Original investigation

Disentangling Within- and Between-Person Effects of Shared Risk Factors on E-cigarette and Cigarette Use Trajectories From Late Adolescence to Young Adulthood

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Abstract

Background: Longitudinal studies report associations between use of electronic cigarettes (ECs) and cigarettes over time among young people, but do not distinguish within- from between-person effects, which complicates interpretation of findings. Further, the role of shared risk factors, such as substance use and mental health, in explaining longitudinal associations between EC and cigarette use remains unclear. This study used within- and between-person analyses to assess longitudinal associations between youths' EC and cigarette use and shared risk factors.

Methods: Between 2015 and 2017, 2039 youths completed three Web-based surveys, allowing us to model EC and cigarette use from ages 16 to 20. Auto-regressive latent growth models with structured residuals (ALT-SR) examined both between-person and within-person associations between past-month frequency of EC use, cigarette use, and third variables (alcohol and marijuana use, mental health symptoms) over time.

Results: Models revealed robust reciprocal associations between EC and cigarette use, such that more frequent EC use at one time predicted more frequent cigarette use at the subsequent time, and vice versa. Between-person analyses showed associations between shared risk factors and both EC and cigarette use. However, shared risk factors did not predict frequency of subsequent EC and cigarette use in within-person analyses.

Conclusions: Findings add to a growing body of research suggesting that EC use among youth is prospectively associated with progression toward greater cigarette use. Shared risk factors may help explain differences in EC and cigarette use patterns *between* young people, but do not appear to influence longitudinal trajectories of EC and cigarette use within individuals.

Implications: This study examined within- and between-person associations between e-cigarette use, cigarette use, and shared risk factors (alcohol use, marijuana use, mental health symptoms) in a longitudinal cohort of youths. Within- and between-person analyses revealed reciprocal prospective associations between e-cigarette and cigarette use, suggesting a progression toward more frequent use of both products over time. The shared risk factors examined here did not affect escalations in e-cigarette or cigarette use over time within individuals, but likely influence which youths use these products. Findings add to a growing body of evidence suggesting that e-cigarette use increases subsequent cigarette use in young people.

Introduction

Electronic cigarettes (ECs) are now the most common type of nicotine/tobacco product used by young people.^{1,2} Although they are not harm-free, ECs yield significantly *lower* concentrations of toxins and are likely less harmful to health than combustible cigarettes.^{3–9} However, health officials and researchers have voiced concerns that EC use *among adolescents and young adults* may increase use of more dangerous products like cigarettes, which could limit ECs' potential to reduce tobacco-related harm.^{9–12} Understanding the longitudinal associations between EC and cigarette use among young people thus has critical implications for public health.

A growing body of evidence suggests that EC use is associated with subsequent cigarette use in young people, despite considerable methodological differences across studies.^{13–20} For example, a recent meta-analysis of nine studies, with follow-up periods ranging from 6 to 18 months and sample ages ranging from 14 to 30 years old, found that baseline never-smokers who used ECs had greater odds of initiating cigarette smoking at follow-up.¹³ Similarly, in a sample of cigarette-naïve college students (ages 18–25) followed across four timepoints over 1.5 years, EC use at wave 1 significantly increased the likelihood of initiating cigarette use across subsequent waves.²¹ In a very different sample of cigarette-naïve high school students (ages 14–18) followed across three timepoints over 2 years, EC use was associated with subsequent cigarette use (*any* past-month use), although cigarette use was *not* associated with future EC use.²²

Cross-sectional research also suggests that concurrent or “dual” use of ECs and cigarettes is common among youth,^{1,23,24} and more frequent EC use is associated with more frequent smoking among dual users.^{25,26} However, less is known about covariation of EC and cigarette use across time, and findings from past studies are mixed. Consistent with studies of smoking onset, some work has shown that EC use is prospectively associated with subsequent escalation in cigarette use. For example, a recent study of young adult non-daily smokers, followed more than 12 months across five timepoints, found that EC use at one timepoint predicted greater frequency and quantity of cigarette smoking in the future.²⁷ In contrast, other work suggests that *cigarette use* in young people may *prospectively predict greater EC use in the future*. A 4-year longitudinal study of young adults (ages 19–23), most (81%) of whom had previously smoked at baseline, examined reciprocal longitudinal associations between *frequency* of past-month EC and cigarette use more than four timepoints and found that cigarette use significantly predicted subsequent EC use; however, EC use did *not* predict subsequent cigarette use.²⁸ This highlights the importance of examining bidirectional associations between EC and cigarette use over time, particularly in samples of older adolescents or young adults who may have already begun experimenting with these products and may be at risk for progressing toward more established use.

At the same time, data also suggest that both EC and cigarette use are associated with similar demographic and psychosocial risk factors, including mental health^{25,29–31} and risky behaviors, such as alcohol and marijuana use.^{25,31–34} Such shared risk factors have been proposed as another explanation^{35,36} for observed associations between EC use and cigarette smoking. Some data suggest that accounting for shared risk factors may attenuate or account for associations between EC use and later cigarette use. For example, a longitudinal study of high school students in Hawaii found that potential mediating variables, including marijuana use, largely accounted for effects of EC use on subsequent cigarette use.³⁷ Accordingly, researchers have called for studies to examine effects of potential

“third” variables such as mental health and other substance use on longitudinal associations between EC use and cigarettes use.³⁶

Another critical methodological issue that has yet to be addressed in this emerging literature is the way in which longitudinal associations between EC and cigarette use are statistically modeled. Common methods for testing reciprocal longitudinal associations between variables (eg, auto-regressive, cross-lagged [ARCL] models) typically yield cross-lagged estimates that represent a combination of both between- and within-person variation.³⁸ These estimates are difficult to interpret and assume that between- and within-person effects are identical. However, *within- and between-person effects are two substantively different levels of analysis* with very different implications. *Between-person effects* provide information on changes in use compared to peers (ie, grand mean) and thus measure trait-like deviations in use. In contrast, *within-person effects* provide information on changes in one's “typical” level (ie, individual mean) of use and measure state-like, time-variant deviations in use.³⁸ Ignoring these distinctions, and conflating between- and within-person variation, may mischaracterize associations between EC use, smoking, and other variables. Recent advances in modeling of longitudinal data can address these limitations. For example, the auto-regressive latent trajectory with structured residuals (ALT-SR)^{38–41} improves prediction by allowing for simultaneous modeling of *between-person* relations among variables of interest (eg, trait-like aspects such as mean levels, growth rates), while also modeling reciprocal relations among variables *within-individuals* over time. This allows for each individual to serve as his/her own control (ie, effectively controlling for all time-invariant variables), and thus strengthens internal validity of reciprocal effects being examined. Disentangling within- and between-person levels of analysis and comparing findings against those from models that *conflate* within- and between-person effects may help to clarify ways in which traditional methods may (or may not) mischaracterize longitudinal associations between EC use, cigarette use, and shared risk factors.

This study addresses gaps in the literature on EC and cigarette use trajectories in young people by using longitudinal data from a large, ethnically diverse California cohort (ages 16–20) to examine reciprocal longitudinal associations between frequency of EC use and cigarette use across three timepoints. We extend prior research in this area by using novel statistical methods (ALT-SR models) to disentangle within- and between-person effects and assessing the impact of shared risk factors (alcohol and marijuana use, mental health symptoms) on longitudinal associations between EC and cigarette use. To illustrate similarities and differences between modeling approaches and interpretations, we compare findings from ALT-SR models against those of ARCL models, which do not distinguish within- and between-person levels of analysis.

Methods

Procedure

Participants were from two cohorts of students in sixth and seventh grade in 2008, followed through 2017. Adolescents ($n = 6509$) were initially recruited from 16 middle schools from three districts in the Los Angeles area as part of a substance use prevention program, CHOICE.⁴² Procedures are reported in detail in the prevention trial.⁴² Briefly, participants completed wave 1 (fall 2008) to wave 5 (spring 2011) during physical education classes. Follow-up rates ranged from 74% to 90%, excluding new youth who could have come in at a subsequent wave. Participants transitioned from middle

schools to more than 200 high schools following wave 5 and were subsequently re-contacted and re-consented to complete annual Web-based surveys. At wave 6 (spring 2013 to spring 2014), 61% of the sample participated in the follow-up survey. At wave 7 (1 year later), we retained 80% of the sample, at wave 8 (1 year later; when most students had completed high school), we retained 90.5% of the sample, and at wave 9 we retained 89.6% of the sample. If a participant did not complete a wave of data collection, they were still eligible to complete all subsequent waves. That is, they did not “dropout” of the study once they missed a survey wave; rather we fielded the full sample at every wave so that all participants had an opportunity to participate in each individual survey. Failure to complete a certain wave was not significantly associated with demographics or risk behaviors, such as alcohol and marijuana use.⁴³ All study procedures were approved by the RAND Institutional Review Board.

Data on mental health, cigarette, alcohol, and marijuana use were collected from wave 1 forward, and we asked about EC use beginning in wave 7. We focus on a timeframe when data were collected on all variables across three timepoints, using data from waves 7–9 collected between 2015 and 2017. The final analytic sample included 2039 young people who provided data in waves 7, 8, and 9. Because data were set up in naturally occurring cohorts (age), we used an accelerated longitudinal cohort design. At wave 7, youth were between the ages of 16 and 18 and at wave 9 between 18 and 20. This creates a planned missing pattern of data whereby participants only contribute data during the three timepoints, yet we can model development from 16 to 20 years old.

Measures

E-Cigarette and Cigarette Use were assessed using items modified from the Monitoring the Future (MTF) survey,² which asked “During the past month (30 days), how many times have you used or tried [an electronic or e-cigarette, cigarettes]?” Items were rated on a seven-point scale (0 = none, 1 = 1 day, 2 = 2 days, 3 = 3–5 days, 4 = 6–9 days, 5 = 10–19 days, 6 = 20–30 days).

Mental Health was assessed using the five-item Mental Health Index (MHI-5),⁴⁴ which assessed frequency of current (past month) mental health symptoms (eg, “Been a very nervous person,” “Felt downhearted and blue”) on a scale from 0 = none of the time to 6 = all of the time. Items were reverse-scored such that higher scores indicated better overall mental health, summed, and transformed to a 0–100 scale.

Alcohol and Marijuana Use were assessed using items from MTF,² which asked “During the past month (30 days), how many times/days have you used or tried [at least one drink of alcohol, marijuana]?” Items were rated on a scale from 0 = none to 6 = 20–30 days.

Sociodemographic Characteristics included biological sex (male, female), education, race/ethnicity (White, Hispanic/Latino(a), Black, Asian/Pacific Islander, other), and mother’s educational attainment, which was used as a proxy for socioeconomic status.

Data Analysis

To understand variation across longitudinal cross-lagged approaches, we fit a series of ARCL and ALT-SR models. First, we fit a taxonomy of ARCL models, which do *not* partition the variance at both within- and between-person levels of analysis, that assessed (1) the cross-lagged association between cigarette and EC use from 16 to 20 years old and (2) how shared risk factors, such as alcohol use,

marijuana use, and mental health, influence cigarette and EC use. We used model constraints that fixed effects of all third variables to zero, allowing the model to only estimate associations between cigarette and EC use. To understand effects of third variables on cigarette and EC use, we lifted constraints and allowed all variances, covariances, and cross-lagged associations to be estimated. We ran three separate models corresponding to the three third variables of interest: alcohol, marijuana, and mental health.

To partition within- and between-person variance, we fit a taxonomy of ALT-SR models. Within the ALT-SR framework, traditional between-person components are captured by latent factor means and covariances. The covariance between our latent growth factors (eg, intercepts and random slopes) extracts the disaggregated between-person effect (represented by φ standardized below), thus pushing the remaining variance into the residual cross-lagged portion of the model. Thus, the cross-lagged and auto-regressive components of this model represent within-person deviations from one’s own typical (or mean) trajectory.

We used a model-building process that allowed us to test for quadratic effects and any potential piecewise growth processes. We found that a linear growth function for all variables of interest fitted the data best. Fit statistics assessed improvement in model specification. We used a comparative fit index of 0.95 or greater, root mean square error of approximation (RMSEA) of 0.05 or less, and standardized root mean square residual (SRMR) of less than 0.08 to indicate good model fit. Use of ECs, cigarettes, alcohol, and marijuana, as well as mental health symptoms, were observed variables at each timepoint. To address missing data, we used the full information maximum likelihood estimator, treating all observed predictors as single-item latent variables. To adjust for any non-normality, all standard errors were bootstrapped (iterations = 5000). Frequency of EC, cigarette, alcohol, and marijuana use was treated as a continuous variable. All models controlled for participant self-reported biological sex, race/ethnicity, mother’s education, and intervention assignment. Analyses were conducted in Mplus version 8.⁴⁵

Results

Sample

The sample was 44% male, 45% Hispanic, 20% White, 21% Asian, 10% multi-ethnic, 2% Black, and 1% other races/ethnicities, and most respondents (55%) reported that their mother had a college degree or higher. Average age was 19.3 ($SD = 0.75$), and 84% were in college or trade school at wave 9. Table 1 shows descriptive information for EC, cigarette, alcohol, and marijuana use, as well as MHI-5 scores for the sample across waves.

ARCL Model Results

Results from ARCL models that estimated EC and cigarette use, while constraining effects of our third variables of interest, indicated a full cross-lagged association between EC and cigarette use from 16 to 20 years old. In addition, when paths for alcohol use were unconstrained, we found full cross-lagged associations between cigarette use and EC use (see Table 2). For example, in Table 2, in the Cross-lag paths rows within the Alcohol column, reporting higher cigarette use is associated with greater EC use ($\beta = 0.17$) and reporting higher EC use is associated with greater cigarette use ($\beta = 0.09$). Youths who reported higher cigarette use than their peers also reported greater alcohol use ($\beta = 0.11$) and vice versa ($\beta = 0.05$).

Table 1. Descriptive Data for e-Cigarette Use, Cigarette Use, Alcohol Use, Marijuana Use, and Mental Health in Waves 7–9

	Wave 7	Wave 8	Wave 9
	%/Mean (SD)	%/Mean (SD)	%/Mean (SD)
Age	17.28 (0.68)	18.29 (0.79)	19.33 (0.75)
Any lifetime e-cigarette use	25.49	37.16	43.11
Past-month e-cigarette use			
Any past-month use	7.92	9.78	8.62
Frequency of past-month use ^a			
1 day	34.16	29.65	28.00
2 days	23.60	17.09	14.29
3–5 days	18.63	14.57	16.00
6–9 days	8.07	12.06	9.14
10–19 days	6.83	11.56	6.86
20–30 days	8.70	15.08	25.71
Any lifetime cigarette use	30.13	38.38	45.54
Past-month cigarette use			
Any past-month use	5.70	8.55	11.82
Frequency of past-month use ^a			
1 day	37.93	29.31	33.75
2 days	16.38	19.54	14.17
3–5 days	19.83	15.52	20.00
6–9 days	6.90	8.62	6.67
10–19 days	11.21	12.07	11.67
20–30 days	7.76	14.94	13.75
Past-month alcohol use			
Any past-month use	27.82	38.67	46.62
Frequency of past-month use ^a			
1 day	33.81	33.76	29.28
2 days	22.12	21.53	20.30
3–5 days	21.77	21.78	25.37
6–9 days	12.74	12.23	13.64
10–19 days	8.32	7.52	9.09
20–30 days	1.24	3.18	2.33
Past-month marijuana use			
Any past-month use	15.63	22.77	27.93
Frequency of past-month use ^a			
1 day	27.36	24.41	23.63
2 days	15.41	14.04	13.40
3–5 days	16.35	17.28	18.17
6–9 days	13.52	9.29	8.64
10–19 days	7.86	12.53	11.99
20–30 days	19.50	22.46	24.16
Mental health symptoms			
MHI-5 score ^b	66.06 (20.51)	65.39 (20.51)	64.27 (21.06)

MHI-5 = five-item Mental Health Index.

^aAmong past-month users.^bScores range from 0 to 100.

Higher EC use was predictive of increased alcohol use the next year ($\beta = 0.08$), but not vice versa ($\beta = 0.02$). Figure 1 illustrates the pathways examined in the final ARCL “third variable” model for marijuana use. Similar to the alcohol model, cross-lagged associations between cigarette and EC use remained when paths for marijuana use were unconstrained (see Table 2, Cross-lag paths rows within the Marijuana column). However, results varied slightly for marijuana compared with alcohol use. Youths reporting higher EC use than their peers also reported greater marijuana use, and vice versa. Unlike alcohol, higher cigarette use was not predictive of subsequent marijuana use, although youth reporting higher marijuana use also reported increased cigarette use the next year. In the final ARCL model for mental health, the full cross-lagged association between EC and cigarette use remained (Table 2, Cross-lag paths rows

within the Mental health column). Further, greater cigarette use was associated with poorer mental health, and in turn, poorer mental health predicted greater cigarette use. No associations were found between mental health and EC use.

ALT-SR Model Results: Between-Person Associations

In an initial ALT-SR model excluding third variables, the between-person association for EC and cigarette use was moderate–strong ($\phi_{\text{standardized}} = 0.81$). In the final models that included third variables of interest, we observed significant between-person associations between intercepts for EC, cigarette use, and third variables (see Table 2, ALT-SR models: Between-person covariances rows). For example, in the final model including alcohol use (Table 2, Between-person covariances rows within the Alcohol column), we found that

Table 2. Results From Final ARCL and ALT-SRThird Variable Models

	Third variable models		
	Alcohol	Marijuana	Mental health (MHI-5)
	Parameter estimate (SE)	Parameter estimate (SE)	Parameter estimate (SE)
ARCL models			
Within-time correlations			
Cigarette with E-cigarette	0.17 (0.03)*	0.17 (0.03)*	0.17 (0.03)*
Cigarette with Third Var	0.21 (0.03)*	0.18 (0.03)*	−0.00 (0.00)
E-cigarette with Third Var	0.17 (0.02)*	0.21 (0.03)*	0.00 (0.01)
Auto-regressive paths			
Cigarette	0.58 (0.06)*	0.59 (0.06)*	0.60 (0.05)*
E-cigarette	0.44 (0.05)*	0.43 (0.05)*	0.44 (0.04)*
Third variable	0.43 (0.03)*	0.53 (0.03)*	0.42 (0.02)*
Cross-lag paths			
Cigarette → E-cigarette	0.17 (0.04)*	0.17 (0.04)*	0.18 (0.04)*
E-cigarette → Cigarette	0.09 (0.04)*	0.09 (0.04)*	0.10 (0.03)*
Cigarette → Third Var	0.11 (0.04)*	0.09 (0.05)	−0.02 (0.01)*
Third Var → Cigarette	0.05 (0.01)*	0.03 (0.01)*	−0.08 (0.03)*
E-cigarette → Third Var	0.08 (0.03)*	0.11 (0.05)*	0.00 (0.01)
Third Var → E-cigarette	0.02 (0.01)	0.03 (0.01)*	0.01 (0.03)
Fit statistics			
CFI	.94	.94	.92
TLI	.90	.91	.88
RMSEA	.04	.03	.05
SRMR	.05	.06	.06
Chi-square	395.1	340.7	455.7
df	90	90	90
ALT-SR models			
Intercepts			
Cigaretteint	2.12 (0.13)*	1.20 (0.05)*	2.11 (0.13)*
E-Cigaretteint	4.73 (1.80)*	1.26 (0.05)*	5.30 (2.60)*
Third Varint	2.62 (0.24)*	2.90 (0.20)*	4.56 (0.15)*
Between-person covariances			
Cigaretteint with E-Cigaretteint	0.90 (0.30)*	0.47 (0.08)*	0.56 (0.72)*
Cigaretteint with Third Varint	0.48 (0.06)*	0.37 (0.10)*	−0.18 (0.05)*
E-Cigaretteint with Third Varint	0.66 (0.31)*	0.20 (0.08)*	−0.17 (0.20)
Residual covariances			
Cigarette€it 1-5	0.99 (0.01)*	0.31 (0.03)*	0.99 (0.01)*
E-Cigarette€it 1-5	0.82 (0.14)*	0.05 (0.05)	0.78 (0.23)*
Third Var€it 1-5	0.92 (0.02)*	0.95 (0.35)*	0.98 (0.01)*
Within-time correlations			
Cigarette with E-cigarette	0.34 (0.03)*	0.20 (0.02)*	0.35 (0.03)*
Cigarette with Third Var	0.19 (0.03)*	0.21 (0.05)*	0.04 (0.03)
E-cigarette with Third Var	0.13 (0.03)*	0.05 (0.04)	0.01 (0.03)
Auto-regressive paths			
Cigarette	0.19 (0.04)*	0.20 (0.04)*	0.19 (0.04)*
E-cigarette	0.42 (0.04)*	0.42 (0.04)*	0.43 (0.04)*
Third variable	0.16 (0.06)*	0.36 (0.08)*	0.15 (0.03)*
Within-person cross-lag paths			
Cigarette → E-cigarette	0.16 (0.04)*	0.17 (0.04)*	0.17 (0.42)*
E-cigarette → Cigarette	0.13 (0.03)*	0.12 (0.03)*	0.14 (0.03)*
Cigarette → Third Var	0.02 (0.06)	0.12 (0.10)	0.94 (0.80)
Third Var → Cigarette	0.01 (0.02)	0.02 (0.02)	0.00 (0.02)
E-cigarette → Third Var	0.09 (0.05)	−0.17 (0.10)	0.13 (0.07)
Third Var → E-cigarette	0.01 (0.02)	−0.04 (0.02)	0.01 (0.02)
Fit statistics			
CFI	.92	.91	.92
TLI	.87	.86	.89
RMSEA	.04	.04	.04
SRMR	.08	.08	.08
Chi-square	562.6	540.7	556.9
df	106	102	102

All models controlled for participant self-reported biological sex, race/ethnicity, mother's education, and intervention status at wave 1.

All models displayed here are final models with all within-time correlations, auto-regressive paths, and cross-lagged effects being estimated. Each column represents the final model for our specific third variables (or shared risk factor) of interest such as alcohol use, marijuana use, and mental health problems. When interpreting results, "third var" is represented by the specific shared variables of interest. For example, one would interpret "third var" as alcohol use when interpreting regression coefficients under the "alcohol" model.

ARCL = auto-regressive cross-lag; ALT-SR = auto-regressive latent trajectory with structured residuals; SE = standard error; CFI = Comparative Fit Index; MHI-5 = five-item Mental Health Index; RMSEA = root mean square error of approximation; TLI = tucker-lewis index; SRMR = standardized root mean square residual; Third Var = entering alcohol, marijuana, or mental health; → represents directional regression coefficient. For example "Cigarette → E-Cigarette" represents the effect of cigarette use predicting E-cigarette use the following year.

* $p < .05$.

individuals reporting more frequent cigarette use also used ECs (Cigaretteint with E-Cigaretteint: $\varphi_{\text{standardized}} = 0.90$) and alcohol (Cigaretteint with Third Varint: $\varphi_{\text{standardized}} = 0.48$) more often. Further, individuals engaging in more EC use also reported higher alcohol use ($\varphi_{\text{standardized}} = 0.66$). Figure 2 provides an illustrative example of the pathways for the final ALT-SR “third variable” models, in this case displaying the model including marijuana use. In the final ALT-SR model including marijuana use, we observed significant between-person associations between higher EC use, cigarette use, and marijuana use (Table 2, Between-person covariances rows within the Marijuana column; Figure 2). For mental health,

we found similar results for between-person associations with EC and cigarette use. However, we found a small between-person negative association for cigarette use and mental health, indicating that poorer mental health is associated with greater cigarette use. No such association was found between EC use and mental health (Table 2, Between-person covariances rows within the Mental health column).

ALT-SR Model Results: Within-Person Associations

Positive auto-regressive relations were evident across EC use, cigarette use, and third variables of interest (alcohol, marijuana, mental health) across all final ALT-SR models (Table 2, ALT-SR models:

Figure 1. ARCL model displaying cross-lagged effects for the final model for e-cigarette, cigarette, and marijuana use. Bold lines indicate significant paths, dashed lines represent nonsignificant paths. Significant parameter estimates (standard error) are shown. Full parameter estimates can be found in Table 2. Ecig = e-cigarette, Cig = cigarette, MJ = marijuana. Each timepoint represents a year lag (eg, Ecig16 to Cig17 represents e-cigarette use at age 16 to cigarette use at age 17). In this model, we constrained cross-lagged effects to be equal across time based on -2 log likelihood ratio tests comparing constrained versus unconstrained parameter estimates.

Figure 2. Auto-regressive latent trajectory with structured residual model displaying within-person cross-lagged effects for the final model between electronic cigarette, cigarette, and marijuana use. Solid lines indicate significant paths, dashed lines represent nonsignificant paths. Significant parameter estimates (standard error) are shown. Full parameter estimates can be found in Table 2. Ecig = e-cigarette, Cig = cigarette, MJ = marijuana. Each timepoint represents a year lag (eg, Ecig16 to Cig17 represents e-cigarette use at age 16 to cigarette use at age 17). In this model, we constrained cross-lagged effects to be equal across time based on -2 log likelihood ratio tests comparing constrained versus unconstrained parameter estimates.

Auto-regressive paths rows). These auto-regressive paths represent remaining variance after accounting for systematic growth functions. Next, we estimated cross-lagged associations between variables. As displayed in Table 2 in the Within-person cross-lag paths rows for the ALT-SR models, we found continued support for a bidirectional association between EC and cigarette use in all final third variable models, whereby individuals reporting higher EC use than their typical use (or individual mean) trajectory also had higher cigarette use than their typical average the following year in age (and vice versa). In contrast to the ARCL models and the between-person effects observed in the ALT-SR models, we found no support for any bidirectional or unidirectional within-person associations between EC or cigarette use and alcohol use, marijuana use, or mental health (see Table 2 and Figure 2 for Marijuana model example).

Discussion

To our knowledge, this is the first study to disentangle within- and between-person effects in EC and cigarette use trajectories in young people. Using both ARCL models, a commonly used approach in trajectory analyses that *does not* differentiate within- and between-person levels of analysis, and ALT-SR models that disentangle within- and between-person effects, we found significant, reciprocal associations between EC and cigarette use. In both types of models, more frequent EC use at one timepoint predicted more frequent cigarette use at the next timepoint, and vice versa. The current study extends prior work indicating positive longitudinal associations between EC and cigarette use^{21,22,27} by showing that these associations are evident at both the within- and between-person levels: in ALT-SR models, between-person effects indicated that more frequent EC use than one's peers predicted more frequent use of cigarettes, and vice versa; within-person effects showed that, for a given person, increases in one's EC use from 1 year to the next predicted subsequent escalation in cigarette use, and vice versa.

Our findings complement those of previous studies examining EC and smoking onset, which suggest that EC use is associated with greater likelihood of future cigarette initiation.^{13,21,22} Of note, the within-person effects described here reflect changes in one's "typical" level of use (ie, individual mean) over time, with each individual serving as his/her own control. Although we did not explicitly test for product initiation (ie, transitioning from a nonsmoker to a smoker), the observed effect of EC use on subsequent increases in cigarette use applies to both baseline users and nonusers in the sample; for those individuals who were cigarette-naïve at baseline, this suggests that increasing one's EC use predicts future cigarette initiation. Such convergent findings across model type and level of analysis, and across studies with considerable methodological differences, reinforce confidence that EC use among youth is prospectively associated with greater cigarette use in the future. Further, that we observed reciprocal longitudinal associations between frequency of using both products suggests that *young people* who use both ECs and cigarettes may progress toward heavier use of both products over time, rather than "switching" to or substituting ECs for cigarettes.³ This is consistent with data from recent studies showing that EC use among adolescent cigarette experimenters (ages 12–17) was associated with subsequent progression to current established smoking⁴⁶; that frequency of EC use predicted smoking heaviness and frequency 6 months later in a sample of 10th grade students (including both smokers and nonsmokers at baseline)⁴⁷; and that EC use predicted more frequent cigarette use over time in young adult

nondaily smokers.²⁷ Progression toward more frequent use of ECs and cigarettes over time could increase total nicotine consumption and risk of nicotine dependence and associated harms as adolescents transition into young adulthood. Thus, efforts to prevent and reduce EC use among young people (eg, through informational campaigns, enacting and enforcing policies to limit youth access to ECs) may help to reduce use of more harmful tobacco products, as has been suggested by other researchers.^{11,13,21,22}

We also assessed contributions of three shared risk factors (alcohol use, marijuana use, mental health symptoms), which are known to correlate with EC and cigarette use. Using ARCL models, we found several significant cross-lagged effects of third variables on EC and cigarette use. For example, more frequent marijuana use at a given age prospectively predicted both more frequent EC use *and* cigarette use in the future. Such third variable effects are consistent with studies showing correlations between substance use and mental health symptoms and both EC and cigarette use^{25,29–31,48} and could be viewed as partial support for the role of shared risk factors in explaining observed associations between EC use and subsequent cigarette use trajectories in young people. This interpretation has implications for efforts to reduce use of nicotine products, such as suggesting that efforts to reduce other substance use and mental health symptoms in young people could in turn reduce escalation in both EC and cigarette use over time (however, note that this would presume a causal relationship between these variables, which cannot be concluded from the current study).

However, using ALT-SR models, different patterns emerged. At the between-person level, we observed associations between EC use, cigarette use, and each of the third variables examined, mirroring results from ARCL models. But at the within-person level, we observed *no effects* of third variables on either the direct associations between use of EC and later use of cigarette, or direct associations between use of cigarettes and later use of ECs. For example, more frequent marijuana use than one's peers was associated with more frequent EC and cigarette use than one's peers; however, reporting higher marijuana use from 1 year to the next (ie, relative to "typical" use) did not affect subsequent EC or cigarette use. In summary, the between-person findings suggest that shared risk factors are important in determining which youths use these products; however, our within-person findings suggest that, *for a given EC and/or cigarette user*, the shared risk factors examined here do not affect *trajectories of EC and cigarette use* (ie, progression toward more frequent use) *over time*. As such, efforts to reduce other risk factors, such as alcohol or marijuana use, may *not* curb EC and cigarette escalation in youth, at least among individuals who already use either product. Intervention efforts may therefore want to target factors specific to EC and cigarette products, such as taste/sensory factors or nicotine dependence, that may be driving heavier EC and cigarette use over time in an individual. This also suggests that efforts to prevent youth from initiating *any* nicotine and tobacco products (eg, limiting youths' access to EC and cigarette products, reducing exposure to product advertising) may be needed to mitigate the potential negative public health effects resulting from youth EC use.

Overall, findings suggest that, in some scenarios, different modeling approaches can lead to differences in how we interpret associations between variables of interest over time. In this study, both ARCL and ALT-SR models showed robust reciprocal associations between frequency of EC and cigarette use across time. With respect to the role of shared risk factors, ARCL models indicated that trajectories of both EC and cigarette use may be influenced by

other substances or mental health problems—suggesting that there are “other reasons” why youth are increasing their EC or cigarette use over time. The ALT-SR models similarly indicate that third variables are important and *partially* replicate the ARCL models in the between-person portion of the model, but support a more nuanced view. When examining within-person relationships, wherein cross-lagged effects reflect more developmentally appropriate estimates and answer questions of “individual level change,” third variables were not prospectively related to EC or cigarette use. This suggests that, in general, youth with more alcohol and marijuana use and poorer mental health may exhibit more EC or cigarette use; but, for a given person, higher EC use predicts higher cigarette use the next year in age (and vice versa), and no “third variables” examined here (alcohol, marijuana, mental health) account for this pattern of reciprocal escalation. This highlights the importance of disentangling within- and between-person effects when characterizing these longitudinal associations.

This study was subject to several limitations. For example, data were self-reported (although rates of EC, cigarette, and other substance use in the sample are largely consistent with those from national samples of youth²). In addition, we do not know type or nicotine content of the ECs used by respondents, which could affect the prospective association between EC use and heaviness of future EC and cigarette use.⁴⁹ Further, the study did not assess physiologic or genetic factors that may contribute to shared liabilities for EC and cigarette use. Finally, the current study examined covariation in frequency of EC and cigarette use over time in relation to other variables of interest; we did not explicitly assess *onset* of EC or cigarette use (ie, transitioning from a nonuser to a user). Future work is needed to address important questions surrounding EC and cigarette initiation—and discontinuation—over time, and the methods presented here can be readily adapted to assess binary status transitions.

Conclusions

Within- and between-person analyses revealed robust reciprocal associations between EC and cigarette use over time, with more frequent use of either product predicting more frequent use of both ECs and cigarettes in the future. These findings add to a growing body of literature suggesting that EC among youth is prospectively associated with greater cigarette use in the future and suggest a progression toward more frequent use of both products over time. Shared risk factors were significantly associated with EC and cigarette use at the between-person level, but did not affect trajectories of EC and cigarette use at the within-person level. Disentangling within- and between-person effects in longitudinal analyses has important implications for how data inform our understanding of adolescent EC and cigarette use and factors that influence patterns of use.

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Declarations of Interest

The authors have no conflicts of interest to declare.

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References

1. Jamal A, Gentzke A, Hu SS, et al. Tobacco use among middle and high school students—United States, 2011–2016. *MMWR*. 2017;66(23):597–603.
2. Johnston LD, O’Malley PM, Miech RA, Bachman JG, Schulenberg JE. *Monitoring the Future National Survey Results on Drug Use, 1975–2015: Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: Institute for Social Research; 2016.
3. Abrams DB, Glasser AM, Pearson JL, Villanti AC, Collins LK, Niaura RS. Harm minimization and tobacco control: reframing societal views of nicotine use to rapidly save lives. *Annu Rev Public Health*. 2018;39:193–213.
4. Farsalinos KE, Kistler KA, Gillman G, Voudris V. Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine Tob Res*. 2015;17(2):168–174.
5. Goniewicz ML, Knysak J, Gawron M, et al. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control*. 2014;23(2):133–139.
6. Hecht SS, Carmella SG, Kotandeniya D, et al. Evaluation of toxicant and carcinogen metabolites in the urine of e-cigarette users versus cigarette smokers. *Nicotine Tob Res*. 2015;17(6):704–709.
7. Shahab L, Goniewicz ML, Blount BC, et al. Nicotine, carcinogen, and toxin exposure in long-term e-cigarette and nicotine replacement therapy users: a cross-sectional study. *Ann Intern Med*. 2017;166(6):390–400.
8. Stephens WE. Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. *Tob Control*. 2018;27:10–17.
9. The National Academies of Sciences Engineering and Medicine. *Public Health Consequences of E-Cigarettes*. Washington, DC: The National Academies of Sciences Engineering and Medicine; 2018.
10. Glantz SA, Bareham DW. E-Cigarettes: use, effects on smoking, risks, and policy implications. *Annu Rev Public Health*. 2018;39:215–235.
11. Kong G, Krishnan-Sarin S. A call to end the epidemic of adolescent E-cigarette use. *Drug Alcohol Depend*. 2017;174:215–221.
12. Rigotti N. E-cigarette use and subsequent tobacco use by adolescents: new evidence about a potential risk of e-cigarettes. *JAMA*. 2015;314(7):673–674.
13. Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr*. 2017;171(8):788–797.
14. Barrington-Trimis JL, Urman R, Berhane K, et al. E-cigarettes and future cigarette use. *Pediatrics*. 2016;138(1):e20160379.
15. Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA*. 2015;314(7):700–707.
16. Miech R, Patrick ME, O’Malley PM, Johnston LD. E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students. *Tob Control*. 2017;26(e2):e106–e111.
17. Primack BA, Soneji S, Stoolmiller M, Fine MJ, Sargent JD. Progression to traditional cigarette smoking after electronic cigarette use among adolescents and young adults. *JAMA Pediatr*. 2015;169(11):1018–1023.
18. Spindle TR, Hiler MM, Cooke ME, Eissenberg T, Kendler KS, Dick DM. Electronic cigarette use and uptake of cigarette smoking: a longitudinal examination of U.S. college students. *Addict Behav*. 2017;67:66–72.
19. Unger JB, Soto DW, Leventhal A. E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. *Drug Alcohol Depend*. 2016;163:261–264.
20. Wills TA, Knight R, Sargent JD, Gibbons FX, Pagano I, Williams RJ. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tob Control*. 2017;26(1):34–39.

21. Loukas A, Marti CN, Cooper M, Pasch KE, Perry CL. Exclusive e-cigarette use predicts cigarette initiation among college students. *Addict Behav.* 2018;76:343–347.
22. Bold KW, Kong G, Carmenga DR, et al. Trajectories of e-cigarette and conventional cigarette use among youth. *Pediatrics.* 2017;141(1):e20171832.
23. Creamer MR, Perry CL, Harrell MB, Diamond PM. Trends in multiple tobacco product use, among high school students. *Tob Regul Sci.* 2015;1(3):204–214.
24. Dutra LM, Glantz SA. Electronic cigarettes and conventional cigarette use among US adolescents: a cross-sectional study. *JAMA Pediatr.* 2014;168(7):610–617.
25. Dunbar MS, Tucker JS, Ewing BA, et al. Frequency of e-cigarette use, health status, and risk and protective health behaviors in adolescents. *J Addict Med.* 2017;11(1):55–62.
26. Goniewicz ML, Leigh NL, Gawron M, et al. Dual use of electronic and tobacco cigarettes among adolescents: a cross-sectional study in Poland. *Int J Public Health.* 2016;61(2):1–9.
27. Doran N, Brikmanis K, Petersen A, et al. Does e-cigarette use predict cigarette escalation? A longitudinal study of young adult non-daily smokers. *Prev Med.* 2017;100:279–284.
28. Selya AS, Rose JS, Dierker L, Hedeker D, Mermelstein RJ. Evaluating the mutual pathways among electronic cigarette use, conventional smoking and nicotine dependence. *Addiction.* 2018;113(2):325–333.
29. Barrington-Trimis JL, Berhane K, Unger JB, et al. Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics.* 2015;136(2):308–317.
30. Leventhal AM, Strong DR, Sussman S, et al. Psychiatric comorbidity in adolescent electronic and conventional cigarette use. *J Psychiatr Res.* 2016;73:71–78.
31. Wills TA, Knight R, Williams RJ, Pagano I, Sargent JD. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents. *Pediatrics.* 2015;135(1):e43–e51.
32. Hughes K, Bellis MA, Hardcastle KA, et al. Associations between e-cigarette access and smoking and drinking behaviours in teenagers. *BMC Public Health.* 2015;15:244.
33. Kristjansson AL, Sigfusdottir ID. E-cigarette use and relations to tobacco and alcohol use among adolescents. *BMC Med.* 2015;13:103.
34. Pentz MA, Shin H, Riggs N, Unger JB, Collison KL, Chou CP. Parent, peer, and executive function relationships to early adolescent e-cigarette use: a substance use pathway? *Addict Behav.* 2015;42:73–78.
35. Etter JF. Gateway effects and electronic cigarettes [published online]. *Addiction.* 2017; doi:10.1111/add.13924
36. Kozlowski LT, Warner KE. Adolescents and e-cigarettes: objects of concern may appear larger than they are. *Drug Alcohol Depend.* 2017;174:209–214.
37. Wills TA, Gibbons FX, Sargent JD, Schweitzer RJ. How is the effect of adolescent e-cigarette use on smoking onset mediated: a longitudinal analysis. *Psychol Addict Behav.* 2016;30(8):876–886.
38. Berry D, Willoughby MT. On the practical interpretability of cross-lagged panel models: rethinking a developmental workhorse. *Child Dev.* 2017;88(4):1186–1206.
39. Curran PJ, Howard AL, Bainter SA, Lane ST, McGinley JS. The separation of between-person and within-person components of individual change over time: a latent curve model with structured residuals. *J Consult Clin Psychol.* 2014;82(5):879–894.
40. Davis JP, Merrin GJ, Berry DJ, Dumas TM, Hong JS, Smith DC. Examining within-person and between-person effects of victimization and social risk on cannabis use among emerging adults in substance-use treatment. *Psychol Addict Behav.* 2016;30(1):52–63.
41. Merrin GJ, Davis JP, Berry D, D'Amico EJ, Dumas TM. The longitudinal associations between substance use, crime, and social risk among emerging adults: a longitudinal within and between-person latent variables analysis. *Drug Alcohol Depend.* 2016;165:71–78.
42. D'Amico EJ, Tucker JS, Miles JN, Zhou AJ, Shih RA, Green HD Jr. Preventing alcohol use with a voluntary after-school program for middle school students: results from a cluster randomized controlled trial of CHOICE. *Prev Sci.* 2012;13(4):415–425.
43. D'Amico EJ, Tucker JS, Miles JN, Ewing BA, Shih RA, Pedersen ER. Alcohol and marijuana use trajectories in a diverse longitudinal sample of adolescents: examining use patterns from age 11 to 17 years. *Addiction.* 2016;111(10):1825–1835.
44. Berwick DM, Murphy JM, Goldman PA, Ware JE Jr, Barsky AJ, Weinstein MC. Performance of a five-item mental health screening test. *Med Care.* 1991;29(2):169–176.
45. Muthén L, Muthén B. *Mplus 6.11*. Los Angeles, CA: Muthén & Muthén; 2011.
46. Chaffee BW, Watkins SL, Glantz SA. Electronic cigarette use and progression from experimentation to established smoking. *Pediatrics.* 2018;141(4):e20173594.
47. Leventhal AM, Stone MD, Andrabi N, et al. Association of e-cigarette vaping and progression to heavier patterns of cigarette smoking. *JAMA.* 2016;316(18):1918–1920.
48. Creamer MR, Portillo GV, Clendennen SL, Perry CL. Is adolescent poly-tobacco use associated with alcohol and other drug use? *Am J Health Behav.* 2016;40(1):117–122.
49. Goldenson NI, Leventhal AM, Stone MD, McConnell RS, Barrington-Trimis JL. Associations of electronic cigarette nicotine concentration with subsequent cigarette smoking and vaping levels in adolescents. *JAMA Pediatr.* 2017;171(12):1192–1199.