the FDA should step in to regulate cigarettes was first broached by public health groups who thought that FDA could present a more muscular counterweight to the tobacco lobby than the FTC or other regulatory agencies. First, Action on Smoking and Health attempted to prod the FDA into action in the late 1970s (*62*). Then, this approach gained some traction when the Coalition on Smoking or Health, representing the major health voluntaries, argued that "light" cigarettes fell under FDA jurisdiction because they made implicit health claims (*58*). Once Kessler had announced his intentions, this issue dominated industry strategy until it was resolved in their favor by the Supreme Court (*63*).

As the focal scientific matters at the core of the battle between tobacco and anti-tobacco forces shifted from harm to addictiveness in the 1990s, the tobacco industry suffered tremendous public embarrassment by arguing the semantics of smoking and addiction in front of Congress in 1995. This led to a rethink on the merits of this

approach, culminating in eventual admissions that cigarettes are indeed addictive. (*35*). While tobacco makers still argue in court that tobacco is not addictive (*64*), they now do so by parsing the semantics of the definition of addiction rather than altogether denying that nicotine delivery is at the core of the smoking experience. This position does not preclude acknowledgement of the outsized role of nicotine in smoking and thus the development of bottom-up products.

Lastly, the relatively strong bond between tobacco manufacturers and growers in the US began to fray due to globalization and increased willingness of manufacturers to import tobacco (*65*, *66*). At the same time, the willingness of farmers to ally strongly with manufacturers on regulatory matters has decreased substantially (*59*), making tobacco companies even less likely to heed the preferences of growers on matters of technology. As a results, a once substantial barrier to bottom-up innovation is a relatively weak factor today, even for major cigarette manufacturers.

Modifying Factors

The strength of each disincentive may vary across firms and time. This section describes why firm type and competitor entry can modify some of the aforementioned disincentives.

Firm Size and Recent Performance

Many of the factors and policies that affect incentives are mentioned in broader debates about innovation (*12*). For example, Schumpeter emphasized the resources of large firms (*67*), while Galbraith emphasized the ability of large firms to absorb risks (*68*). In addition, their larger resource base allows them to more confidently wage regulatory battles over marketing or FDA classification. On the other hand, with the

exception of the possibility of bankrupting liability, indirect disincentives are almost always lower for smaller firms who are less worried about cannibalizing their revenue streams or implicitly disparaging the cigarette brands that are already in the marketplace. Besides firm size, the rate of change in market share is also critical. Projected into the future, declining revenue theoretically lowers the expected revenues of existing brands absent new innovations (and thus the expected losses in the event of new innovations). Small and declining firms can be grouped together as "dissatisfied" with their status quo market position, while large and growing firms can be considered "satisfied." New entrants face no indirect disincentives at all by definition.

Offense vs. Defense

The magnitude of many of these indirect incentives shifts according to whether a company wants to go on offense or needs to play defense. The strength of many indirect incentives wanes once a competitor introduces a new feature that appeals to consumers. Brand-switching is now a *fait accompli*. At this point, the marginal reduction in existing revenue streams from introducing a competing product is dampened. In sports parlance, this is the difference between playing defense and going on offense. Offensive innovations include the first introduction in each product category, such as the first filters, charcoal filters, low tar, very low tar, catalyzed smoke, heated tobacco cigarettes, and aerosol cigarettes. Marketing activities can also be classified as offensive, to the degree that their messaging revolves around the health issue. Indirect disincentives apply more strongly to offensive innovations than defensive. Figure 2 looks at the market share of major tobacco firms over time, marking offensive innovations. The pattern that

emerges is one where small or declining firms show a much greater willingness to go on offense than large firms.

Swimming Against the Tide: Patterns of Offensive Cigarette Innovation

Filter cigarettes were the most immediate response to the health scare of the early 1950s. In some ways, because liability and other concerns were not yet central to tobacco industry thinking on this issue, this era most resembles our own in terms of the level and type of disincentive that each company faces. Figures 3 and 4 show that low market-share companies were much quicker to adopt filters than the market leaders. In particular, American, the leader in the non-filter world of 1952, was by far the slowest to switch to filter brands. A similar patterns can be seen with e-cigarettes. First, an outsider made the first entry. Next, a small company, Lorrilard, entered the market. Lastly, the major players enter the marketplace, albeit with very subdued marketing and a suspiciously dire warning label (*69*) that seems to insinuate that they would rather e-cigarettes not existed at all.

Discussion

This review contains many lessons for theory and practice. The core lesson to draw from this history is applicable far beyond the case of tobacco, to any innovation that has the potential for high social benefit and high economic disruption. It is difficult to make sense of the fact that Hon Lik, a single pharmacist in Hong Kong, was able to successfully invent the e-cigarette in 2003 with hardly any resources at all while the multibillion dollar tobacco industry research efforts never produced a product of comparable significance (*38*). He faced neither the direct incentives related to FDA regulation, nor the indirect disincentives applicable to cigarette makers. Consider that

Altria waited 8 years after e-cigarettes first entered the market to finally attempt to sell their own e-cigarette market, and this was approximately 20 years after they had first developed a workable non-tobacco cigarette product themselves (*55*, *56*).

In terms of policy solutions, this history suggests that innovative activities that stall due to indirect disincentives warrant a different policy approach than those that stall due to direct disincentives. If a product is not expected to be directly profitable, but is recognized as representing a likely social benefit, then the returns to developing that product need to be increased. Policy options would include stronger intellectual property rights or an outright subsidization scheme. The NCI actually attempted to spearhead the less hazardous cigarette research effort due in part to frustrations about progress in the private sector (Parascondola 2005). However, if instead innovative activity stalls due to indirect disincentives, subsidization may not be the only or best option. Strong indirect disincentives are an implied indictment of the market structure. One option is softer regulations for standalone firms in terms of taxation or marketing restrictions. The goal is to facilitate the spinning off of innovative product capabilities into separate corporate entities without cross ownership from tobacco firms, as this cross-ownership entails substantial fetters to progress due to the accompanying indirect disincentives.

Conclusions

Can we assume that the tobacco industry, deceptive and unscrupulous for decades, will continue to undermine public health today? Many of the disincentives that previously hindered tobacco industry research efforts are absent or diminished in the present context. The threat of lawsuits related to new product innovation has receded for the time being, FDA is becoming less hostile to nontobacco nicotine, and tobacco

companies no longer deny the harms of their products. Yet, many other disincentives remain, such as the implicit anti-cigarette message implied by health-oriented marketing or the potential for less hazardous products to cannibalize tobacco cigarette revenue streams. Hence the reluctance of cigarette makers to make an early entry into the market. Nevertheless, even large tobacco companies have now proven that they are willing to develop non-tobacco cigarette products. The first move has already been made, along with hundreds of competitive responses at this point (*70*), such that destabilization and loss of market share are already occurring. Future developments may lead to novel products that are more hazardous than those of today (*71*), including heated tobacco hybrid products that will potentially reverse many of the health advantages to non-tobacco nicotine products (*72*). However, the fact that big tobacco makers are moving into the non-tobacco space after all these decades shows that a chasm has finally been crossed. As Fox and Cohen warn, "If the industry changes and the tobacco control community is not prepared to deal with an industry that is not easily demonized, the tobacco control community may lose its own credibility" (*73*).

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Tables and Figures

Figure 1: Strength of Disincentives Over Time

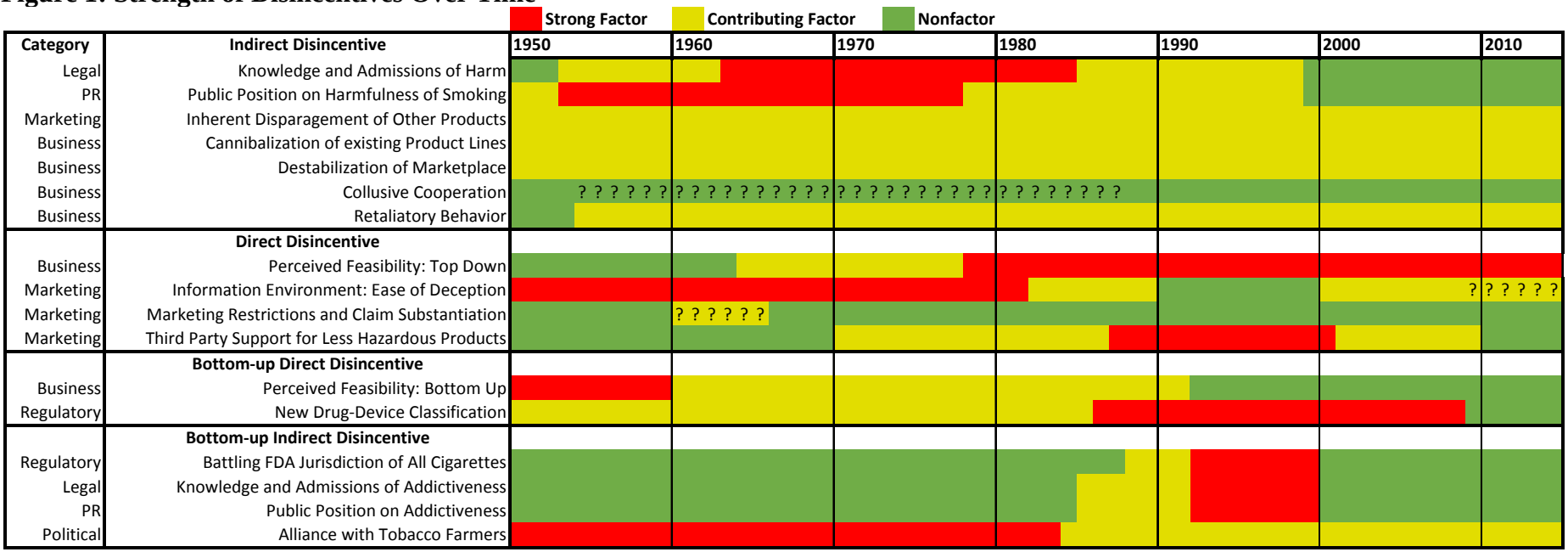

Figure 2: Offensive Innovations in the Tobacco Industry, 1950-2008

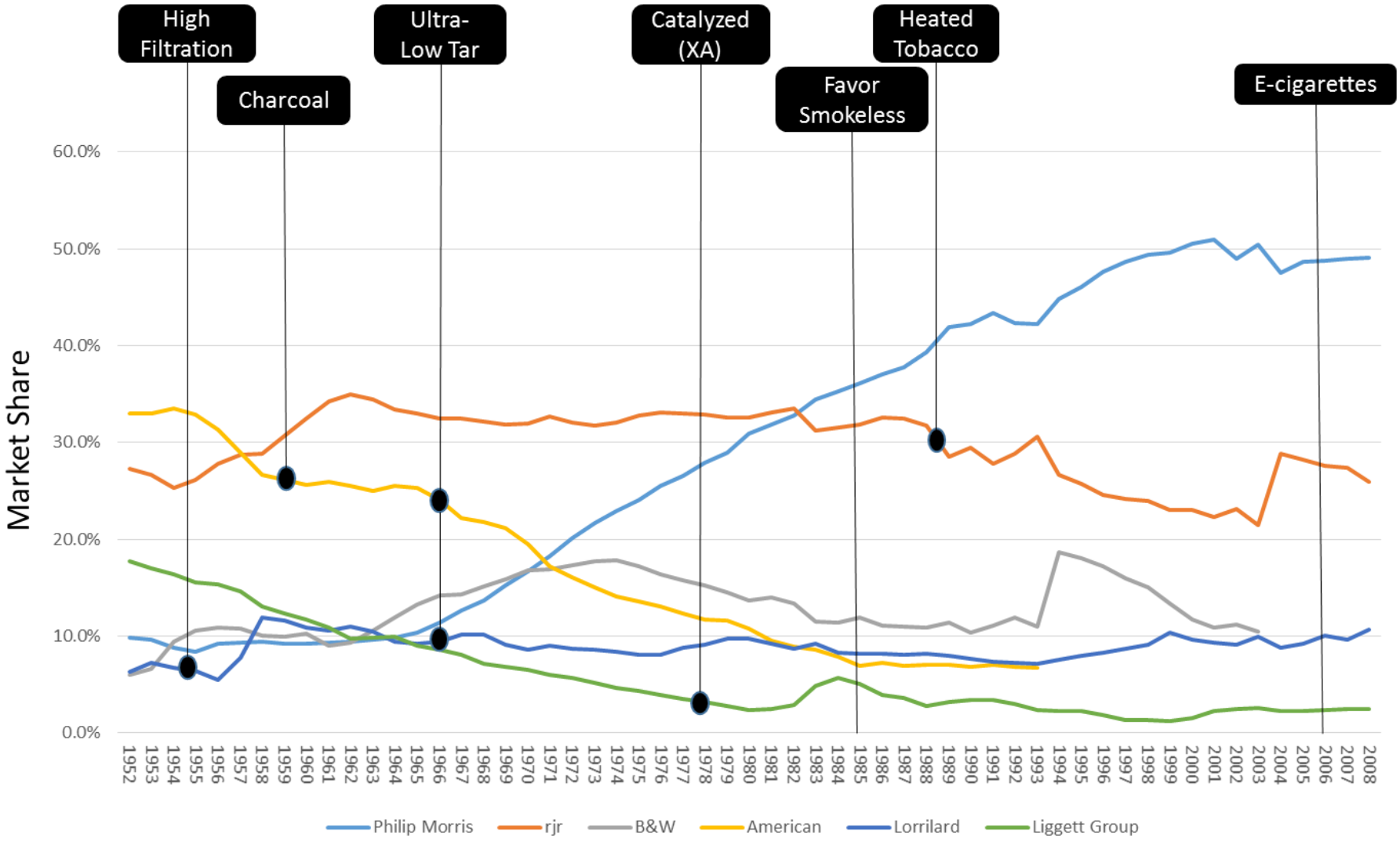

Figure 3: Tobacco Company Market Share 1950-1960

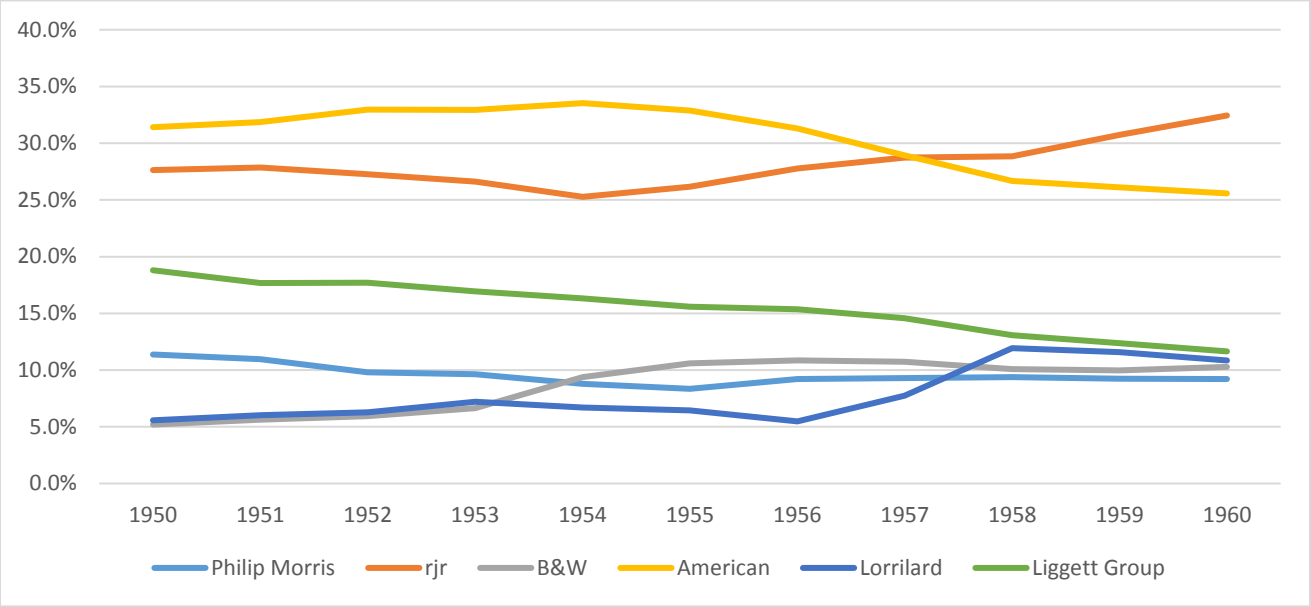

Figure 4: Tobacco Company Filter Share of Sales 1950-1960

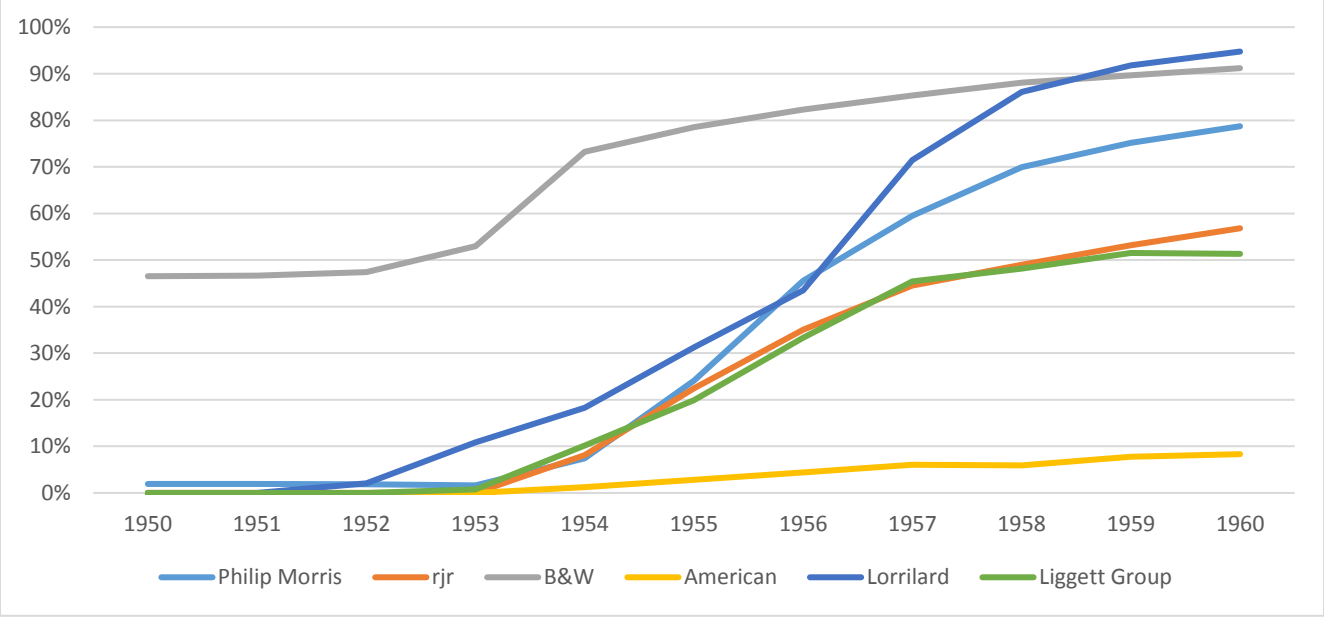

Table 1: How Disincentive Strength Varies With Company Type

Category	Indirect Disincentive	Effect on Small Co's	Effect on New Entrants
Legal	Knowledge and Admissions of Harm	Same as Large	No effect
PR	Public Position on Harmfulness of Smoking	Less than Large	No effect
Marketing	Inherent Disparagement of Other Products	Less than Large	No effect
Business	Cannibalization of existing Product Lines	Less than Large	No effect
Business	Destabilization of Marketplace	No Effect	No effect
Business	Collusive Cooperation	More than Large	No effect
Business	Retaliatory Behavior	More than Large	More than Large
	Direct Disincentive		
Business	Perceived Feasibility: Top Down	Same as Large	Same as Large
Marketing	Information Environment: Ease of Deception	Same as Large	Same as Large
Marketing	Marketing Restrictions and Claim Substantiation	Same as Large	Same as Large
Marketing	Lack of Third Party Support	Same as Large	Less than Large?
	Bottom-up Direct Disincentive		
Business	Perceived Feasibility: Bottom Up	Same as Large	Same as Large
Regulatory	New Drug-Device Classification	Same as Large	Same as Large
	Bottom-up Indirect Disincentive		
Regulatory	Battling FDA Jurisdiction of All Cigarettes	Same as Large	No effect
Legal	Knowledge and Admissions of Addictiveness	Same as Large	No effect
PR	Public Position on Addictiveness	Less than Large	No effect
Political	Alliance with Tobacco Farmers	Less than Large	No effect

Chapter 3. Assessing "Renormalization" of smoking: How does peer e-cigarette use affect perceived peer smoking rates?

Introduction

Reduced denormalization, often referred to as "renormalization", has been theorized to be a major potential hazard associated with e-cigarettes (1). Various studies have shown the effectiveness of the denormalization campaign on lowering smoking prevalence. Reduced denormalization threatens to reverse this apparent success. While there has been considerable debate about the possible consequences of renormalization, as well as the normative merits of prioritizing denormalization over more concrete public health objectives (2,3), there has been no quantitative empirical investigation into whether renormalization is actually occurring. This paper seeks to fill this gap by attempting to assess whether peer vaping has a measurable impact on an individual's perception of peer smoking. The study population will be middle and high school students, which is when most smoking initiation occurs (4).

Background

Defining Renormalization

There are at least two ways that "renormalization" is used in the literature. Many authors are concerned that nicotine use is renormalized through e-cigarettes, pointing to the impact of e-cigarette prevalence on overall nicotine prevalence (5), particularly among youth. The existence of this phenomenon is not controversial – few would argue that e-cigarettes provide an additional means of nicotine consumption that faces somewhat reduced stigma. However, this paper concerns the much more pernicious potential for e-cigarettes to lead to the renormalization of *smoking*, not just nicotine. It is stated most precisely by Schneider and Diehl:

> According to this hypothesis, the increasing popularity of e-cigarette use leads to individuals seeing more users in public and in their own surroundings. The fact that many e-cigarettes look like tobacco cigarettes could mean that tobacco smoking may be "renormalized" by the often similar consumption patterns and product characteristics of tobacco and e-cigarettes. (6)

Put another way, renormalization of *smoking*, rather than nicotine or something else, occurs if bystanders perceive vaping to be smoking due to confusion or conflation. Either a bystander cannot distinguish vaping from smoking because they are so similar in appearance (confusion), or they do not believe there to be an important distinction between vaping and smoking such that they consider the behaviors to be essentially the same (conflation).

Perception is at the heart of denormalization and related concepts. Social Norms Theory (SNT) holds that perceptions of the prevalence of a behavior among one's peers causes an increased probability in engaging in that behavior because of an individual's desire to conform to social expectations (7–9). Studies have confirmed both that youths generally overestimate cigarette rates, often significantly, and that the level of overestimation can predict future smoking behavior (10–13). Thus, if peer vaping causes a greater perception of peer smoking, there is evidence to suggest that this misperception will in turn cause increased smoking.

Framing Perception

There are not many well-established health science conceptual models designed to explain perception. More typically, perception is a key supporting explanatory variable in a conceptual model that seeks to explain behaviors. Previous studies that seek to explain the determinants of perceived smoking prevalence have used the relatively encompassing "socio-ecological model" (12,14) that holds that perceptions are affected by variables at many levels of

analysis, including household, school, and community. Looking only at the individual may miss these environmental influences. This is particularly important to consider for this study, where the key explanatory variable is a school-level factor. This study seeks to determine whether peer vaping affects students' perception of peer smoking.

Methods

Dataset and Study Population

The National Youth Tobacco Survey (NYTS) is administered in intermittent years beginning in 1999. The survey is a representative sample of American middle and high school students, stratified to guarantee a consistent mix of schools. Schools are stratified based on the predominant minority group (Hispanic or black), the minority proportion of the school (4 levels from low to high), and whether the school is urban or rural. Students are surveyed while taking required classes, such that each student within each school has an equal probability of selection. Versions of the survey in 2011, 2012, 2013, and 2014 ask about e-cigarette use. These years, along with 2009, also have school identifiers. Only 2012 and 2013 ask students about their perception of peer tobacco use, so the dataset is a pooled cross section of students embedded in schools in 2012 and 2013.

NYTS does not include geographic variables, limiting our ability to control for factors and policies that might occur at the state, or national level. However, students are asked about behavior of other people in their household as well as their perceived level of exposure to tobacco advertising and product placement. This allows us to measure environmental variables even without geographic identifiers. In addition, the presence of school identifiers allows for the creation of school-level rates for demographic variables as well as smoking and vaping.

There is the potential for reverse causality to occur, where an individual's over-perception of the smoking rate (an established risk factor for smoking) leads to an increased likelihood of them becoming a smoker. This can then increase the likelihood that this individual uses e-cigarettes and in turn influence their peer's smoking and vaping behavior. If this is the case, then any correlation that is detected between peer vaping and smoking perception might be the result of the latter causing the former. To rule this out, this study will focus on students who have never smoked, to sever the causal pathway that leads from an individual's smoking perception back to their peer smoking and vaping behavior. In addition to reducing reverse-causality, it is the never-smoking population that is at risk for becoming smokers and where understanding risk factors is most critical.

Measures

This section will elaborate on the construction of the variables that will be used to model renormalization.

Focal Relationship

Perceived Peer Smoking Rate. Students were asked: "Out of 10, how many students in your grade smoke cigarettes?" A students' response to this question was divided by 10 to give a rough percentage estimate of the share of smoking among a student's school peers.

Actual Peer Smoking Rate. Students were asked: "During the past 30 days, on how many days did you smoke cigarettes?" Since we are trying to find recent visible smoking among peers, and perceived smoking is measured in the present tense, we defined current smokers as any student who reports smoking at least 1 day. The number of current smokers was divided by the total number of student respondents within that school to give an estimate of the actual peer smoking rate within a school. A similar measure was created for each grade within a school.

Actual Vaping Rates. Students were asked: "During the past 30 days, which of the following products have you used on at least one day?" and presented with a list of nicotine and tobacco products that includes e-cigarettes. Past 30-day e-cigarette users were consider *current vapers*. *Peer vaping rates* were calculated summing the students within a school who report current e-cigarette use is then divided by the total number of student respondents within that school to give an estimate of the actual peer vaping rate within a school. While students who have smoked are removed from the sample, students who vape or have vaped remain. Since there is a strong possibility that an individual who vapes is more likely to be around smokers, vaping status is included in the model.

Demographics

Age. Students self-reported their age in years.

Grade. Students self-reported their grade level. These were split into a set of dummy variables.

Race. Students self-reported their race. Race information was split into dummy variables for Black, White, and Asian students.

Potential Confounders of Perceived Smoking

In addition to individual vaping status, several other individual confounders are included in the model.

Ad Exposure. Self-reported exposure to ads included internet, newspaper, and in-store ads. For each category, students were asked if they see these ads most times, sometimes, rarely, or never when they are in potential contact with each medium. Degree of exposure was split out into dummy variables for rare, sometime, and most time ad contact. Never exposure is the reference category.

Media Exposure. Self-reported exposure to smoking on TV and in movies was also split out into dummy variables for rare, sometime, and most time exposure. Never exposure was the reference category.

School-Level Demographics

School and Grade Racial Composition. The racial makeup of each school and grade was compiled in a similar manner to smoking rates, where the % of White, Black, and Asian students were calculated using school identifiers.

Analytic Strategy

This study relies on a relatively simple model where perceived smoking rate is the dependent variable, while smoking rate, vaping rate, vaping status, and the various potential confounders of peer smoking serve as independent variables. If youths are confusing or conflating vaping with smoking, then we would expect vaping rates to have an effect on perceived peer smoking after controlling for actual peer smoking and other potential confounders. If youths are able to distinguish peer vaping from peer smoking, then we should expect no correlation between peer vaping and peer smoking.

Because of the multilevel nature of the data, where students are nested within grades, which are nested within schools, this analysis will use a hierarchical linear model to assess the impact of peer vaping on peer smoking. The base model will look at smoking behavior rates and vaping status only, while the fuller model will include potential confounders. More specifically, model 1 will include only variables associated with the focal relationship. Model 2 will add demographics, individual vaping status, and individual smoking perception confounders. Model 3 will add school level demographics.

Peer contextual variables were constructed at the school-level instead of the grade level for two main reasons. First, the Intraclass Correlation Coefficient (ICC) from the unconditional means model suggested that there was much more variance in the dependent variable at the school level than the grade level. Second, the school level averages had less statistical noise embedded within them because they were constructed from a larger sample (approximately three times larger for middle schools, and four times larger for high schools)

Results

Table 1 shows the crosstabs for never-smoking students, with middle and high school crosstabs reported separately in the 2nd and 3rd columns and overall means in the first. Rates of vaping are very low among the never-smoking population during these years, at 0.21% and 0.44% for middle and high school students respectively. Peer (school-mate) vaping rates are considerably higher, at 0.95% and 3.35% for middle and high school students, indicating that the vast majority of e-cigarette users in this sample have smoked a cigarette before. Peer smoking rates are 3.06% and 12.16% for middle and high schoolers, while the average perceived smoking rates are 21.76% and 38.87% for middle and high schoolers respectively. This indicates a substantial overestimation of peer smoking compared to the average of self-reported smoking.

Tables 2 and 3 report the hierarchical model results for high schools and middle schools respectively. Coefficients and p-values are reported for models 1 through 3 described above, for each school type. Using an unconditional means model, the ICC for high schools was determined to be 0.17 for school, 0.03 for grade, and 0.80 at the individual level. The ICC for middle school students was 0.09 for school, 0.06 for grade, and 0.85 at the individual level. Thus, the relative importance of grade environment compared to school environment in predicting perceived peer smoking is greater in middle schools than high schools. This is also clear from the p-values on

the grade dummy variables, which are significant for middle school students but not high school students.

Table 2 shows that there is a significant inverse correlation between school vape rate and perceived peer smoking among high school students, whether or not confounders are included. In the full model (model 3), a 1 percentage point increase in school vaping rate as associated with a 0.5 percentage point decrease in perceived smoking rate. Comparing model 3 to model 2, we can see that the addition of school-level demographics increases the p-value associated with school-level vape rate. This suggests that at least some of the correlation between vaping rate and perceived smoking rate in models 1 and 2 is attributable to the tendency for whiter schools to have both higher vaping rates and lower over-estimation of smoking rates. Table 3 shows that there is no significant relationship between school vape rate and perceived peer smoking among middle school students for all models.

Racial demographics are uniformly significant for all models where they are included in both school types. Black students perceive greater smoking rates among school peers, while White and Asian students perceive lower smoking rates. All media exposure variables show a significant association with perceived peer smoking for both middle school and high school students, where greater exposure correlates with greater perceived smoking rate. Cohabitation with smokers also increases students' perception of smoking rates for both high school and middle school students. Students attending schools with a greater proportion of White and Asian students perceived lower smoking rates.

Discussion

The key result of this paper is that there is no apparent positive association between peer vaping and the perception of peer smoking in a population of never smokers. Following from the lack of a statistical relationship between peer vaping and perceived peer smoking, one can conclude that youths were not confusing or conflating vaping with smoking during the study period. If anything, the relationship appears negative among high schoolers, where higher peer vaping lowers students' perceived peer smoking. This is especially notable because other researchers have pointed out that vaping is substantially easier to do during the school day than smoking because it is so much harder to detect in indoor spaces (6). As a result, there is a likelihood that vaping would occur during the school day even when smoking would not, and thus be more visible to school peers. Perhaps the same differences that make vaping more difficult to detect are those that aid students in distinguishing it from smoking.

While this result undermines the notion that vaping necessarily leads to renormalization, possible external validity issues mean that renormalization cannot be ruled out entirely as a potential issue for policymakers to consider. This study looks only at a youth population, but other scholars have indicated the possibility that renormalization may be occurring among older ex-smokers (15). Also, this study looks at a timeframe in 2012 and 2013, but there may be more or less confusion today. Thus, although renormalization may not be occurring to the extent that is often assumed, policymakers should not ignore the continuing potential for e-cigarettes to be conflated or confused with cigarettes. Certainly, there is a similarity in appearance. In addition, some e-cigarette makers are purposefully trying to conflate the two in their advertising (15), while some anti-vaping campaigns do the same (16). One policy solution that has been proposed is to restrict cig-a-like e-cigarettes from being used in public spaces, while allowing more

obviously distinct devices to be used (2). This would be a relatively unrestrictive means of stemming renormalization if it were found to be occurring.

There are other results in this analysis that do not have direct bearing on the issue of renormalization but may be of interest to tobacco control researchers more generally. The association between media exposure to smoking advertising and perceived smoking rate among one's peers demonstrates how cigarette marketing increases smoking risk among youth. It is conceivable that some of these ads are actually e-cigarette ads, or soon will be.

Strengths and Limitations

This paper attempts to fill a major gap in the literature by analyzing the link between vaping and renormalization that is often supposed but has not been empirically estimated. It focuses on a nationally representative population of youths, which is where the vast majority of smoking initiation takes place. In addition, it includes school-level factors which are rarely included in studies of this nature.

Limitations include the fact that the identification strategy is simplistic and susceptible to residual confounding due to unobservable variables. These may include geographic variables, which are not included in the public NYTS dataset. A seemingly high proportion of students claimed that 100% of their peers smoked cigarettes, which may indicate a lack of understanding or sincerity on the part of respondents. Various modeling choices needed to be made about how to define smoking and vaping rates and how to parametrize potential confounders, some of which were necessarily arbitrary. Sensitivity analyses were conducted to minimize the prospect that arbitrary decisions would have an outsized impact on the final result. Lastly, this paper only focuses on one aspect of the gateway effect. While this is by design, it is possible that there other

causal pathways will outweigh the results found here and so there is a clear necessity for further research.

Conclusions

This paper sought to determine whether renormalization of smoking was occurring in middle and high schools by estimating the effect of peer vaping on perceived peer smoking independent of actual peer smoking. The results provide no evidence that renormalization of smoking is occurring. The correlation among high school students appears to actually go in the opposite direction, although it is not statistically significant when school-level confounders are included in the model and may not be meaningful. Overall, this paper does not find evidence to support speculation that e-cigarette use is confused or conflated with tobacco cigarette use in the study population. Concerns about renormalization of smoking due to vaping may not be invalid but cannot be substantiated.

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Table 1. Bivariate analyses examine predictors of perceived smoking among never smokers

	All Students		Middle School		High School		
	N=29561		N=15734		N=13827		
Variable	M or N	SD or %	M or N	SD or %	M or N	SD or %	p
Sociodemographics							
Black	6050	20.47%	2995	19.04%	3055	22.09%	<.0001
White	18366	62.13%	10145	64.48%	8221	59.46%	<.0001
Asian	2294	7.76%	1140	7.25%	1154	8.35%	0.000
Hispanic	6031	20.92%	3012	19.81%	3019	22.16%	<.0001
Female	14844	50.22%	7872	50.04%	6972	50.43%	0.512
Key Individual Variables							
Current EC User	94	0.32%	33	0.21%	61	0.44%	0.000
Perceived Smoke Rate	29.76%	29.48%	21.76%	27.70%	38.87%	28.79%	<.0001
Media Environment							
See Internet Ads							
Rarely	10574	35.77%	5427	34.49%	5147	37.22%	<.0001
Sometimes	9118	30.84%	4521	28.73%	4597	33.25%	<.0001
Most Times	3263	11.04%	1797	11.42%	1466	10.60%	0.025
See Ads Papers							
Rarely	8455	28.60%	4278	27.19%	4177	30.21%	<.0001
Sometimes	7302	24.70%	3421	21.74%	3881	28.07%	<.0001
Most Times	2939	9.94%	1418	9.01%	1521	11.00%	<.0001
See Ads Store							
Rarely	3670	12.42%	2168	13.78%	1502	10.86%	<.0001
Sometimes	6411	21.69%	3328	21.15%	3083	22.30%	0.017
Most Times	15556	52.62%	7744	49.22%	7812	56.50%	<.0001
See Smoking TV/Movies							
Rarely	5705	19.30%	3336	21.20%	2369	17.13%	<.0001
Sometimes	12149	41.10%	6177	39.26%	5972	43.19%	<.0001
Most Times	8176	27.66%	4117	26.17%	4059	29.36%	<.0001
Does Smoking Look Cool?							
Def	583	1.97%	300	1.91%	283	2.05%	0.388
Prob	1667	5.64%	866	5.50%	801	5.79%	0.283
Prob Not	3144	10.64%	1613	10.25%	1531	11.07%	0.022
Household Environment							
Cohabit Smoker	8024	27.36%	4481	28.74%	3543	25.79%	<.0001
School Environment							
School Size	128.66	51.65	110.44	45.32	149.38	50.60	<.0001
School Smoke Rate	7.32%	7.00%	3.06%	3.03%	12.16%	7.09%	<.0001
School Vape Rate	2.07%	2.63%	0.95%	1.26%	3.35%	3.14%	<.0001
Black %	20.80%	23.49%	19.69%	23.71%	22.07%	23.16%	<.0001
White %	61.61%	26.88%	63.46%	26.03%	59.51%	27.67%	<.0001
Asian %	7.61%	10.71%	7.24%	10.34%	8.03%	11.11%	<.0001
Hisp %	22.18%	22.95%	20.91%	22.39%	23.63%	23.50%	<.0001

Table 2. Multilevel regression predicting perceived peer smoking rate among nonsmoking high school youths

	Model 1		Model 2		Model 3	
	Coef	P value	Coef	P value	Coef	P value
Intercept	0.30	<.0001	0.04	0.515	0.13	0.094
Focal Relationship						
School Smoke Rate	0.91	<.0001	0.88	<.0001	0.92	<.0001
School Vape Rate	-0.73	0.006	-0.60	0.011	-0.50	0.031
Ecig User Dummy			0.04	0.200	0.04	0.214
Demographics						
Black			0.02	0.005	0.02	0.009
White			-0.06	<.0001	-0.06	<.0001
Asian			-0.05	<.0001	-0.05	<.0001
Age			0.01	0.001	0.01	0.001
Grade6						
Grade7						
Grade8						
Grade9			0.00	0.847	0.00	0.836
Grade10			0.00	0.984	0.00	0.978
Grade11			0.00	0.895	0.00	0.902
Grade12			0.00	.	0.00	.
Smoking Propensity						
See Internet Ads						
Rarely			0.00	0.573	0.00	0.576
Sometimes			0.03	<.0001	0.03	<.0001
Most Times			0.12	<.0001	0.12	<.0001
See Ads Papers						
Rarely			0.01	0.047	0.01	0.045
Sometimes			0.01	0.029	0.01	0.027
Most Times			0.03	0.001	0.03	0.001
See Ads Store						
Rarely			0.02	0.021	0.02	0.019
Sometimes			0.01	0.249	0.01	0.227
Most Times			0.02	0.047	0.02	0.039
See Smoking TV/Movies						
Rarely			0.02	0.026	0.02	0.024
Sometimes			0.02	0.064	0.02	0.058
Most Times			0.08	<.0001	0.08	<.0001
Does Smoking Look Cool?						
Def			0.08	<.0001	0.08	<.0001
Prob			0.05	<.0001	0.05	<.0001
Prob Not			0.00	0.942	0.00	0.941
Cohabit with Smoker			0.03	<.0001	0.03	<.0001
School Level						
black %					-0.04	0.405
white %					-0.13	0.003

asian %			-0.13	0.132
Fit Statistics				
ICC School				
ICC Grade				
-2 Log Likelihood	2656.9	1646.8	1632.3	
AIC (Smaller is Better)	2668.9	1708.8	1700.3	
AICC (Smaller is Better)	2668.9	1709	1700.4	
BIC (Smaller is Better)	2692	1828.2	1831.2	

Table 3. Multilevel regression predicting perceived peer smoking rate among nonsmoking middle school youths

	Model 1		Model 2		Model 3	
	Coef	P value	Coef	P value	Coef	P value
Intercept	0.16	<.0001	0.01	0.871	0.17	0.004
Focal Relationship						
School Smoke Rate	1.83	<.0001	1.52	<.0001	1.41	<.0001
School Vape Rate	-0.19	0.672	0.47	0.294	0.50	0.236
Ecig User Dummy			0.18	<.0001	0.18	<.0001
Demographics						
Black			0.03	<.0001	0.03	<.0001
White			-0.03	<.0001	-0.02	<.0001
Asian			-0.05	<.0001	-0.04	<.0001
Age			0.01	0.002	0.01	0.002
Grade6			-0.09	<.0001	-0.09	<.0001
Grade7			-0.02	0.002	-0.02	0.001
Grade8			0.00	.	0.00	.
Grade9						
Grade10						
Grade11						
Grade12						
Smoking Propensity						
See Internet Ads						
Rarely			0.01	0.028	0.01	0.024
Sometimes			0.03	<.0001	0.03	<.0001
Most Times			0.09	<.0001	0.09	<.0001
See Ads Papers						
Rarely			0.01	0.086	0.01	0.082
Sometimes			0.01	0.103	0.01	0.098
Most Times			0.04	<.0001	0.04	<.0001
See Ads Store						
Rarely			0.01	0.232	0.01	0.214
Sometimes			0.00	0.885	0.00	0.865
Most Times			0.03	0.000	0.03	<.0001
See Smoking TV/Movies						
Rarely			-0.01	0.231	-0.01	0.250
Sometimes			0.00	0.477	0.00	0.529
Most Times			0.03	<.0001	0.03	<.0001
Does Smoking Look Cool?						
Def			0.16	<.0001	0.16	<.0001
Prob			0.06	<.0001	0.06	<.0001
Prob Not			0.00	0.620	0.00	0.617
Cohabit with Smoker			0.03	<.0001	0.03	<.0001
School Level						
black %					-0.11	0.004
white %					-0.19	<.0001

asian %			-0.21	0.001
Fit Statistics				
ICC School				
ICC Grade				
-2 Log Likelihood	1759.7	404.4	368.4	
AIC (Smaller is Better)	1771.7	464.4	434.4	
AICC (Smaller is Better)	1771.7	464.5	434.6	
BIC (Smaller is Better)	1796.2	587.3	569.6	

Chapter 4. Characteristics of smokers purchasing e-cigarettes and the association with cessation: An examination using a national USA consumer panel

Introduction

There is limited conclusive data about which smokers are most likely to use e-cigarettes and whether e-cigarettes help or hinder cessation efforts. This study uses an observational, longitudinal cohort design to examine which cigarette smokers use e-cigarettes – either experimentally or repeatedly – and the potential harm reduction impact of e-cigarettes on smokers by following a cohort of smokers over time.

First, important questions to address are: which smokers experiment with e-cigarettes and which are likely to become regular users of e-cigarettes? To answer these questions, we must document differences in smoking behaviors among smokers. The type (e.g., menthol vs. non-menthol), price, and volume of cigarettes consumed at baseline might be predictive of e-cigarette initiation and may impact the likelihood of continued use of e-cigarettes. For example, heavy smokers may be more likely to become intensive e-cigarette users than light smokers (1).

Additionally, understanding one's motivation for using e-cigarettes and potentially quitting them is important. One study noted that "curiosity" was the most commonly reported reason for initially trying e-cigarettes and that the most common reason for discontinuing e-cigarette use was that participants were "just experimenting" with them (2). Another study documented that the most common reasons current and former smokers used e-cigarettes were for harm reduction and cessation (3). The most common reason for discontinued e-cigarette use among current smokers was because

they were using other tobacco products, while the most common reason for discontinued e-cigarette use among former smokers was because they quit the use of all nicotine/tobacco (3). Thus, indicators regarding motivation to quit smoking, such as prior NRT purchasing or previous gaps in purchase (potentially marking prior quit attempts), may be important predictors of e-cigarette initiation and may lead to more regular use. Indeed, prior research suggests that e-cigarette users report a higher number of previous quit attempts and intention to quit (4).

From a broader socioecological perspective, little is known about the impact of the tobacco control environment on initiation and continued use of e-cigarettes. For example, stricter policies could promote denormalization of tobacco and nicotine use altogether or promote the use of e-cigarettes in order to facilitate cessation. As such, accounting for these contextual findings may provide a more comprehensive account of how these factors might impact e-cigarette use over time.

In terms of the effect of e-cigarette use on smoking cessation, findings have been mixed. Two cohort studies found that e-cigarette use was negatively associated with cessation (5,6). Another two cohort studies found no significant association between e-cigarette use and cessation (7,8). Lastly, two studies documented that certain types of e-cigarette use predicted cessation. A UK study found that daily tank users had increased odds of cessation, nondaily cigalike users have decreased odds, and all others demonstrated no difference in odds of cessation from nonusers of e-cigarettes (9). Another study of smokers in Dallas and Indianapolis from 2011-2014 found an increase in the odds of smoking cessation among intensive e-cigarette users but no effect among

intermittent e-cigarette users (1). Thus, quantifying and characterizing e-cigarette use is important.

Given disparate findings reported by these prior observational studies, attention must be paid to the potential reasons for these differences. First is the timing and frequency of assessments. Some studies measure e-cigarette use only at baseline (5,6,8). If a study focuses on a cohort that is smoking at baseline and measures e-cigarette use at baseline only, ex-smokers who experienced an e-cigarette-associated quit pre-baseline would be excluded, biasing the results. On the other hand, others measure e-cigarette use only at follow up, which also limits the ability to determine sequencing of events in some cases (7). Second, some studies distinguished between different types of e-cigarette users (1,8,9), while others did not (5–7). This is important for two reasons: 1) experimenters versus more intensive users may have different characteristics at baseline (1,2); and 2) as with NRT, the causal impact of e-cigarette use on cessation is likely low among those that only briefly experiment with them. As such, greater attention must be given to understanding the characteristics of smokers who use e-cigarettes as well as characteristics of their use.

Given the aforementioned literature, the aims of the current study are: 1) to examine predictors of single and repeat e-cigarette purchasing among panelists that consistently purchasers cigarettes at baseline, and 2) to identify whether e-cigarette purchasing predicts tobacco cigarette smoking cessation (defined as no purchases for at least 6 months and no subsequent purchases until the end of 2013) in a longitudinal national U.S. consumer panel. In support of the study aims, we will also examine whether quitting is concurrent with the initiation of e-cigarette purchasing. Lastly, we will present

trends in NRT use to assess whether the growth in e-cigarette use reduces the amount of people using NRT.

Methods

The consumer purchasing data for our study is derived from the Nielsen Homescan Panel, which provides a record of consumer packaged goods purchases for a nationally representative panel of U.S. households. To construct our sample, we began with any household who remained in the sample from 2011 to 2013 (N = 47,489) and bought cigarettes at some point (23.3%, N = 11,060). We then restricted to households who: 1) made at least two cigarette purchases in 2011; 2) made at least one cigarette purchase in 2012 or later; 3) purchased at least four cigarette packs between 2011 and 2013; and 4) made consistent purchases with no gaps of greater than 180 days between purchases. Households with nonsensical price data (priced below tax level or above $20 per pack) were also removed, leaving a final analytic sample of 2,854 panelists.

Measures

Outlined below are the variables included in this analysis.

Smoking Cessation. Our primary outcome for the second study aim was tobacco cigarette smoking cessation. Panelists were categorized to have "quit" if they did not purchase a pack of cigarettes for at least 180 days at any point during the observational window and did not purchase cigarettes again subsequently until the end of the observation window.

E-Cigarette Use. E-cigarette purchase was the primary outcome for our first aim and our primary predictor of interest for our second aim. E-cigarette purchasers were stratified into single purchasers and repeat purchasers, following other studies that have

found different motivations(2) and effects(1,8,9) between experimenters versus more intensive users.

For our analyses focusing on cessation, e-cigarette use was also split into pre-baseline use (2011) and post-baseline use (2012-13), depending on when a panelist initiated e-cigarette purchasing. Note that a repeat user who initiates in 2011 will be categorized as a pre-baseline repeat user whether or not they continue using after baseline. This allowed us to accurately capture the prospective effect of e-cigarette use without ignoring past use or erroneously treating past users as non-users. Also, note that, for cessation analyses, e-cigarette purchases made in the last 180 days of 2013 were excluded, as the impact of these late purchases on cessation could not be examined because we do not have the data to prospectively follow these users for 180 days to determine impact on cessation.

Sociodemographic Characteristics. Precision regarding sociodemographics is limited because the panel operates at the level of the household. As such, we included age, race/ethnicity, household composition, and household income level in our analyses. Specifically, either the age of single adult household members or the average age of adults in multiple adult households was used. Exploratory analyses indicated that quit rates among Black panelists was significantly different from other races; thus, we categorized race/ethnicity as Black versus other races. We also included Hispanic ethnicity. Additionally, we created a variable for single male, single female, and multiple adult households.

State Tobacco Control Environment. We augmented the individual consumer information with data on state-level tobacco control funding, cigarette excise taxes, and

smoke-free restrictions per CDC's State Tobacco Activities Tracking and Evaluation (STATE) System. The variable for *% CDC control funding* was defined as the state's level of funding divided by funding recommended by CDC. *Cigarette excise taxes* were defined as the state level of cigarette taxes. To assess *smoke-free restrictions*, each smoker was matched to their respective state's level of smoke-free policies in four common venues – restaurants, bars, government workplaces, and private workplaces. In each venue, smoke-free restrictions were assigned one of three values: 0 for no restriction, .5 for partial, and 1 for a complete. We took the average of the smoke-free restrictions across bars, restaurants, and workplaces.

Purchasing Characteristics. Purchase-related variables were calculated from pre-baseline data to prevent reverse causal effects of e-cigarette or NRT use after baseline. We included menthol, pack price, monthly cigarette volume, purchase frequency, and recency. *Menthol* purchasing was operationalized based on whether at least 50% of a participants' cigarette spending was allocated to menthol cigarettes. *Pack price* was defined as the average price paid per pack. *Monthly cigarette volume* was calculated as the number of packs purchased per month. *Purchase frequency* was operationalized as the average number of days between purchases. *Recency* was operationalized as the gap in time between baseline and the most recent purchase before baseline.

NRT Use. Users of NRT were stratified into single and repeat purchasers, although the meaning of single purchase may be different, as a single purchase may include an entire recommended schedule for NRT. It is also split into pre-baseline and post-baseline purchasing as with e-cigarettes. As with e-cigarettes, these categories are mutually exclusive. A repeat user who initiated in 2011 was categorized as a 2011 repeat

user whether or not they continued using into 2012 or 2013. Usage during the final 180 days was excluded for the cessation analysis parallel to how e-cigarettes were treated.

Statistical Analyses

Descriptive analyses of participant baseline characteristics were conducted. Bivariate analyses were conducted examining correlates of single and repeat e-cigarette use at any point from 2011-13. For continuous variables, statistical significance was assessed using ordered logistic regression. For categorical variables, a standard Chi-square test was used. We then conducted a multinomial logistic regression to determine predictors of single and repeat e-cigarette use in 2012 or 2013. Next, we conducted bivariate analyses examining predictors of cessation in 2012-13 (using bivariate logistic regression). Binary logistic regression was used for the multivariable analyses, jointly examining all predictors of cessation. After conducting our cessation analysis, we investigated whether quitting was occurring at or around first use of e-cigarettes or NRT. Lastly, we explored whether e-cigarette use appeared to displace NRT use in this population. All statistical models were estimated using SAS 9.4.

Results

Participant Characteristics

The sample was on average 58.86 years old (SD=9.72) and was 10.65% Black, 84.37% White, and 3.50% Hispanic. Overall, 73.09% lived in multiple adult households; the average income was $47,926 (SD=$27,487; Table 1).

E-Cigarette Purchasing

Bivariate analyses indicated that e-cigarette use was correlated with lower levels of smoke-free policies (P=0.014), lower cigarette prices (P<0.001), higher monthly

cigarette volume ($P<0.001$), higher purchase frequency ($P=0.004$), greater likelihood of NRT purchasing ($P=0.022$), and greater likelihood of cessation, with single purchasers having the lowest quit rates and repeat purchasers having the highest ($P=0.043$; Table 1). In multivariable analysis, single e-cigarette purchase was associated with whether the panelist resided in a single male household ($P=0.045$) and bought a higher volume of cigarettes ($P=0.042$; Table 2). Repeat purchase was predicted by higher cigarette taxes ($P=0.020$), less stringent public smoke-free policies ($P=0.011$), lower cigarette prices ($P=0.018$), and more frequent cigarette purchasing ($P=0.017$).

Cessation

Cessation was associated with younger age ($P<0.001$), being White ($P=0.015$), residing in a multiple-person household ($P=0.040$), living in a state with more stringent smoke-free policies ($P=0.020$), purchasing fewer cigarettes per month ($P<0.001$), purchasing cigarettes less frequently ($P<0.001$), purchasing cigarettes less recently ($P<0.001$), making a single e-cigarette purchase before cessation ($P=0.022$), and making repeat NRT purchases after baseline ($P=0.034$; Table 3). In multivariable analyses, repeat e-cigarette use ($P=0.010$) and repeat NRT use ($P=0.007$) after baseline were both associated with cessation. Younger age ($P=0.001$), lower monthly cigarette volume ($P<0.001$), less frequent purchasing of cigarettes ($P<0.001$), less recent cigarette purchase at baseline ($P=0.001$), and single e-cigarette purchase before baseline ($P=0.020$) were also associated with cessation.

Figure 1 shows how time between e-cigarette and NRT users' quitting and date of first purchase of e-cigarettes and NRT. The figure plots the final cigarette purchase over time, with the initial e-cigarette or NRT purchase considered to be time 0. There was a

spike in final cigarette purchases close to e-cigarette or NRT initiation date. NRT purchase was most frequently within 1 month after the final cigarette purchase; e-cigarette purchase was estimated at 1-2 months after final cigarette purchase.

NRT Displacement

Figure 2 estimates how NRT purchasing was affected by the emergence of e-cigarettes. Overall, e-cigarettes did not appear to substantially displace NRT purchases. Although 16.5% of e-cigarette purchasers also purchased NRT, there was not an obvious reduction in the amount of NRT purchases over time.

Discussion

This study was the first cohort study using consumer purchase data to examine correlates of e-cigarette initiation and repeated use as well as the impact of e-cigarette use on cessation. Our main finding was that repeat e-cigarette purchasing was associated with smoking cessation, while single e-cigarette purchase was not. Moreover, predictors of repeat e-cigarette use included more frequent cigarette purchases before baseline, suggesting that these panelists would have lower propensity to quit at baseline. However, multivariable analysis suggested significantly higher likelihood of quitting. This may suggest a causal role of e-cigarettes in abetting smoking cessation, which is in line with prior findings (1). However, it is important to interpret these findings with caution. It is possible that repeat e-cigarette use selects for motivated smokers who may have quit regardless of e-cigarette use. That said, the fact that single e-cigarette use was not associated with higher quit rates suggests that selection alone was unlikely to explain the apparent effect of repeat use.

There are other findings related to cessation that are worth noting. All smoking intensity variables were associated with decreased odds of cessation. Also, while previous studies have found that smoking cessation is predicted by NRT in real-world samples (10,11), previous looks at NRT in the Nielsen sample have not examined the impact on cessation (12). Cessation was predicted by repeat NRT purchase, although, as in the case of e-cigarettes, we could not disentangle the degree to which NRT use selects for quit intention. Single e-cigarette use before baseline was also associated with cessation, but there were only twelve single e-cigarette users before baseline, of which five quit after baseline, so this result may not hold outside of this sample.

Additionally, e-cigarette use was predicted by smoking intensity measures, similar to prior findings (1). Specifically, higher volume smokers were more likely to make a single e-cigarette purchase, while more frequent cigarette purchasers were more likely to make repeat e-cigarette purchases. Repeat e-cigarette purchase was predicted by lower per-pack cigarette cost, suggesting that e-cigarettes might appeal to more price-sensitive smokers. As for policy, some of the associations between e-cigarette use and policy were intuitive (higher cigarette taxes are associated with repeat e-cigarette use), while others may be more surprising. The finding that higher levels of smoke-free policies are associated with *lower* rates of repeat e-cigarette use is interesting. This may be explained by cultural differences between states that pass more comprehensive smoke-free policies versus those lagging in that area. It may also be easier to vape indoors in states that do not have smoking bans, since the applicability of smoke-free policies to e-cigarettes is often not stipulated.

Our finding that e-cigarette purchases do not seem to displace NRT purchase echoes findings from a UK sample (13). Overall, it is unlikely that the emergence of e-cigarettes is leading to more smoking but rather has led to somewhat less smoking.

The current study has important implications for research and practice. In research, characterization of e-cigarette types and usage patterns is necessary, especially with rapidly proliferating new product types (14). More detailed study of the interrelationships between quit intention, quit propensity, and e-cigarette use is also necessary to better control for selection effects. Additionally, other forms of verification beside purchase scanning are necessary in order to have more specific and precise measures of product usage. In practice, policymakers must be informed of the differential impact of e-cigarettes on smokers versus the nonsmoking population in order to develop appropriate policies. Clinicians need better resources to aid them in discussions with patients about the state of the science regarding e-cigarettes and cessation.

Limitations

Limitations include the lack of online purchases in the Nielsen dataset and the possibility that heavier smokers may finish and dispose of cigarette packs before scanning. Filtering for smokers who make regular purchases mitigates this weakness. Also, there is a lack of psychosocial measures, particularly those related to quit intention and reasons for using e-cigarettes. An arbitrary determinations of eligibility criteria, cessation outcome, e-cigarette usage variables, etc. was necessary although sensitivity to these decisions was tested and they did not impact the core conclusions. The older average age of this sample may not allow for generalizability to younger populations. Also, looking only at Nielsen participants who are willing to scan all of their purchases

may limit generalizability. We also did not include all tobacco control policies in our models, such as private home and vehicle bans, as there was little variability compared to the policies included in the current study. Lastly, it is difficult to give a precise quit date for any smoker in the sample since we could only note the last date that a cigarette purchase was made. Depending on the size of that purchase and the smoking intensity of the household, the true cessation date could be a month or more after the final purchase.

Conclusions

Our key finding is that repeat e-cigarette purchasing predicts discontinuation of cigarette purchasing, as is the case with NRT. Other results include that higher cigarette taxes and greater smoking intensity predicted more e-cigarette use, while paying more per pack and facing stricter smoke-free policies predicted less e-cigarette use. Further research is needed to add to these findings and inform policy.

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Ethics Statement

The Emory University Institutional Review Board approved this study.

Table 1. Bivariate analyses examining predictors of e-cigarette purchases among consistent smokers

	All Consistent Smokers		Never Purchasers		Single Purchasers		Repeat Purchasers		
	N=2854		N=2454		N=201		N=199		
Variable	M or N	SD or %	M or N	SD or %	M or N	SD or %	M or N	SD or %	p
Sociodemographics									
Age (SD)	58.86	9.72	58.97	9.84	57.32	8.94	58.99	8.89	0.153
Race (%)									
Black	304	10.65%	267	10.88%	23	11.44%	14	7.04%	0.223
White	2408	84.37%	2066	84.19%	168	83.58%	174	87.44%	0.455
Asian	30	1.05%	26	1.06%	3	1.49%	1	0.50%	0.621
Other	112	3.92%	95	3.87%	7	3.48%	10	5.03%	0.683
Ethnicity (%)									
Hispanic	100	3.50%	86	3.50%	6	2.99%	8	4.02%	0.854
Non-Hispanic	2754	96.50%	2368	96.50%	195	97.01%	191	95.98%	0.854
Household Composition (%)									
Single female	519	18.19%	440	17.93%	40	19.90%	39	19.60%	0.680
Single male	249	8.72%	215	8.76%	19	9.45%	15	7.54%	0.783
Multiple adults	2086	73.09%	1799	73.31%	142	70.65%	145	72.86%	0.714
Income (SD)	$47,926	$27,487	$48,204	$27,414	$46,776	$28,535	$45,663	$27,311	0.174
State Tobacco Control Environment									
% CDC control funding (SD)	17.61%	13.68%	17.48%	13.71%	18.44%	14.33%	18.42%	12.72%	0.200
State cigarette tax (SD)	$1.28	$0.82	$1.29	$0.82	$1.21	$0.82	$1.26	$0.82	0.256
Smoke-free policy index (SD)	0.66	0.34	0.67	0.34	0.63	0.35	0.62	0.35	0.014
Smoking Characteristics									
Menthol (%)	925	32.41%	799	32.56%	64	31.84%	62	31.16%	0.906
Pack price (SD)	$4.92	$1.40	$4.96	$1.43	$4.70	$1.19	$4.65	$1.19	<0.001
Monthly cigarette volume (SD)	21.28	20.76	20.59	20.35	25.01	23.22	26.13	22.16	<0.001
Purchase frequency (SD)	16.60	18.29	16.99	18.51	16.31	19.70	12.17	12.62	0.004
Recency (SD)	16.35	23.39	16.54	23.71	15.20	20.11	15.14	22.56	0.275

NRT purchases (%)									
Never	2502	87.67%	2168	88.35%	169	84.08%	165	82.91%	0.022
Single	167	5.85%	137	5.58%	15	7.46%	15	7.54%	0.317
Repeat	185	6.48%	149	6.07%	17	8.46%	19	9.55%	0.080
Cessation (%)	484	16.96%	423	17.24%	22	10.95%	39	19.60%	0.043

Table 2. Multinomial logistic regression predicting single or repeat e-cigarette purchase among consistent smokers

	Single Use				Repeat Use			
		CI				CI		
Variables	OR	Lower	Upper	p	OR	Lower	Upper	p
Sociodemographics								
Age	0.98	0.96	1.00	0.098	1.01	0.99	1.03	0.409
Black (vs. other)	1.20	0.64	2.25	0.565	0.52	0.23	1.15	0.107
Hispanic (vs. non)	1.39	0.54	3.55	0.493	1.46	0.65	3.29	0.364
Single female household (vs. multiple)	1.41	0.85	2.35	0.182	1.34	0.84	2.16	0.221
Single male household (vs. multiple)	1.82	1.01	3.27	0.045	0.99	0.51	1.91	0.977
Income	1.00	1.00	1.01	0.489	1.01	1.00	1.01	0.142
State Tobacco Control Environment								
% CDC control funding	1.00	0.99	1.02	0.551	1.01	1.00	1.02	0.164
Cigarette tax	1.01	0.74	1.40	0.937	1.41	1.05	1.88	0.020
Smoke-free policy index	0.74	0.41	1.36	0.337	0.50	0.29	0.85	0.011
Smoking Characteristics								
Menthol	1.01	0.67	1.53	0.953	1.11	0.76	1.61	0.600
Pack price	0.92	0.76	1.11	0.389	0.80	0.67	0.96	0.018
Monthly cigarette volume	1.00	1.00	1.00	0.042	1.00	1.00	1.00	0.081
Purchase frequency	1.00	0.99	1.02	0.431	0.98	0.96	1.00	0.017
Recency	1.00	0.99	1.01	0.988	1.00	1.00	1.01	0.463
NRT Purchase (vs. never)								
Single	1.30	0.62	2.74	0.486	1.48	0.77	2.85	0.234
Repeat	1.44	0.74	2.83	0.287	1.45	0.79	2.64	0.228

Table 3. Bivariate analyses examine predictors of cessation among consistent smokers

	All Consistent Smokers		No Cessation		Cessation		
	N=2854		N=2370		N=484		
Variable	M or N	SD or %	M or N	SD or %	M or N	SD or %	p
Sociodemographics							
Age (SD)	58.86	9.72	59.18	9.51	57.27	10.55	<0.001
Race (%)							
Black	304	10.65%	262	11.05%	42	8.68%	0.122
White	2408	84.37%	1982	83.63%	426	88.02%	0.015
Asian	30	1.05%	27	1.14%	3	0.62%	0.307
Other	112	3.92%	99	4.18%	13	2.69%	0.124
Ethnicity (%)							
Hispanic	18	0.63%	1	0.04%	82	16.94%	0.778
Non-Hispanic	2754	96.50%	2288	96.54%	466	96.28%	0.778
Household Composition (%)							
Single female	519	18.19%	443	18.69%	76	15.70%	0.120
Single male	249	8.72%	213	8.99%	36	7.44%	0.271
Multiple adults	2086	73.09%	1714	72.32%	372	76.86%	0.040
Income (SD)	$47,926	$27,487	$47,725	$27,431	$48,909	$27,763	0.388
State Tobacco Control Environment							
% CDC control funding (SD)	17.61%	13.68%	17.55%	13.73%	17.89%	13.46%	0.621
State cigarette tax (SD)	$1.28	$0.82	$1.27	$0.82	$1.33	$0.81	0.132
Smoke-free policy index (SD)	0.66	0.34	0.66	0.34	0.69	0.34	0.020
Smoking Characteristics							
Menthol (%)	925	32.41%	775	32.70%	150	30.99%	0.464
Pack price (SD)	$4.92	$1.40	$4.91	$1.38	$4.97	$1.50	0.391
Monthly cigarette volume (SD)	21.28	20.76	22.77	21.24	14.00	16.43	<0.001
Purchase frequency (SD)	16.60	18.29	14.54	15.23	26.69	26.75	<0.001
Recency (SD)	16.35	23.39	14.62	21.19	24.80	30.72	<0.001
E-cigarette and NRT Purchasing							

E-cigarette purchases (%)							
Never	2567	89.94%	2136	90.13%	431	89.05%	0.919
Single, 2011	12	0.42%	7	0.30%	5	1.03%	0.022
Repeat, 2011	19	0.67%	15	0.63%	4	0.83%	0.633
Single, 2012-13	117	4.10%	103	4.35%	14	2.89%	0.142
Repeat, 2012-13	139	4.87%	109	4.60%	30	6.20%	0.136
NRT purchases (%)							
Never	2540	89.00%	2126	89.70%	414	85.54%	0.004
Single, 2011	53	1.86%	42	1.77%	11	2.27%	0.457
Repeat, 2011	103	3.61%	84	3.54%	19	3.93%	0.682
Single, 2012-13	76	2.66%	57	2.41%	19	3.93%	0.058
Repeat, 2012-2013	82	2.87%	61	2.57%	21	4.34%	0.034

Table 4. Binary logistic regression predicting cessation among consistent smokers

Variables	OR	CI Lower	CI Upper	p
Sociodemographics				
Age	0.98	0.97	0.99	0.001
Black (vs. other)	0.75	0.52	1.08	0.125
Hispanic (vs. non)	0.84	0.48	1.46	0.532
Single female household (vs. multiple)	0.78	0.59	1.05	0.102
Single male household (vs. multiple)	0.92	0.62	1.36	0.684
Income	1.00	1.00	1.00	0.998
State Tobacco Control Environment				
% CDC control funding	1.00	0.99	1.01	0.837
Cigarette tax	1.07	0.91	1.26	0.410
Smoke-free policy index	1.39	0.98	1.97	0.069
Smoking Characteristics				
Menthol	0.97	0.78	1.22	0.817
Pack price	0.97	0.88	1.06	0.484
Monthly cigarette volume	1.00	1.00	1.00	<0.001
Purchase frequency	1.02	1.02	1.03	<0.001
Recency	1.01	1.00	1.01	0.001
E-cigarette and NRT purchases				
E-cigarette purchases (vs. never)				
Single, 2011	4.35	1.26	15.03	0.020
Repeat, 2011	1.52	0.48	4.87	0.477
Single, 2012-13	0.66	0.36	1.21	0.177
Repeat, 2012-13	1.79	1.15	2.77	0.010
NRT purchases (vs. never)				
Single, 2011	1.32	0.65	2.67	0.444
Repeat, 2011	1.16	0.68	1.98	0.586
Single, 2012-13	1.58	0.90	2.77	0.109
Repeat, 2012-2013	2.09	1.22	3.59	0.007

Figure 1. Temporal proximity of last cigarette purchase to first e-cigarette or NRT purchase

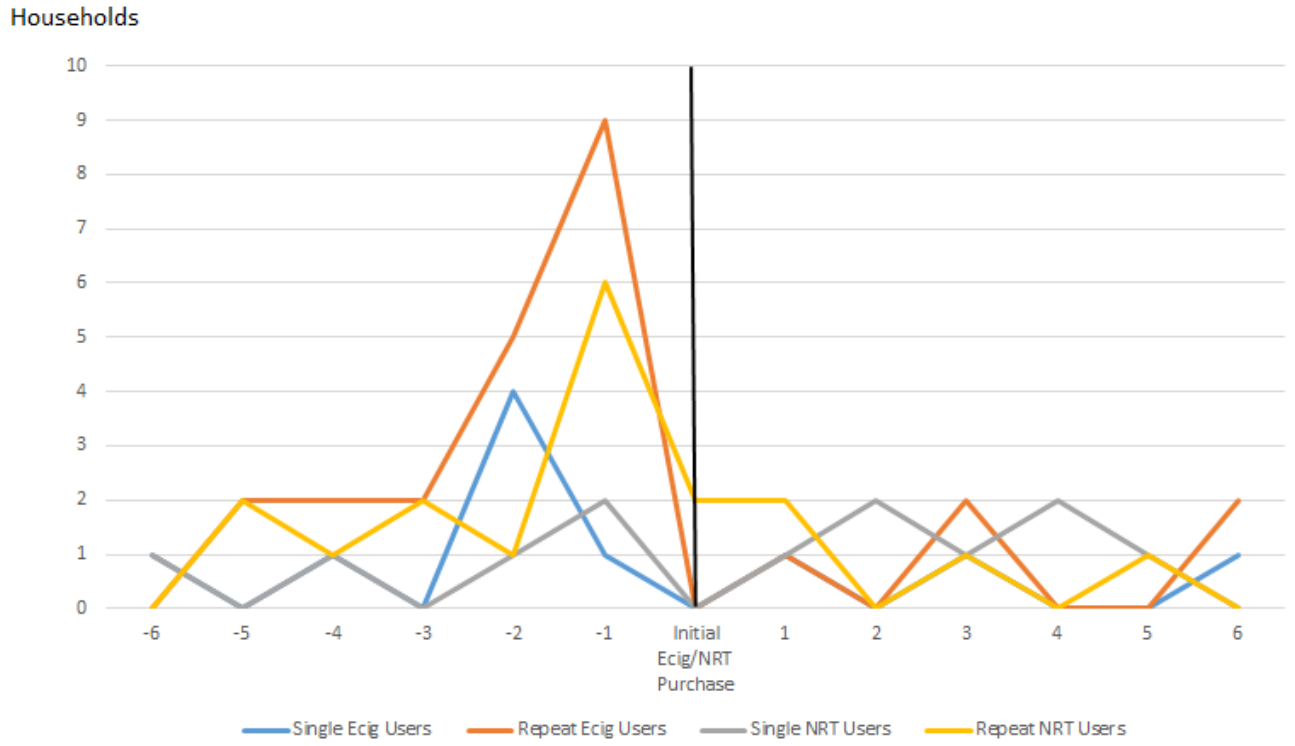
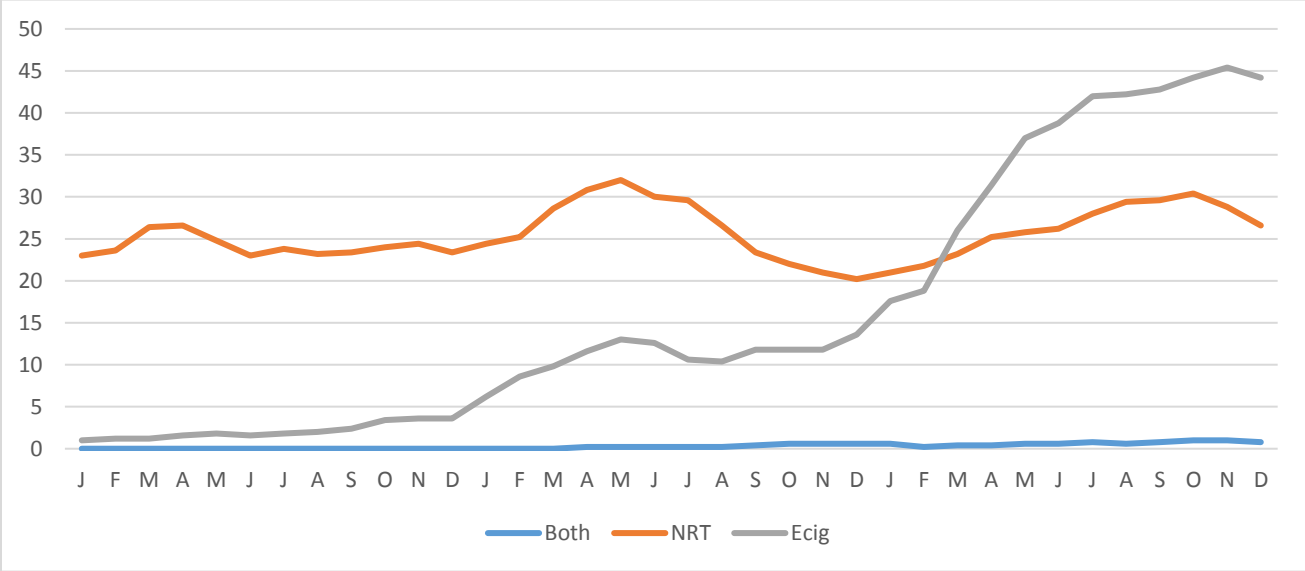


Figure 2. Households Making E-cigarette and NRT purchases over time, January 2011 to December 2013



Chapter 5. Lessons for E-cigarette Research and Policy

Lessons for Researchers

The preceding two chapters contribute to an assessment of whether theorized gateway or cessation effects operate in the real world. However, these assessments are necessarily incomplete. Individual studies cannot give a universal and definitive measure of the population effects of e-cigarettes. Even more, the totality of all evidence on e-cigarettes from all studies conducted to this point does not, and cannot, fully answer these questions. Even though the literature on e-cigarettes is rapidly expanding every week, there remain enormous obstacles to comprehensively answering causal questions about the effect of using one substance on use of another. The preceding chapters address these obstacles intermittently, but it is worth zooming out to fully consider what makes these research questions so difficult to answer. This will first address the difficulties in assessing population effects. It will then address ways of facing these difficulties, including strategies employed in the preceding chapters as well as strategies that have been or could be employed by others.

Difficulties in Assessing Population Effects

How do we distinguish true causal effects from patterns of behavior that do *not* involve a causal gateway or cessation relationship between e-cigarettes and tobacco cigarettes? Erroneous causal conclusions are likely to result from insufficient attention to at least three aspects of study design: timing of use or assessment, selection of users, and intensity of use.

The most glaring timing issue is reverse causality, particularly for cross-sectional studies. E-cigarettes use among smokers is sometimes taken as evidence of a pathway

from using e-cigarettes to tobacco cigarettes even when temporal precedence has not been established (1). However, correlations between e-cigarette use and cigarette use may only mean that e-cigarettes are likely to appeal to those who already smoke. Similarly, for studies of cessation effects, it is possible that long-time ex-smokers may initiate e-cigarette use, which could be mistakenly interpreted as evidence of e-cigarette use causing cessation if temporal precedence has not been established. This is not to discount the possibility that, even without temporal precedence, e-cigarettes may lead to a quicker escalation in smoking behavior among those who have already smoked or a reduced chance of relapsing back to cigarette smoking behavior among those who had already quit. The point is that with currently collected data we simply do not and cannot know the true direction of causality in many cases, making the overall strength of evidence quite weak.

Chapter 4 addressed how, for longitudinal studies where temporal precedence can be more easily established, there is a second timing issue concerning whether e-cigarette use is measured at baseline, follow up, or, ideally, both. In particular, measuring e-cigarette use at baseline is particularly problematic for studies of cessation because many e-cigarette associated quits may have theoretically happened before baseline. These ex-smokers could drop out of a study that requires all participants to be smokers at baseline. Purging e-cigarette users who have already quit would bias a study that compares the remaining e-cigarette users to never-users. Longitudinal studies with frequent assessments, such as the Population Assessment of Tobacco and Health (PATH) collaboration between FDA and NIH (2), are necessary to accurately describe the

interrelationships between e-cigarette and tobacco use. In chapter 4, we were able to use the Nielsen Consumer Panel for this purpose.

In terms of study population, attention must be paid to the characteristics and tobacco use history of participants to truly examine gateway or cessation/harm reduction effects. For gateway studies, use of e-cigarettes may be driven by some of the same risk factors that drive tobacco smoking. Some of these risk factors are observable and can potentially be controlled for analytically, but many of the most important risk factors are not easily observed or measured. Risk-taking propensity, for example, is likely to affect both e-cigarette and tobacco cigarette use. Correlations between e-cigarette use and smoking may result when one of these unobserved factors drives the use of both products, even if there is no causal impact of the use of one product on the other. Previous theoretical work on the marijuana gateway effect on hard drug use can serve as a guide for the obstacles to causal inference that nicotine researchers currently face (3–5). For cessation studies, the concern is that e-cigarette use might select for (or against) pre-existing propensity to quit. This might entail an association between e-cigarette use and smoking intensity, quit intention, or sociocontextual factors known to affect smoking cessation.

Lastly, it is it is important to characterize e-cigarette use. Consider the intensity of e-cigarette use. If a smoker or nonsmoker experiments with e-cigarettes very briefly and then stops, it is difficult to imagine a plausible causal mechanism linking this fleeting e-cigarette use to initiation or cessation of tobacco smoking. Rather, the most plausible explanation of a finding that brief experimentation is associated with increased initiation or cessation of smoking is the aforementioned selection issue. In addition, there may be

differential effects on smoking depending on the type of e-cigarette under consideration (e.g. tank-style of cig-a-like) (6).

Designing Studies to Uncover Population Effects

There are three approaches that must all be leveraged to infer true population effects: 1) classic clinical trials with manipulated randomization (7) strong natural experiments and other econometric methods (8,9) that can overcome selection issues "as-if" they were truly random (10), and 3) careful causal reasoning utilizing combinations of observational results to yield analytical leverage on causal questions (9,11,12). This dissertation has focused on the third strategy, but it is worth going into more detail on the others.

Randomized controlled trials (RCT) are considered the "gold standard" of causal research. In the context of e-cigarette research, an RCT could involve participants being randomized into equivalent groups, one of which is given an intervention supporting e-cigarette use and the other is not. Unfortunately, RCTs face at least two major drawbacks. First, while some intermediate outcomes can be studied experimentally (13), gateway effects are not generally amenable to randomized experiments because it is unethical to give nicotine products to those that have never used them before. In addition, apparent effects found in RCTs may be absent or insubstantial when we generalize to the larger population where smokers may be more or less motivated to quit than the study population. As such, the fundamental questions concerning total population harm are not likely be addressed through RCTs alone.

Another research approach is to identify an exogenous source of variation that affects e-cigarette use. For example, Tuchman (2015) used variation in e-cigarette

advertising between individuals on either side of semi-arbitrary Nielsen media boundary lines to show that e-cigarette advertising causes a decrease in cigarette consumption. Friedman (2015) looked at state-level variation in e-cigarette minimum age requirements and found that minimum age requirements actually lead to more smoking. In general, policy variation across both geography and time can allow for difference-in-difference or instrumental variable analysis with relatively high internal validity.

Clean natural experiments suffer some of same issues as RCTs, namely that they are not always practicable and cannot always capture how *substantial* an effect is at the population level. We can still gain insight into which causal effects appear more or less likely, and how substantial these effects appear to be, by carefully examining controlled associations between e-cigarette use and tobacco smoking behavior. For example, Beiner and Hargraves (2015) examined a cohort of smokers over 2.5 years, with about 50% first trying e-cigarettes between baseline and follow-up (11). They compared quit rates across intensive, intermittent, and light or nonuse of e-cigarettes during the entire period before follow-up, finding a substantially higher quit rate among intensive e-cigarette users, with no effect among intermittent users. The fact that intermittent use has no effect suggests the overall impact of intensive use is not merely a selection issue where likely quitters decide to try e-cigarettes. Rather, the combined results suggest that e-cigarettes abet quitting among intensive users and cast some doubt on the alternative explanations that they hinder quitting or have no effect. The results from chapter 4 are consistent with these findings.

Fixed effects designs such as this, which theoretically control for between-individual effects and isolate within-individual effects over time, may help to identify a

causal effect when the unobservable confounder is time-invariant (e.g., geographic location, gender, some policy variables). However, the core weakness of fixed effects designs is that they cannot account for unobserved time-varying confounders. Hernandez and Pudney pointed out that the assumption that unobserved confounders are time-invariant "is particularly strong in the context of the behavior of young people, who are undergoing complex developmental and socialization processes, and it conflicts with many of the ideas of developmental psychology and sociology" (14).

As chapters 3 and 4 demonstrate, a lack of randomization or exogenous variation does not mean that study results cannot have any causal bearing. Often meaningful comparisons can be made between only high-propensity and low propensity smoking initiators (9), among only quit attempters (12), between intensive and experimental users (11), or between nicotine replacement therapy users and e-cigarette users (12) as in chapter 4. These comparisons can give causal insight even if the ultimate conclusion is not as definitive as a randomized experiment would be. A set of observational results can, in combination, affect our assessment over whether a relationship is likely to be causal. Perhaps one explanation among many can be ruled out, or perhaps a result that has been established in an experimental setting may be shown to have an insubstantial effect in the real world.

Another option is to break down the causal chain to find an intermediate outcome that is less susceptible to the aforementioned obstacles. Chapter 3 largely sidesteps the issues of reverse causality and known unobservable confounders by predicting a known risk factor for smoking – overestimation of peer smoking rate – rather than smoking itself. After controlling for actual peer smoking rates, tobacco media exposure, and

demographics, it is reasonable to assume that the gateway pathway of interest – peer vaping leading to a perception of peer smoking – would be the most likely reason for a positive correlation between peer vaping and perceived peer smoking.

Ultimately, a convincing answer to the question of population effects requires various methodological approaches. Clinical trials can most firmly address whether a statistically significant relationship exists and whether that relationship is causal, but their external validity issues undermine their ability to identify whether the ultimate impact of e-cigarettes is *substantial*. Well-designed observational studies analyzing individual-level data that can be generalized to a wider population may be better suited to detect whether a causal impact, if identified, is substantial. Also, they can identify which effects outweigh others if many are taking place simultaneously. When there is no clear identification strategy, then it is particularly important that assumptions, selection issues, and possible alternative explanations are discussed explicitly.

Lessons for Policymakers

The first half of this chapter has laid out the difficulties that researchers will face in developing policy knowledge in this field and given some suggestions on how to address these difficulties. The remainder of this chapter will focus on how policymaking can move forward given the unavoidable uncertainties that they will face in this field. First, I will discuss some factors that have altered the tobacco policymaking environment in recent years, particularly in the US. Then, I will discuss what approaches and specific policies are warranted given the current policy environment and state of knowledge.

Kingdon in Reverse

Kingdon's conception of "policy streams" has become a canonical starting point for scholars of policymaking (15). This theory holds that problems, proposed solutions, and political will to implement solutions all must line up together for policy change to occur. While all theories of policy have some explanation for how issues arrive on the agenda and solutions are proposed, the notion that there is an essentially separate and distinct political stream that is largely independent of the emergence of problems and solutions is the distinctive aspect of Kingdon's work. This approach remains particularly relevant to modern US policy because divided government, or even a minority party holding enough Senators to sustain a filibuster, are often sufficient to keep a policy window closed. Political windows will open and close in any Democratic system, but the US system is rife with veto points that make the openings fewer and farther between (16). As a result, a defining characteristic of policymaking in the US is that policy ideas need to wait for appropriate political conditions to arrive in order to be realized.

Notably, Kingdon's stream schema applies to policymaking that requires legislative or executive bodies to act, bodies that will experience substantial ideological swings across time, but it is less relevant in cases where the bureaucracy has substantial autonomy. In these cases, the political window essentially remains open indefinitely. The Federal Reserve, for example, will respond to economic conditions with little regard for the partisan makeup on Capitol Hill and in the White House. No bureaucracy acts completely autonomously, and Congress possesses various tools for bringing the bureaucracy to heel, such (17). Nevertheless, to the degree that bureaucratic actors have

comprehensive and autonomous authority over a policy domain, the impact of the political stream becomes marginalized.

In a sense, tobacco control policy on e-cigarettes is Kingdon in reverse. Typically, the ordering of policymaking starts with the arrival of a problem, followed by sets of proposed solutions, followed by the opening of a political window. In this case, the political window was opened first. It so happened that e-cigarettes began to gain a foothold in the American market in the months following the first instance of unified filibuster-proof Democratic control since 1965. As a result, the political window for action had opened up, and action had been taken in response to pent up policy solutions that had built up over the previous two decades, before e-cigarettes themselves became the central focus of tobacco control policymaking. This action, the 2009 Family Smoking Prevention and Tobacco Control Act (18) (hereafter "Tobacco Act") represented a profound shift in tobacco policy authority, with substantial power delegated to the FDA.

The shift of tobacco policymaking to the FDA represents a major change from the past century of smoking policymaking. Previously, tobacco control advocates went "venue shopping" (19) for sympathetic voices within the government, at various times making policy through the FTC, FCC, FAA, FDA, and in the states (20–22). Tobacco interests responded by fighting these actions in the courts and seeking allies in Congress to enact legislation that would supersede bureaucratic authority (20–22). The Tobacco Act delegates substantial authority to the FDA, particularly regarding less hazardous cigarettes which finally have a clear regulatory home. This is one way in which tobacco policymaking today differs from in the past, but it is not the only one.

Interest Groups

The interest group environment (23) is substantially different today than in years past. Consider the tobacco industry. The tobacco industry of old was less monolithic than commonly portrayed (see chapter 2), but the nicotine industry today far more diverse and diffuse than ever before. First of all, there are a number of standalone e-cigarette companies that do not make tobacco cigarettes. Second, sophisticated electronics makers that have been servicing the marijuana industry, such as Pax, are now entering the nicotine space (24,25). Third, even the old guard companies have expanded into the e-cigarette space, exposing potential conflicts of interests within companies where new products are competing against existing ones. Notably, there is an apparent cleavage within the tobacco industry between Altria/Philip Morris and other tobacco companies, the former supporting the Tobacco Act and all others opposed (26). On the retail side, the emergence of "vape shops" that exclusively sell e-cigarettes represent a new interest group with different characteristics than traditional tobacco retail channels (27).

The most consequential shift in the interest group landscape may end up being the politicization of nicotine consumers, especially e-cigarette users (vapers). Formally represented by the Consumer Advocates for Smokefree Alternatives Association (CASAA) in the US (28), vapers congregate in online forums to discuss and review new products and discuss political activities (29). While they might lack the inherent sympathy in the general population of cancer or AIDS patients, their activism can nonetheless impact FDA activities in similar ways (30).

Unambiguous End Goals

The political science of policy is necessarily general, but policymakers within a given policy area will encounter features that vary across policy areas. A critical and distinctive aspect of modern tobacco control policy is that the ultimate goal – to eliminate tobacco-related morbidity and mortality (31) – is relatively straightforward. There may be value tradeoffs involved in the means of achieving this end goal. Or, there may be opportunity costs, associated either with pursuing this end goal instead of others, or with one strategy of reaching this goal against competing strategies. However, all tobacco control policy arguments have the same end goal in mind. This can be contrasted with policy areas where there is 1) considerable disagreement about the end goal, such as in the case of social issues or agricultural policy; 2) considerable ambiguity surrounding an abstract end goal, such as "security" (32) or "sustainability (33,34); or 3) potential tradeoffs between multiple unambiguous end goals, such as inflation control and growth in monetary policy or access and quality in health care policy (35). Because the end goal or reducing tobacco smoking is straightforward and uncontroversial, values and arguments center almost entirely on means to reach this goal. Thus the emergence of e-cigarettes has sharpened disagreements about the optimal way forward.

Prudent Policymaking Under Uncertainty

At this time, the obstacles to a full understanding of the population effects of e-cigarettes outweigh the available evidence. The most obvious strategy to combat uncertainty is to run a number of studies using the approaches from the previous section in order to reduce this uncertainty. Clearly, there is much work to be done in uncovering the presence and magnitudes of the various gateway and cessation effects. But the reality

is that a full picture of the population effects may not be available for many years. Unfortunately, while there are increasing amounts of data on e-cigarette use being collected, this data is not always easily obtained and analyzed. Current research is unable to meet the demand of policymakers who are forced to regulate e-cigarettes with incomplete information. On top of the internal validity difficulties that have been discussed already, there are a number of external validity issues that add further uncertainty into the situation. Nationally representative data that comes available is typically several years old by the time access is granted to most researchers. Timeliness is critical because of the quick evolution of e-cigarette technology (36). Also, over time different populations of smokers and nonsmokers trying the products. The initial wave of e-cigarette triers were early adopters, and later adopters may have different characteristics. Lastly, there may be different experiences with e-cigarettes in different places. To this point, the possible cessation benefit of e-cigarettes appears particularly promising in the UK (12), while the potential harms of the gateway effect appears particularly alarming in Poland (37,38).

Without full knowledge of whether e-cigarettes are harming or improving public health in the short term, how should policymakers approach these products? First, beware of policy implications stemming from on research designs that are faulty or inherently misleading. To give one prominent example, many suggest that e-cigarettes may reduce the odds of cessation among smokers based on cohort studies that measure e-cigarette use at baseline (39). However, chapter 4 has shown that these studies select out most quits associated with e-cigarettes because these quits are most likely to occur before baseline,

concurrent with initial e-cigarette use. We simply cannot conclude anything meaningful from the reported effects without any accounting for this selection effect.

Second, consider unintended consequences. Policy efforts should aim to hinder gateway pathways and facilitate cessation pathways where possible, focusing on approaches where achieving one goal is unlikely to inhibit the other. The primary virtue of the harm reduction framework is not that it leads to a conclusion that harm reduction is advisably always, usually, sometimes, or never. Rather, it is that harm reduction strategies and use reduction strategies will always trade off in some way, as reducing the harm associated with a behavior will automatically increase its marginal utility, and so it is important to consider ways to pursue one approach with minimal adverse effect on the other.

For potential gateway mechanisms, bans on advertising and sales to minors, increased messaging to youth on the dangers and costs of nicotine addiction, and disallowing cross-branding of cigarette and e-cigarette products can all help hinder gateway mechanisms without also substantially hindering cessation mechanisms.

Facilitating the development of products that smokers find appealing and discouraging tobacco-only retailers where non-tobacco nicotine products are unavailable can help facilitate cessation mechanisms without enhancing gateway mechanisms. Taxation proportional to harm (40), clearly distinguishing between vaping and smoking to avoid conflation, communicating accurate relative risk information, mandating an arms-length relationship between e-cigarette and tobacco cigarette makers and giving a competitive edge to the former, encouraging explicit anti-smoking messaging in e-

cigarette marketing, and restricting pro-smoking messaging can all both facilitate cessation mechanisms and hinder gateway mechanisms.

Third, maintain flexibility. The state of evidence is currently weak, but new studies are accumulating all the time. Any short-term policy implemented today should be amenable to becoming either more restrictive or more permissive according to what these studies contain. FDA is now beginning to implement safety standards which are long overdue. It is important to implement some level of standards to allow for regulatory flexibility to move in either direction. If e-cigarettes are more harmful or less beneficial than they currently appear, these standards can be modified accordingly. If not, these standards will be necessary to win the backing of currently skeptical members of public health and the medical establishment. Public confidence that e-cigarettes are less harmful than cigarettes is eroding (41). It will not be possible to outright recommend the use of e-cigarettes until there is substantial regulatory oversight over safety. Without such recommendation, many smokers will continue to believe that e-cigarettes do not represent a substantial health improvement. Thus, safety standards are not just important in their own right, but are an important component of a flexible approach going forward.

Finally, tread cautiously. While there is no consensus on a precise ethical framework through which to judge the merits of health policies, there is broad agreement on the importance of at least these 4 principles: respect for autonomy, beneficence, nonmaleficence, and justice (42). Of these, nonmaleficence – "to do no harm" – is arguably the most fundamental obligation. Violations of nonmaleficence have unique capacity to threaten the professional virtue of health practitioners because they are so jarringly dissonant with our "legitimate moral expectations that medicine will serve our

good" (43). In practice, this cannot mean that medical professionals must refrain from any action that might lead to harmful consequences, since some level of risk is unavoidable. Sharpe offers, "one ought not to inflict evil or harm," and, "one ought not to impose unnecessary or unreasonable risks of harm." Distilled to its essence, nonmaleficence "reflects an apparent need for cautious behavior…a need repeatedly rediscovered" (44).

In this sense, the initial FDA approach to e-cigarettes, where they were required to meet drug standards or be taken off of the market, represented a suboptimal approach. (45). Tobacco cigarettes are grandfathered onto the market, and they are, by far, the deadliest consumer product available. Until more is known about the effect of e-cigarettes on smoking rates, health authorities have an obligation to allow a reasonable range of products onto the market for adult smokers seeking an alternative. There are not enough proven harms relative to the extreme harms associated with tobacco cigarettes to justify taking away the option from smokers. As Michael Russell wrote 25 years ago:

> Until they have thought it through, those in the antismoking movement may fear that their clear simple message will be complicated and undermined. It need not be changed. There is only one fight and that is against tobacco and tobacco-related disease. It is important that this battle is maintained. Nicotine replacement could not compete unless awareness of the health risks of tobacco remains high. Availability of substitutes for tobacco will help the anti-smoking message to be heeded (46)

A robust market for cigarette alternatives can allow for increasingly aggressive antismoking policies that might otherwise verge on draconian. By giving space to market forces in the form of alternative nicotine products, the product mix that results from these market forces can in turn expand the regulatory options available to the next generation of tobacco control practitioners.

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