Examining trends, predictors, and mediators of e-cigarette use and smoking among Canadian youth: Findings from the COMPASS study

by

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Author's declaration

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true coy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Statement of Contributions

This thesis consists of three manuscripts- two of which have been submitted for publication and one of which has been prepared for publication. Exceptions to sole authorship:

Chapter 6: Aleyan, S., Hitchman, S.C., Ferro, M.A., & Leatherdale, S.T. (2020). Trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use among youth in Canada. *Addictive Behaviors*, *109*. https://doi.org/10.1016/j.addbeh.2020.106481

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As lead author of these three chapters (Chapters 6 to 8), I was responsible for formulating the research questions, conducting the literature review, leading the study design, conducting the statistical analyses, interpreting the study findings, and drafting all three manuscripts. My co-authors provided their guidance and feedback on drafts of the manuscripts. Dr. Leatherdale provided significant guidance and direction throughout this process.

Under Dr. Leatherdale's supervision, I also prepared the remaining chapters of this thesis, which were not written for publication.

Abstract

The objectives of this dissertation were to (1) examine trends and predictors of youth e-cigarette use and cigarette smoking, (2) explore potential mediators of the association between initial e-cigarette use and cigarette smoking uptake, and (3) evaluate the impact of Ontario's introduction of e-cigarette minimum legal sales age (MLSA) laws on youth e-cigarette use. The study objectives were explored in three separate manuscripts using data gathered from a sample of students in two Canadian provinces, Ontario and Alberta, that participated in a school-based study (COMPASS).

Using longitudinal data from students in Ontario and Alberta, the first manuscript examined changes in the prevalence of exclusive e-cigarette use, exclusive smoking and dual use of e-cigarettes and cigarettes over time. This manuscript also examined how frequency of e-cigarette use and smoking (i.e., number of days used in the past month) predicted exclusive e-cigarette use, exclusive cigarette smoking and dual use of both products after a one- and two-year follow-up period. Study findings showed an increase in all usage categories over time. Findings also demonstrated some differences in predictors of exclusive e-cigarette use, exclusive smoking and dual use. For instance, frequent e-cigarette use (i.e., use for 4 or more days in past month) was not a significant predictor of exclusive smoking at either follow-up time point, but did predict dual use at both the one- and two-year follow-up. Notably, findings also showed that students who reduced their frequency of e-cigarette use were less likely to report being exclusive e-cigarette users and dual users at the two-year follow-up.

The second manuscript investigated whether having one or more smoking friends mediated the association between initial e-cigarette use and cigarette smoking onset among a longitudinal sample of youth who were never smokers at baseline. Longitudinal findings showed that having one or more smoking friends did not mediate the association between e-cigarette use and subsequent cigarette smoking. Similarly, longitudinal results showed that having smoking friends did not mediate the association between e-cigarette use and subsequent dual

use of e-cigarettes and cigarettes. Rather, our study findings indicated that smoking friends significantly predicted both e-cigarette use and cigarette smoking among youth.

The third manuscript evaluated the influence of an e-cigarette law introduced in Ontario using a quasi-experimental design. In January 2016, Ontario implemented a law restricting the sale of e-cigarettes to those 19 and over. At that time, Alberta did not have a similar law in effect. Using a repeat cross-sectional sample, we examined the impact of Ontario's law on the school-level prevalence of e-cigarette use among a sample of Ontario schools versus Alberta schools. Furthermore, using a longitudinal sample of students, we evaluated the impact of this law on the individual likelihood of e-cigarette use among students in Ontario versus Alberta schools. Findings based on the repeat cross-sectional sample showed that the changes in the average school-level prevalence of e-cigarette use within the Ontario sample were not significantly different from the changes seen in the Alberta sample. Findings based on the longitudinal sample showed increases in e-cigarette use over time among students in Ontario and Alberta. However, the increase observed among students in Alberta (i.e., where no e-cigarette MLSA law was implemented) was larger than the increase seen among students in Ontario (i.e., where an e-cigarette MLSA law was implemented).

The studies examined within this dissertation project contribute towards our understanding of e-cigarette use and cigarette smoking among Canadian youth. Longitudinal findings indicated that having one of more smoking friends is a common risk factor that is associated with both e-cigarette use and cigarette smoking among youth. These findings suggest that the role of peers should be considered within the design of youth-based prevention interventions. Longitudinal findings showed an increase in e-cigarette use over time among youth in our study sample. Longitudinal findings also indicated that Ontario's introduction of e-cigarette MLSA laws had an impact in attenuating these increases in e-cigarette use, but did not reverse the overall increasing trend in use among youth in our sample. Collectively, our study findings suggest the need for a more comprehensive approach to address the rise in e-cigarette use among Canadian youth.

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To my thesis advisory committee, thank you for your invaluable support and feedback on my dissertation project.

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To my family - Mom, Noor, Feras and Ali, your love and support mean the world to me.

To my incredible husband, Nader, no words can describe how grateful I am for your love and support. You are my rock.

Dedication

This thesis is dedicated in loving memory of my father, Shawket Abdul Hadi Aleyan, who taught me the meaning of strength and perseverance.

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List of Terms

COMPASS: A research system designed to evaluate the impact of ongoing changes in school-based/provincial policies, programs and changes in the built environment on youth health behaviors

Dual users: Individuals who report using both cigarettes and electronic cigarettes (or e-cigarettes) at least once within the last 30 days

Electronic cigarettes (or e-cigarettes): A diverse range of battery-operated devices that heats a liquid typically comprised of flavoring agents, additives, propylene glycol and sometimes nicotine

Exclusive cigarette smokers: Individuals who report using *only* cigarettes at least once within the last 30 days

Exclusive e-cigarette users: Individuals who report using *only* e-cigarettes at least once within the last 30 days

List of Abbreviations

Cq: COMPASS student questionnaire designed to examine various health outcomes, including tobacco and substance use use, mental health outcomes, physical activity etc.

MLSA: Minimum legal sales age; referring to laws that introduce minimum legal age restrictions around the sale of a product

SHP: School Health Profile; customized health profiles that are distributed to each of the COMPASS schools that provides student-level data on key health behaviors and topic-specific evidence-based recommendations for school-based policies and programming

SPP: School Policies and Practices questionnaire; questionnaire designed to identify changes in school-level policies, programming and built environment that is generally filled out by a school administrator that is most knowledgeable about the school policy environment

TTI: Theory of Triadic Influence; a comprehensive framework grounded in various social and psychological theories that has been used to assess the complex range of influences that predict youth tobacco use

TVPA: Tobacco and Vaping Products Act; the national framework introduced within Canada to regulate the sale and marketing of electronic cigarettes (also known as vaping products)

1.0 Background

Since the late 1990s, Canada has witnessed significant declines in the prevalence of cigarette smoking among youth. For instance, national estimates demonstrated significant declines in the prevalence of ever smoking cigarettes among Canadian youth from approximately 50% in 1999 to 16.4% in 2017 (Reid et al., 2019). Relative to 27% of Canadian youth that reported being current smokers in 1999, this number dropped to roughly 8% in 2017 (Reid et al., 2019). However, the tobacco and nicotine product market has been evolving considerably with respect to the number and use of alternative tobacco products. Specifically, electronic cigarettes (e-cigarettes) have grown in popularity among youth in Canada (Cole, Aleyan, Battista, & Leatherdale, 2020; Hammond, Reid, Cole, & Leatherdale, 2017; Hammond et al., 2019; Montreuil et al., 2017; Zuckermann et al., 2019). E-cigarettes are defined within this dissertation as a diverse range of battery-operated devices that heat a liquid typically comprised of flavoring agents, additives, propylene glycol and sometimes nicotine (Hajek, Etter, Benowitz, Eissenberg, & Mcrobbie, 2014). According to national estimates, e-cigarette use in the past 30 days has doubled from 14.6% in 2017 to 29.4% in 2019 among Canadian students in grades 10 to 12 (Health Canada, 2019; Reid et al., 2019). Furthermore, recent national data showed that among past 30-day e-cigarette users, roughly 40% also reported smoking cigarettes in the past 30 days, suggesting that dual use of e-cigarettes and cigarettes is common (Reid et al., 2019).

The rise in e-cigarette use among youth has prompted researchers to examine correlates of use (Azagba, 2018a; Bold, Kong, Cavallo, Camenga, & Krishnan-Sarin, 2016; Demissie, Everett Jones, Clayton, & King, 2017a; Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2015; Milicic & Leatherdale, 2017; Patrick et al., 2016; Thomas A Wills, Knight, Williams, Pagano, & Sargent, 2015). Recent studies have demonstrated differences in socio-demographic and behavioral correlates of exclusive e-cigarette users (i.e., individuals who report using only e-cigarettes in the past 30 days) versus dual users of e-cigarettes and cigarettes (i.e., individuals who report using both e-cigarettes and cigarettes within the past 30 days) (Demissie et al., 2017; Goniewicz et al., 2016; Wills, Knight, Williams, Pagano, & Sargent, 2015). However, a key limitation of the majority of these studies is that they are based on cross-sectional designs. Moving forward, additional

longitudinal work could provide valuable insight regarding temporal trends and predictors of exclusive e-cigarette use, exclusive cigarette use and dual use. Future longitudinal work may also assist in identifying potentially promising interventions that are effective in reducing rates of e-cigarette use among youth.

This dissertation filled a knowledge gap by examining trends and predictors of smoking and e-cigarette use among a sample of Canadian youth, potential mediators of the relationship between e-cigarette use and cigarette smoking and the potential influence of new provincial e-cigarette laws on rates of youth e-cigarette use. Specifically, this research project focused on (1) assessing whether the frequency of e-cigarette use and cigarette smoking predicted subsequent patterns of dual use, exclusive e-cigarette use, exclusive cigarette smoking (vs. non-use); (2) identifying whether having smoking friends mediated the relationship between e-cigarette use and smoking behaviors; and, (3) evaluating whether e-cigarette minimum legal sales age (MLSA) laws that restricted e-cigarette sales to those 19 and over had an impact on rates of e-cigarette use among a sample of Canadian youth.

1.1 Structure of thesis dissertation

Chapter 1 provides a general overview of background information on youth e-cigarette use and cigarette smoking. Chapter 2 provides a brief literature review on (1) socio-demographic and behavioral correlates of youth e-cigarette use and cigarette smoking, (2) associations between youth e-cigarette use and cigarette smoking, (3) prominent theories regarding the association between e-cigarette use and smoking and (4) a review of identified characteristics of effective youth access restriction laws. Chapter 3 provides an overview of the study rationale and research questions for each of the three manuscripts. Chapter 4 discusses the theoretical framework that guided this dissertation, in addition to details regarding the research methodology. Chapter 5 provides an overview of the analytic approach that was used for each of the three manuscripts. Chapters 6 to 8 set out Manuscripts 1, 2 and 3 respectively. Lastly, Chapter 9 provides a summary of key findings across all three manuscripts and discusses the implications of these findings for future research and policy.

1.2 Electronic cigarette use among youth within Canada

There are a range of factors that may have contributed to the rise in awareness and use of e-cigarettes among Canadian youth. For instance, recent U.S. studies have noted the proliferation of e-cigarette promotion through a number of different channels including radio, television, celebrity endorsements and online media platforms (Duke et al., 2014; Farrelly et al., 2015; Kornfield, Huang, Vera, & Emery, 2015; Vasiljevic, Petrescu, & Marteau, 2016). Recent studies that have examined advertising claims made on e-cigarette retail websites have also demonstrated that e-cigarettes are often marketed by the industry as lifestyle choices and statements of identity, backed with fashionable designs and associations with celebrity icons that appeal to younger populations (Grana & Ling, 2014; Huang, Kornfield, & Emery, 2016). Within Canada, the Tobacco and Vaping Product Act (TVPA) that was introduced in May 2018 prohibited specific types of advertising that were considered appealing to youth, lifestyle advertising (with some exceptions) and advertising that entailed endorsements and sponsorship promotion (Health Canada, 2017). Figure 1 below provides a timeline of federal tobacco control policies that were in effect during the study period.

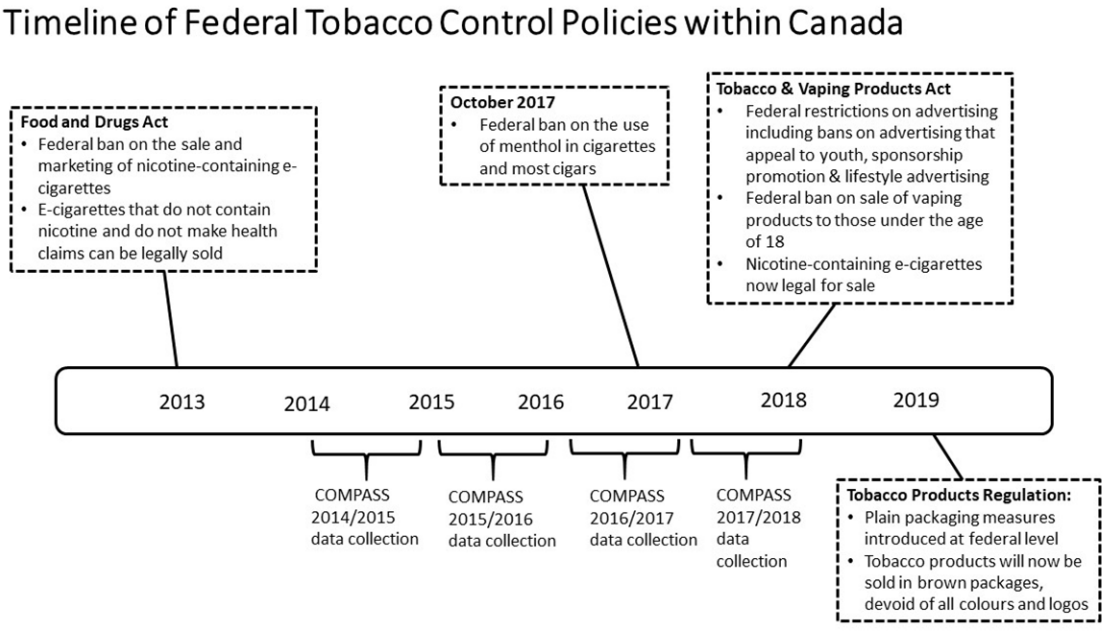


Figure 1. Overview of federal tobacco control policies that were in effect within Canada during the study period.

Aside from the proliferation of e-cigarette promotion, the availability of a diverse range of flavors that can be used in e-cigarettes has been shown to be particularly appealing to youth (Hoffman, Salgado, Dresler, Faller, & Bartlett, 2016). Previous U.S. studies have demonstrated that the availability of appealing flavors is often cited as one of the primary reasons for using e-cigarettes among youth (Bold et al., 2016; Kong et al., 2015; Tsai et al., 2018). Furthermore, data stemming from Canada has shown that among e-cigarette users, the most popular flavor youth reported using were fruit-flavored e-cigarettes (Reid et al., 2019). This data was also supported by a recent review by Hoffman and colleagues indicating that children and adolescents exhibited a preference for sweetened flavoring agents (e.g., cherry, strawberry etc.), in comparison to adults (Hoffman et al., 2016). Currently, there are over 7,000 flavors for the e-liquid solutions present in e-cigarettes (Zhu et al., 2014).

Other features that have been found to be particularly appealing to youth include rapid innovations in design features of newer brands of e-cigarettes. In contrast to older versions of e-cigarettes that resembled cigarettes (i.e., cig-a-likes), newer features of 'next generation' brands that utilize pod-devices (e.g., JUUL devices) have been found to be particularly appealing to youth (Barrington-Trimis et al., 2018; Huang et al., 2019; Willett et al., 2019). A recent review by Fadus et al. (2019) sought to identify key factors influencing the use of e-cigarettes and pod devices among adolescents and young adults (Fadus, Smith, & Squeglia, 2019). These findings indicated that pod devices have become increasingly popular among youth due to their novelty, sleek design, user-friendly functions and ability to be used in a discrete manner in places where smoking is forbidden (Fadus et al., 2019).

1.3 Concerns regarding e-cigarette use among youth

There are a number of arguments that have been raised by the public health community as to why the rise in e-cigarette use among Canadian youth is a source of concern. First, the use of e-cigarettes may promote the initiation of cigarette smoking behaviors among non-smoking youth by re-normalizing smoking behaviors. Secondly, youth e-cigarette use has been shown to co-occur with other risky behaviors including cigarette smoking, resulting in a sub-group of youth

that are dual users (i.e., youth who use e-cigarettes and cigarettes concurrently). Third, the widespread availability and use of nicotine-containing e-cigarettes within Canada has fueled concerns that the increasing popularity of e-cigarettes may result in a new generation of nicotine dependent youth (Czoli, Goniewicz, Palumbo, White, & Hammond, 2018; Hamilton et al., 2015; Hammond et al., 2015; Reid et al., 2019).

Various studies to date have examined the relationship between e-cigarette use and cigarette smoking among youth populations. A number of longitudinal studies have demonstrated that the use of e-cigarettes among non-smoking youth has been associated with an increased odds of cigarette smoking uptake (Barrington-Trimis et al., 2016; Berry et al., 2019; Hammond, Reid, Cole, & Leatherdale, 2017; Leventhal et al., 2015; Miech, Patrick, O'Malley, & Johnston, 2017; Primack, Soneji, Stoolmiller, Fine, & Sargent, 2015; Soneji, Barrington-Trimis, Wills, et al., 2017). In light of this evidence , concerns have been raised from the public health community that e-cigarette use may lead to the re-normalization of smoking behaviors as a result of social and behavioral mechanisms that increase access and exposure to cigarettes, and promote ritualistic procedures associated with smoking behaviors (Pepper et al., 2013; Schneider & Diehl, 2016).

Various studies conducted in the United States and Canada have demonstrated that a substantial number of youth report using both e-cigarettes and cigarettes concurrently, resulting in a sub-group of dual users (Dutra & Glantz, 2014; Hughes et al., 2015; Kristjansson, Mann, & Sigfusdottir, 2015; Milicic & Leatherdale, 2017). Studies have shown that dual users represent a 'high-risk' category of youth that are more likely to engage in risky behaviors including e-cigarette use and cigarette smoking at higher frequencies (compared to non-users and exclusive e-cigarette users) (Goniewicz et al., 2016; McCabe, West, Veliz, & Boyd, 2017; Wills, Knight, Williams, Pagano, & Sargent, 2015). Recent cross-sectional studies have also found that ever use of e-cigarettes among experimental smokers was associated with a higher odds of current cigarette smoking and lower odds of abstaining from cigarettes (relative to non-users) (Chaffee, Watkins, & Glantz, 2018; Dutra & Glantz, 2014). These findings have raised concerns that e-

cigarette use among adolescent experimental smokers may lead to the maintenance and/or escalation of cigarette consumption patterns.

Although recent studies have demonstrated that e-cigarettes are less harmful than combustible cigarettes (McNeill et al., 2019; McNeill et al., 2018), exposure to nicotine during early adolescence has been shown to have adverse effects with respect to both cognitive function and development (National Health Center for Chronic Disease Prevention and Health Promotion, 2014). Of particular importance, recent changes in federal regulations brought forth through the TVPA now provides a legal framework for the sale and distribution of nicotine-containing e-cigarettes (Health Canada, 2018). This change in legislation will likely result in large shifts within the Canadian nicotine landscape. For instance, high concentration nicotine-based e-cigarettes like JUUL that deliver nicotine more effectively through the use of nicotine salts are now available for sale within Canada (Goniewicz, Boykan, Messina, Eliscu, & Tolentino, 2018; Talih et al., 2019). Concerns have been raised that the widespread availability of these highly effective nicotine delivery devices may pose a potential threat to youth who are particularly vulnerable to nicotine dependence (Counotte, Smit, Pattij, & Spijker, 2011; Yuan, Cross, Loughlin, & Leslie, 2015).

1.4 E-cigarettes as a potential harm reduction tool

Although e-cigarette use (particularly among non-smoking youth) has raised various concerns within the public health community, others have drawn attention to its potential utility as a harm reduction tool among adult established smokers (Dib et al., 2017; Hartmann-Boyce, McRobbie, Begh, Stead, & Hajek, 2016; Malas et al., 2016). In a Cochrane review conducted by Hartmann-Boyce et al. (2016), the authors concluded that using e-cigarettes with nicotine assisted adult smokers in quitting smoking, compared to e-cigarettes without nicotine (Hartmann-Boyce et al., 2016). Another systematic review by Malas et al. (2016) concluded that the effectiveness of e-cigarettes as a potential cessation aid was inconclusive, due to various methodological weaknesses including sampling issues and limited number of well-designed studies (Malas et al., 2016). In a systematic review and meta-analysis by Dib et al. (2017) which included three randomized control trials and nine cohort studies, the authors concluded that due to the low quality of evidence available to date, drawing strong inferences regarding whether e-

cigarettes promote or hinder smoking cessation was impossible (Dib et al., 2017). A more recent Cochrane review found moderate evidence that e-cigarettes with nicotine increased quit rates at six months or longer, compared to non-nicotine e-cigarettes and compared to nicotine replacement therapy (Hartmann-Boyce et al., 2020). Though some evidence exists suggesting a positive relationship between e-cigarette use and smoking cessation outcomes among adult smokers, these reviews have noted the need for additional evidence stemming from well-designed randomized control trials and longitudinal population studies (Dib et al., 2017; Hartmann-Boyce et al., 2016; Malas et al., 2016; Hartmann-Boyce et al., 2020).

In contrast to studies based on adult smokers, e-cigarette use does not appear to encourage smoking cessation among youth smokers. For instance, in a U.S. study by Dutra et al. (2014), current e-cigarette use among current cigarette smokers (who had smoked 100 or more cigarettes) were less likely to report abstaining from cigarettes after 30 days, 6 months and 1 year (Dutra & Glantz, 2014). Among dual users of e-cigarettes and cigarettes, current e-cigarette use has also been shown to be negatively associated with intentions to quit smoking cigarettes and quit attempts (Huang et al., 2016). A more recent U.S. study demonstrated that among dual users of e-cigarettes and cigarettes, over half of the sample remained dual users after a 12-month follow-up (Vogel, Prochaska, Ramo, Andres, & Rubinstein, 2019). These findings offer little evidence for a possible smoking cessation benefit among youth dual users. However, these findings are also not surprising, as recent studies that have investigated reasons for use indicate that a small proportion of youth report using e-cigarettes for the purposes of smoking cessation/reduction (Bold et al., 2016; Kong et al., 2015; Tsai et al., 2018). Rather, recent studies have shown that the most commonly reported reasons for using e-cigarettes included use by a family or friend, curiosity and the availability of different flavors; less than 10% of youth reported using e-cigarettes to assist in quitting/reducing smoking behaviors (Bold et al., 2016; Kong et al., 2015; Tsai et al., 2018).

2.0 Literature Review

Chapter 2 is divided into three sections (2.1, 2.2 and 2.3). Each of these three sections coincides with the literature review for each of the three manuscripts (to be described in further detail in Chapter 3). Each section provides a relevant literature review and concludes with a summary of the evidence to date, in addition to identified research gaps.

2.1 Sociodemographic and behavioral correlates of e-cigarette, cigarette & dual use behaviors

As described in Section 1.1, recent data has demonstrated that many Canadian youth have used e-cigarettes; in 2017, 14.6 % of youth in grades 10-12 had used e-cigarettes within the past 30 days (Reid et al., 2019). Of concern, recent national estimates indicate that ~40% of past 30-day e-cigarette users also report smoking cigarettes, suggesting that dual use of e-cigarettes and cigarettes is common (Reid et al., 2019). The phenomenon of dual use that has been observed among youth is particularly concerning, as cigarette smoking during early adolescence, even at lower levels, has been shown to significantly increase the risk of regular cigarette smoking in the future (Hwang & Park, 2014; Reidpath, Davey, Kadirvelu, Soyiri, & Allotey, 2014; Reidpath, Ling, Wellington, Al-Sadat, & Yasin, 2013). Despite this, there is limited data that reports on current trends in dual use behaviours among Canadian youth. Longitudinal data on dual use behaviours among Canadian youth could provide valuable insight on trends in e-cigarette use and cigarette smoking during adolescence.

Despite the prominence of dual use behaviours among youth, few studies to date have examined correlates that distinguish exclusive e-cigarette users, exclusive cigarette smokers and dual users. Among the few studies conducted to date (Azagba, 2018; Cooper, Case, Loukas, Creamer, & Perry, 2016; Kristjansson et al., 2015; McCabe et al., 2017), key differences have been noted among non-users, exclusive e-cigarette users, exclusive cigarette smokers and dual users. With respect to sociodemographic characteristics, recent cross-sectional studies have demonstrated that dual users were more likely to be males, compared to non-users (Cooper et al., 2016). Dual users were also more likely to identify as White, compared to exclusive smokers and non-users (Cooper, Case, Loukas, Creamer, & Perry, 2016). Studies have also shown

differences in the substance use risk profiles of dual users, exclusive e-cigarette users and cigarette smokers and non-users. For instance, recent cross-sectional studies have noted that dual users were more likely to engage in frequent/daily cannabis use, relative to exclusive e-cigarette users, exclusive cigarette smokers and non-users (Azagba, 2018; Demissie et al., 2017; McCabe et al., 2017). Similar differences in associations have been documented with other substance use behaviours including binge drinking and illicit drug use (Demissie et al., 2017; Kristjansson et al., 2015; McCabe et al., 2017). Recent cross-sectional studies have shown that dual users of e-cigarettes and cigarettes were more likely to report using e-cigarettes at higher frequencies, relative to exclusive cigarette smokers and exclusive e-cigarette users (Demissie et al., 2017; McCabe et al., 2017). Collectively, these studies suggest that dual users represent a high-risk sub-group of youth that engage in risky behaviours at higher frequencies, whereas exclusive e-cigarette users represent an intermediate level risk group that fall somewhere between non-users and exclusive cigarette smokers/dual users (Azagba, 2018; Demissie et al., 2017; McCabe et al., 2017). However, it is important to note that a key limitation of the current evidence on dual use behaviours is that it is primarily derived from studies that are cross-sectional in nature. As such, inferences regarding the temporality of these associations cannot be inferred. Additional longitudinal studies could provide valuable information regarding what specific risk factors predict involvement in exclusive e-cigarette use, cigarette smoking, dual use and non-use among Canadian youth.

Various longitudinal studies to date have demonstrated associations between past 30-day e-cigarette use and subsequent cigarette smoking (Aleyan, Cole, Qian, & Leatherdale, 2018; Leventhal et al., 2015; Milicic & Leatherdale, 2017; Primack et al., 2015; Soneji, Barrington-Trimis, Willis, et al., 2017). Some evidence also exists that these associations can be bi-directional, whereby having tried smoking a cigarette also predicts subsequent use of e-cigarettes (East et al., 2018; Penzes et al., 2018). However, it remains unclear how frequency of e-cigarette use and cigarette smoking (i.e., number of days that e-cigarettes were used in the past month) may influence subsequent patterns of exclusive e-cigarette use, cigarette smoking and dual use over time. Moving forward, additional longitudinal studies that utilise more granular measures (e.g., number of days used within the past month) could provide additional insight into how frequency

of e-cigarette use and cigarette smoking is related to subsequent use of e-cigarettes and cigarettes among youth.

2.1.1 Summary & Research Gaps

The current evidence to date indicates that e-cigarette use is on the rise among Canadian youth and that roughly 40% of e-cigarette users report smoking cigarettes concurrently (i.e., dual users) (Hammond et al., 2017; Reid et al., 2019; Zuckermann et al., 2019). Despite this, there is a lack of studies examining longitudinal trends in exclusive cigarette smoking, exclusive e-cigarette use and dual use among Canadian youth. Though recent cross-sectional studies suggest that dual users have distinct risk profiles from exclusive e-cigarette users and cigarette smokers (Azagba, 2018; Cooper et al., 2016; Demissie, Everett Jones, Clayton, & King, 2017; McCabe et al., 2017; Wills et al., 2015), there is a clear need for additional longitudinal studies that can identify what risk factors predict exclusive e-cigarette use, exclusive smoking, dual use and non-use.

2.2 Associations between youth e-cigarette and cigarette use

In response to concerns raised by the public health community that e-cigarette use may re-normalize smoking behaviors (Arrazola et al., 2015; Reid et al., 2017; Stanbrook, 2016; Stanwick, 2015), various studies have been conducted to explore the associations between the initial use of e-cigarettes and subsequent cigarette smoking uptake among youth populations. In a recent study that examined a cohort of 2,530 grade 9 students, non-smoking youth who had reported trying e-cigarettes at baseline were 2.65 times more likely to report smoking cigarettes after a year, after adjusting for sociodemographic, environmental and intra-personal risk factors for smoking (Leventhal et al., 2015). These associations have also been demonstrated among non-smoking individuals who were not attitudinally susceptible to smoking cigarettes in the future (Aleyan et al. 2018). Specifically, this study found that among a sample of 9,501 never-smokers in grades 9 and 10, non-susceptible never smokers (i.e., low-risk youth) that reported using e-cigarettes at baseline were 5.28 times more likely to report smoking cigarettes after a 2-year follow-up period (Aleyan, Cole, & Qian, 2018). Links between initial e-cigarette use and subsequent smoking uptake have been shown in studies conducted across various countries including the Unites States, Canada, England and Scotland (Aleyan, Cole, Qian, et al., 2018; Best et al., 2017; Conner et al., 2017; East et al., 2018; Hammond et al., 2017). In a recent meta-analysis that assessed 9 longitudinal studies that included samples of youth and young adults, the authors concluded that individuals who reported using e-cigarettes were 3.63 times more likely to report smoking cigarettes at follow-up, after adjusting for a range of cigarette-related risk factors (Soneji, Barrington-Trimis, Wills, et al., 2017). A more recent meta-analysis by Khouja et al. that examined 17 studies that included samples of youth and young adults showed similar findings whereby non-smokers who had used e-cigarettes were 4.59 times more likely to report being smokers than those who had not (Khouja, Suddell, Peters, Taylor, & Munafò, 2020).

2.2.1 Theories that may explain the association between e-cigarette and cigarette use

Various theories have been put forth within the tobacco control community to explain the associations observed between youth e-cigarette use and subsequent smoking behaviors. Advances in product innovation and design have resulted in the creation of effective nicotine

delivery devices (Goniewicz et al., 2018; Talih et al., 2019). E-cigarettes offer consumers a large degree of control over extensive features and operating conditions, that allow for a range of nicotine yields to be acquired (Goniewicz et al., 2018; Talih et al., 2019). Prior research has shown that adolescents exhibit an enhanced sensitivity to the effects of nicotine; early exposure to nicotine among youth may result in nicotine dependence and an increased liability to experiment with other nicotine products (i.e., combustible cigarettes). (Counotte et al., 2011; Yuan et al., 2015). Others have argued that the associations observed between e-cigarette use and smoking initiation may be the result of unmeasured common factors that increase an individual's likelihood of using both cigarettes or e-cigarettes (Vanyukov et al., 2012). According to the Common Liability Theory, young individuals may share common factors (e.g., risk-taking tendencies, rebelliousness) that make them more likely to experiment with both vaping and smoking (irrespective of which order they are used in) (Vanyukov et al., 2012) .

Aside from the theories noted above, others have drawn attention to the role of social contexts in influencing youth smoking (Poland et al., 2006; Wills, Gibbons, Sargent, & Schweitzer, 2016). Extensive research has shown that social settings (e.g., family circles, peer circles) represent critical microsystems that can influence adolescent smoking behaviors (Lakon et al., 2015; U.S. Department of Health and Human Services, 2012; Wellman et al., 2016; Wills et al., 2016) . For example, having parents/siblings who smoke has been shown to predict adolescent smoking initiation (Tyas & Pederson, 1998). Similarly, having friends who smoke has been shown to be a reliable predictor of smoking initiation (Kobus, 2003; Mayhew, Flay, & Mott, 2000; Tyas & Pederson, 1998). Furthermore, a large proportion of adolescents that use e-cigarettes also smoke cigarettes and e-cigarette users tend to have friends who also use e-cigarettes (Azagba, Kah, & Latham, 2019; Montreuil et al., 2017). Therefore, youth who use e-cigarettes and are affiliating with e-cigarette users are likely to come into contact with cigarettes. These peer affiliations may provide youth with access to cigarettes, encourage and model smoking behaviors (Bandura, 1987; Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2016; Sussman, Pokhrel, Ashmore, & Brown, 2007).

Though various theories, described above, have been put forth to explain associations

between youth e-cigarette use and cigarette smoking, many of them have not been tested and it remains unclear as to *why* youth e-cigarette use is linked to smoking uptake. Only two studies to date have utilized mediation models to investigate potential explanations for the relationship between youth e-cigarette use and cigarette smoking behaviors. The first study conducted among sample of youth in the United Kingdom sought to investigate (a) whether the escalation of e-cigarette use mediated the relationship between initial e-cigarette use and subsequent smoking onset and (b) whether the escalation of cigarette use mediated the relationship between initial cigarette use and subsequent e-cigarette use (East et al., 2018). The authors concluded that both e-cigarette escalation and smoking escalation did not explain these relationships (East et al., 2018). The second study examined the role of various cognitive and social factors mediating the relationship between e-cigarette use at baseline and smoking onset at follow-up among a sample of 2,338 grade 9 and 10 students in Hawaii (Wills et al., 2016). The study found that changes in social and cognitive factors including smoking-related expectancies, peer smoking affiliations and cannabis use were all significant pathways linking e-cigarette use and subsequent smoking onset (Wills et al., 2016).

2.2.2 Summary and Research Gaps

There is consistent evidence of the association between e-cigarette use and subsequent smoking uptake among youth populations examined in various countries (Aleyan, Cole, Qian, et al., 2018; Barrington-Trimis et al., 2016; Hammond et al., 2017; Leventhal et al., 2015; Soneji, Barrington-Trimis, Wills, et al., 2017). Despite this, limited studies have tested possible theories for the observed association between e-cigarette use and subsequent smoking onset using rigorous methods, such as mediational models (East et al., 2018; Wills et al., 2016). There is a clear need for additional longitudinal studies that seek to identify possible underlying mechanism(s) linking e-cigarette use and subsequent smoking behaviors. This data can provide a deeper understanding of the relationship between e-cigarette and cigarette use. Furthermore, this information can be used to inform the design of appropriate interventions that seek to prevent and reduce cigarette consumption.

2.3 Distinct regulatory approaches surrounding e-cigarette use

In response to rising rates of e-cigarette use, various governments have taken distinct approaches to regulate e-cigarettes. Within Canada, the Tobacco and Vaping Products Act (TVPA) was introduced in May 2018 providing a regulatory framework for the sale, manufacturing and marketing of nicotine-containing e-cigarettes (Health Canada, 2018). Some of the measures within the TVPA included restricting the marketing of flavors that would be considered appealing to youth (e.g., bubble-gum, candy flavors) and restricting promotional efforts that would be considered appealing to youth (Health Canada, 2018). Within the United States (U.S.), federal regulations were introduced in 2016 aimed at preventing youth access to e-cigarettes, including restrictions of e-cigarette sales to anyone under the age of 18 (Food and Drug Administration, 2016). Within Europe, the EU Tobacco Products Directive introduced measures aimed at regulating e-cigarettes across the 28 member states, including restrictions on the sale of nicotine-containing e-liquids with nicotine concentrations of more than 20 mg/ml (European Parliament and the Coucil of the European Union, 2014). As new regulations relating to e-cigarettes are introduced globally, evaluations of these regulatory changes (i.e., natural experiments) offer an ideal opportunity to gather timely and relevant 'practice-based' evidence to inform the design of future policies (Leatherdale, 2018; Petticrew et al., 2005).

2.3.1 Restrictions on youth access to tobacco

A widely adopted regulatory approach aimed at restricting youth access to tobacco include the introduction of minimum legal sales age (MLSA) laws. Various reviews have demonstrated that the introduction of MLSA laws may have the potential to reduce youth purchasing behaviors, perceived access to cigarettes and the prevalence of youth cigarette use (Richardson et al., 2009; Stead & Lancaster, 2005). A Cochrane review by Stead and Lancaster (2005) that examined the impact of interventions focused on reducing underage access to tobacco concluded that legislation alone was not sufficient to prevent the sale of tobacco to minors; rather, a comprehensive approach that incorporated consistent and ongoing enforcement of MLSA laws and community policies aimed at improving retailer compliance were necessary components of effective policy (Stead & Lancaster, 2005). The authors of this review

also made note of the challenges in drawing conclusions about the effectiveness of interventions in reducing access to tobacco by minors, in cases where retailers continued to sell tobacco to minors (i.e., failed to comply with policies) (Stead & Lancaster, 2005). Similar to earlier findings, a more recent review by Richardson et al. (2009) that included 20 intervention studies relating to access restriction of tobacco among minors concluded that comprehensive interventions involving retail inspections, consistent enforcement practices and general awareness of MLSA laws were associated with decreases in illegal sales of tobacco (Richardson et al., 2009). It is important to note that the majority of the studies included within this review examined the effect of access restriction interventions on illegal sales; less evidence exists regarding the impact of these interventions on youth smoking behaviors (Richardson et al., 2009). However, the few studies conducted to date that have examined the impact of introducing MLSA laws have reported reductions in the prevalence of cigarette smoking among youth populations (Fidler & West, 2010; Millett, Lee, Gibbons, & Glantz, 2011; Rimpelä & Rainio, 2004).

2.3.1.1 Extending minimum legal sales age (MLSA) restrictions to e-cigarettes

Given the rise in e-cigarette use among youth populations (Glantz & Bareham, 2018), many countries have extended MLSA laws to e-cigarettes within recent years. Despite this, limited evidence exists regarding the impact of e-cigarette MLSA laws on youth e-cigarette use. Rather, the majority of studies to date have focused on evaluating the effects of e-cigarette MLSA restrictions on youth tobacco use (as measures of e-cigarette use were only added in more recent survey years) (Dutra, Glantz, Arrazola, & King, 2018; Friedman, 2015; Pesko, Hughes, & Faisal, 2015). The first study by Friedman (2015) found that states which introduced e-cigarette MLSA laws had a significant 0.9 percent increase in past 30-day smoking rates among U.S. adolescents, relative to states without such restrictions (Friedman, 2015) . The second study by Pesko et al. (2015) also used state-level data to examine how e-cigarette MLSA laws influenced the use of cigarettes, cigars, smokeless tobacco and cannabis among a nationally representative sample of adolescents from the United States (Pesko et al., 2015). The study findings demonstrated that that e-cigarette MLSA laws were not associated with cigar use, smokeless tobacco use or cannabis use (Pesko et al., 2015). In contrast, MLSA laws were associated with a 0.8 increase in regular adolescent cigarette use (defined as at least 20 days out of past 30 days) (Pesko et al.,

2015). However, more recent U.S. studies that have assessed the effects of e-cigarette MLSA laws using individual-level data have shown conflicting findings (Abouk & Adams, 2017; Dutra et al., 2018). For instance, a study by Abouk et al. (2017) that used individual-level data from a sample of high school seniors that participated in Monitoring the Future (MTF) study found that MLSA laws were associated with reductions in past 30-day cigarette smoking (Abouk & Adams, 2017). Another study conducted by Dutra et al. (2018) found that after adjusting for e-cigarette use and other tobacco use, MLSA laws were not significantly associated with past 30-day cigarette smoking among a sample of youth aged 12-17 (Dutra et al., 2018). These conflicting results may be attributable to differences in retailer awareness of MLSA laws, compliance with existing laws and consistency of enforcement practices exercised by relevant authorities.

Currently, only one study to date has examined the impact of e-cigarette MLSA laws on youth e-cigarette use. This repeat cross-sectional study by Nguyen et al. (2019) showed an increase in e-cigarette use among youth across all Canadian provinces. Nguyen et al. also showed that increases seen were 4.3 percentage points lower in Canadian provinces where e-cigarette MLSA laws were implemented, relative to provinces that had not (Nguyen et al., 2019). Given the currently limited evidence base, additional research focused on evaluating the impact of e-cigarette MLSA laws is needed to identify their effectiveness. This information could offer timely and relevant information that can be used to inform future decision-making and policy development.

2.3.2 Use of natural experiments to advance the evidence base

Currently, large gaps exist between the kind of public health evidence available to policy-makers and the type of evidence needed to inform real-world decision-making processes (Green, 2006; Leatherdale, 2019; Petticrew et al., 2005). This mismatch has been echoed by policy-makers and researchers alike that have called for more timely and relevant research that has applicability for policy and practice in 'real-world' settings (Brownson, Fielding, & Maylahn, 2009). As noted by Green (2006), in order to advance evidence-based practices, there is a need for more practice-based evidence (i.e., evidence generated in 'real-world' settings) (Green, 2006). One strategy that can be used to assist in the generation of practice-based evidence

includes the evaluation of natural experiments. Researchers can capitalize on opportunities offered by natural experiments in order to evaluate the impact of emerging health policies. In the same way that evidence-based medicine has been built on evaluation studies of treatment options, the foundation of an evidence-based policy must begin with building a database from the rigorous evaluation of health policies (Fong et al., 2006; Green, 2006). The evaluation of natural experiments (e.g., e-cigarette MLSA laws) may offer locally relevant and timely practice-based evidence to decision-makers that can be used to amend existing laws or inform the design of novel laws (Green, 2006; Petticrew et al., 2005).

2.3.2.1 Using natural experiments to evaluate e-cigarette MLSA laws

On January 1st, 2016, the province of Ontario (Canada) introduced a provincial MLSA law restricting the sale of e-cigarettes to those 19 years of age and over (Government of Ontario, 2015). At that time, no provincial law prohibiting the sale of e-cigarettes to minors was in effect in Alberta. These differences in provincial laws provide a timely opportunity to evaluate the effectiveness of Ontario's e-cigarette MLSA law within the context of a natural experiment. This data can be used to determine whether this law has been effective in achieving its intended outcomes and assist in identifying key components of effective e-cigarette access restriction laws.

Within Ontario and Alberta, there are provincial data systems in place (COMPASS) that can be used to robustly measure the impact of Ontario's e-cigarette MLSA law on youth e-cigarette use. COMPASS is a longitudinal cohort study designed to gather information on various health behaviors from a sample of Canadian high school students (Leatherdale et al., 2014). The COMPASS study provided data on high school students within Ontario and Alberta both pre- and post- implementation of Ontario's e-cigarette MLSA law; this presented a unique opportunity to evaluate this natural experiment and generate timely and relevant practice-based evidence within the Canadian context.

2.3.3 Summary and Research Gaps

Overall, there is limited evidence regarding the impact of e-cigarette MLSA laws on youth

e-cigarette use. Most evaluations conducted to date have focused on examining the influence of e-cigarette MLSA laws on youth cigarette smoking (as older surveys did not contain measures of e-cigarette use) (Dutra et al., 2018; Friedman, 2015; Pesko et al., 2015). Including e-cigarette use as a proximal indicator of policy impact is key to establishing whether MLSA laws are effective in preventing e-cigarette use among youth. Furthermore, there is a lack of longitudinal research focused on examining the effects of e-cigarette MLSA laws on trends in youth e-cigarette use. Moving forward, additional longitudinal work is needed to assess what impact e-cigarette MLSA laws have had on changes in youth e-cigarette use over time.

3.0 Study Rationale & Research Questions

This dissertation was divided into three distinct manuscripts. The study rationale, implications, research questions and hypotheses for each manuscript are described below.

3.1 Manuscript 1: Trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use among youth in Canada

As described in Section 2.1, roughly 40% of Canadian youth who report using e-cigarettes also smoke cigarettes, suggesting that dual use is common (Reid et al., 2019). Despite this, limited Canadian data exists regarding trends and predictors of dual use among youth populations. Recent studies have demonstrated that dual users have distinct risk profiles from exclusive e-cigarette users, exclusive cigarette smokers and non-users (Hanewinkel & Isensee, 2015; Smith et al., 2019). For example, associations between higher frequency use of e-cigarettes and dual use have been documented in recent cross-sectional studies (Demissie et al., 2017; McCabe et al., 2017). Moving forward, additional longitudinal studies are needed to explore trends and predictors of exclusive e-cigarette use, exclusive cigarette smoking and dual use in Canada.

Implications

Gaining a deeper understanding of predictors of exclusive e-cigarette use, exclusive cigarette smoking, dual use, and non-us provides valuable information that can be used to inform the design of youth-focused policies and programming. Examining what risk factors predict involvement in specific behaviors (e.g., dual use) may assist in identifying high-risk sub-groups; this information can then be used to inform the development of targeted programs.

3.1.1 Manuscript 1 Research Questions

Research Question 1:

(a) What is the prevalence of exclusive e-cigarette use, exclusive cigarette smoking and dual use at each wave?

(b) Does the prevalence of exclusive e-cigarette use, exclusive cigarette smoking and dual use change over time?

Research Question 2:

Adjusting for relevant sociodemographic and behavioral covariates,

(a) How does frequency of e-cigarette use and cigarette smoking measured at baseline predict dual use versus exclusive e-cigarette use versus exclusive cigarette smoking versus non-use after a *1-year* follow-up period?

(b) How does frequency of e-cigarette use and cigarette smoking measured at baseline predict dual use versus exclusive e-cigarette use versus exclusive cigarette smoking versus non-use after a *2-year* follow-up period?

Research Question 3:

Adjusting for relevant sociodemographic and behavioral covariates, how do changes in frequency of e-cigarette use and cigarette smoking over time predict dual use versus exclusive e-cigarette use versus exclusive cigarette use versus non-use after a *2-year* follow-up period?

3.1.2 Manuscript 1 Hypotheses

Hypothesis 1:

(a) Consistent with recent national estimates (Health Canada, 2017), I hypothesized that the prevalence of past 30-day e-cigarette use would be 13-16%, with higher prevalence estimates observed among older youth. I also hypothesized that roughly ~40% of past 30-day e-cigarette users would report smoking cigarettes in the past 30 days (i.e., dual use) (Reid et al., 2019). Lastly, I hypothesized that the prevalence of past 30-day cigarette smoking would be 8-11% (Health Canada, 2017).

(b) I hypothesized that there would be a significant increase in the prevalence of exclusive e-cigarette use, exclusive cigarette smoking and dual use over time.

Hypothesis 2:

(a) Consistent with previous research (Demissie et al., 2017; McCabe et al., 2017), I hypothesized that individuals who report using e-cigarettes and cigarettes at higher frequencies would be more likely to report being dual users after the 1-year follow up period.

(b) Consistent with previous research (Demissie et al., 2017; McCabe et al., 2017), I hypothesized that individuals who report using e-cigarettes and cigarettes at higher frequencies would be more likely to report being dual users after the 2-year follow up period.

Hypothesis 3:

I hypothesized that individuals who increased their frequency of e-cigarette use over time would be more likely to report being dual users at the 2-year follow-up. Similarly, I hypothesized that individuals who increased their frequency of cigarette smoking over time would be more likely to report being dual users at the 2-year follow-up.

3.2 Manuscript 2: Does having one or more smoking friends mediate the transition from e-cigarette use to cigarette smoking: a longitudinal study of Canadian youth

As described in Section 2.2, various longitudinal studies have demonstrated an association between e-cigarette use and cigarette smoking uptake among youth (Soneji, Barrington-Trimis, Willis, et al., 2017). Though various theories have been put forth seeking to explain these associations, few studies to date have tested these theories. As such, it remains unclear as to *why* e-cigarette use is linked to subsequent cigarette smoking among youth. Extensive evidence has outlined the key role of social contexts (e.g., friends' circles, family circles) in influencing youth tobacco use (Lakon et al., 2015; U.S. Department of Health and Human Services, 2012; Wellman et al., 2016). It is possible that these social contexts play a role in mediating the relationship between e-cigarette use and cigarette smoking behaviors.

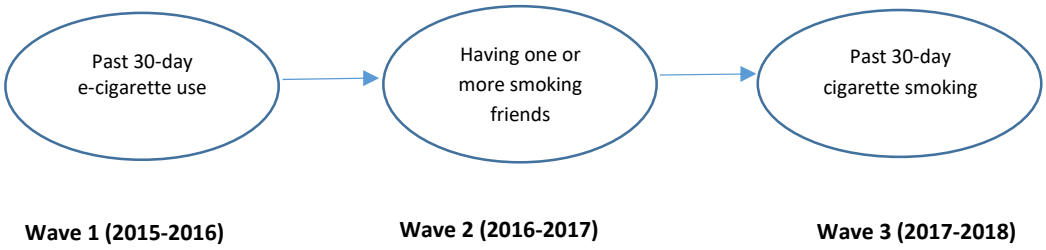
Implications

Although youth e-cigarette use has been related to subsequent cigarette smoking, there is a limited understanding of the mechanism(s) through which this occurs. Being able to examine and test potential mediating factors linking e-cigarette use and subsequent smoking uptake allows us to identify possible explanations for these associations. In other words, identifying these mediating factors provides us with a better understanding of the association between e-cigarette use and cigarette smoking. This data provides valuable information to inform ongoing debates about the association between e-cigarette use and subsequent smoking among youth.

3.2.1 Manuscript 2 Research Questions

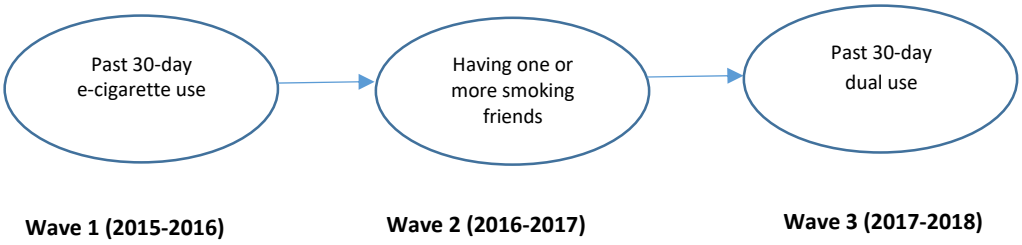
Research Question 1:

Does having smoking friends mediate the association between past 30-day e-cigarette use and cigarette smoking onset?



Research Question 2:

Does having smoking friends mediate the association between past 30-day e-cigarette use and subsequent dual use?



3.2.2 Manuscript 2 Hypotheses

Hypothesis 1: Consistent with previous research (Wills et al., 2016), I hypothesized that having smoking friends would mediate the association between e-cigarette use and subsequent cigarette smoking.

Hypothesis 2: I hypothesized that having smoking friends would mediate the association between e-cigarette use and subsequent dual use.

3.3 Manuscript 3: Do e-cigarette minimum legal sales age laws influence current e-cigarette use among Canadian youth: Cross-sectional and longitudinal findings from the COMPASS study

As noted in Section 3.2, various countries have introduced e-cigarette MLSA laws in recent years. Despite this, limited evidence exists regarding the effectiveness of e-cigarette MLSA laws in reducing youth e-cigarette use, as most studies to date have focused on the outcome of tobacco use. Furthermore, there is a lack of longitudinal research focused on assessing the impact of e-cigarette MLSA laws on trends in youth e-cigarette use over time. Moving forward, additional studies using robust quasi-experimental designs are needed to evaluate the effectiveness of these laws.

In Ontario, a provincial MLSA law was introduced on January 1st, 2016 restricting the sale of e-cigarettes to those 19 years of age and older. At that time, no provincial e-cigarette MLSA law existed within Alberta. The differences in provincial laws provided an opportunity to evaluate the impact of this natural experiment. Within Ontario and Alberta, there are provincial data systems in place (COMPASS) that can be used to robustly measure the impact of Ontario's e-cigarette MLSA law on youth e-cigarette use. COMPASS is a longitudinal school-based study designed to gather information on various health behaviors (including e-cigarette use) from a sample of Canadian high school students (Leatherdale et al., 2014). The COMPASS study provides data on high school students within Ontario and Alberta both pre- and post- implementation of Ontario's e-cigarette MLSA law. This presented a unique opportunity to evaluate the effectiveness of this law in reducing youth e-cigarette use.

Implications

This study provided timely and relevant practice-based evidence regarding the effectiveness of e-cigarette MLSA laws within the Canadian context (Green, 2006; Petticrew et al., 2005). This data can be used by policy makers to inform the development of appropriate regulations.

3.3.1 Manuscript 3 Research Questions

Research Question 1:

Does the introduction of e-cigarette minimum legal sales age laws within Ontario influence the average school-level prevalence of *past 30-day e-cigarette use* over time?

Research Question 2:

Does the introduction of e-cigarette minimum legal sales age laws within Ontario influence the individual likelihood of being a past 30-day e-cigarette user over time?

3.3.2 Manuscript 3 Hypotheses

Hypothesis 1:

I hypothesized that the introduction of e-cigarette MLSA laws within Ontario would result in reductions in the school-level prevalence of past 30-day e-cigarette use over time among Ontario schools versus Alberta schools. This hypothesis was based on (1) recent qualitative work that had shown that vendor compliance with Ontario's provincial law was generally high and (2) quantitative evidence from tobacco control studies demonstrating the potential effectiveness of MLSA laws in reducing tobacco use (Abouk & Adams, 2017; Borland, Dubray, Chaiton, & Schwartz, 2017).

Hypothesis 2:

I hypothesized that Ontario's introduction of e-cigarette MLSA laws would result in a reduced risk of past 30-day e-cigarette use among students in Ontario, compared to students in Alberta.

4.0 Methodology

4.1 Theoretical Framework

A range of theories have been used to gain a deeper understanding of the complex range of factors that influence tobacco use behaviors among youth populations. This dissertation was guided by the Theory of Triadic Influence (TTI).

4.1.1 Theory of Triadic Influence

A major contemporary theory that has been used to explain adolescent tobacco use is The Theory of Triadic Influence (TTI). TTI is grounded in various sociological and psychological theories of behavior change, and provides a unified framework to assess the complex range of influences that predict tobacco use among youth (Flay & Petraitis, 1994; Flay, Snyder, & Petraitis, 2009). According to TTI, causal influences of tobacco use can be classified into three streams: cultural-environmental, social/normative and intra-personal influences (Flay & Petraitis, 1994; Flay et al., 2009) (Refer to Figure 2 below) . The first stream of influence includes features of the broader cultural environment that contribute towards an adolescent's attitude towards tobacco use (Flay & Petraitis, 1994; Flay et al., 2009) . Examples of cultural-environmental influences may include the presence of national and provincial policies relating to tobacco use. The second stream of influence includes characteristics of a youth's more immediate social situation that contribute towards an adolescent's social normative beliefs surrounding tobacco use (i.e., perceptions of pressure to partake in tobacco use) (Flay & Petraitis, 1994; Flay et al., 2009). Examples of social/normative influences may include tobacco use by peers, siblings or parents. The third stream of influence includes an adolescent's biological and personality traits that contribute towards an individual's sense of self-efficacy in resisting tobacco use (Flay & Petraitis, 1994; Flay et al., 2009). Examples of intra-personal influences may include an individual's openness to new experiences and levels of extraversion.

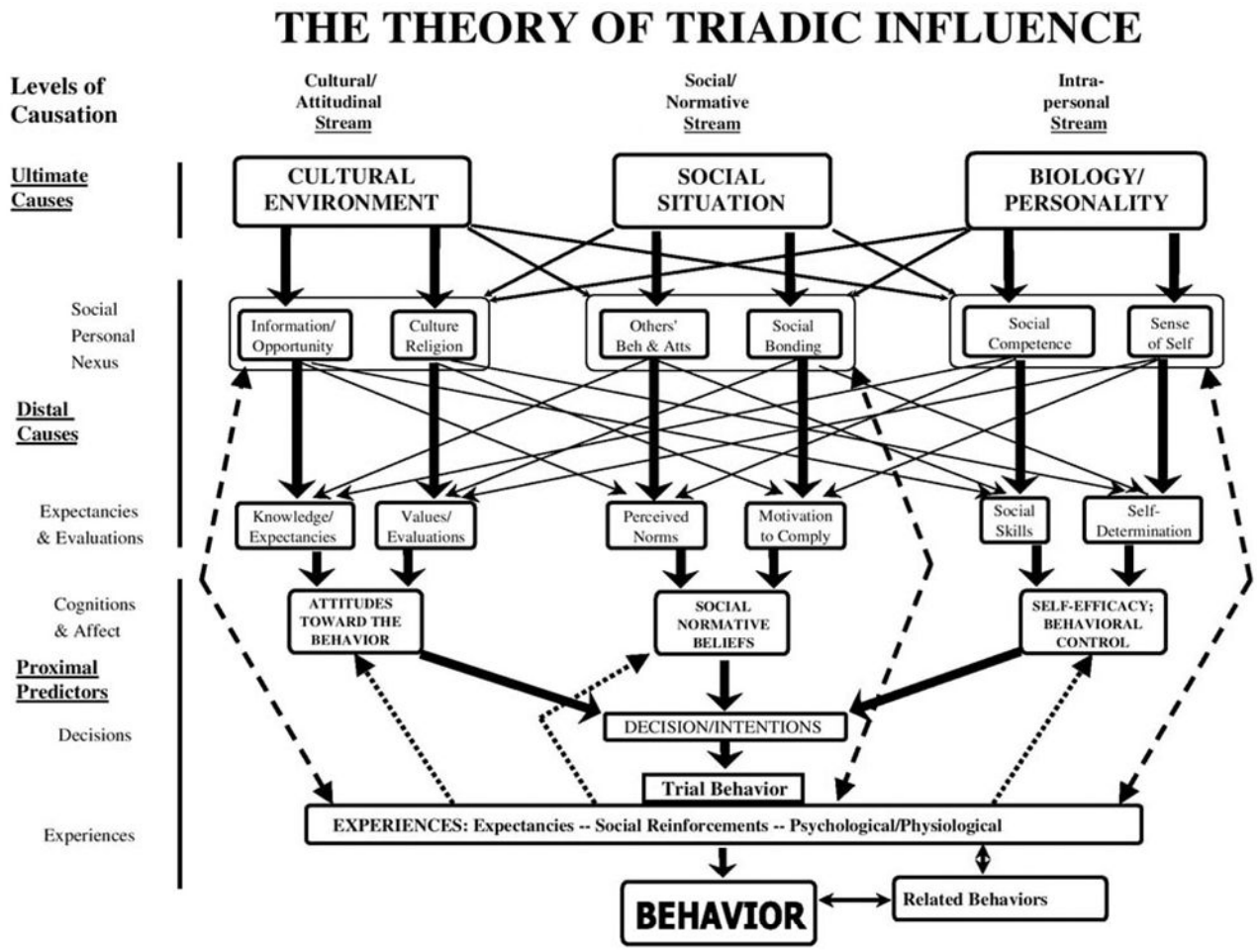


Figure 1: Theory of Triadic Influence. Reprinted from Emerging Theories in Health Promotion Practice and Research (Second ed., p. 455), by R. J. DiClemente, M. C. Kegler, and R. A. Crosby (Eds.), 2009, New York: Jossey-Bass. Copyright 2009 by John Wiley and Sons. Reprinted with permission.

According to TTI, the three streams of influence, described above, that predict tobacco use among youth can be organized into three levels (or tiers) of causation: ultimate, distal and proximal (Flay & Petraitis, 1994; Flay et al., 2009). Ultimate-level predictors are generally stable and characterized as causes that individuals generally have little to no control over, such as the introduction of governmental policies (Flay & Petraitis, 1994; Flay et al., 2009). This level of influence, if changed, can produce the greatest effect in the long-term on a broad range of behaviors (Flay et al., 2009). Distal-level predictors are variables affecting behaviors that

individuals are likely to have some control over, such as the level of bonding with parental or peer role models (Flay & Petraitis, 1994; Flay et al., 2009). Proximal-level predictors are precursors of specific behaviors and lie within the control of the individual, such as an individual's intentions to smoke cigarettes (Flay & Petraitis, 1994; Flay et al., 2009).

TTI was the theoretical framework that guided this project as it makes note of the various levels and streams of influence that impact e-cigarette and tobacco use that are subsequently explored within this dissertation. In conjunction with TTI that notes the influence of social contexts/situations on subsequent norms and behaviors, this dissertation explored whether having friends who smoked mediated the association between e-cigarette use and cigarette smoking onset. In alignment with TTI that discusses the role of environmental influences on e-cigarette and tobacco use behaviors, this dissertation explored the influence of provincial e-cigarette MLSA laws within Ontario on youth e-cigarette use.

4.2 Data Source

COMPASS is a longitudinal cohort study designed to collect data on youth health behaviors from students in grades 9-12 attending a convenience sample of Canadian secondary schools (Leatherdale et al., 2014). The COMPASS study uses a number of measurement tools including the student questionnaire (also referred to as Cq), the School Policies and Practices questionnaire (also referred to as SPP) and the COMPASS School Environment Application (also called Co-SEA). For the purposes of this study, I used student-level data derived from the COMPASS student questionnaire (referred to as Cq). The Cq collects individual student data pertaining to a range of health behaviors (e.g., tobacco use, marijuana use) and demographic characteristics (e.g., gender, age).

4.2.1 The COMPASS study

COMPASS is a research platform used to evaluate ongoing natural experiments to enable the generation of practice-based evidence to advance youth health (Leatherdale et al., 2014). Specifically, COMPASS was designed to evaluate how changes in school environment characteristics and provincial/school-level policies are associated with changes in health

behaviors among youth (Leatherdale et al., 2014). COMPASS also facilitates knowledge transfer and exchange by providing each school participating in the study with access to a knowledge broker (KB) and a customized School Health Profile (SHP) annually (Leatherdale et al., 2014). Each SHP report provides schools with data on various health behaviors, makes comparisons with provincial and/or national guidelines and provides evidence-based suggestions for school-based interventions (programs and/or policies) (Leatherdale et al., 2014).

4.2.2 School board and school recruitment

COMPASS was not designed to be nationally representative; as such, school boards and schools were purposefully sampled. After a school board granted their approval, eligible schools were approached for recruitment. Board-level inclusion criteria included being a secondary school board that permitted the use of active-information passive-consent parental permission protocols (Leatherdale et al., 2014). The University of Waterloo Office of Research Ethics and participating school boards approved all procedures used within the COMPASS study, including the use of passive consent procedures.

4.2.3 Participant selection and recruitment

In participating schools, student recruitment took place through the use of active-information passive-consent permission protocols (Leatherdale et al., 2014). This approach involved the parent or guardian of the student being mailed an information letter that provided an overview of the COMPASS study and the contact details of the COMPASS recruitment coordinator (both a 1-800 phone number and their email address), should they choose not to have their child participate in the study (Leatherdale et al., 2014). All eligible students whose parents or guardians do not contact the COMPASS team to withdraw their child from the study are eligible to participate. Eligible students are able to refuse to participate in the study or withdraw from the study at any point in time (Leatherdale et al., 2014).

4.2.4 Data Collection Protocols

Consistent with previous research, the COMPASS student questionnaire (i.e., Cq) was developed to facilitate large-scale school-based data collections (Elton-Marshall et al., 2011;

Leatherdale, McDonald, Cameron, & Brown, 2005; Leatherdale & Papadakis, 2011). On the day of the data collections, teachers administered the student questionnaire in their classrooms following the instructions provided to them in their classroom questionnaire bundle. A 'Teacher Instruction Questionnaire Letter' was given to teachers in advance as a guide to assist them in the administration of the student questionnaire to eligible students. All students who were present within the class and were not on the 'No Permission' List completed the student questionnaire in one 30-40 minute class period (Leatherdale et al., 2014).

The COMPASS questionnaire collected individual student data pertaining to a range of health behaviors including obesity, physical activity, dietary intake, marijuana use, e-cigarette use, tobacco use, alcohol use, sleep, bullying, academic outcomes, mental health outcomes and demographic characteristics. The questionnaire was purposefully made short (12 pages in length) to facilitate its administration in one class period (usually 30-40 minutes in length). The items present on the questionnaire were consistent with national measures and public health guidelines and have been shown to be reliable and valid (Brener, McManus, Galuska, Lowry, & Wechsler, 2003; Elton-Marshall et al., 2011; Leatherdale & Laxer, 2013).

4.2.5 Data Linkage Procedures

In order to link the data of students that participated in multiple waves of the study, the cover page of the Cq contained specific measures used to produce a unique self-generated code for each participant within a school based on a series of questions (Bredin & Leatherdale, 2013). Consistent with previous research, these unique codes were used in order to link each student's unique identifier data over multiple waves of the study, while ensuring the anonymity of study participants was maintained (Bredin & Leatherdale, 2013; Kearney, Hopkins, Mauss, & Weisheit, 1984). Additional technical details relating to the linkage procedures used within the COMPASS study can be found elsewhere (Qian, Battista, Bredin, Brown, & Leatherdale, 2015).

4.3 Measures

The following section describes the measures that were used for the purposes of this dissertation. Cigarette smoking measures included within the COMPASS student questionnaire

were previously validated among Canadian youth and aligned with national surveillance measures (Wong, Shields, Leatherdale, Malaison, & Hammond, 2012; Health Canada, 2019). E-cigarette use and substance use measures within the questionnaire were consistent with national surveillance measures and previous research (Elton-Marshall et al., 2011; Patte, Qian, & Leatherdale, 2018). Furthermore, socio-demographic and psycho-social measures included within the questionnaire were consistent with those used in previous school-based surveys (Bredin & Leatherdale, 2014).

4.3.1 Measures used to examine e-cigarette use and cigarette smoking

Individuals who reported using e-cigarettes in the past 30 days were classified as *current (past 30-day) e-cigarette users*. Similarly, those who reported using cigarettes in the past 30 days were classified as *current (past 30-day) cigarette users.* Consistent with prior research (Azagba, 2018; Demissie et al., 2017), these two measures were combined into a 4-level variable with mutually exclusive categories: non-users, exclusive e-cigarette users, exclusive cigarette smokers and dual users. Non-users were defined as individuals who reported not having used cigarettes or e-cigarettes within the past 30 days. Exclusive e-cigarette users were defined as individuals who reported using only e-cigarettes within the past 30 days. Similarly, exclusive cigarette smokers were defined as those who reported using only cigarettes within the past 30 days. Dual users included individuals who reported using e-cigarettes and cigarettes concurrently within the past 30 days.

Individuals were asked to report, 'In the last 30 days, did you use any of the following? (mark all that apply)' with a list of options given to them including 'e-cigarettes (electronic cigarettes that look like cigarettes/cigars, but produce vapour instead of smoke)'. Those who marked this option were classified as past 30 day e-cigarette users.

In order to assess frequency of e-cigarette use, individuals were asked to report, 'On how many days within the past 30 have you used e-cigarettes?', with response options of 'None', '1 day', '2-3 days', '4-5 days', '6-10 days', '11-20 days', '21-29 days' and '30 days (every day)'. Response options were collapsed into a three-category variable consisting of: (1) *non-users* (used 0 days in past month); (2) *infrequent users* (used 1-3 days in the past month); and (3) *frequent*

users (used 4 or more days in the past month). It is worth noting that our categorization of *frequent users* differed slightly from prior youth-based studies that have used a cut-off of '3 or more days' to classify frequent users (Barrington-Trimis, Kong, et al., 2018; Goldenson, Leventhal, Stone, McConnell, & Barrington-Trimis, 2017), due to the response options given within the COMPASS student questionnaire. To measure frequency of cigarette smoking, students were asked, 'On how many days of the last 30 days did you smoke one or more cigarettes?', with response options ranging from 'None' to '30 days (every day)'. Similar to the categorization scheme used for e-cigarettes, response options were collapsed into a three-category variable consisting of: (1) *non-smokers* (smoked 0 days in past month); (2) *infrequent smokers* (smoked 1-3 days in past month); and (3) *frequent smokers* (smoked 4 or more days in past month).

4.3.2 Measures used to examine substance use behaviors

Binge drinking behaviors were measured by asking students, "In the last 12 months, how often did you have 5 drinks of alcohol or more on one occasion?". Individuals who reported consuming 5 or more drinks on one occasion at least once a month were classified as *current (past 30-day) binge drinkers*. Cannabis use was measured by asking students, "In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)?" Individuals who reported using cannabis at least once a month were classified as *current (past 30-day) cannabis users*.

4.3.3 Measures used to assess socio-demographic & psychosocial characteristics

Students were asked to self-report their sex ("male" or "female") and ethnicity ("White", "Black", "Asian", "Latin American" or "Other"). Students were also asked what grade they were in, with response options of "grade 9", "grade 10", "grade 11" and "grade 12". Students were asked, "About how much money do you usually get each week to spend on yourself or to save?", with response options ranging from "Zero" to "More than $100". A separate variable for province was also created based on which province students resided within (Ontario or Alberta). Students were also asked, "How many of your closest friends smoke cigarettes?", with response options ranging from 'Zero' to '5 or more friends'.

5.0 Statistical Analyses

The statistical analyses that were conducted in each of the three manuscripts are described below.

5.1 Manuscript 1: Trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use among youth in Canada

The analyses were conducted using linked longitudinal data derived from three waves of the COMPASS study (Wave 1: 2015-2016; Wave 2: 2016-2017; Wave 3: 2017-2018). The target population included students who could be followed across all three time points. Additional details regarding linkage procedures used to form the linked longitudinal sample are provided within the Methods section (Refer to Section 4.2.4).

In order to answer Research Question 1, descriptive statistics were used to compute the prevalence of exclusive e-cigarette use, exclusive cigarette smoking, dual use and non-use of either product within each of the three waves examined. McNemar-Bowker tests were used to assess whether there are significant differences in the proportion of exclusive e-cigarette users, cigarette users and dual users respectively over time within the linked longitudinal sample. McNemar-Bowker tests act as appropriate tests, as they can be used to examine changes in repeated measurements (McNemar, 1947).

In order to answer Research Question 2(a), a multinomial logistic regression model was used to examine the association between frequency of e-cigarette use and cigarette smoking at baseline and subsequent e-cigarette use and cigarette smoking at the *1-year follow-up* (Model 1). Multinomial logistic regression is an extension of binary logistic regression that allows for more than two categories for the outcome of interest. Multinomial logistic regression was an appropriate modelling approach given that our outcome of interest consisted of four categories: non-users, exclusive e-cigarette users, exclusive cigarette smokers and dual users. For the purposes of these analyses, ‘non-users’ were classified as the Reference group. In order to answer Research Question 2(b), a similar modelling approach was used to examine associations between frequency of e-cigarette use and cigarette smoking and subsequent e-cigarette use and

cigarette smoking at the *2-year follow-up* (Model 2). To account for potential confounding effects, Models 1 and 2 adjusted for sex, ethnicity, weekly spending money (used as a proxy for socio-economic status), number of friends who smoke, monthly cannabis use and binge-drinking at baseline within modelling procedures. Student-level covariates were chosen based on previous literature demonstrating associations with tobacco and vaping product use (Hanewinkel & Isensee, 2015; Milicic & Leatherdale, 2017; Tyas & Pederson, 1998; Wills, Knight, Williams, Pagano, & Sargent, 2015). Province was also accounted for in both models, based on recent data showing differences in provincial estimates of youth e-cigarette use (Reid et al., 2019). Given the hierarchical nature of the data (Leatherdale et al., 2014), all modelling procedures accounted for the nested structure of the data (i.e., students nested within schools).

In order to answer Research Question 3, a multinomial logistic regression model was used to examine the association between changes in frequency of e-cigarette use and cigarette smoking and subsequent e-cigarette use and cigarette smoking at the 2-year follow-up (Model 3). To assess changes in frequency of e-cigarette use and cigarette use between Wave 1 and Wave 2 (i.e., the key predictor of interest in this model), a measure of change was created. With respect to how change was defined, those who reported increases in frequency of e-cigarette use between Wave 1 and Wave 2 (e.g., going from using 1 day/past month at W1 to 6-10 days/past month at W2) were classified as 'Increase'. Students who reported decreases in frequency of e-cigarette use between W1 and W2 (e.g., going from using 4-5 days/past month at W1 to 1 day/past month at W2) were classified as 'Decrease'. Those who reported no change in their frequency of e-cigarette use between W1 and W2 (e.g., maintained use at 1 day/past month at W1 and W2, maintained non-use at W1 and W2) were classified as 'No change'. A similar categorization scheme ('Increase', 'Decrease', 'No change') was used to assess changes in frequency of cigarette smoking between Wave 1 and Wave 2. To account for confounding effects, Model 3 also adjusted for baseline covariates including gender, ethnicity, province, weekly spending money, having friends who smoke, monthly cannabis use, binge drinking, e-cigarette use and cigarette smoking. Similar to Models 1 and 2, Model 3 also accounted for the nested structure of the data.

5.2 Manuscript 2: Does having one or more smoking friends mediate the transition from e-cigarette use to cigarette smoking: a longitudinal study of Canadian youth

The research questions in Manuscript 2 were focused on examining whether having smoking friends mediated the relationship between e-cigarette use and subsequent smoking onset. These analyses were conducted using linked longitudinal data derived from three waves of the COMPASS study (wave 1: 2015-2016; wave 2: 2016-2017; wave 3: 2017-2018). The target population included students that could be followed across all three time points who were never smokers at baseline. Additional details regarding linkage procedures used to form the linked longitudinal sample are provided within the Methods section (Refer to Section 4.2.4).

To address Research Question 1, a series of multi-level logistic regression models were used to test the hypothesis that having smoking friends at wave 2 mediated the relationship between past 30-day e-cigarette use at wave 1 and past 30-day cigarette smoking at wave 3. A theoretical mediation model for research question 1 is demonstrated below in Figure 1 below.

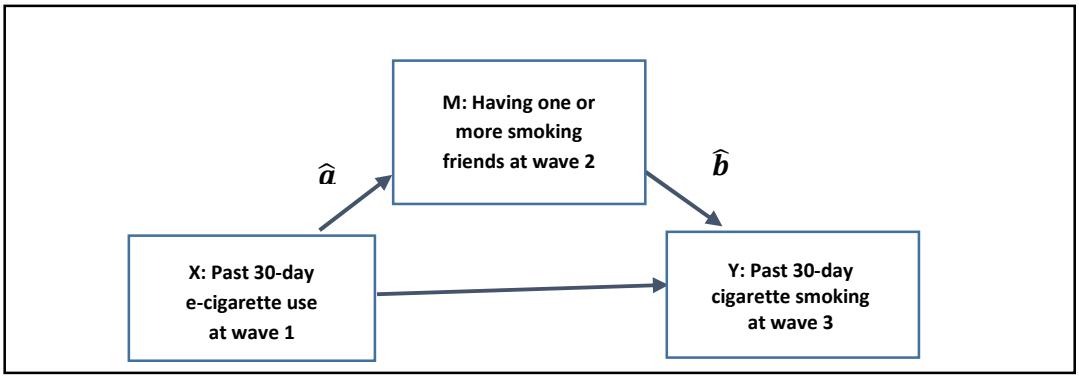


Figure 1. Hypothesis of Mediational Relationship between past 30-day e-cigarette use and past 30-day cigarette smoking among the sample of youth never smokers at baseline (i.e., wave 1).

In order to assess the potential mediating effects of having smoking friends, the products of coefficients method was used (MacKinnon, 2008). The products of coefficients method has been shown to produce more accurate Type I errors and greater statistical power, in comparison to more traditional causal step approaches (MacKinnon, 2008; MacKinnon, Lockwood, Hoffman,

West, & Sheets, 2002). This approach is based on the rationale that mediation depends on the extent to which e-cigarette use impacts having smoking friends, $\hat{a}$, and the extent to which having smoking friends impacts cigarette smoking, $\hat{b}$. As described by MacKinnon, the product of coefficients approach involves computing the product of $\hat{a}$ and $\hat{\mathbf{b}}$, $\hat{\mathbf{a}}\hat{\mathbf{b}}$, to form the mediated or indirect effect (MacKinnon, 2008). In order to examine the statistical significance of the mediated effect, the estimate of the mediated effect was divided by the standard error of the mediated effect; this value was then compared to the normal distribution (MacKinnon, 2008). To estimate the standard error of the mediated effect, the Sobel test was utilized (Sobel, 1982). The Sobel test was calculated using the following equation, $\sqrt{\hat{a}^2 s_{\hat{b}}^2 + \hat{b}^2 s_{\hat{a}}^2}$, where $s_{\hat{a}}^2$ and $s_{\hat{b}}^2$ represented the squared standard errors of $\hat{a}$ and $\hat{b}$ respectively (MacKinnon, 2008; Sobel, 1982). The Sobel method currently represents one of the most widely utilized methods for estimating the standard error of mediated effect (MacKinnon, 2008; Sobel, 1982). The mediation model described above also adjusted for relevant covariates including gender, ethnicity, province, weekly spending money, current cannabis use and binge drinking behaviors.

Similarly, in order to answer Research Question 2, a series of multi-level logistic regression models were used to assess whether having smoking friends at wave 2 mediated the relationship between past 30-day e-cigarette use at wave 1 and past 30-day dual use at wave 3. As described in Research Question 1, similar steps were taken to compute the mediated effect and assess the significance of the mediated effect. A theoretical mediation model for research question 2 is demonstrated below in Figure 2 below.

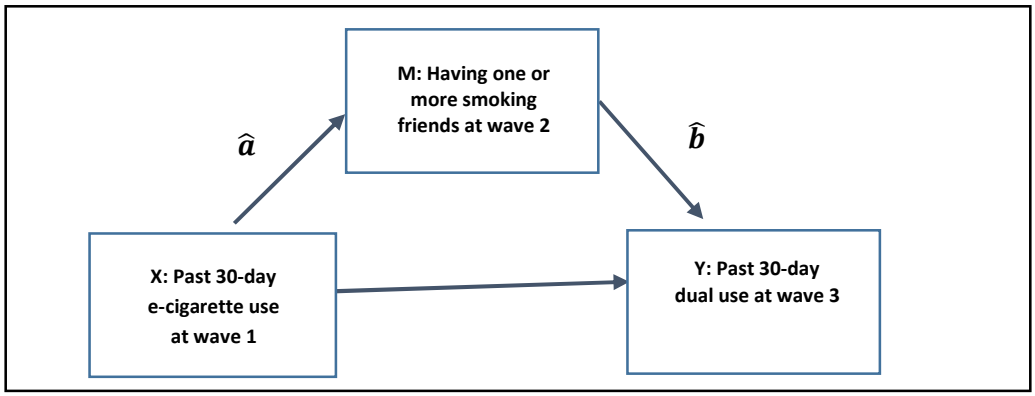


Figure 2. Hypothesis of Mediational Relationship between past 30-day e-cigarette use and past 30-day dual use among the sample of youth never smokers at baseline (i.e., wave 1).

5.3 Manuscript 3: Do e-cigarette minimum legal sales age laws influence current e-cigarette use among Canadian youth: Cross-sectional and longitudinal findings from the COMPASS study

5.3.1 Analysis for Research Question 1

In order to answer Research Question 1, a *repeat-cross sectional* quasi-experimental research design was used to evaluate the impact of Ontario's e-cigarette MLSA law on the average school-level prevalence of past 30-day e-cigarette use within Ontario schools, relative to Alberta schools where no provincial e-cigarette MLSA law was in effect (Leatherdale, 2019). The analyses for Research Question 1 utilized repeat-cross sectional data derived from three waves of the COMPASS study (T_1: 2014-2015, T_2: 2015-2016, T_3: 2016-2017). Unlike Manuscripts 1 and 2, an earlier wave (T_1: 2014-2015) was included in Manuscript 3 to provide a baseline datapoint (i.e., pre-implementation of law) for this evaluation. The target population for the analyses conducted in Research Question 1 included the full sample of gr.9-12 students attending Ontario and Alberta schools participating in the COMPASS study. Specifically, the analytic sample used for these cross-sectional analyses was comprised of 64 Ontario and Alberta schools that participated at all three time points of the COMPASS study. The same sample of COMPASS schools was used at each time point to mitigate potential confounding effects due to school-level differences.

For Research Question 1, difference-in-difference (DiD) models were used to examine changes in the prevalence of past 30-day e-cigarette use over time among the sample of Ontario schools impacted by the provincial e-cigarette MLSA law (Intervention group) relative to the sample of Alberta schools where no provincial e-cigarette MLSA law was in effect (Control group) (Shadish, Cook, & Campbell, 2002). As shown in Figure 3 below, to evaluate the impact of this law, students attending COMPASS schools were placed into one of three groups: (1) Ontario schools where T2 data collection occurred <u>after</u> the e-cigarette MLSA law was passed *[Intervention group 1*]; (2) Ontario schools where T2 data collection occurred <u>before</u> the e-cigarette MLSA law was passed [*Intervention group 2]* and (3) Alberta schools where no provincial e-cigarette MLSA law was in effect [*Control group*].

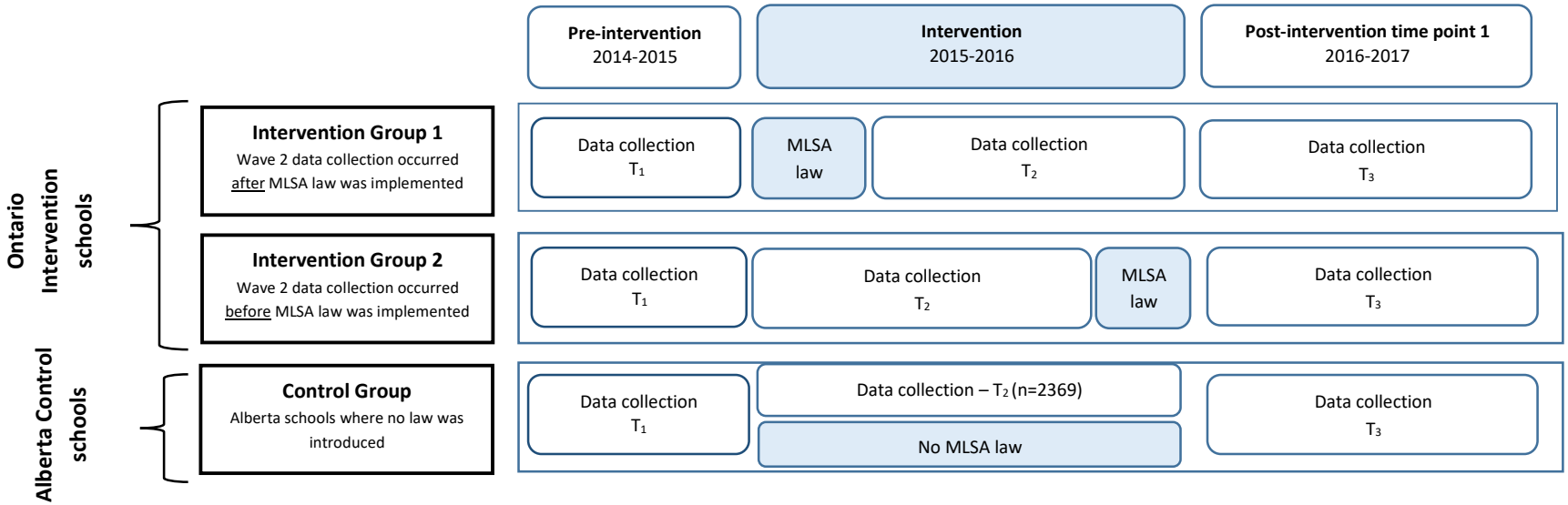


Figure 3. Illustration of the quasi-experimental design that will be used to evaluate the impact of the e-cigarette minimum legal age restrictions introduced within Ontario. The diagram above demonstrates the grouping of Ontario and Alberta schools into Intervention and control groups based on when data collections took place and whether schools were affected by Ontario's e-cigarette MLSA law.

5.3.2 Analysis for Research Question 2

In order to answer research question 2, a *longitudinal* quasi-experimental research design was used to evaluate the impact of Ontario's e-cigarette MLSA law on the likelihood of a student reporting past 30-day e-cigarette use (Leatherdale, 2019). The analyses for Research Question 2 utilized linked longitudinal data derived from three waves of the COMPASS study (T_1: 2014-2015, T_2: 2015-2016, T_3: 2016-2017). The target population included students who could be followed across all three time points. Additional details regarding linkage procedures used to form the linked longitudinal sample are provided within the Methods section (Refer to Section 4.2.4).

For Research Question 2, Generalized Estimating Equations (GEE) were used to estimate the effects of the Ontario's e-cigarette MLSA law on the relative increase/decrease in likelihood of a student in an Ontario Intervention group being a past 30-day e-cigarette user over time, relative to a student within the Alberta Control group (Refer to Figure 5 above). Generalized Estimating Equations were used to account for the hierarchical structure of the longitudinal data (i.e., students nested within schools over time) (Zeger & Liang, 1986). Similar to research question 1, students attending COMPASS schools were grouped into one of three groups: 1) Ontario schools where T2 data collection occurred <u>after</u> the e-cigarette MLSA law was passed [*Intervention group 1*]; (2) Ontario schools where T2 data collection occurred <u>before</u> the e-cigarette MLSA law was passed [*Intervention group 2]* and (3) Alberta schools where no provincial e-cigarette MLSA law was in effect [*Control group*] (Refer to Figure 5 above). The outcome of interest (past 30-day e-cigarette use) was treated as a binary outcome. The model adjusted for the effects of gender, ethnicity, weekly spending money, having one or more friends who smoke, current binge drinking, current cannabis use and current cigarette smoking. This model, Model 1, is set out below:

$$\boldsymbol{Model\ 1}\text{:}\ \ \boldsymbol{log(\pi_{it}) = \beta_0 + \beta_1 X_{it} + \beta_2 G_{ik} + \beta_3 Wave_t + (G_{ik} * Wave_t)\alpha}$$

where X_{it} represents the set of socio-demographic and behavioral covariates that were included in the model to control for confounding effects and β_1 represents the effects of these covariates;

G_{ik} represents the measure for the intervention of interest (i.e., presence/absence of MLSA

law) where G_{ik}=1 if a student i is from the kth intervention group (i.e., Ontario schools) and G_{ik}=0 if student i is from the Control group (i.e., Alberta schools);

$Wave_t$ represents the wave-specific indicator of time; and

α, the interaction effect and the main parameter of interest, represents the effect of the e-cigarette MLSA law on changes in past 30-day e-cigarette use over time.

6.0 Manuscript 1

Trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use among youth in Canada

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6.1 Abstract

Background

Few studies have examined predictors of exclusive e-cigarette use, exclusive smoking and dual use among youth. We investigated whether frequency of e-cigarette use and cigarette smoking predicted involvement in different usage groups after a 1- and 2-year follow-up among a sample of Canadian youth.

Methods

A longitudinal sample of youth who participated in three waves of COMPASS [Wave 1 (W_1) 2015/16, Wave 2 (W_2) 2016-17, Wave 3 (W_3) 2017/18] was identified (N=5,704). Multinomial logistic regression was used to examine whether frequency of e-cigarette use and cigarette smoking at W_1 predicted involvement in different usage groups at W_2 and W_3. Similarly, we examined whether changes in frequency of e-cigarette use and cigarette smoking between W_1 and W_2 predicted involvement in different usage groups at W_3.

Results

E-cigarette users reporting use on 4 or more days per month at W_1 had greater odds of dual use at W_2, compared to non-users (aOR=11.22, $p<0.0001$). Those who reduced their frequency of e-cigarette use between W_1 and W_2 had lower odds of exclusive e-cigarette use and dual use at W_3 (aOR=0.18 and 0.17 respectively; both $p<0.05$). Those who increased their frequency of cigarette smoking between W_1 and W_2 had higher odds of exclusive smoking and dual use at W_3 (aOR=22.65 and aOR=9.92 respectively; both $p<0.0001$).

Discussion

Reductions in frequency of e-cigarette use appeared to have a protective effect of reducing exclusive e-cigarette use and dual use at follow-up. Increases in frequency of cigarette smoking were a significant predictor of exclusive smoking and dual use.

Key Words: e-cigarettes, cigarettes, smoking, dual use, youth, predictors

6.2 Background

Evidence suggests that e-cigarettes are being used by many Canadian youth (Hammond et al., 2019; Reid et al., 2019). In 2017, 14.6% of grade 10-12 students reported using an e-cigarette within the past month (Reid et al., 2019). Data from the 2017 Canadian Student Tobacco Alcohol and Drugs Survey (CSTADS) survey also showed that among e-cigarette users between the ages of 15-19, 38.2 % also smoked cigarettes in the past month (Reid et al., 2019); these data suggest that dual use (i.e., use of both e-cigarettes and cigarettes) is common among e-cigarette users. Recent studies have raised concerns that for at least some users, dual use may lead to the maintenance/escalation of smoking behaviours and nicotine dependence among youth (Azagba & Wolfson, 2018; Doran et al., 2017; Soneji, Barrington-Trimis, Willis, et al., 2017). In light of these findings, gaining a better understanding of exclusive versus dual use of cigarettes and e-cigarettes among Canadian youth is warranted.

Currently, few studies have examined what correlates distinguish exclusive e-cigarette users, exclusive smokers, and dual users among youth. Of the few studies conducted to date, key differences have been identified in risk factors that predict different usage groups (Azagba, 2018; Cooper et al., 2016; Kristjansson et al., 2015). For instance, recent studies have shown that dual users are more likely to report using both e-cigarettes and cigarettes at higher frequencies, compared to exclusive e-cigarette users and exclusive smokers (Demissie et al., 2017; Wills et al., 2015). Dual users are also more likely to smoke cigarettes at a greater intensity (i.e., more cigarettes per day), relative to exclusive smokers (Goniewicz et al., 2016). Other studies have found that dual users are more likely to report using cannabis, illicit drugs and alcohol at greater frequencies, compared to non-users (Azagba, 2018; Demissie et al., 2017). These findings suggest that dual users represent a high-risk group of youth that engage in risky behaviours at higher frequencies, compared to exclusive product users and non-users; in contrast, exclusive e-cigarette users appear to represent an intermediate risk group of youth that fall somewhere between non-users and exclusive smokers/dual users. However, a key limitation of the current evidence base is that it is primarily derived from cross-sectional studies. Data from longitudinal studies could provide valuable insight as to what risk factors predict exclusive e-cigarette use, exclusive smoking and dual use.

Available longitudinal evidence suggests that past 30-day e-cigarette use predicts subsequent smoking among youth (Aleyan et al., 2018; Hammond et al., 2017; Soneji et al., 2017). More recent work has shown that these associations can be bi-directional, whereby having tried smoking a cigarette also predicts subsequent use of e-cigarettes (East et al., 2018; Pénzes et al., 2018). However, it remains unclear how frequency of e-cigarette use and cigarette smoking (i.e., number of days used in the past month) predicts exclusive e-cigarette use, exclusive cigarette smoking and dual use. Moving forward, longitudinal studies that utilise more granular measures (e.g., number of days used within the past month) could provide additional insight on this matter.

The current study used data from a sample of secondary students from the provinces of Ontario and Alberta, Canada to estimate the prevalence of exclusive e-cigarette users, exclusive cigarette smokers and dual users across three waves (2015/2016, 2016/2017, 2017/2018) and to test whether there were changes in prevalence estimates over time. Secondly, the study examined how frequency of e-cigarette use and cigarette smoking measured at baseline predicted e-cigarette use and cigarette smoking after a 1- and 2-year follow-up period. Lastly, the study examined how changes in frequency of e-cigarette use and cigarette smoking over time predicted e-cigarette use and cigarette smoking after a 2-year follow-up period.

6.3 Methods

6.3.1 Design

COMPASS is a 9-year longitudinal cohort study (2012-2021) designed to collect information on various health behaviours among a sample of grade 9-12 students attending Canadian secondary schools (Leatherdale et al., 2014), aged approximately 13-18 years old. The data used within our study were collected from students in Ontario and Alberta using the COMPASS student questionnaire. Inclusion criteria for recruitment included being a secondary school that permitted the use of active-information passive-consent permission protocols (Leatherdale et al., 2014). Passive-consent permission protocols have been shown to be important in gathering robust data on self-reported risk behaviours, such as tobacco use, while maintaining student anonymity (Thompson-Haile et al., 2013; White et al., 2004). The current study reports on longitudinal data from Year 4 (2015/2016), Year 5 (2016/2017)

and Year 6 (2017/2018). Year 4 will be referred to as 'wave 1 (W_1: baseline)', Year 5 as 'wave 2 (W_2)' and Year 6 as 'wave 3 (W_3)'. Additional details on COMPASS can be found in print (Leatherdale et al., 2014) and online (https://uwaterloo.ca/compass-system/). All procedures used in COMPASS received ethics approval from University of Waterloo Office of Research Ethics, and participating school boards.

6.3.2 Sample

A total of 6,190 students participated in all three waves of the study. Students who provided contradictory responses relating to outcomes of interest in W_1 (n=98), W_2 (n=157) and W_3 (n=231) were excluded. The COMPASS student questionnaire had two measures to assess past month e-cigarette use (described below); contradictory responses resulted from individuals providing conflicting information when answering these questions. After excluding these individuals, the final sample consisted of 5,704 students.

6.3.3 Predictors

To measure frequency of e-cigarette use, students were asked 'In the last 30 days, did you use any of the following? (Mark all that apply), with a list of products, including 'e-cigarettes (electronic cigarettes that look like cigarettes/cigars but produce vapour instead of smoke)'. Students were also asked, "On how many days of the last 30 did you use an e-cigarette?", with response options of 'None', '1 day', '2-3 days', '4-5 days', '6-10 days', '11-20 days', '21-29 days' and '30 days (every day)'. Response options were collapsed into a three category variable consisting of (1) *non-users* (0 days in the past month), (2) *infrequent users* (1-3 days in the past month) and (3) *frequent users* (4 or more days in the past month). To measure frequency of cigarette smoking, students were asked, "On how many days of the last 30 days did you smoke one or more cigarettes?", with response options ranging from 'None' to '30 days (every day)'. Similar to the categorization scheme used for e-cigarettes, response options were collapsed into a three category variable consisting of (1) *non-smokers* (smoked 0 days in the past month), (2) *infrequent smokers* (smoked 1-3 days in the past month) and (3) *frequent smokers* (smoked 4 or more days within the past month). As noted in previous studies (Goldenson et al., 2017; Leventhal et al., 2016), this categorization scheme was used due to low frequency counts in categories of greater use.

A measure of *change* was also created to examine changes in frequency of e-cigarette use between W_1 and W_2. With respect to how *change* was defined, those who reported increases in frequency of e-cigarette use between W_1 and W_2 (e.g., going from using 1 day/past month at W_1 to 6-10 days/past month at W_2) were classified as 'Increase'. Students who reported decreases in frequency of e-cigarette use between W_1 and W_2 (e.g., going from using 4-5 days/past month at W_1 to 1 day/past month at W_2) were classified as 'Decrease'. Those who reported no changes in frequency of e-cigarette use between W_1 and W_2 (e.g., maintained use at 1 day/past month at W_1 and W_2, maintained non-use at W_1 and W_2) were classified as 'No change' (Reference group). A similar categorization scheme (i.e., 'Increase', 'Decrease', 'No change') was used to measure *changes* in frequency of cigarette smoking between W_1 and W_2.

Students were asked to provide demographic data including sex, ethnicity and weekly spending money. Ethnicity was classified into five categories: White, Black, Asian, Latin American and Other. Weekly spending money was classified into five categories: $0, 1-20, 20-100, over $100 and I don't know. Students were also categorized by province of residence (Ontario, Alberta). With respect to substance use behaviours, students were asked how often they had used cannabis within the past year. Those who reported using cannabis at least once a month were classified as *current cannabis users;* otherwise, they were categorized as *non-current cannabis users*. Students were asked how often they had 5 or more drinks of alcohol on one occasion within the past year. Students who reported consuming 5 or more drinks on one occasion at least once a month were classified as *current binge drinkers*; otherwise, they were classified as *non-current binge drinkers.* Students were also asked to report how many of their closest friends smoked cigarettes. Response options were categorized as: 'None', '1', '2' or '3 or more'.

6.3.4 Outcome Measures

Consistent with prior research (Azagba, 2018; Demissie et al., 2017), students who reported having used only e-cigarettes within the past month were defined as *exclusive e-cigarette users*. Students who reported having used only cigarettes within the past month were defined as *exclusive smokers.* Those who reported using both products within the past

month were defined as *dual users*. Those who had not used either product in the past month were defined as *non-users.*

6.4 Analysis

Descriptive statistics were used to examine characteristics of the sample at W_1. Chi-squared tests were used to examine differences in student-level characteristics among exclusive e-cigarette users, exclusive smokers, dual users and non-users. To address our first research question, McNemar-Bowker tests were used to estimate changes in the prevalence of exclusive e-cigarette use, exclusive smoking and dual use across three waves (McNemar, 1947).

Multinomial logistic regression was used in all modelling procedures, given that the outcome of interest consisted of four categories: exclusive e-cigarette users, exclusive smokers, dual users and non-users (Reference group). To address our second research question, regression models were used to estimate how frequency of e-cigarette use and cigarette smoking measured at W_1 predicted e-cigarette use and cigarette smoking status at W_2 (Model 1) and W_3 (Model 2). To address our third research question, a regression model was used to estimate how *changes* in the frequency of e-cigarette use and frequency of cigarette smoking between W_1 and W_2 predicted e-cigarette use and cigarette smoking status at W_3 (Model 3). All models, described above, were not limited to participants who reported exclusive e-cigarette use/exclusive cigarette smoking at W_1, but also included dual users. All models adjusted for sex, ethnicity, province, weekly spending money (a proxy measure for socio-economic status), having close friends who smoke, past month cannabis use and binge drinking at baseline. Model 3 also adjusted for the frequency of e-cigarette use and cigarette smoking measured at W_1. These covariates were included in modelling procedures based on previous literature (Hanewinkel & Isensee, 2015; Milicic & Leatherdale, 2017; Wills et al., 2015). Generalized estimating equation (GEE) models were used to account for the nested structure of the data (i.e., students clustered within schools). Using GEE models, missing data were treated as missing completely at random and excluded on an analysis-by-analysis basis in each model conducted (Zeger & Liang, 1986). Analyses were conducted using SAS 9.4.

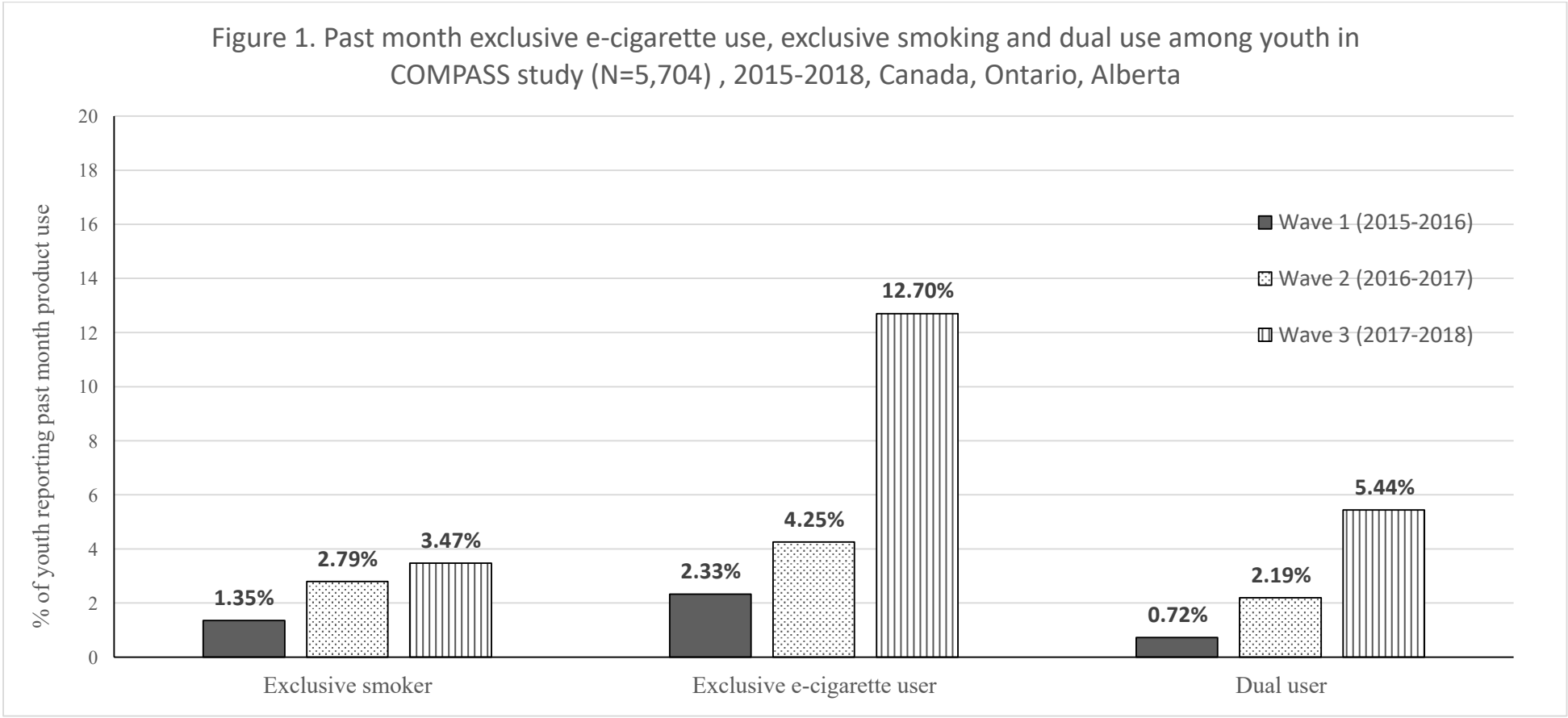
6.5 Results

With respect to sample characteristics, 54.6% were female, 72.5% identified as White and the majority resided in Ontario. Furthermore, 26.9% reported having at least $20 CAD in weekly spending money. Differences in socio-demographics and behavioural characteristics were demonstrated by usage groups (all $p<0.0001$; Table 1).

Table 1: E-cigarette use and cigarette smoking status by socio-demographic and behavioural characteristics at baseline (wave 1), COMPASS study, 2015-2016 (N=5704)										
		Non-users [a] (n=5303)		Exclusive e-cigarette users [a] (n=129)		Exclusive smokers [a] (n=75)		Dual users [a] (n=40)		p-value [b]
		N	%	N	%	N	%	N	%	
Sex	Male	2366	44.9	87	67.4	25	33.8	24	60.0	<0.0001
	Female	2905	55.1	42	32.6	49	66.2	16	40.0	
Grade	9	3078	58.1	63	48.8	30	40.0	11	27.5	<0.0001
	10	2220	41.9	66	51.2	45	60.0	29	72.5	
Ethnicity	White	3820	72.3	104	80.6	55	73.3	29	72.5	<0.0001
	Black	234	4.5	6	4.7	2	2.7	2	5.0	
	Asian	434	8.2	4	3.1	1	1.3	3	7.5	
	Latin American	165	3.2	4	3.1	1	1.3	0	0.0	
	Other	628	11.8	11	8.5	16	21.4	6	15.0	
Weekly spending money	$0	1210	22.9	15	11.6	8	10.8	6	15.0	<0.0001
	$1-20	1973	37.4	40	31.0	27	36.5	14	35.0	
	$20-100	1066	20.2	43	33.3	19	25.7	13	32.5	
	Over $100	306	5.8	14	10.9	14	18.9	7	17.5	
	I don’t know	719	13.7	17	13.2	6	8.1	0	0.0	
Number of close friends who smoke	None	4413	84.2	64	49.6	18	24.0	4	10.0	<0.0001
	1 friend	499	9.5	38	29.5	17	22.7	6	15.0	
	2 friends	180	3.4	13	10.1	14	18.7	5	12.5	
	3 or more friends	152	2.9	14	10.8	26	34.6	25	62.5	
Province	Ontario	5038	95.0	109	84.5	57	76.0	35	87.5	<0.0001
	Alberta	265	5.0	20	15.5	18	24.0	5	12.5	
Past month cannabis use	No	5122	98.1	102	80.3	39	54.2	19	47.5	<0.0001
	Yes	101	1.9	25	19.7	33	45.8	21	52.5	
Past month binge-drinking	No	5063	95.7	80	62.0	45	60.0	15	38.5	<0.0001
	Yes	229	4.3	49	38.0	30	40.0	24	61.5	

[a] ‘Non-users’ refers to students who have used neither e-cigarettes or cigarettes within the past month ; ‘Exclusive e-cigarette users’ refers to students who used only e-cigarettes within the past month; ‘Exclusive smokers’ refers to students who used only cigarettes within the past month; ‘Dual users’ refers to those who reported using e-cigarettes and cigarettes concurrently within the past month.

[b] p-values based on Chi-squared tests



Note: Percentage of youth who reported being non-users of e-cigarettes and cigarettes are not shown in Figure 1.

There were significant differences in the prevalence of exclusive e-cigarette use, exclusive smoking and dual use over time ($W_{1\text{-}2}$: $p<0.0001$; $W_{2\text{-}3}$: $p<0.0001$; $W_{1\text{-}3}$: $p<0.0001$; Figure 1). Findings showed a 157% increase in the prevalence of exclusive smokers between W_1 and W_3. Findings also demonstrated a 445% increase in the prevalence of exclusive e-cigarette users between W_1 and W_3. There was a 655% increase in the prevalence of dual users between W_1 and W_3.

Table 2: Multivariate logistic regression model examining associations between frequency of e-cigarette use and smoking measured at wave 1 and subsequent e-cigarette use and cigarette smoking status at wave 2 **(MODEL 1)**

Baseline characteristics at *wave 1*		E-cigarette use and cigarette smoking status at *wave 2*					
		Exclusive e-cigarette users vs. Non-users [c]		Exclusive Cigarette smokers vs. Non-users [c]		Dual users vs. Non-users [c]	
		AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value
Frequency of e-cigarette use in past month [ł]	Non-users (0 days) [a]	---	---	---	---	---	---
	Infrequent users (1-3 days) [a]	**5.74 (3.33-9.89)**	<0.0001	**3.00 (1.47-6.10)**	0.0024	**6.67 (3.48-12.78)**	<0.0001
	Frequent users (4 or more days) [a]	**4.91 (1.91-12.64)**	0.001	1.35 (0.38-4.76)	0.6404	**11.22 (4.70-26.78)**	<0.0001
Frequency of cigarette smoking in past month [ł]	Non-smokers (0 days) [b]	---	---	---	---	---	---
	Infrequent smokers (1-3 days) [b]	1.75 (0.67-4.56)	0.2505	**3.94 (1.81-8.57)**	0.0005	**3.71 (1.57-8.78)**	0.0029
	Frequent smokers (4 or more days) [b]	1.80 (0.42-7.67)	0.4278	**12.53 (4.78-32.81)**	<0.0001	**5.15 (1.61-16.42)**	0.0056

[a] 'Non-users' refer to students who have not reported using e-cigarettes in the past month (this also includes students who have never tried using e-cigarettes); 'Infrequent users' refer to students who reported using e-cigarettes 1-3 days in the past month; 'Frequent users' refer to students who reported using e-cigarettes 4 or more days in the past month.
[b] 'Non-smokers' refer to students who have not reported smoking cigarettes in the past month (this also includes students who have never smoked cigarettes); 'Infrequent smokers' refer to students who reported smoking cigarettes 1-3 days in the past month; 'Frequent smokers' refer to students who reported smoking cigarettes 4 or more days in the past month.
[c] 'Non-users' refers to students who have used neither e-cigarettes or cigarettes within the past month; 'Exclusive e-cigarette users' refers to students who used only e-cigarettes within the past month; 'Exclusive smokers' refers to students who used only cigarettes within the past month; 'Dual users' refers to those who reported using both e-cigarettes and cigarettes within the past month.
[ł] 'Frequency of e-cigarette use in past month' included both exclusive e-cigarette users and dual users; 'Frequency of smoking in past month' included both exclusive smokers and dual users.
Note: Odds Ratios (ORs) adjusted for sex, ethnicity, province, weekly spending money, number of friends who smoke, past month cannabis use and binge-drinking at baseline.
Note: Bolded estimates are significant at p<0.05.

Adjusting for relevant covariates, infrequent and frequent e-cigarette users at W_1 were more likely to report being exclusive e-cigarette users, exclusive smokers and dual users at W_2, compared to non-users (Table 2). Notably, frequent e-cigarette users at W_1 had the highest odds of being dual users at W_2 (aOR=11.22; Table 2). Infrequent and frequent smokers at W_1 were more likely to report being exclusive smokers and dual users at W_2, compared to non-smokers. Specifically, frequent smokers at W_1 had 12.5 times higher odds of being exclusive smokers at W_2. In contrast, infrequent and frequent smokers at W_1 did not have a significantly higher odds of being exclusive e-cigarette users at W_2, compared to non-smokers (p=0.25 and p=0.43 respectively; Table 2). Similar findings, to those described above, were observed between W_2 and W_3, with respect to associations between frequency of e-cigarette use/cigarette smoking and subsequent e-cigarette use and cigarette smoking status (Supplementary Table 1).

Table 3: Multivariate logistic regression model examining associations between frequency of e-cigarette use and cigarette smoking measured at wave 1 and subsequent e-cigarette use and cigarette smoking status at wave 3 **(MODEL 2)**

Baseline characteristics at *wave 1*		E-cigarette use and cigarette smoking status at *wave 3*					
		Exclusive e-cigarette users vs. Non-users [c]		Exclusive smokers vs. Non-users [c]		Dual users vs. Non-users [c]	
		AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value
Frequency of e-cigarette use in past month [ɬ]	Non-users (0 days) [a]	---	---	---	---	---	---
	Infrequent users (1-3 days) [a]	**3.99 (2.39-6.68)**	<0.0001	**2.52 (1.13-5.66)**	0.0247	**6.90 (3.96-11.99)**	<0.0001
	Frequent users (4 or more days) [a]	**5.17 (2.21-12.02)**	0.0001	0.42 (0.05-3.53)	0.4254	**4.18 (1.66-10.48)**	0.0023
Frequency of smoking in past month [ɬ]	Non-smokers (0 days) [b]	---	---	---	---	---	---
	Infrequent smokers (1-3 days) [b]	1.64 (0.77-3.53)	0.1993	**5.56 (2.51-12.29)**	<0.0001	**2.32 (1.06-5.07)**	0.0353
	Frequent smokers (4 or more days) [b]	0.73 (0.17-3.13)	0.6745	**8.63 (2.93-25.38)**	<0.0001	**4.83 (1.67-13.97)**	0.0037

[a] 'Non-users' refer to students who have not reported using e-cigarettes in the past month (this also includes students who have never tried using e-cigarettes); 'Infrequent users' refer to students who reported using e-cigarettes 1-3 days in the past month; 'Frequent users' refer to students who reported using e-cigarettes 4 or more days in the past month.

[b] 'Non-smokers' refer to students who have not reported smoking cigarettes in the past month (this also includes students who have never smoked cigarettes); 'Infrequent smokers' refer to students who reported smoking cigarettes 1-3 days in the past month; 'Frequent smokers' refer to students who reported smoking cigarettes 4 or more days in the past month.

[c] 'Non-users' refers to students who have used neither e-cigarettes or cigarettes within the past month; 'Exclusive e-cigarette users' refers to students who used only e-cigarettes within the past month; 'Exclusive smokers' refers to students who used only cigarettes within the past month; 'Dual users' refers to those who reported using both e-cigarettes and cigarettes within the past month.

[ɬ] 'Frequency of e-cigarette use in past month' included both exclusive e-cigarette users and dual users; 'Frequency of smoking in past month' included both exclusive smokers and dual users.

Note: Odds Ratios (ORs) adjusted for sex, ethnicity, province, weekly spending money, number of friends who smoke, past month cannabis use and binge-drinking at baseline.

Note: Bolded estimates are significant at p<0.05.

Adjusting for relevant covariates, infrequent e-cigarette users at W_1 were more likely to report being in all usage groups at W_3, compared to non-users (Table 3). In contrast, frequent users of e-cigarettes at W_1 did not have a significantly higher odds of being exclusive smokers at W_3, compared to non-users (p=0.43; Table 3). Infrequent and frequent smokers at W_1 were more likely to report being exclusive smokers and dual users at W_3, compared to non-smokers. Specifically, frequent smokers at W_1 had the greatest odds of being exclusive smokers at W_3 (aOR=8.63, Table 3). In contrast, infrequent and frequent smokers did not have a significantly higher odds of being exclusive e-cigarette users at W_3, compared to non-smokers (p=0.19 and p=0.67 respectively; Table 3).

Table 4: Multivariate logistic regression model examining associations between changes in frequency of e-cigarette use and cigarette smoking between wave 1 and wave 2 and subsequent e-cigarette use and cigarette smoking status at wave 3 **(MODEL 3)**

Changes in frequency of e-cigarette use		E-cigarette use and cigarette smoking status at *wave 3*					
		Exclusive e-cigarette users vs. Non-users [c]		Exclusive smokers vs. Non-users [c]		Dual users vs. Non-users [c]	
		AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value
Changes in frequency of e-cigarette use between wave 1 and wave 2	No change [a]	---	---	---	---	---	---
	Increase [a]	**12.86 (9.21-17.96)**	<0.0001	1.92 (0.93-3.94)	0.0766	**15.63 (10.23-23.91)**	<0.0001
	Decrease [a]	**0.18 (0.04-0.75)**	0.0187	1.15 (0.09-14.72)	0.9136	**0.17 (0.04-0.76)**	0.0203
Changes in frequency of cigarette smoking between wave 1 and wave 2	No change [b]	**---**	---	---	---	**---**	---
	Increase [b]	1.48 (0.87-2.51)	0.1452	**22.65 (13.85-37.02)**	<0.0001	**9.92 (6.13-16.04)**	<0.0001
	Decrease [b]	0.63 (0.09-4.67)	0.6533	0.31 (0.06-1.66)	0.1695	0.27 (0.05-1.42)	0.1242

[a] 'No change' refers students who maintained the same frequency of e-cigarette use between W_1 and W_2 ; 'Increase' refers to students who escalated the frequency at which they engaged in e-cigarette use between W_1 and W_2; 'Decrease' refers to students who reduced the frequency at which they engaged in e-cigarette use between W_1 and W_2.

[b] 'No change' refers students who maintained the same frequency of smoking between W_1 and W_2 ; 'Increase' refers to students who escalated the frequency at which they engaged in smoking between W_1 and W_2; 'Decrease' refers to students who de-escalated the frequency at which they engaged in smoking W_1 and W_2.

[c] 'Non-users' refers to students who have used neither e-cigarettes or cigarettes within the past month; 'Exclusive e-cigarette users' refers to students who used only e-cigarettes within the past month; 'Exclusive smokers' refers to students who used only cigarettes within the past month; 'Dual users' refers to those who reported using both e-cigarettes and cigarettes within the past month.

Note: Odds Ratios (ORs) adjusted for sex, ethnicity, province, weekly spending money, number of friends who smoke, past month cannabis use, past month binge-drinking, frequency of e-cigarette use and frequency of cigarette smoking at baseline

Note: Bolded estimates are significant at p<0.05.

Adjusting for relevant covariates, students who increased their frequency of e-cigarette use between W_1 and W_2 were more likely to report being exclusive e-cigarette users and dual users at W_3, compared to those who reported no changes in frequency of use (aOR= 12.86 and aOR= 15.63 respectively; Table 4). Students who reduced their frequency of e-cigarette use between W_1 and W_2 were less likely to report being exclusive e-cigarette users and dual users at W_3, compared to those who reported no changes in frequency of use (aOR=0.18 and aOR=0.17 respectively; Table 4). Students who reduced their frequency of cigarette smoking between W_1 and W_2 did not have a significantly reduced odds of belonging to any of the 3 usage groups after a 2-year follow-up, compared to those who reported no changes in frequency of smoking (Table 4).

6.6 Discussion

This is the first study to investigate trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use within a large longitudinal sample of Canadian youth. An increase in all categories of e-cigarette use and cigarette smoking was observed over time. Our study demonstrated that being a frequent e-cigarette user at baseline was the strongest predictor of dual use after 1-year follow-up. Study findings also showed that being a frequent smoker was the strongest predictor of exclusive smoking at both follow-up time points. Notably, youth who reduced their frequency of e-cigarette use between W_1 and W_2 were less likely to be exclusive e-cigarette users and dual users at the 2-year follow-up. Although youth-based programming is frequently informed by prevention approaches that emphasize abstinence, our findings suggest that interventions aimed at reducing frequency of e-cigarette use may also carry benefits to some youth.

Consistent with US studies (Gentzke et al., 2019; Johnston et al., 2019), our findings showed a rise in e-cigarette use among youth in our sample; a notable increase in exclusive e-cigarette use and dual use was observed between 2016-2017 and 2017-2018. Increases in e-cigarette use may reflect advances in e-cigarette product design observed within recent years. Specifically, the design of newer generation pod-based devices (e.g., JUUL) have gained popularity among youth (Fadus, Smith, & Squeglia, 2019; Goniewicz et al., 2018). Devices like JUUL entered the Canadian market after the introduction of the Tobacco and Vaping Products Act (TVPA); the TVPA was implemented in May 2018 to provide a legal framework for the sale and marketing of nicotine-containing e-cigarettes (Health Canada, 2018). The rise in e-cigarette use and dual use may also reflect youth exposure to advertising. A recent Canadian study demonstrated associations between exposure to vaping product ads and youth e-cigarette use and that more than a third of Canadian youth reported that ads made e-cigarettes seem appealing (Cho et al., 2019). It is also likely that increases in e-cigarette use and dual use observed in our study are partially attributable to age-related effects (i.e., the sample aging over time).

Study findings showed that there were some differences in what risk factors predicted being in different usage groups. Frequent e-cigarette use and cigarette smoking were consistent predictors of dual use at both the 1- and 2-year follow-up time points. In contrast,

frequent e-cigarette use was not a significant predictor of exclusive smoking at either time-point. Similarly, our findings showed that frequent cigarette smoking was not a significant predictor of exclusive e-cigarette use at either time-point. Given the limited research examining longitudinal predictors of dual versus exclusive use of e-cigarettes/cigarettes (Conner et al., 2019), additional work is needed to provide a better understanding of what other risk factors (e.g., accessibility of cigarettes/e-cigarettes) may be linked to different usage groups.

Students who increased their frequency of e-cigarette use between W_1 and W_2 were 15 times more likely to report being dual users after a 2-year follow-up, compared to those who reported no changes in frequency of use. This association may be a reflection of the peer circles in which youth engage. Youth who use e-cigarettes may be more likely to come into contact with smokers and dual users; this may result in greater opportunities to access cigarettes and greater exposure to social cues/pressures to smoke (Bandura, 1987; Kong et al., 2016). These findings may also reflect changes in perceptions of harms of smoking among those use e-cigarettes; previous research has demonstrated that e-cigarette users were more likely to move away from the perception that cigarettes were a 'great risk' the following year, compared to non-users (Miech et al., 2017). Findings may also reflect the development of nicotine dependence, resulting in youth seeking out multiple sources of nicotine (i.e., e-cigarettes and cigarettes). Although the sale of nicotine-containing e-cigarettes was illegal during the first two waves of study, nicotine-containing e-cigarettes were still widely available in the Canadian market (Hammond et al., 2015). Notably, our study findings also showed that those who reduced their frequency of e-cigarette use between W_1 and W_2 were less likely to report being dual users and exclusive e-cigarette users at the 2-year follow-up. Additional studies are needed to identify mediators of the relationship between frequency of e-cigarette use and subsequent smoking to gain a better understanding of underlying mechanisms driving this association.

Study findings showed that those who increased their frequency of cigarette smoking between W_1 and W_2 were more likely to report being exclusive smokers and dual users at the 2-year follow-up point. The associations observed between frequency of smoking and subsequent dual use may reflect smokers using e-cigarettes as an additional source of nicotine in places where smoke-free policies are in effect; previous research suggests that

part of the appeal of e-cigarettes among youth is the ability to use them anywhere (Bold et al., 2016; Kong et al., 2015). Overall, findings suggest that e-cigarettes are simply being added to the diverse array of products youth use (i.e., resulting in dual use of e-cigarettes and cigarettes). Given the limited evidence base regarding youth dual use, continued monitoring of trends and predictors of dual use is warranted.

Our findings hold important implications at a time when Health Canada is considering additional regulatory measures to the TVPA, including further restrictions on the placement of advertisements to limit youth exposure to ads at point of sale, public places, broadcast media and social media platforms (Health Canada, 2019). Our findings lend support for the need for additional regulatory measures aimed at curbing rates of e-cigarette use and dual use among youth.

In terms of study strengths, our study utilized data from a large sample of youth from two Canadian provinces: Ontario and Alberta. Furthermore, this study represents the first investigation of predictors of exclusive e-cigarette use, smoking and dual use among a sample of Canadian youth. With respect to study limitations, we did not have measures to distinguish whether youth were using nicotine/non-nicotine containing e-cigarettes. Secondly, there were relatively fewer youth who reported frequent use of e-cigarettes and cigarettes (i.e., using 4 or more days in the past month) within our sample. Lastly, the study relied on self-reported measures of e-cigarette use and cigarette smoking; as such, findings may reflect some under-reporting bias which is common in youth smoking research. However, COMPASS data are based on previously validated measures of self-reported measures of youth smoking (Wong et al., 2012).

6.7 Conclusions

Findings showed an increase in all usage categories across the three waves, including exclusive e-cigarette use, exclusive smoking and dual use. Findings also demonstrated some differences in predictors of exclusive e-cigarette use, exclusive smoking and dual use. Notably, reductions in frequency of e-cigarette use had a protective effect of reducing the odds of dual use and exclusive e-cigarette use at follow-up. Moving forward, additional research seeking to identify potential mediators of these associations is warranted.

7.0 Manuscript 2

Does having one or more smoking friends mediate the transition from e-cigarette use to cigarette smoking: A longitudinal study of Canadian youth

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7.1 Abstract

Purpose

Studies have shown consistent associations between youth e-cigarette use and subsequent smoking uptake. However, it remains unclear why, as limited evidence exists regarding the mechanisms underlying these associations. Our study investigated whether having one or more smoking friends mediated the association between e-cigarette use and cigarette smoking onset among a longitudinal sample of Canadian youth who were never smokers at baseline.

Methods

A longitudinal sample of youth that participated in three waves of the COMPASS study (2015-16 to 2017-18) was identified (N= 5,535). The product of coefficients method was used to assess whether having one or more smoking friends mediated the association between: (1) past 30-day e-cigarette use and cigarette smoking onset and (2) past 30-day e-cigarette use and subsequent dual use of e-cigarettes and cigarettes.

Results

Having one or more smoking friends did not mediate the association between (1) past 30-day e-cigarette use and cigarette smoking onset (β= 0.38, 95% CI: -0.12, 0.89) or (2) past 30-day e-cigarette use and subsequent dual use (β= 0.46, 95% CI: -0.16, 1.07). Post hoc tests indicated that smoking friends significantly predicted past 30-day e-cigarette use and cigarette smoking at wave 3 (aOR = 1.68 and 2.29 respectively).

Conclusion

Having smoking friends did not explain the association between e-cigarette use and smoking uptake despite being a common risk factor for both e-cigarette use and cigarette smoking. Prevention efforts should consider how best to incorporate effective programming to address these social influences.

Key words: youth; e-cigarettes; smoking; longitudinal study; mediation

7.2 Background

Tobacco smoking is a major preventable cause of many chronic conditions, including several types of cancer, cardiovascular disease and respiratory illnesses (United States Department of Health and Human Services, 2014). Despite steady declines in cigarette smoking observed in Canada, the tobacco and nicotine product market has been evolving, with an increase in the number and use of alternative products (Reid et al., 2019). Specifically, the emergence of electronic cigarettes (e-cigarettes) has proliferated among youth, internationally and within Canada (Arrazola et al., 2015; Dutra et al., 2018; Hammond et al., 2019; Montreuil et al., 2017; Zuckermann et al., 2019). National data indicates that among Canadian students in grades 10 to 12, e-cigarette use in the past 30 days has doubled from 14.6% in 2017 to 29.4% in 2019 (Health Canada, 2019; Reid et al., 2019). The use of e-cigarettes among youth has raised concerns regarding the potential public health implications of this behaviour.

Our previous work has demonstrated an association between e-cigarette use and cigarette smoking uptake among Canadian youth (Aleyan, Cole, Qian, et al., 2018; Hammond et al., 2017). Using longitudinal data from the COMPASS study, our first study found that non-smoking youth who used e-cigarettes in the past 30 days were twice as likely to report trying cigarettes one year later (Hammond et al., 2017). Our second study showed similar findings: among a sample of youth never-smokers, e-cigarette users were at a greater risk of smoking uptake after a two-year follow-up (Aleyan, Cole, Qian, et al., 2018). This association was also observed among low-risk youth who were not susceptible to smoking in the future (Aleyan, Cole, Qian, et al., 2018). Overall, these studies contribute to a growing evidence base showing a consistent association between youth e-cigarette use and smoking uptake (Aleyan, Cole, Qian, et al., 2018; Barrington-Trimis et al., 2016; Barrington-Trimis, Kong, et al., 2018; Best et al., 2017; Conner et al., 2017; East et al., 2018; Hammond et al., 2017; Khouja et al., 2020; Leventhal et al., 2015; Primack et al., 2015).

Currently, it remains unclear *why* youth e-cigarette use is associated with smoking uptake, as there is limited evidence on possible mechanisms underlying this association. To date, only two studies have investigated possible mediating factors between e-cigarette use and smoking uptake (East et al., 2018; Wills et al., 2016). The first study conducted among a

sample of 1,152 English youth found that escalation of e-cigarette use did not explain the association between e-cigarette use and subsequent smoking behaviours (East et al., 2018). The second study conducted among 2,238 students in Hawaii found that the association between e-cigarette use and smoking onset was partly attributable to changes in smoking-related expectancies and affiliations with smoking friends (Wills et al., 2016).

There are several possible explanations for the associations between youth e-cigarette use and subsequent smoking uptake. Some have argued that exposure to nicotine via e-cigarettes may result in nicotine dependence and an increased liability to use other nicotine products (Counotte et al., 2011; Yuan et al., 2015). In contrast, the Common Liability Theory argues that associations between e-cigarette use and smoking may be a result of unmeasured common risk factors (e.g., risk-taking tendencies) that increase an individual's likelihood of using both e-cigarettes and smoking (Vanyukov et al., 2012).

Other theories have drawn attention to the role of social contexts (e.g., peer circles) in influencing e-cigarette use and smoking behaviours (Bandura, 1987). Having friends who smoke has been shown to be a strong predictor of smoking uptake (Liu, Zhao, Chen, Falk, & Albarracín, 2017; Wellman et al., 2016). Furthermore, a large proportion of youth who use e-cigarettes also smoke cigarettes, and e-cigarette users tend to have friends that also use e-cigarettes (Azagba et al., 2019; Montreuil et al., 2017). It may be that non-smoking youth who use e-cigarettes are more likely to have smoking friends. E-cigarette users with smoking friends may be at a greater risk of taking up smoking due to increased contact and exposure to smokers who model smoking behaviours and provide access to cigarettes (Bandura, 1987; Kong et al., 2016; Sussman et al., 2007).

Building off our initial work that demonstrated an association between initial e-cigarette use and smoking uptake among a sample of Canadian youth (Aleyan, Cole, Qian, et al., 2018; Hammond et al., 2017), this follow-up aimed to investigate potential mediating factors linking these two behaviours. Thus, using three waves of longitudinal data from a sample of Canadian youth never smokers, we examined whether having smoking friends mediated the association between (1) past 30-day e-cigarette use and cigarette smoking onset and (2) past 30-day e-cigarette use and subsequent dual use (e-cigarette use and cigarette smoking). We hypothesized that the association between (1) past 30-day e-cigarette

use and cigarette smoking onset and (2) past 30-day e-cigarette use and subsequent dual use would be mediated by having friends who smoke.

7.3 Methods

7.3.1 Design

COMPASS is a prospective cohort study designed to follow a sample of grade 9-12 students attending Canadian secondary schools, aged approximately 13-18 years old (Leatherdale et al., 2014). Specifically, COMPASS collects data on how changes in the school environment (policies, programs, built environment) influence student health behaviours (Leatherdale et al., 2014). Data regarding student health behaviours are gathered during class-time using the COMPASS questionnaire (Leatherdale et al., 2014). The questionnaire was created to gather data from students relating to demographics and various health behaviours, including tobacco and e-cigarette use (Leatherdale et al., 2014). Additional details on COMPASS methodology can be found here (Leatherdale et al., 2014) (www.compass.uwaterloo.ca).

7.3.2 Study Sample

This study used data from Ontario and Alberta schools in Year 4 (2015-2016), Year 5 (2016-2017) and Year 6 (2017-2018) of COMPASS. Year 4 will be referred to as 'wave 1', Year 5 as 'wave 2' and Year 6 as 'wave 3'. The sample consisted of students attending schools in Ontario and Alberta who participated in waves 1 to 3. Details regarding the procedures used to form the longitudinal sample can be found elsewhere (Qian et al., 2015). Students who reported ever having smoked a cigarette at wave 1 were excluded from the sample (n=655), resulting a final longitudinal sample of 5,535 students who were never smokers at wave 1.

With respect to missing data, non-response rates for outcome measures including past 30-day cigarette smoking and dual use were low: 0.5% and 0.9% respectively. Similarly, non-response rates for baseline demographic and behavioural covariates were also quite low (<1%).

7.3.3 Measures

Past 30-day e-cigarette use: “On how many of the last 30 days did you use an e-cigarette?” Students who reported using e-cigarettes within the past month were classified as *past 30-day e-cigarette users*; otherwise they were categorized as *non past 30-day users.*

Past 30-day cigarette smoking: “On how many of the last 30 days did you smoke one or more cigarettes?” Students who reported smoking cigarettes within the past month were classified as *past 30-day smokers;* otherwise they were categorized as *non past 30-day smokers.*

Past 30-day Dual use*:* A derived variable for dual use was created based on measures of past 30-day e-cigarette use and cigarette smoking. Students who reported smoking cigarettes and using e-cigarettes were classified as *past 30-day dual users;* otherwise, they were classified as ‘other’.

Smoking friends: “Your closest friends are the friends you like to spend the most time with. How many of your closest friends smoke cigarettes?”, with response options ranging from ‘None’ to ‘5 or more friends’. Response options were dichotomized as: ‘having at least one friend’ versus ‘none’, given the low proportion of students who reported having more than one close friend who smoked.

Demographic Covariates: Gender (male, female), grade (9,10,11,12), ethnicity (White, Black, Asian, Latin American, Other) and weekly spending money ($0, $1-20, $20-100, over $100, I don’t know), province (Ontario, Alberta).

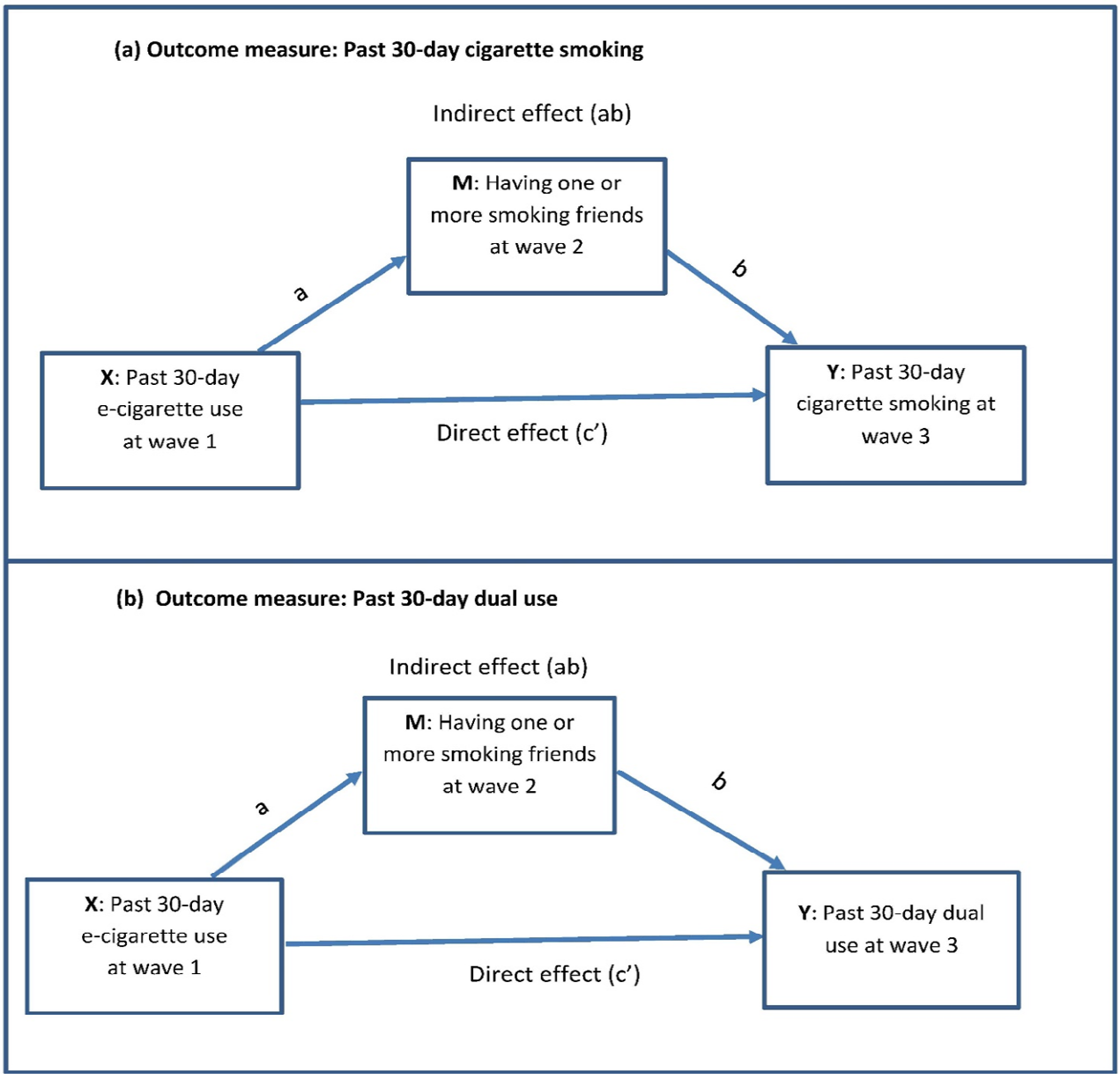
Behavioural covariates: Students were asked how often they used cannabis in the past year. Those who had used cannabis within the past month were classified as past 30-day cannabis users; otherwise, they were classified as non past 30-day cannabis users. Students were also asked how often they had 5 or more drinks of alcohol on one occasion in the past year. Those who had had 5 or more drinks of alcohol on one occasion in the past month were classified as past 30-day binge drinkers; otherwise, they were classified as non past 30-day binge-drinkers.

7.4 Analysis

Descriptive statistics were used to examine the sociodemographic and behavioural characteristics of the sample at wave 1. To address our main research objectives, a series of multi-level logistic regression models were used to examine whether having smoking friends at wave 2 mediates the association between: (a) past 30-day e-cigarette use at wave 1 and past 30-day cigarette smoking at wave 3 and; (b) past 30-day e-cigarette use at wave 1 and past 30-day dual use at wave 3 (Refer to Figure 1a, b). Specifically, the products of coefficient method was used to estimate the potential mediating effect of smoking friends (MacKinnon, 2008). This approach is based on the rationale that mediation depends on the extent to which e-cigarette use leads to having smoking friends, $\widehat{\boldsymbol{a}}$, and the extent to which having smoking friends leads to cigarette smoking, $\widehat{\boldsymbol{b}}$. The products of coefficients approach involves estimating the product of $\widehat{\boldsymbol{a}}$ and $\widehat{\boldsymbol{b}}$, $\hat{\mathbf{a}}\hat{\mathbf{b}}$, to form the mediated effect (MacKinnon, 2008). To estimate the standard error of the mediated effect, the Sobel test was used (Sobel, 1982). In order to evaluate the statistical significance of the mediated effect, the estimate of the mediated effect was divided by the standard error of the mediated effect; this value was then compared with the normal distribution (MacKinnon, 2008). All mediation models adjusted for demographic and behavioural covariates, described above. Students with missing data for the outcome or any covariates were excluded from regression models using listwise deletion.

Given the absence of significant mediating effects (described below), post hoc analyses were also conducted to test whether having smoking friends was a confounding variable in the association between e-cigarette use and subsequent smoking uptake. Specifically, the Change-in-Estimate criterion was used to statistically test the potential confounding influence of smoking friends (Greenland & Pearce, 2015). Using the CIE criterion, a change of ≥10% in the effect of e-cigarette use on smoking onset between unadjusted regression models and regression models adjusted for having smoking friends was used as a cut-off for identifying whether smoking friends was a confounding variable (Greenland & Pearce, 2015). We also examined whether having smoking friends met the two criteria to qualify as a confounding variable: (1) it is associated with the exposure (i.e., past 30-day e-cigarette use) and (2) it is a predictor of the outcome of interest (i.e., past 30-day cigarette smoking/dual use). All analyses were conducted using SAS 9.4.

Fig 1 Hypothesized mediation models examining associations between past 30-day e-cigarette use, having one or more smoking friends and **(a)** past 30-day cigarette smoking, and **(b)** past 30-day dual use, among the sample of never smokers at wave 1 (N=5,535)



7.5 Results

Table 1 reports the demographic and behavioural characteristics of the sample of never-smokers at wave 1. Within our study sample, 53.4% of students were females and 73% identified as White. 95.1% of students within the sample were from Ontario and 27.1% reported having at least twenty dollars in weekly spending money.

Table 1: Characteristics of the Wave 1 (2015-16) sample of never smokers in the COMPASS study, Ontario, Alberta, Canada (N=5,535)

Variables		*N*	*%*
Gender	Female	2940	53.4
	Male	2570	46.6
Grade	9	3160	57.1
	10	2227	40.3
	11	140	2.5
	12	4	0.1
Ethnicity	White	4029	73.0
	Black	241	4.4
	Asian	447	8.1
	Latin American	181	3.3
	Other	615	11.2
Province	Ontario	5266	95.1
	Alberta	269	4.9
Weekly spending money	$0	1245	22.6
	$1-20	2020	36.7
	$20-100	1143	20.8
	Over $100	344	6.3
	I don't know	756	13.6
Having 1 or more smoking friends	Yes	811	14.7
	No	4693	85.3
Past 30-day e-cigarette use	Yes	124	2.3
	No	5308	97.7
Past 30-day cannabis use	Yes	97	1.8
	No	5385	98.2
Past 30-day binge drinking	Yes	241	4.4
	No	5281	95.6

Table 2. Regression coefficient estimates and standard errors of the **a**, **b, c'** and indirect (**ab**) effects of past 30-day cigarette smoking and past 30-day dual use among past 30-day e-cigarette users, via having one or more close friends who smoke, COMPASS study (2015-2018), Ontario, Alberta, Canada

Model	Effect	Estimate (SE) [c]	95% CI	z-statistic [d]
Model 1 [a]	E-cigarette use → Having ≥ 1 smoking friends (**a**)	0.36 (0.24)	[-0.11, 0.83]	---
	Having ≥ 1 smoking friends→ Cigarette smoking (**b**)	1.06 (0.10) ***	[0.86, 1.27]	---
	E-cigarette use → Cigarette smoking (**c'**)	1.06 (0.28) ***	[0.52, 1.60]	---
	Indirect effect (**ab**)	0.38 (0.26)	[-0.12, 0.89]	1.48
Model 2 [b]	E-cigarette use → Having ≥ 1 smoking friends (**a**)	0.36 (0.24)	[-0.11, 0.83]	--
	Having ≥ 1 smoking friends→ Dual use (**b**)	1.29 (0.13) ***	[1.03, 1.56]	--
	E-cigarette use → Dual use (**c'**)	1.31 (0.24) ***	[0.84, 1.79]	--
	Indirect effect (**ab**)	0.46 (0.31)	[-0.16, 1.07]	1.45

[a] Refer to the mediation model shown in Figure 1a.
[b] Refer to the mediation model shown in Figure 1b.
[c] Values shown above adjust for gender, ethnicity, weekly spending money, province, past 30-day binge drinking and past 30-day cannabis use
[d] z-statistic > 1.96 indicates that the mediated effect is statistically significant
Note: * p<0.05, ** p<0.01, *** p<0.001; ---: not applicable

As shown in Table 2, the direct effect of being a past 30-day e-cigarette user at wave 1 significantly predicted past 30-day cigarette smoking and dual use at wave 3 ($p<0.05$ for both). However, the effect of past 30-day e-cigarette use on subsequent past 30-day cigarette smoking was not mediated by having friends who smoke at wave 2 (β= 0.38, 95% CI: -0.12, 0.89, z = 1.48. Similarly, the effect of past 30-day e-cigarette use on subsequent dual use was not mediated by having friends who smoke at wave 2 (β= 0.46, 95% CI: -0.16, 1.07, z = 1.45).

Post hoc tests that were conducted to investigate the role of smoking friends in the association between e-cigarette use and subsequent smoking showed that having friends who smoke was a confounding factor: a change of ≥10% was observed in parameter estimates between unadjusted models and models adjusting for having friends who smoke (Table 3). These findings were reinforced by post hoc tests showing that having friends who smoke at wave 1 was significantly associated with past 30-day e-cigarette use (i.e., exposure of interest)

and predictive of past 30-day cigarette smoking (i.e., outcome of interest; Supplementary Table 1).

Table 3. Unadjusted and adjusted regression coefficient estimates (β) in the association between e-cigarette use and cigarette smoking/dual use among youth in the COMPASS study (2015-2018), Ontario, Alberta, Canada

	Past 30-day Cigarette Smoking at wave 3			Past 30-day Dual Use at wave 3		
	Unadjusted	Adjusted [a]	**Δ %**	Unadjusted	Adjusted [a]	**Δ %**
Past 30-day e-cigarette use at wave 1	1.80	1.63	10.4	2.13	1.96	8.5
	Past 30-day Cigarette Smoking at wave 3			Past 30-day Dual Use at wave 3		
	Unadjusted	Adjusted [b]	**Δ %**	Unadjusted	Adjusted [b]	**Δ %**
Past 30-day e-cigarette use at wave 2	2.03	1.64	23.8	2.34	1.94	20.0

[a] Adjusted for having close friends who smoke at wave 1
[b] Adjusted for having close friends who smoke at wave 2
Δ %: Percentage change in β-coefficients, when adjusting for having friends who smoke in modelling procedures

Supplementary Table 1: Associations between having smoking friends and e-cigarette use/smoking behaviours among youth in the COMPASS study (2015-2018), Ontario, Alberta, Canada

		Model 1 [a]	Model 2 [b]	Model 3 [c]	Model 4 [d]	Model 5 [e]
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Having smoking friends	None	--	--	--	--	--
	One or more	2.31 *** (1.57-3.39)	1.56 *** (1.20-2.02)	2.59 *** (1.76-3.82)	1.68 *** (1.38-2.04)	2.29 *** (1.78-2.94)

[a] Model 1: Association between smoking friends at wave 1 and past 30-day *e-cigarette use* at *wave 1*
[b] Model 2: Association between smoking friends at wave 1 and past 30-day *e-cigarette use* at *wave 2*
[c] Model 3: Association between smoking friends at wave 1 and past 30-day *cigarette smoking* at *wave 2*
[d] Model 4: Association between smoking friends at wave 1 and past 30-day *e-cigarette use* at *wave 3*
[e] Model 5: Association between smoking friends at wave 1 and past 30-day *cigarette smoking* at *wave 3*
Note: All models shown above are adjusted for gender, ethnicity, weekly spending money, province, past 30-day cannabis use and binge drinking. Models 2-5 also adjusted for past 30-day e-cigarette use at wave 1.
Note: *: p<0.05; **: p<0.01; ***: p<0.001

7.6 Discussion

This is the first study to investigate what role having one or more smoking friends has on the association between e-cigarette use and subsequent cigarette smoking onset using three waves of data from a large, longitudinal sample of youth. Our findings showed that past 30-day e-cigarette use was significantly associated with cigarette smoking onset. However, contrary to our initial hypotheses, having one or more smoking friends did not mediate the association between past 30-day e-cigarette use and cigarette smoking onset. Rather, the study findings indicated that having one or more friends who smoked was a significant predictor of both past 30-day e-cigarette use and past 30-day cigarette smoking. Overall, these findings suggest that having smoking friends represents a confounding factor in the e-cigarette use-cigarette smoking pathway.

The associations observed between past 30-day e-cigarette use and subsequent smoking onset in our study are consistent with recent systematic reviews and meta-analyses (Khouja et al., 2020; Soneji, Barrington-Trimis, Wills, et al., 2017). Our findings regarding the role of smoking friends in the e-cigarette use-smoking pathway is inconsistent with earlier evidence, but aligns with more recent work (Conner et al., 2019; Wills et al., 2016). Overall, our findings are in line with the Common Liability Theory that argues that there are common underlying risk factors (e.g., shared social or environmental factors) that increase an individual's propensity to use nicotine (Vanyukov et al., 2012) ; having one or more close friends who smoke appears to represent a common risk factor that is associated with using both e-cigarettes and cigarettes according to our findings. It is possible that having smoking friends may provide a shared access point for both products (i.e., e-cigarettes and cigarettes); in this way, the presence of smoking friends may offer increased opportunities for youth to use both products.

The study findings did not support the role of smoking friends as a mediating factor in the association between past 30-day e-cigarette use and subsequent past 30-day dual use. However, a significant association between having one or more close friends who smoke and subsequent past 30-day dual use was observed among never smokers. This is noteworthy as it may be the case that having at least one close friend who smokes represents a proxy/marker for which youth will eventually go on to engage in multiple risky behaviours. The clustering of

risky behaviours has been widely documented in various youth-based studies (Azagba, 2018; Mehra, Keethakumar, Bohr, Abdullah, & Tamim, 2019; Milicic & Leatherdale, 2017; Zuckermann et al., 2019).

Implications for Programming & Research

Our findings indicate that having one or more close friends who smoke represents a key social factor that is linked to both past 30-day e-cigarette use and past 30-day cigarette smoking. Our findings suggest the need to consider the role of social influences within the design of future interventions focused on preventing youth uptake of e-cigarettes and cigarettes. Prevention programs combining social competence (i.e., teaching problem solving and cognitive skills to resist personal and media influences) and social influence curricula (i.e., teaching skills to resist offers of tobacco/deal with peer pressure) have been shown to be effective in preventing youth smoking uptake (Thomas, McLellan, & Perera, 2015). Involvement of influential student leaders within the design of prevention initiatives has also been shown to be a key component of effective tobacco programming (Campbell et al., 2008; Macarthur et al., 2016). Specifically, previous evaluations have shown that student-led interventions aimed at de-normalizing smoking behaviours can be effective in reducing smoking uptake (Campbell et al., 2008; Macarthur et al., 2016). Future prevention efforts should consider how best to incorporate key components of evidence-based tobacco programming noted above. Given the currently limited evidence base to inform the design of e-cigarette prevention programs, future work would also benefit from identifying key components of effective e-cigarette programming moving forward.

Study Strengths & Limitations

The strengths of our study include the use of a large, three-year longitudinal sample of youth from two Canadian provinces: Ontario and Alberta. Furthermore, our study makes use of an under-utilized analytic approach within applied health research to investigate mediating factors that may explain the association between youth e-cigarette use and smoking uptake. Our study also had some limitations. First, we did not have measures to assess whether students were using nicotine or non-nicotine containing e-cigarettes. As such, we could not examine whether there were potential differences in these associations among sub-groups of e-cigarette users. We also did not have access to other social norm measures

that may have played a role in the e-cigarette use-cigarette smoking pathway (e.g., having friends who use e-cigarettes, having a sibling/family member who uses e-cigarettes/smokes). Lastly, the study relied on non-probability sampling methods; as such, the results may not be representative of all Ontario and Alberta secondary schools.

7.7 Conclusions

Our findings indicate that having one or more smoking friends does not explain the association between past 30-day e-cigarette use and cigarette smoking onset. Rather, it represents a common risk factor that is linked to past 30-day use of both products. These findings suggest the need to consider the role of social influences within the design of future prevention intervention efforts.

8.0 Manuscript 3

Do e-cigarette minimum legal sales age laws influence current e-cigarette use among Canadian youth? Cross-sectional and longitudinal findings from the COMPASS study

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8.1 Abstract

Background

The province of Ontario (Canada) implemented a law restricting the sale of e-cigarettes to those 19 and over in January 2016. At that time, the province of Alberta (Canada) had not implemented a similar law. We examined the impact of Ontario's law on: (1) the average school-level prevalence of e-cigarette use within schools in Ontario versus Alberta; and, (2) the individual likelihood of e-cigarette use among students in Ontario relative to Alberta.

Methods

Data from three waves of COMPASS, a prospective study of grade 9 to 12 students (13 to 18 years of age) were used as both repeat cross-sectional [T1 (2014-2015): n=31,200; T2 (2015-2016): n= 31,120; T3 (2016-2017): n=30,086] and longitudinal samples [T1-3: n=6950]. Schools were placed into three groups: (1) Ontario schools where T2 data collection occurred post-implementation of Ontario's law [*Intervention Group 1]*; (2) Ontario schools where T2 data collection occurred pre-implementation of Ontario's law [*Intervention Group 2*] and; (3) Alberta schools where no law was in effect [*Control Group*]. Difference-in-difference models and Generalized Estimating Equations tested changes in (a) the mean school-level prevalence of past 30-day e-cigarette use; and (b) individual likelihood of a student being a past 30-day e-cigarette user respectively, comparing Intervention and Control groups.

Results

Repeat cross-sectional findings showed insignificant changes in the mean school-level prevalence of e-cigarette use from T1 to T3 within Ontario (Groups 1 and 2) compared to changes in the Alberta group (+1.27% and -1.46% respectively, both $p > 0.05$). Adjusting for sociodemographic and behavioural covariates, longitudinal analysis showed students in Ontario (Groups 1 and 2) had a lower risk of e-cigarette use by T3, compared to students in the Alberta group (RR=0.68, 95% CI: 0.47-0.99 and RR=0.57, 95% CI: 0.39-0.84 respectively).

Discussion

Repeat cross-sectional findings showed small changes in the average school-level prevalence of e-cigarette use after the implementation of Ontario's law. Longitudinal individual-level findings suggest that this law attenuated increases in e-cigarette use among youth within our study sample, but did not prevent the increasing trend in use among Ontario youth over time.

8.2 Background

Electronic cigarette (e-cigarette) use among Canadian youth has increased substantially in the last three years (Cole et al., 2020; Hammond et al., 2019). According to national estimates, 29.4% of Canadian youth in grades 10 to 12 reported using e-cigarettes in the past 30 days in 2018-2019, an increase from 14.6% in 2016-2017 (Health Canada, 2017; Health Canada, 2019). The use of e-cigarettes among youth (particularly among never smokers) has raised public health concerns and prompted calls for further regulatory action to deter use among youth.

One regulatory approach to preventing e-cigarette use among youth is the implementation of minimum legal sales age (MLSA) laws. Currently, there is limited evidence regarding the effectiveness of e-cigarette MLSA laws in reducing e-cigarette use among youth, as most studies to date have focused on the outcome of cigarette smoking (Dutra et al., 2018; Pesko et al., 2015). Only one study to date has evaluated the impact of e-cigarette MLSA laws on youth e-cigarette use (Nguyen, 2019). This repeat cross-sectional study showed an increase in e-cigarette use among individuals aged 15-18 across all Canadian provinces, but that these increases were 4.3 percentage points lower in provinces with an e-cigarette MLSA law compared to provinces without one (Nguyen, 2019). Given the currently limited evidence base, additional quasi-experimental studies evaluating the impact of e-cigarette MLSA laws on youth e-cigarette use could provide valuable insight into their effectiveness.

In the province of Ontario (Canada), an e-cigarette MLSA law was implemented on January 1st, 2016 restricting the sale of e-cigarettes to those 19 years of age and over (Government of Ontario, 2017). At that time, the province of Alberta (Canada) did not have a provincial e-cigarette MLSA law in effect. These differences in provincial laws across Canada provide a timely opportunity to evaluate the impact of e-cigarette MLSA laws within the context of a natural experiment. This evaluation could assist in the formulation of relevant practice-based evidence that could be used to determine whether Ontario's e-cigarette MLSA law was effective in achieving its intended outcomes (Leatherdale, 2018).

Using three waves of repeat-cross-sectional data from a sample of Canadian youth attending schools in Ontario and Alberta, the first research objective was to examine whether Ontario's e-cigarette MLSA law had an impact on the average school-level prevalence of

current e-cigarette use within Ontario schools versus Alberta schools. Secondly, using three waves of longitudinal data, we sought to examine whether Ontario's e-cigarette MLSA law influenced the individual likelihood of a student being a current e-cigarette user over time. We hypothesized that Ontario's e-cigarette MLSA law would result in a reduced risk of current e-cigarette use among students in Ontario, relative to students in Alberta.

8.3 Methods

8.3.1 Study Design & Sample

COMPASS is a prospective cohort study designed to evaluate how changes in policies, programming, and the built environment impact youth health behaviours including e-cigarette use and tobacco use (Leatherdale et al., 2014). Data regarding youth health behaviours were collected using the COMPASS student questionnaire (Leatherdale et al., 2014). The COMPASS student questionnaire was administered during class-time among grade 9-12 students (aged approximately 13-18 years old) (Bredin & Leatherdale, 2014). Additional details regarding the COMPASS methodology can be found elsewhere (https://uwaterloo.ca/compass-system/) (Bredin & Leatherdale, 2014; Leatherdale et al., 2014). This quasi-experimental study used data derived from Wave 1 (T1 [2014-2015]: pre-implementation baseline time point), Wave 2 (T2 [2015-2016]: e-cigarette MLSA law implemented in Ontario) and Wave 3 (T3 [2016-2017]: post-implementation follow-up) as both *repeat cross-sectional* and *longitudinal* samples (described below; See Figure 1 a, b).

Repeat Cross-Sectional Sample

The repeat cross-sectional sample consisted of grade 9-12 students attending Ontario and Alberta schools participating in the COMPASS study (mean age: 15.6). Specifically, the analytic sample used for cross-sectional analyses was comprised of 64 Ontario and Alberta schools that participated at all three time points of the COMPASS study (T1: n=31,200; T2: n= 31,120; T3: n=30,086). The same sample of COMPASS schools was used at each time point to mitigate potential confounding effects due to school-level differences. A break-down of the cross-sectional samples is provided in Appendix B (Refer to Supplementary Table 1).

Longitudinal Sample

To assess longitudinal changes among individuals, we linked student responses at T1, T2 and T3 using a unique code generated for each student (Qian et al., 2015). The analytic sample used for longitudinal analyses consisted of students (mean age: 14.6) who could be followed across all three time points (n=6,950). A breakdown of the longitudinal sample is provided in Appendix B (Refer to Supplementary Table 2).

8.3.2 Exposure to Intervention

COMPASS schools were classified into one of three groups: (1) Ontario schools where T2 data collection occurred after the e-cigarette MLSA law was implemented [N=39; *Intervention Group 1]*; (2) Ontario schools where T2 data collection occurred before the e-cigarette MLSA law was implemented [N=18; *Intervention Group 2*] and; (3) Alberta schools where no provincial e-cigarette MLSA law was in effect at the time [N=7; *Control Group*]. This was then used to create the variable 'group' for whether schools were exposed to Ontario's e-cigarette MLSA law. An overview of the quasi-experimental design used and specific sample sizes within each of these groups are outlined below (Refer to Figure 1 a, b).

Figure 1a. Student-level sample size for the *repeat cross-sectional* samples in the quasi-experimental design evaluating the impact of Ontario's implementation of e-cigarette minimum legal sales age laws using data from the COMPASS study (2014-2015 to 2016-2017)

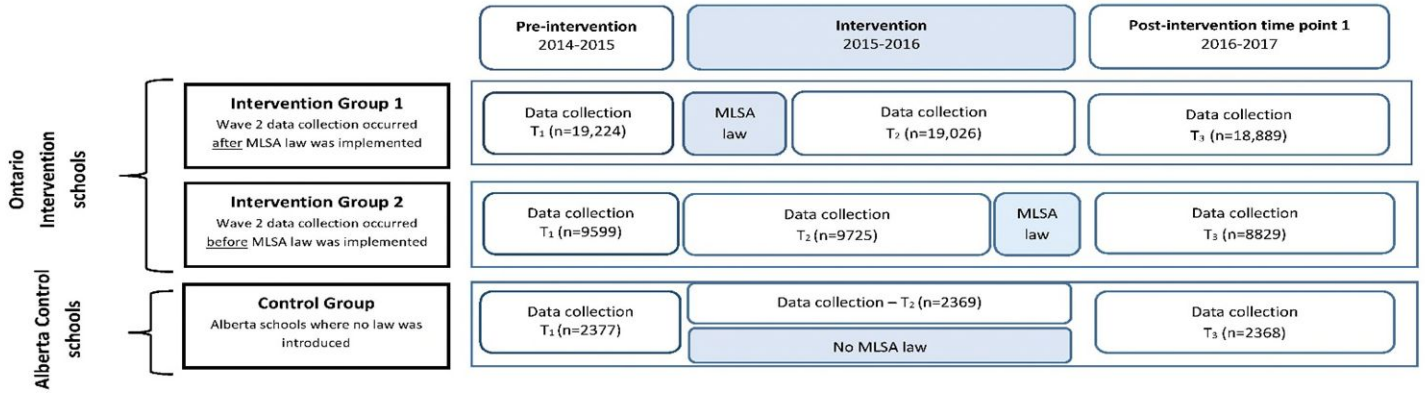
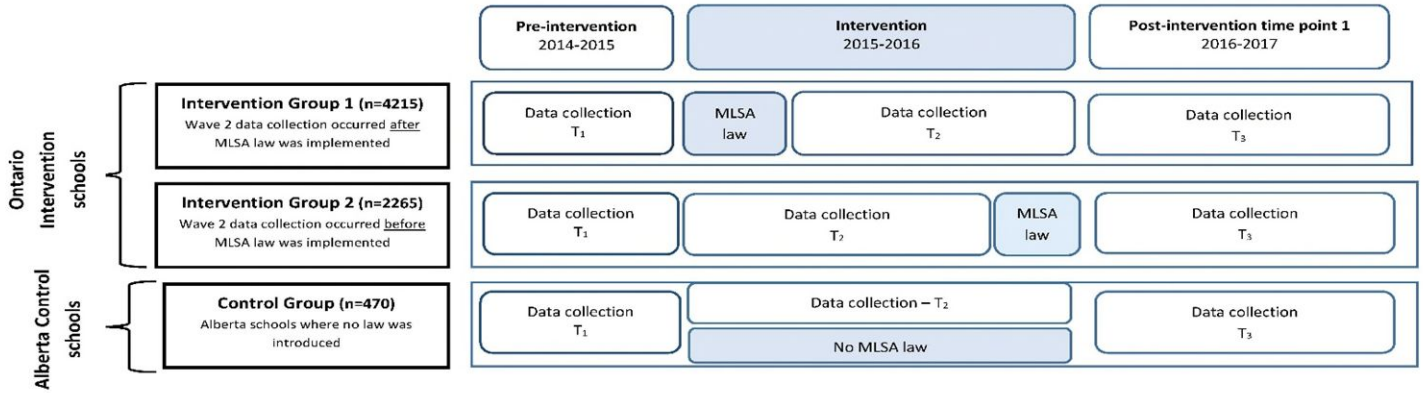


Figure 1b. Student-level sample size for the *longitudinal* samples in the quasi-experimental design evaluating the impact of Ontario's introduction of e-cigarette minimum legal sales age laws using data from the COMPASS study (2014-2015 to 2016-2017)



8.3.3 Outcome Measures

Student-level e-cigarette use. Students at each wave were asked whether they had used e-cigarettes in the past 30 days. Consistent with previous research (Aleyan, Gohari, Cole, & Leatherdale, 2019; Cole, Aleyan, & Leatherdale, 2019; Hammond et al., 2017), students who reported using e-cigarettes any time in the past 30 days were classified as *past 30-day e-cigarette users*; otherwise they were classified as *non past 30-day e-cigarette users*.

School-level prevalence of e-cigarette use. Using student data from the repeat cross-sectional samples, the school-specific prevalence of past 30 day e-cigarette use was determined within each of the 64 schools at each time point.

8.3.4 Covariates

Students were asked to report their gender (male, female), ethnicity (White, Black, Asian, Latin American, Other), amount of weekly spending money (proxy for socio-economic status) and whether they had close friends who smoked. Students were asked to report how often they had had 5 or more drinks of alcohol on one occasion in the past year. Those who reported having 5 or more drinks of alcohol on one occasion in the past month were categorized as past 30-day binge-drinkers; otherwise, they were classified as non past 30-day binge-drinkers. Students were asked how often they had used cannabis in the past year. Those who reported using cannabis in the past month were categorized as past 30-day cannabis users; otherwise, they were classified as non past 30-day cannabis users. Students were also asked to report on how many of the last 30 days they had smoked one or more cigarettes, with response options ranging from 'None' to '30 days (every day)'. Those who reported smoking cigarettes on one or more days within the past 30 were classified as past 30-day cigarette smokers; otherwise, they were classified as non-past 30-day cigarette smokers.

8.4 Analysis

To address our first research objective (which was based on the repeat cross-sectional sample), descriptive statistics were used to estimate the mean school-level prevalence of e-cigarette use at each time point within the Ontario Intervention groups and the Alberta Control group. Difference-in-difference models were used to estimate changes in the mean

school-level prevalence of past 30-day e-cigarette use from T1 to T3 within Ontario Intervention Groups 1 and 2 (i.e., schools impacted by Ontario's e-cigarette MLSA law), relative to the changes seen within the Alberta Control Group (i.e., schools where no provincial e-cigarette MLSA law was in effect at the time) (Refer to Figure 1a) (Shadish et al., 2002). Difference-in-difference estimates were obtained by testing the interaction between group (i.e., proxy for exposure to e-cigarette MLSA law) and time using a linear regression model (SAS Institute Inc., 2018).

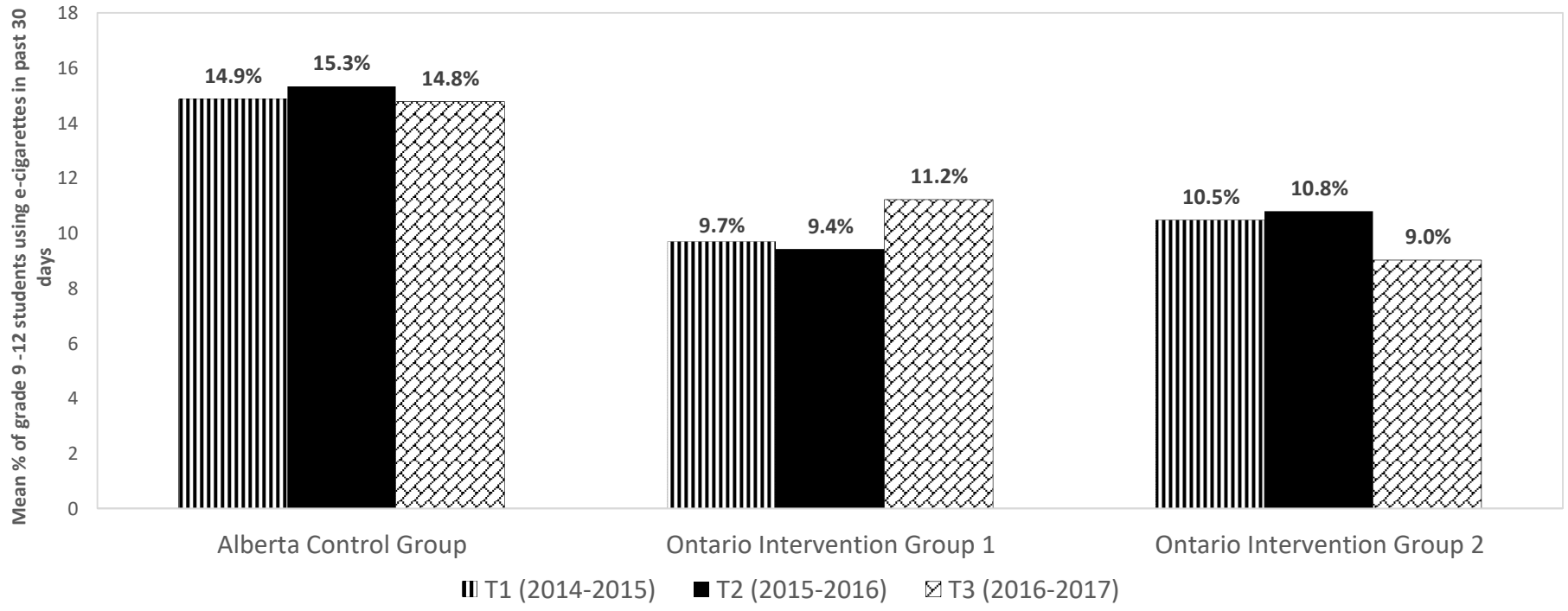
To address our second research objective (which was based on the longitudinal sample), descriptive statistics were used to estimate the proportion of e-cigarette users at each time point by group. Generalized Estimating Equation (GEE) models were used to estimate the effects of Ontario's provincial e-cigarette MLSA law on the relative increase/decrease in likelihood of a student in an Ontario Intervention group being a past 30-day e-cigarette user over time, relative to a student within the Alberta Control group (Refer to Figure 1b). The outcome of interest (past 30-day e-cigarette use) was treated as a binary outcome. Generalized Estimating Equations (GEE) were used to account for the hierarchical structure of the data and the use of repeated measures (i.e., students nested within schools over time) (Zeger & Liang, 1986). Models were adjusted for the effects of gender, ethnicity, weekly spending money, having friends who smoke, current binge drinking, current cannabis use, and current cigarette smoking. Model estimates were then exponentiated to obtain Relative Risks (RR).

8.5 Results

Figure 2 provides the mean school-level prevalence estimates of past 30-day e-cigarette use within each of the groups from T1 (i.e., baseline time point pre-implementation of MLSA law) to T3 (post-implementation follow-up). Across 7 Alberta schools within the Control Group, the mean school-level prevalence of past 30-day e-cigarette use was 14.9% (range from 8.6% to 22.3%) in T1, 15.3% (range from 8.5% to 24.9%) in T2, and 14.8% (range from 8.6% to 20.0%) in T3. Across 39 Ontario schools within Intervention Group 1, the mean school-level prevalence of past 30-day e-cigarette use was 9.7% (range from 4.3% to 18.2%) in T1, 9.4% (range from 3.1% to 22.2%) in T2, and 11.2% (range from 1.8% to 27.5%) in T3. Across 18 Ontario schools within Intervention Group 2, the mean school-level prevalence of past 30-day e-cigarette use was 10.5% (range from 4.3% to 19.8%) in T1, 10.8% (range from 4.1% to 17.0%) in T2, and 9.0% (range from 3.2% to 14.5%) in T3.

Within the Alberta Control Group, the 0.1% change in the mean school-level prevalence of past 30-day e-cigarette use between T1 to T3 represents a 0.6% decrease in past 30-day e-cigarette use. In contrast, within Ontario Intervention Group 1, the 1.5% change in the mean school-level prevalence of past 30-day e-cigarette use between T1 to T3 represents a 15.8% increase in past 30-day e-cigarette use. Within Ontario Intervention Group 2, the 1.5% change in the mean school-level prevalence of past 30-day e-cigarette use reflects a 15.9% decrease in past 30-day e-cigarette use.

Figure 2. Mean school-level prevalence of past 30-day e-cigarette use within the repeat cross-sectional samples of grade 9 to 12 students, COMPASS study, Ontario, Alberta, Canada, 2014-15 to 2016-17



Note: Alberta Control group: Alberta COMPASS schools where no provincial e-cigarette MLSA law was in effect at the time; Ontario Intervention Group 1: Ontario COMPASS schools where the T2 data collection (2015-2016) occurred **after** the implementation of e-cigarette MLSA laws on Jan 1st, 2016; Ontario Intervention Group 2: Ontario COMPASS schools where the T2 (2015-2016) data collection occurred **before** the implementation of e-cigarette MLSA laws on Jan 1st, 2016.

Table 1. Difference-in-difference (DiD) estimates within the *repeat cross-sectional* samples of grade 9 to 12 students, COMPASS study, Ontario, Alberta, Canada, 2014-2015 to 2016-2017

		Mean School-Level Prevalence of past 30-day e-cigarette use	
		Percentage Point Change (Difference in Difference)	p-value
	Changes over time pre- and post-law		
Ontario Intervention Group 1 vs. Alberta Control Group [a]	T2 vs. T1	-0.73	0.766
	T3 vs. T1	1.62	0.5235
Ontario Intervention Group 2 vs. Alberta Control Group [a]	T2 vs. T1 [b]	---	---
	T3 vs. T1	-1.35	0.6197

[a] Alberta Control group: Alberta COMPASS schools where no provincial e-cigarette MLSA law was in effect at the time; Ontario Intervention Group 1: Ontario COMPASS schools where the T2 data collection (2015-2016) occurred **after** the implementation of e-cigarette MLSA laws on Jan 1st, 2016; Ontario Intervention Group 2: Ontario COMPASS schools where the T2 (2015-2016) data collection occurred **before** the implementation of e-cigarette MLSA laws on Jan 1st, 2016.

[b] The difference-in-difference estimate is not presented in this row, due to the timing of T2 data collection within this group of Ontario schools.

Repeat cross-sectional findings showed that changes in the mean school-level prevalence of past 30-day e-cigarette use from T1 to T3 within Ontario Intervention Group 1 (i.e., schools affected by provincial e-cigarette MLSA laws) were not significantly different from the changes observed within the Alberta Control Group (p=0.52; See Table 1). From T1 to T3, findings also showed that the changes in the mean school-level prevalence of past 30-day e-cigarette use within Ontario Intervention Group 2 (i.e., schools affected by provincial e-cigarette MLSA laws) were not significantly different from the changes observed in the Alberta Control Group (p=0.62; See Table 1).

Figure 3. Proportion of students who reported past 30-day e-cigarette use within the *longitudinal* sample of students, COMPASS study, Ontario, Alberta, Canada, 2014-15 to 2016-17

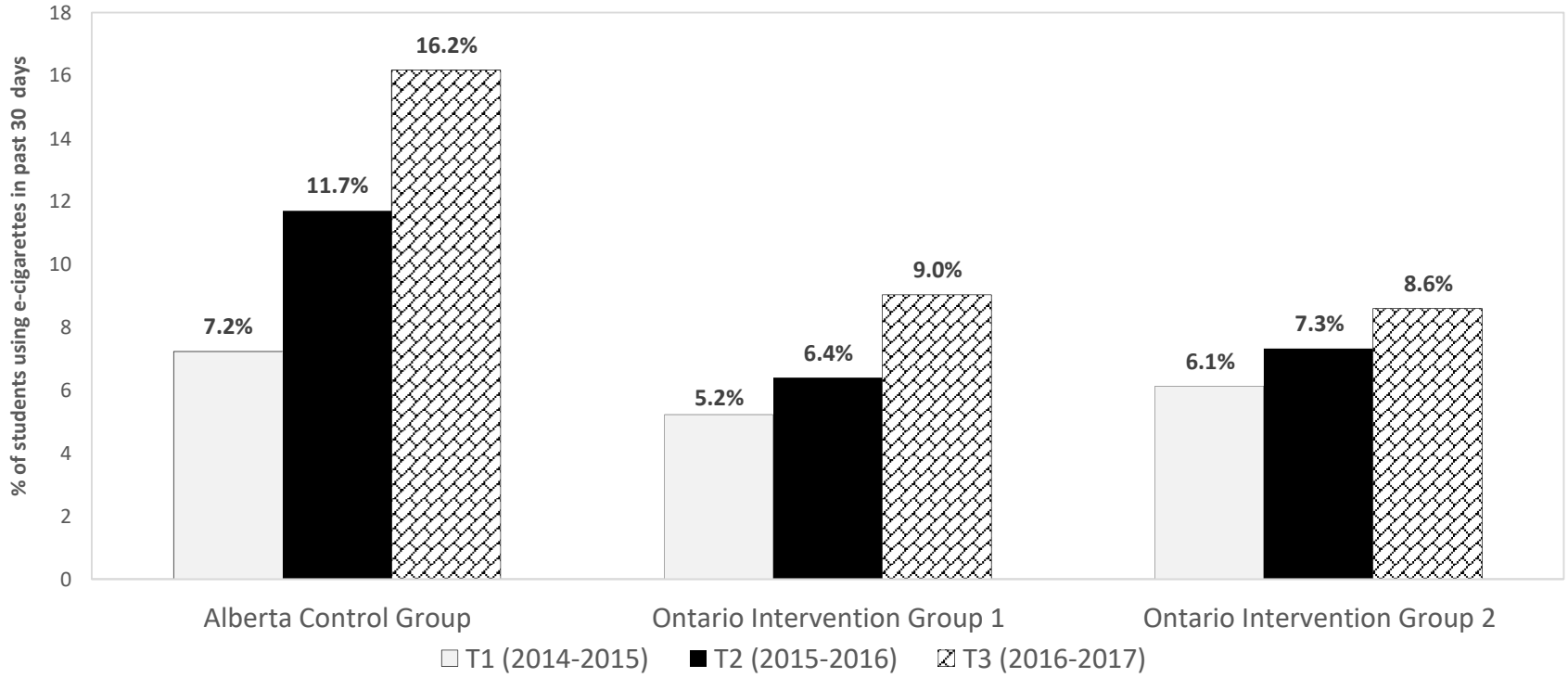


Figure 3 shows the proportion of students in the longitudinal sample who reported using e-cigarettes in the past 30 days within each of the groups from T1 (i.e., pre-implementation of Ontario's MLSA law) to T3 (i.e., post-implementation follow-up). As shown in Figure 3, there was an increase in the proportion of past 30-day e-cigarette users from T1 to T3 across all groups. However, the increase seen in the Alberta group (+123%), was larger than the increases seen in the Ontario groups where e-cigarette MLSA laws were implemented (Ontario Group 1: +72%; Ontario Group 2: +40%).

Table 2. Adjusted GEE models evaluating the impact of Ontario's MLSA law on the likelihood of a student being a past 30-day e-cigarette user within the *longitudinal* sample of students, COMPASS study, Ontario, Alberta, Canada, 2014-15 to 2016-17

		Past 30-day e-cigarette use	
		Relative Risk (95% CI)	p-value
	Changes over time pre- and post-law		
Ontario Intervention Group 1 vs. Alberta Control Group [a]	T2 vs. T1	0.70 (0.47, 1.03)	0.0721
	T3 vs. T1	**0.68 (0.47, 0.99)**	0.047
Ontario Intervention Group 2 vs. Alberta Control Group [a]	T2 vs. T1 [b]	--	--
	T3 vs. T1	**0.57 (0.39, 0.84)**	0.0048

[a] Alberta Control group: Alberta COMPASS schools where no provincial e-cigarette MLSA law was in effect at the time; Ontario Intervention Group 1: Ontario COMPASS schools where the T2 data collection (2015-2016) occurred **after** the implementation of e-cigarette MLSA laws on Jan 1st, 2016; Ontario Intervention Group 2: Ontario COMPASS schools where the T2 (2015-2016) data collection occurred **before** the implementation of e-cigarette MLSA laws on Jan 1st, 2016.

[b] The Relative Risk estimate is not presented in this row, due to the timing of T2 data collection within this group of Ontario schools.

Note: Estimates shown above are adjusted for gender, ethnicity, weekly spending money, having friends who smoke, current cigarette smoking, current binge drinking and current cannabis use. Estimates also adjusted for the nested structure of the data (i.e., students nested within schools over time).

Adjusting for sociodemographic and behavioural covariates, longitudinal findings showed that changes in past 30-day e-cigarette use from T1 to T3 in Ontario Intervention Group 1 were significantly lower than the changes seen in the Alberta Control group (RR=0.68; see Table 2). Similarly, the changes in past 30-day e-cigarette use in Ontario Intervention Group 2 were significantly lower than the changes seen in the Alberta Control group (RR=0.57; see Table 2). In other words, the increases in past 30-day e-cigarette use within the Ontario groups (where an e-cigarette MLSA law was implemented), were significantly lower than the increases seen within the Alberta group (where no provincial e-cigarette MLSA law was in effect).

8.6 Discussion

This is the first study to date to examine the impact of Ontario's provincial e-cigarette MLSA law on past 30-day e-cigarette use using both aggregate repeat cross-sectional and individual-level longitudinal data from a sample of Canadian youth across three waves. Findings based on the repeat cross-sectional sample showed that the changes in the average school-level prevalence of past 30-day e-cigarette use (i.e., pre- and post-implementation of Ontario's e-cigarette MLSA law) did not significantly differ between the Ontario Intervention Groups and the Alberta Control group. Findings based on the longitudinal sample showed an increase in past 30-day e-cigarette use over time among youth in the Ontario Intervention groups and the Alberta Control group. However, the increases observed among youth in the Ontario Intervention groups (where an e-cigarette MLSA law was implemented) were significantly lower than the increases seen in the Alberta Control group (where no e-cigarette MLSA law was in effect).

Longitudinal findings suggest that Ontario's e-cigarette MLSA law had a modest protective effect of attenuating increases in e-cigarette use, as indicated by the reduction in risk of e-cigarette use among students within the Ontario Intervention groups (Group 1 and 2) versus students in the Alberta Control group. However, this law did not effectively prevent the increase in e-cigarette use observed over time among youth in the Ontario groups (Group 1 and 2). One plausible explanation for these findings could be that youth are acquiring e-cigarettes through social sources. Recent work has shown that a large proportion of youth report obtaining e-cigarettes through a friend or relative (Braak, Cummings, Nahhas, Reid, & Hammond, 2020). Another reason may include lack of compliance with Ontario's law prohibiting the sale of e-cigarettes to minors. Previous research has shown that e-cigarettes can easily be purchased by youth through online vendors (Collier, 2017; Williams, Derrick, & Ribisl, 2015).

Contrary to initial hypotheses, difference-in-difference model results based on the repeat cross-sectional sample showed that the changes in the average school-level prevalence of e-cigarette use (i.e., pre- and post-implementation of the provincial law) within the Ontario Intervention Groups were not significantly different from the changes seen in the Alberta Control Group. These findings were inconsistent with previous cross-sectional data; specifically, Nguyen

(2019) demonstrated that increases in e-cigarette use were significantly lower in provinces with e-cigarette MLSA laws, compared to provinces without one (Nguyen, 2019). The discrepancy in findings may be a function of differences in sampling methods used. While previous evidence was based on nationally representative data (Nguyen, 2019), the COMPASS study was not designed to be provincially or nationally representative.

At the individual-level, longitudinal findings suggest that Ontario's e-cigarette MLSA law had a moderate effect of attenuating increases in youth e-cigarette use, as indicated by the reduced risk of e-cigarette use among students in the Ontario Groups versus those in the Alberta group. However, the effects seen in at the individual-level did not translate to a significant reduction in e-cigarette use at the population-level (i.e., school-level), as indicated by the findings of difference-in-difference models based on the repeat cross-sectional sample. Overall, our findings suggest that an e-cigarette MLSA law alone is not sufficient to prevent increases in e-cigarette use among youth. Given the range of factors influencing youth e-cigarette use, a comprehensive and coordinated approach will be needed to achieve significant reductions in e-cigarette use (as was found to be effective in the case of tobacco control) (Pierce, White, & Emery, 2012; U.S. Department of Health and Human Services, 2012).

These findings hold important implications given the recent adoption of e-cigarette MLSA laws across a growing number of countries. For instance, within Canada, as of May 2018, new federal laws have been implemented that restrict the sale of e-cigarettes to those 18 years of age and older under the Tobacco and Vaping Products Act (Health Canada, 2018). Longitudinal findings suggest that Ontario's provincial laws restricting e-cigarette sales to those 19 and over had an impact in attenuating increases in e-cigarette use, but did not effectively prevent the overall increasing trend in use observed among Ontario youth in our study sample. Our study findings suggest that e-cigarette MLSA laws will likely need to be supplemented with additional measures, including the consistent enforcement of e-cigarette MLSA laws and the implementation of rigorous age verification systems by e-cigarette retailers.

Study Strengths & Limitations

Study strengths include the use of a robust quasi-experimental design and three waves of data from two distinct Canadian provinces: Ontario and Alberta. However, our study was also subject to limitations. The COMPASS study used non-probability sampling methods; as such, the samples used may not be representative of all youth within Ontario and Alberta or within Canada. The COMPASS student questionnaire also asked students to report whether they had used e-cigarettes in the past month. Given the rapidly evolving language used to refer to e-cigarettes among youth (e.g., vaping, JUUL-ing) (Huang et al., 2019; Willett et al., 2019), our study may under-estimate the prevalence of e-cigarette use among youth. Furthermore, the difference-in-difference analysis based on the repeat cross-sectional sample could not account for the dependence of observations at the student-level, as student data was collapsed to a higher unit of analysis (i.e., school-level prevalence of e-cigarette use). However, the analytic approach used within our study was consistent with previous research (Leatherdale & Cole, 2015; Leatherdale, Stefanczyk, & Kirkpatrick, 2016). Lastly, this study was restricted to the outcome of past 30-day e-cigarette use; as such, we could not draw inferences regarding the effects of Ontario's e-cigarette MLSA law on other behaviours, including cigarette smoking.

Conclusions

Repeat cross-sectional findings showed small changes in the average school-level prevalence of e-cigarette use pre- and post- implementation of Ontario's e-cigarette MLSA law. However, individual-level longitudinal findings suggest that Ontario's provincial law had an effect in attenuating the increases in e-cigarette use observed over time among youth in our study sample. As this is the first study to examine the impact of e-cigarette MLSA laws on youth e-cigarette use longitudinally, additional evidence stemming from other jurisdictions/settings is needed to identify key components of effective legislation, moving forward.

9.0 General Discussion

9.1 Overview

Chapter 6 was based on Manuscript 1 which aimed to examine predictors and trends of past 30 day exclusive e-cigarette use, exclusive smoking and dual use among a longitudinal sample of Canadian youth. Chapter 7 was based on Manuscript 2 which aimed to identify potential mediators of the association between youth e-cigarette use and cigarette smoking onset that has been documented in previous research (Aleyan, Cole, Qian et al., 2018; Best et al. 2017; East et al., 2018; Hammond et al., 2017). Chapter 8 was based on Manuscript 3, which sought to evaluate the effectiveness of e-cigarette MLSA laws in reducing youth e-cigarette use using repeat cross-sectional data and longitudinal data from a sample of Canadian youth. This chapter, Chapter 9, will provide a summary of key findings observed across all three manuscripts, an overview of the strengths and limitations of this dissertation and the implications of our findings for future research and policy.

9.2 Summary of Key Findings

Using three waves of longitudinal data (2015-2016 to 2017-2018), Chapter 6 showed an increase in exclusive e-cigarette use, exclusive smoking and dual use over time among youth within our study sample. Specifically, an increase from 4.25% to 12.70% was observed in youth exclusive e-cigarette use between 2016-2017 and 2017-2018. Findings also demonstrated an increase in dual use of e-cigarettes and cigarettes from 2.19% to 5.44% during this period. These findings coincide with U.S. and Canadian studies documenting a rise in youth e-cigarette use in recent years (Gentze et al., 2019; Johnston et al., 2019; Hammond et al., 2019; Cole et al., 2020). Our findings suggest the need for additional regulatory measures aimed at curbing increases in e-cigarette use and dual use observed among Canadian youth.

Longitudinal findings from Chapter 6 indicated some differences in what risk factors predicted being in different usage groups (i.e., being an exclusive e-cigarette user, exclusive smoker or dual user) among youth in our study sample. For instance, frequent smoking (4 or more days in the past 30) was a significant predictor of exclusive smoking and dual use at both

follow-up time points. In contrast, frequent smoking did not predict exclusive e-cigarette use at either follow-up time point. Findings also showed that youth who increased their frequency of e-cigarette use between 2015-2016 and 2016-2017 were more likely to report being exclusive e-cigarette users and dual users at the two-year follow-up period, relative to those who reported no changes in frequency of use. Notably, our findings also demonstrated that reductions in frequency of e-cigarette use had a protective effect of reducing the odds of exclusive e-cigarette use and dual use among youth in our study sample at the 2-year follow-up. Although youth-based programming is frequently informed by prevention approaches that emphasize abstinence, our study findings suggest that interventions aimed at reducing frequency of e-cigarette use may also carry benefits to some youth.

Using three waves of longitudinal data (2015-2016 to 2017-2018), Chapter 7 examined whether having one or more smoking friends mediated the relationship between initial e-cigarette use and subsequent smoking onset among a sample of youth never smokers at baseline. Overall, longitudinal findings showed that the direct effect of being a past 30-day e-cigarette user at baseline (2015-2016) predicted past 30-day cigarette smoking and dual use at the 2-year follow-up (2017-2018). However, contrary to initial hypotheses, having one or more smoking friends did not mediate the association between past 30-day e-cigarette use and subsequent smoking uptake. Rather, longitudinal results demonstrated that having one or more smoking friends was a significant predictor of past 30-day e-cigarette use and cigarette smoking. Our findings regarding the role of smoking friends in the e-cigarette use-smoking pathway was inconsistent with earlier research, but did align with more recent evidence (Will et al., 2016; Conner et al., 2019).

Using three waves of repeat cross-sectional and longitudinal data from Ontario and Alberta schools participating in the COMPASS study (T_1: 2014-2015; T_2: 2015-2016; T_3: 2016-2017), Chapter 8 evaluated the impact of Ontario's introduction of an e-cigarette MLSA law in January 2016, relative to Alberta where no provincial e-cigarette MLSA law was in effect at the time. COMPASS schools were classified into three groups: (1) Ontario schools where 2015-2016 data collection occurred after the implementation of the law [*Intervention Group 1*]; (2) Ontario

schools where 2015-2016 data collection occurred before the implementation of the law [*Intervention Group 2*] and; (3) Alberta schools where no e-cigarette MLSA law was in effect at the time [*Control group*]. Using a quasi-experimental design, we examined the impact of this provincial law on (i) the average school-level prevalence of e-cigarette use; and (ii) the individual likelihood of a student being an e-cigarette user, comparing Intervention and Control groups. Based on findings from the previous chapter indicating that having smoking friends was a significant predictor of past 30-day e-cigarette use, this covariate was included within longitudinal models testing the impact of Ontario's e-cigarette MLSA law on trends in youth e-cigarette use. Aggregate data from the repeat cross-sectional sample showed that changes in the mean school-level prevalence of past 30-day e-cigarette use (pre- and post-implementation of Ontario's e-cigarette MLSA law) among the Ontario Intervention Groups were not significantly different from the changes seen in the Alberta Control Group. Our study findings were inconsistent with previous cross-sectional evidence evaluating the impact of provincial e-cigarette MLSA laws on individual e-cigarette use among a nationally representative sample of Canadian youth (Nguyen et al., 2019). This discrepancy in findings may be due to differences in the sampling methods used; the evaluation by Nguyen et al. (2019) was based on nationally representative data, while COMPASS was not designed to be either nationally or provincially representative.

Longitudinal findings from Chapter 8 showed an increase in past 30-day e-cigarette use from 2014-2015 to 2016-2017 (i.e., before and after Ontario's introduction of an e-cigarette MLSA law) within the Ontario Intervention Groups and the Alberta Control group (Ontario Intervention Group 1: 5.2% to 9.0%; Ontario Intervention Group 2: 6.1% to 8.6%; Alberta Control Group: 7.2% to 16.2%). However, longitudinal models showed that the increases within the Ontario groups were significantly lower than the increases seen in the Alberta group. These findings suggest that Ontario's e-cigarette MLSA law had a modest protective effect of attenuating the increase in e-cigarette use over time, however it did not effectively prevent the increase in e-cigarette use observed over time among Ontario youth. This is the first longitudinal study to date to examine the influence of an e-cigarette MLSA law on youth e-cigarette use using a rigorous quasi-experimental design. Thus, our findings contribute novel practice-based

evidence regarding the effectiveness of these laws. The data gathered from the evaluation of this natural experiment offers timely and locally relevant evidence that is particularly valuable to policy makers who are concerned with policy effectiveness in 'real-world' settings (O'Donoughue Jenkins, Kelly, Cherbuin, & Anstey, 2016). This type of evidence is often viewed as more relevant to policy makers as it provides an accurate reflection of the realities of policy implementation and can be used to inform future decision-making (O'Donoughue Jenkins et al., 2016).

Across both Manuscripts 1 and 3, longitudinal findings showed an increase over time in past 30-day e-cigarette use among youth in our study sample. Specifically, longitudinal findings drawn from Chapter 8 demonstrated an overall increase in past 30-day e-cigarette use between 2014-2015 to 2016-2017 in each of the Ontario Intervention Groups despite the introduction of a provincial law restricting the sale of e-cigarettes to those aged 19 years of age and over. The increase in e-cigarette use observed among youth in our study sample may be partly explained by advances in e-cigarette product design observed in recent years. Recent studies have shown that newer generation pod-based devices have become increasingly popular among youth (Fadus, Smith, & Squeglia,2019; Goniewicz et al., 2019). Pod-based devices like JUUL and Vype entered the Canadian market in May 2018 after the implementation of the Tobacco and Vaping Products Act which provided a legal framework for the sale and marketing of nicotine containing e-cigarettes (Health Canada, 2018). These increases may also be partially attributable to youth exposure to e-cigarette marketing (Cho et al., 2019). A recent Canadian study found that increased exposure to e-cigarette marketing was strongly associated with increases in e-cigarette use among Canadian youth (Hammond, Reid, Burkhalter, & Rynard, 2020). Overall, our study findings suggest that a more comprehensive approach that goes beyond restricting the sale of e-cigarettes to minors will be needed in order to address rising rates of e-cigarette use (as was found to be effective in the case of tobacco control) (Pierce et al., 2012; U.S. Department of Health and Human Services, 2012).

Across both Manuscripts 1 and 2, we identified youth who reported dual use of both e-cigarettes and cigarettes. For instance, longitudinal findings drawn from Chapter 6 demonstrated a 655% increase in the prevalence of youth dual use from 2015-2016 to 2017-2018. These

findings are consistent with previous studies that have documented the co-occurrence of risky behaviours among Canadian youth (Zuckermann et al., 2019; Zuckermann et al., 2020). Dual use of e-cigarettes and cigarettes among youth is a problematic issue, as it has been positively associated with other risky behaviours including illicit substance use and alcohol use (McCabe, West, Veliz et al., 2017; Azagba, 2018; Kristjansson et al., 2015). Furthermore, recent studies have raised concerns that for at least some users, dual use of e-cigarettes and cigarettes may lead to the maintenance/escalation of smoking behaviours and the development of dependence among youth (Azagba & Wolfson, 2018; Doran et al., 2017). Our study findings exemplify the need for continued monitoring and surveillance of trends in dual use among Canadian youth.

Consistent with the Theory of Triadic Influence (TTI) (Flay et al., 2009), our study findings identified social influences for youth e-cigarette and cigarette use. For instance, longitudinal findings drawn from Chapter 7 showed that having friends who smoked was a key social factor that predicted *both* past 30-day e-cigarette use and past 30-day cigarette smoking. The role of smoking friends in influencing youth smoking uptake has been widely documented in previous research (Kobus, 2003; Mayhew, Flay, & Mott, 2000; Sussman, Pokhrel, Ashmore, & Brown, 2007). Our study findings offer new evidence that a similar influence may also extend to e-cigarette use. It is possible that having friends who smoke may influence these behaviours by providing access to these products and offering opportunities to use them in social settings.

9.3 Overall Strengths

This dissertation project provided novel findings that contribute towards addressing research gaps within Canada. Specifically, there is a lack of longitudinal data on e-cigarette and tobacco use among youth populations in Canada. This dissertation project included the first longitudinal study examining trends and predictors of exclusive e-cigarette use, exclusive smoking and dual use among a sample of Canadian youth. It also includes the first longitudinal study to evaluate the impact of e-cigarette MLSA laws on trends in e-cigarette use among Canadian youth. The findings presented here offer novel 'real world' practice-based evidence that advances our understanding of the influence of e-cigarette MLSA laws on youth e-cigarette use. Another key strength included the use of three waves of longitudinal data from a large

sample of youth from two Canadian provinces: Ontario and Alberta. Utilizing three waves of data provided us with the opportunity to evaluate trends in youth e-cigarette use and cigarette smoking over time. Furthermore, the use of passive consent procedures maximized the number of students that participated in the study, resulting in robust participation rates. Passive consent procedures have been found to be particularly important in gathering robust data on self-reported risk behaviours, such as tobacco use, while maintaining student anonymity (Thompson-Haile et al., 2013; White, Hill, & Effendi, 2004). Lastly, this dissertation project employed a complex analytic approach (mediation analysis) that is generally under-utilized in applied health research to advance our understanding of what may be driving the associations between e-cigarette use and smoking uptake among youth. Using this novel analytic approach, we were able to explore what potential factors mediate the association between e-cigarette use and cigarette smoking uptake among youth never smokers.

9.4 Overall Limitations

Inevitably, the three studies that this thesis dissertation was comprised of were also subject to various limitations. First, when this study was conducted, the COMPASS study did not include measures that allowed us to assess whether youth were using nicotine or non-nicotine containing e-cigarettes. As such, we could not examine whether there were sub-group differences between nicotine versus non-nicotine e-cigarette users. Second, the measures used within our study were based on self-reported measures of e-cigarette use and cigarette smoking. Thus, this study may have been subject to underreporting bias which is a common issue in youth smoking research. Third, the COMPASS study also relied on non-probability sampling methods; as such, our findings may not be generalizable of all youth within Ontario or Alberta. However, given the lack of Canadian data on youth e-cigarette use, the longitudinal study design and large study sample used, our findings hold important implications for research and policy. The e-cigarette measure used within the COMPASS study asked youth to report whether they had used e-cigarettes within the past 30 days. However, given the evolving language that youth tend to use to refer to e-cigarettes (e.g., JUUL-ing, vaping) (Huang et al., 2019; Willett et al., 2019), the estimates produced within our study may have underestimated the prevalence of e-cigarette use. Lastly, we were limited by the measures that were available in the COMPASS questionnaire.

For instance, the COMPASS questionnaire did not include any measures to assess whether individuals reported having close friends, a sibling or a family member who used e-cigarettes.

9.5 Implications for Policy

Consistent with prior evidence documenting the rise in e-cigarette use among Canadian youth (Cole et al., 2020; Hammond et al., 2019), longitudinal findings showed an increase in past 30-day e-cigarette use among youth within our sample. Overall, these findings suggest that additional measures will be needed to reduce the appeal and use of e-cigarettes among Canadian youth. There are a variety of intervention approaches that may help in reducing youth e-cigarette use. For instance, further restrictions on e-cigarette advertising and promotion may be helpful in reducing e-cigarette use, given the high advertising exposure reported among Canadian youth (Cho et al., 2019). A recent Canadian study found that comprehensive provincial restrictions on e-cigarette marketing were associated with a reduced prevalence of e-cigarette use among youth (Hammond et al., 2020). Evidence from tobacco control has also shown that comprehensive tobacco control programs involving well-designed mass media campaigns, price increases, the implementation of school-based programming, comprehensive smoke-free policies and restrictions on youth access to cigarettes were effective in preventing smoking uptake among youth (National Health Center for Chronic Disease Prevention and Health Promotion, 2014; Pierce et al., 2012). Building off of lessons from tobacco control, a comprehensive strategy involving a combination of prevention approaches will be needed to achieve significant reductions in e-cigarette use among youth.

Our findings also showed that Ontario's introduction of e-cigarette MLSA laws had a modest effect in attenuating increases in past 30-day e-cigarette use among youth. However, it did not effectively prevent the overall increase in e-cigarette use seen over time among Ontario youth in our study sample. Overall, our study findings suggest that the e-cigarette MLSA laws will likely need to be supplemented with additional measures to improve their effectiveness. For instance, regular inspections are needed to ensure that brick-and-mortar e-cigarette retailers are complying with e-cigarette MLSA laws. Furthermore, consistent and strict enforcement of the law is needed to deter retailers from selling to minors. These measures have been identified as

key components of effective youth access restriction interventions (Richardson et al., 2009). With respect to the sale of e-cigarettes online, the implementation of rigorous age verification systems by e-cigarette vendors may also assist in ensuring that youth are not circumventing these age restrictions.

Our findings also demonstrated that having one or more close friends who smoked was a common risk factor that predicted past 30-day e-cigarette use and past 30-day cigarette smoking among youth. These findings suggest that the role of friends/peers should be considered within the design of youth-based interventions aimed at addressing youth e-cigarette and tobacco use. Evidence drawn from tobacco control has shown that youth-led interventions aimed at de-normalising smoking behaviors were effective in reducing smoking uptake (Macarthur et al., 2016; Campbell et al., 2008). Furthermore, the involvement of influential peers within the design and delivery of youth-based initiatives has been shown to be a key component of tobacco prevention programming (Macarthur et al., 2016; Campbell et al., 2008).

9.6 Directions for Future Research

The results of this dissertation present directions for future research which are outlined below:

1. *Identify how youth are obtaining e-cigarette products in Canada.* Despite Ontario's provincial law restricting the sale of e-cigarettes to those 19 and over, our study findings suggest that many youth are still able to obtain e-cigarettes (as indicated by the increase in e-cigarette use observed over time). Currently, there is limited evidence regarding how Canadian youth are obtaining these products (Braak et al., 2020). Additional research seeking to identify key sources of youth access is warranted. This knowledge could provide valuable insight that could assist in the formulation of relevant and targeted measures aimed at restricting youth access. This information would also provide a better understanding of where intervention efforts need to be directed, moving forward.
2. *Examine the effects of changes in e-cigarette regulatory restrictions on youth e-cigarette use.* In light of the increases in e-cigarette use observed among Canadian youth (which was also supported by our study findings), various changes in provincial and federal

restrictions have recently been introduced. For instance, of as July 2020, new provincial measures in Ontario have been implemented under the Smoke-free Ontario Act (i) restricting the sale of flavoured e-cigarettes to specialty vape stores/licensed cannabis retail stores, (ii) restricting the sale of vaping products with nicotine concentrations greater than 20 mg/ml to specialty vape stores and (iii) ensuring that indoor displays and promotion of vaping products within specialty vape stores are not visible from outside their stores (Smoke-Free Ontario Act, 2020). The evaluation of these natural experiments can assist in generating timely and relevant practice-based evidence that can be used to inform future decision-making (Green, 2006; Leatherdale 2012). Moving forward, longitudinal studies utilizing robust quasi-experimental designs are needed to assess the impact of changes in provincial/federal regulatory restrictions on subsequent product use. This knowledge could assist in identifying key components of effective regulatory measures aimed at preventing e-cigarette use among youth.

3. *Explore the impact of e-cigarette MLSA laws on youth cigarette smoking and dual use.* The implementation of e-cigarette MLSA laws may have an impact on more than just youth e-cigarette use. Previous cross-sectional studies have shown that the introduction of e-cigarette MLSA laws was associated with other youth behaviours, including tobacco use (Dutra et al., 2018; Pesko et al., 2015). Moving forward, longitudinal work focused on evaluating the influence of e-cigarette MLSA laws on changes in cigarette smoking over time could provide valuable information. This knowledge would allow us to examine whether this law may have any unintended consequences (negative or positive) on youth smoking behaviours.

9.7 Conclusions

The studies examined within this dissertation project add towards our understanding of e-cigarette use and smoking among Canadian youth. Study findings demonstrate that having one or more close friends who smoke is a common risk factor linked to both e-cigarette use and cigarette smoking among youth. Furthermore, our findings demonstrated an increase in e-cigarette use over time among youth within our study sample. Although the introduction of provincial e-cigarette MLSA laws had an impact in attenuating increases in e-cigarette use, it did

not effectively prevent the overall increase in e-cigarette use observed over time among youth within our sample. Collectively, our findings suggest the need to consider a more comprehensive approach in order to address the issue of youth access to and use of e-cigarettes.

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Appendix A Supplementary material for Manuscript 1

Supplementary Table 1: Multivariate logistic regression model examining associations between frequency of e-cigarette use and cigarette smoking measured at *wave 2* and subsequent e-cigarette use and cigarette smoking status at *wave 3*

Characteristics at *wave 2*		E-cigarette use and cigarette smoking status at *wave 3*					
		Exclusive e-cigarette users vs. Non-users [c]		Exclusive smokers vs. Non-users [c]		Dual users vs. Non-users [c]	
		AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value
Frequency of e-cigarette use in past month	Non-users (0 days) [a]	---	---	---	---	---	---
	Infrequent users (1-3 days) [a]	**9.02 (6.23-13.03)**	<0.0001	1.28 (0.60-2.72)	0.5186	**7.67 (4.80-12.24)**	<0.0001
	Frequent users (4 or more days) [a]	**10.0 (5.29-19.0)**	<0.0001	0.95 (0.28-3.23)	0.9395	**13.35 (6.58-27.1)**	<0.0001
Frequency of smoking in past month	Non-smokers (0 days) [b]	---	---	---	---	---	---
	Infrequent smokers (1-3 days) [b]	1.18 (0.65-2.10)	0.585	**5.59 (3.01-10.38)**	<0.0001	**5.21 (3.05-8.91)**	<0.0001
	Frequent smokers (4 or more days) [b]	2.12 (0.85-5.30)	0.1068	**24.71 (10.71-81.80)**	<0.0001	**12.52 (5.47-28.64)**	<0.0001

[a] 'Non-users' refer to students who have not reported using e-cigarettes in the past month (this also includes students who have never tried using e-cigarettes); 'Infrequent users' refer to students who reported using e-cigarettes 1-3 days in the past month; 'Frequent users' refer to students who reported using e-cigarettes 4 or more days in the past month.
[b] 'Non-smokers' refer to students who have not reported smoking cigarettes in the past month (this also includes students who have never smoked cigarettes); 'Infrequent smokers' refer to students who reported smoking cigarettes 1-3 days in the past month; 'Frequent smokers' refer to students who reported smoking cigarettes 4 or more days in the past month.
[c] 'Non-users' refers to students who have used neither e-cigarettes or cigarettes within the past month; 'Exclusive e-cigarette users' refers to students who used only e-cigarettes within the past month ; 'Exclusive smokers' refers to students who used only cigarettes within the past month ; 'Dual users' refers to those who reported using both e-cigarettes and cigarettes within the past month.
Note: Odds Ratios (ORs) adjusted for sex, ethnicity, province, weekly spending money, number of friends who smoke, past month cannabis use and binge-drinking.
Note: Bolded estimates are significant at p<0.05.

Appendix B Supplementary Material for Manuscript 3

Supplementary Table 1. Characteristics of the repeat cross-sectional sample of grade 9-12 students, COMPASS study, Ontario, Alberta, Canada, 2014-2017				
		T1: 2014-2015 (n=31,200)	*T2: 2015-2016 (n=31,120)*	*T3: 2016-2017 (n=30,086)*
		N (%)	*N (%)*	*N (%)*
Gender	Female	15232 (49.3)	14985 (48.8)	14496 (48.9)
	Male	15655 (50.7)	15696 (51.2)	15140 (51.1)
Age	13	363 (1.1)	384 (1.2)	317 (1.1)
	14	6299 (20.2)	6310 (20.3)	5774 (19.2)
	15	8354 (26.8)	7947 (25.5)	7896 (26.2)
	16	7679 (24.6)	7786 (25.0)	7553 (25.1)
	17	6354 (20.4)	6420 (20.6)	6274 (20.9)
	18	2000 (6.4)	2087 (6.7)	2107 (7.0)
Grade	9	8165 (26.3)	8240 (26.7)	7744 (25.9)
	10	8417 (27.1)	8117 (26.3)	8190 (27.4)
	11	7742 (24.9)	7781 (25.2)	7526 (25.12)
	12	6713 (21.7)	6778 (21.9)	6456 (21.6)
Ethnicity	White	22096 (71.4)	21697 (70.3)	20641 (69.0)
	Black	1768 (5.7)	1816 (5.9)	1680 (5.6)
	Asian	2191 (7.1)	2301 (7.5)	2462 (8.1)
	Latin American	1011 (3.3)	992 (3.2)	1052 (3.5)
	Other	3872 (12.5)	4051 (13.1)	4087 (13.7)
Weekly spending money	$0	5148 (16.7)	5182 (16.8)	5002 (16.8)
	$1-20	8757 (28.3)	8319 (27.0)	7706 (25.9)
	$20-100	7871 (25.5)	7719 (25.1)	7533 (25.3)
	Over $100	5395 (17.5)	5919 (19.2)	5888 (19.8)
	I don't know	3729 (12.1)	3661 (11.9)	3673 (12.2)
Having friends who smoke	Yes	10901 (35.6)	10330 (33.8)	9921 (33.6)
	No	19742 (64.4)	20206 (66.2)	19598 (66.4)

Past 30-day cannabis use	Yes	5169 (17.0)	4988 (16.4)	4881 (16.6)
	No	25329 (83.0)	25359 (83.6)	24480 (83.4)
Past 30-day binge drinking	Yes	6980 (22.4)	6525 (21.0)	6281 (21.0)
	No	24121 (77.6)	24473 (79.0)	23680 (79.0)
Past 30-day cigarette smoking	Yes	3471 (11.1)	3703 (11.9)	3472 (11.7)
	No	27729 (88.9)	27417 (88.1)	26212 (88.3)

Supplementary Table 2. Baseline characteristics of the longitudinal sample of students (N=6,950), COMPASS study, Ontario, Alberta, Canada, 2014-2015		
Variables		*N (%)*
Gender	Female	3587 (51.9)
	Male	3329 (48.1)
Grade	9	3795 (54.8)
	10	2948 (42.5)
	11	186 (2.7)
Age	13	128 (1.9)
	14	2996 (43.3)
	15	3088 (44.5)
	16	682 (9.8)
	17	34 (0.5)
Ethnicity	White	5245 (76.0)
	Black	281 (4.1)
	Asian	448 (6.5)
	Latin American	185 (2.7)
	Other	740 (10.7)
Weekly spending money	$0	1555 (22.6)
	$1-20	2603 (37.8)
	$20-100	1383 (20.1)
	Over $100	431 (6.3)
	I don't know	917 (13.2)
Having friends who smoke	Yes	1556 (22.6)
	No	5328 (77.4)
Past 30-day cannabis use	Yes	417 (6.1)
	No	6452 (93.9)
Past 30-day binge drinking	Yes	636 (9.2)
	No	6308 (90.8)
Past 30-day cigarette smoking	Yes	271 (3.9)
	No	6679 (96.1)