

HHS Public Access

Author manuscript JAMA. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

JAMA. 2016 November 08; 316(18): 1918-1920. doi:10.1001/jama.2016.14649.

Association of e-Cigarette Vaping and Progression to Heavier Patterns of Cigarette Smoking

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E-cigarette vaping is reported by 37% of US 10th-grade adolescents¹ and is associated with subsequent initiation of combustible cigarette smoking.² Whether individuals who vape and

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Author Contributions: Dr Leventhal had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis *Concept and design:* Leventhal, Strong, Sussman, Audrain-McGovern. *Acquisition, analysis, or interpretation of data:* Leventhal, Stone, Andrabi, Barrington-Trimis, Sussman, Audrain-McGovern. *Drafting of the manuscript:* Leventhal, Andrabi *Critical revision of the manuscript for important intellectual content:* Leventhal, Stone, Barrington-Trimis, Strong, Sussman, Audrain-McGovern. *Statistical analysis:* Leventhal *Administrative, technical, or material support:* Stone, Andrabi *Study supervision:* Leventhal, Sussman, Audrain-McGovern

Additional Contributions: We thank Chih-Ping Chou, PhD, Jennifer B. Unger, PhD, Jonathan M. Samet, MD, MS (each with the Department of Preventive Medicine, University of Southern California, Keck School of Medicine, Los Angeles), and Nathanial Riggs, PhD (Department of Human and Family Development, Colorado State University, Ft Collins), for providing editorial feedback on drafts; each was compensated for his/her contribution. Drs Chou, Unger, and Riggs also provided consultation to assist with data collection.

transition to combustible cigarettes are experimenting or progress to more frequent and heavy smoking is unknown. In addition, because some adolescents use e-cigarettes as a smoking cessation aid,³ adolescent smokers who vape could be more likely to reduce their smoking levels over time. Therefore, associations of vaping with subsequent smoking frequency and heaviness pattern among adolescents were examined.

Methods

Respondents were students in 10 public high schools in Los Angeles County, California, enrolled in a longitudinal study approved by the University of Southern California institutional review board and detailed elsewhere.² This analysis used data from surveys administered during fall (baseline for this report) and spring (6-month follow-up) of 10th grade (2014-2015).

Surveys included e-cigarette and combustible cigarette use questions from prior research,^{1,2} Which were used to create variables for baseline vaping (never, prior [ever-vaper with no past 30-day vaping], infrequent [vaped 1-2 days during past 30 days], or frequent [vaped 3 days]), and baseline and follow-up past 30-day smoking frequency (nonsmoker, infrequent smoker [1-2 days], frequent smoker [3 days]) and heaviness (0, <1, 1, or 2 cigarettes per day on smoking days).

Generalized estimating equation ordinal (cumulative logit) logistic regression models were used to assess the association between baseline vaping and follow-up frequency or heaviness of smoking, with adjustment for baseline smoking frequency or heaviness using SAS (SAS Institute), version 9.3. The baseline vaping × baseline smoking interaction term was then added to test differential associations of baseline vaping with follow-up smoking by baseline smoking status. Each model was retested after adjusting for age, sex, ethnicity, highest parental education, whether the student lived with both parents, ever use of alcohol or drugs, ever use of any combustible tobacco product, family history of smoking, depressive symptoms (Cronbach $\alpha = .94$), UPPS Impulsive Behavior Scale lack of premeditation ($\alpha = .$ 94) and sensationseeking ($\alpha = .91$) subscales, delinquent behavior ($\alpha = .81$), peer smoking, smoking susceptibility ($\alpha = .87$), and smoking expectancies ($\alpha = .46$). Details on covariate measures are reported elsewhere.² Significance was .05 (2-tailed). See modeling details in Table 1.

Results

Among 4100 eligible students, 3396 (82.8%) provided assent and parental consent to enroll in the study. Data were obtained from 3282 students (96.6%) at baseline and 3251 (95.0%) at follow-up. Students with complete vaping and smoking data at both time points constituted the analytic sample (N = 3084;54.3% girls,47.3% Hispanic, baselinemean age, 15.5 years).

The prevalence rates of past 30-day vaping and smoking were low overall. Smoking frequency at follow-up was proportionately greater with successively higher levels of baseline vaping: never-vapers (infrequent smokers: 0.9%; frequent smokers: 0.7%), prior

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vapers (4.1% and 3.3%, respectively), infrequent vapers (9.0% and 5.3%), and frequent vapers (11.6% and 19.9%; Table 2). Similar trends were found for smoking heaviness.

Adjusting for baseline smoking, each increment higher on the 4-level baseline vaping frequency continuum was associated with proportionally higher odds of smoking at a greater level of frequency (odds ratio [OR], 2.17; 95% CI, 1.95-2.42) and heaviness (OR, 2.19; 95% CI, 1.85-2.58) by follow-up; associations persisted in covariate-adjusted analyses (Table 1).

The positive association between baseline vaping and follow-up smoking frequency was stronger among baseline nonsmokers (n = 2966; OR, 2.51; 95% CI, 2.30-2.75) than baseline infrequent (n = 63; OR, 1.47; 95% CI, 0.98-2.23) and frequent (n = 53; OR, 1.06; 95% CI, 0.72-1.55) smokers (P<.001 for interaction; Table 1 and Table 2). Similar trends were found for smoking heaviness (Table 1).

Discussion

In this study of adolescents, vaping more frequently was associated with a higher risk of more frequent and heavy smoking 6 months later. Adolescent smoking patterns overrepresented by more frequent vapers in this study (ie, weekly smoking, >2 cigarettes per day) have been previously linked with high risk of nicotine dependence during adulthood.⁵ Although some youth use e-cigarettes for cessation purposes,³ vaping was not associated with smoking reductions in baseline smokers. However, because reason for vaping was not assessed, further investigation is required.

The role of nicotine and generalizability of these results to other locations and ages, longer follow-up periods, and non– self-report assessments are unknown and merit further inquiry. The transition from vaping to smoking may warrant particular attention in tobacco control policy.

Acknowledgments

Funding/Support: This research was supported bygrants R01-DA033296 and P50-CA180905 from the National Institutes of Health.

Role of the Funder/Sponsor: The National Institutes of Health had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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	Parameter Estimate for Ass	ociation With Sr	noking Frequency or Heavine	ss at Follow-
	Frequency ^b		Heaviness ^c	
	Odds Ratio (95%CI)	P Value	Odds Ratio (95%CI)	P Value
Initial Models ^d				
Baseline smoking	4.30 (3.07-6.03) ^e	<.001	3.07 (2.40-3.93) ^f	<.001
Vaping (4-level continuum)	2.17 (1.95-2.42)	<.001 <i>g</i>	2.19 (1.85-2.58)	<.001g
Vaping (4-level continuum) \times smoking ^h	0.63 (0.53-0.73) ^e	<.001 ^g	$0.67 (0.61-0.76)^{f}$	<.001 ^g
Post hoc pairwise contrasts ^{i}				
Prior (vs never) vaper	4.61 (2.49-8.53)	<.001	5.01 (2.72-9.22)	<.001
Infrequent (vs never) vaper	6.60 (3.48-12.51)	<.001	8.80 (4.63-16.75)	<.001
Frequent (vs never) vaper	10.62 (6.46-17.46)	<.001	10.53 (5.33-20.83)	<.001
Infrequent (vs prior) vaper	1.43 (0.82-2.49)	.21	1.76 (0.93-3.31)	.08
Frequent (vs prior) vaper	2.30 (1.22-4.36)	.01	2.10 (1.14-3.88)	.02
Frequent (vs infrequent) vaper	1.61 (0.67-3.86)	.29	1.20 (0.59-2.41)	.62
Adjusted Models ^j				
Baseline smoking	1.64 (1.19-2.27) ^e	.003	$1.54(1.14-2.07)^{f}$.005
Vaping (4-level continuum)	1.37 (1.16-1.61)	<.001 ^g	1.26 (1.07-1.48)	.006 ^g
Vaping (4-level continuum) × smoking ^{h}	$0.82 (0.69-0.96)^{\mathcal{C}}$.02 ^g	$0.78 (0.71 - 0.86)^f$	<.001g
Post hoc pairwise contrasts ^{i}				
Prior (vs never) vaper	1.51 (0.78-2.93)	.22	1.44 (0.79-2.64)	.23
Infrequent (vs never) vaper	1.94 (0.97-3.91)	.06	2.02 (1.16-3.53)	.01
Frequent (vs never) vaper	2.64 (1.43-4.87)	.002	1.96 (1.12-3.41)	.02
Infrequent (vs prior) vaper	1.28 (0.73-2.27)	.39	1.40 (0.73-2.71)	.31
Frequent (vs prior) vaper	1.74 (0.94-3.22)	.08	1.36 (0.69-2.67)	.38
Frequent (vs infrequent) vaper	1.36 (0.56-3.30)	.50	0.97 (0.45-2.08)	.93

Ţ	Table 1			
Association of Baseline e-Cigarette	Vaping	With Smoking	at 6-Month	Follow-up ^a

^aScore tests for violation of proportional odds assumptions for all models were nonsignificant, supporting ordinal modeling. The variance inflation factor estimates were 2.2 or less for all regressors and covariates in tests of multicollinearity across all models. The range of quasi likelihood was 1103.4 to 1239.9 under the independence model criterion fit indices across all models.

^bOrdinal logistic regression generalized estimating equation (GEE) model of proportional odds for being at a higher smoking frequency outcome (ie, days smoked in the past 30 days; nonsmoker, 0; infrequent smoker [1-2 days], 1; frequent smoker [3 days], 2) accounting for clustering of data by school in sample with complete vaping and smoking frequency data (n = 3084).

^{*C*}Ordinal logistic regression GEE model of proportional odds for being at a higher smoking heaviness outcome (ie, cigarettes per day on smoking day in the past 30 days; no smoking, 0; <1 cigarette, 1; 1 cigarette, 2; 2 cigarettes, 3) accounting for clustering of data by school in sample with complete vaping, smoking frequency, and smoking heaviness data (n = 3052).

 $d_{\text{Initial models without interaction term include only vaping and respective baseline smoking variable as the sole regressors.}$

^eParameter estimate for the baseline 3-level continuous smoking frequency variable (no smoking vs infrequent smoking vs frequent smoking) or its interaction with baseline vaping.

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fParameter estimate for the baseline 4-level continuous smoking heaviness variable (0 vs <1 vs 1 vs 2 cigarettes) or its interaction with baseline vaping.

gStatistically significant (P<.05) following application of the Benjamini-Hochberg adjustment for multiple comparisons to control study-wise false discovery rate for parameter estimates of associations involving the 4-level vaping variables tested in primary models.

^hInteraction term added in subsequent model; parameter estimates for other regressors are from models excluding the interaction term.

Pairwise contrast estimates tested in separate models in which vaping was treated as a categorical indicator reported for descriptive purposes (all other elements of these models matched those applied in the parallel a priori models with the continuous vaping terms).

^JAdjusted for demographic, environmental, and psychosocial covariates described in the Methods. To address missing covariate data in adjusted models, 5 multiply-imputed data sets were generated, each with imputed values that were missing on covariates via the Markov-chain Monte Carlo

method with available covariate data.⁴ The parameter estimates from models in each imputed data set were pooled and presented as a single estimate. The available data for each covariate ranged across variables from 2678 to 3080.

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Prevalence of Cigarette Smoking at Follow-up by Baseline e-Cigarette Vaping in Overall Sample and by Baseline Smoking Status

		Baseline Vaj	oing Status ^a			
Follow-up Smoking Status	Overall Sample ^d	Never	Prior	Infrequent	Frequent	P Value
Frequency in overall sample b	3084	2075	730	133	146	
Nonsmokers	2933 (95.1)	2043 (98.5)	676 (92.6)	114 (85.7)	100 (68.5)	
Infrequent smokers	77 (2.5)	18 (0.9)	30 (4.1)	12 (9.0)	17 (11.6)	<.001 c
Frequent smokers	74 (2.4)	14 (0.7)	24 (3.3)	7 (5.3)	29 (19.9)	
Heaviness in overall sample ^d	3052	2054	723	130	145	
0 cigarettes per day	2904 (95.2)	2024 (98.5)	666 (92.1)	109 (83.9)	105 (72.4)	
<1 cigarette per day	66 (2.2)	11 (0.5)	29 (4.0)	14 (10.8)	12 (8.3)	0
1 cigarette per day	34 (1.1)	10 (0.5)	11 (1.5)	2 (1.5)	11 (7.6)	<.001
2 cigarettes per day	48 (1.6)	9 (0.4)	17 (2.4)	5 (3.9)	17 (11.7)	
Frequency in baseline nonsmokers	2966	2059	702	112	93	
Nonsmokers	2872 (96.8)	2034 (98.8)	659 (93.9)	100 (89.3)	79 (85.0)	
Infrequent smokers	55 (1.9)	15 (0.7)	27 (3.9)	8 (7.1)	5 (5.4)	<.001
Frequent smokers	39 (1.3)	10 (0.5)	16 (2.3)	4 (3.6)	9 (9.7)	
Frequency in baseline infrequent smokers	63	6	18	15	21	
Nonsmokers	38 (60.3)	5 (55.6)	14 (77.8)	11 (73.3)	8 (38.1)	
Infrequent smokers	14 (22.2)	2 (22.2)	2 (11.1)	3 (20.0)	7 (33.3)	$\mathcal{D}60$
Frequent smokers	11 (17.5)	2 (22.2)	2 (11.1)	1 (6.7)	6 (28.6)	
Frequency in baseline frequent smokers	55	7	10	9	32	
Nonsmokers	23 (41.8)	4 (57.1)	3 (30.0)	3 (50.0)	13 (40.6)	
Infrequent smokers	8 (14.6)	1 (14.3)	1 (10.0)	1 (16.7)	5 (15.6)	.83 <i>c</i>
Frequent smokers	24 (43.6)	2 (28.6)	6 (60.0)	2 (33.3)	14 (43.8)	

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^aData are expressed as No. or No. (%). The percentages reflect the proportion for the column by row grouping. Never-vaper was defined as a student who never used an e-cigarette at baseline; prior vaper, used e-cigarette but no vaping during past 30 days; infrequent vaper, used e-cigarettes on 3 or more days during past 30 days.

^bIndicates the No. of days smoked during past 30 days (nonsmoker, 0 days; infrequent smoker, 1-2 days; frequent smoker, 3 days).

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^c Calculated using the Spearman ρ test for linear association between 2 ordinal variables of vaping (never-vapers, 0; prior vapers, 1; infrequent vapers, 2; frequent vapers, 3) and smoking frequency (0, nonsmokers;1, infrequent smokers; 2, frequent smokers).

 $d_{\rm indicates}$ the No. of cigarettes per day on smoking days during the past 30 days.

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e Calculated using the Spearman p test for linear association between 2 ordinal variables of baseline vaping (0, never-vapers;1, prior vapers; 2, infrequent vapers; 3, frequent vapers) and smoking heaviness (0; 1, <1 cigarette; 2, a whole cigarette; 3, 2 cigarettes).