EXPOSURE TO TOXIC VOLATILE ORGANIC CHEMICALS FROM E-CIGARETTE USE IN ADOLESCENTS

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Disclosures

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Background

- E-cigarettes are marketed to promote cessation or harm reduction in adults.

Background

- Marketing strategies clearly have a broader population in mind.

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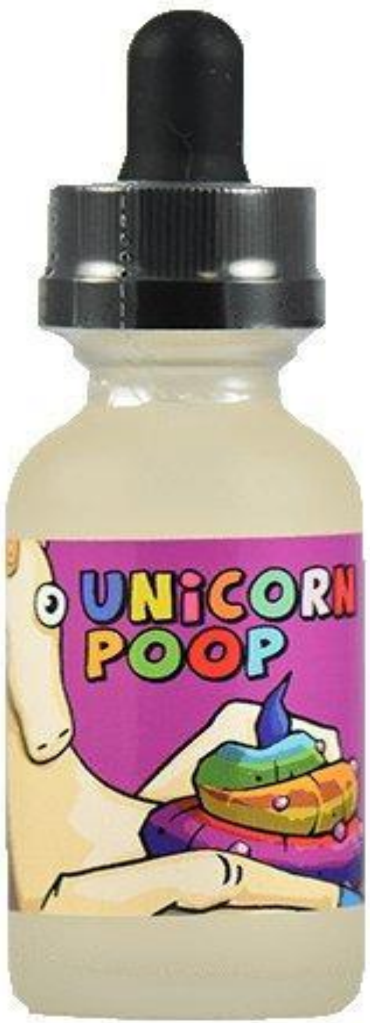
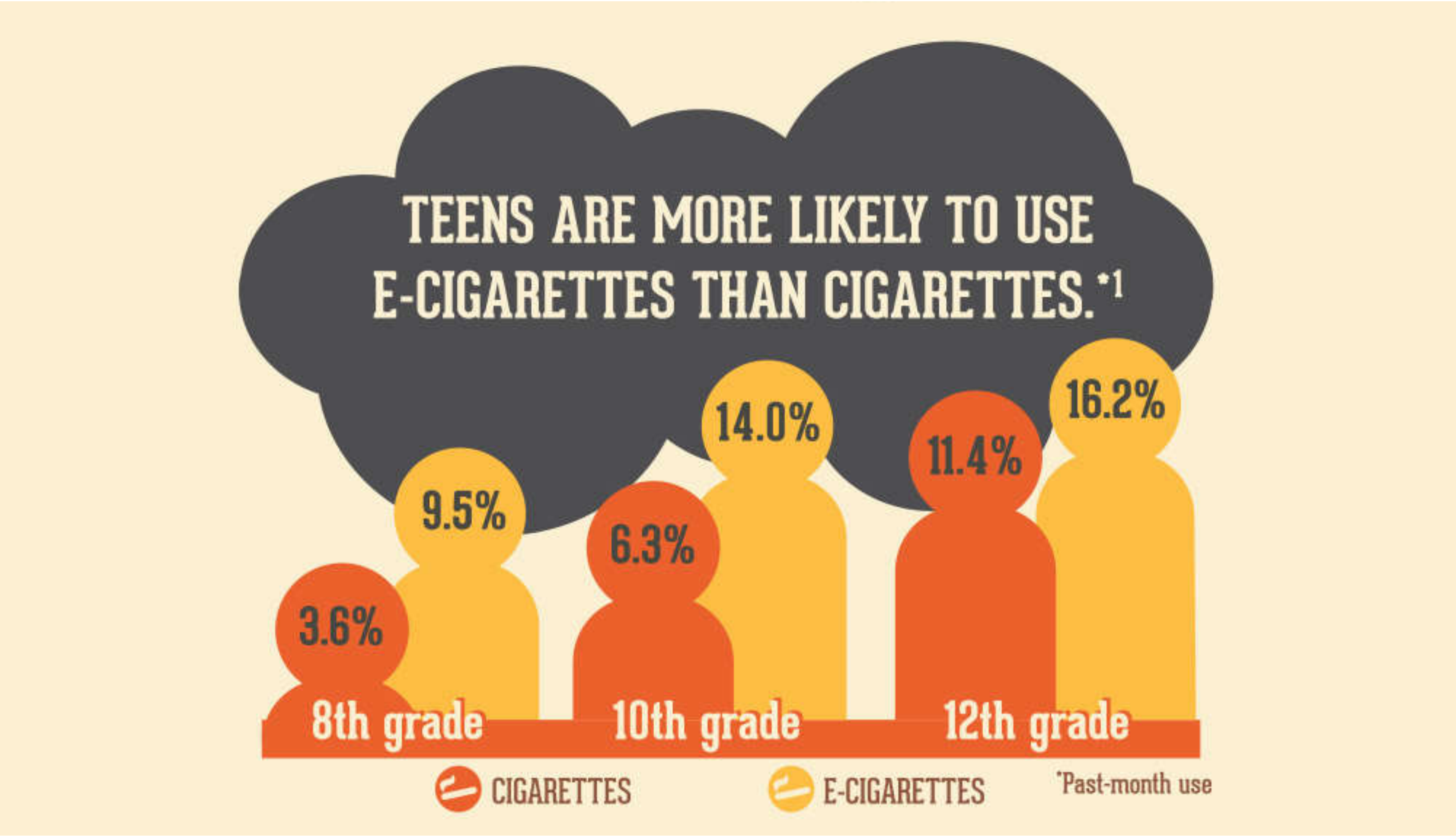


Background

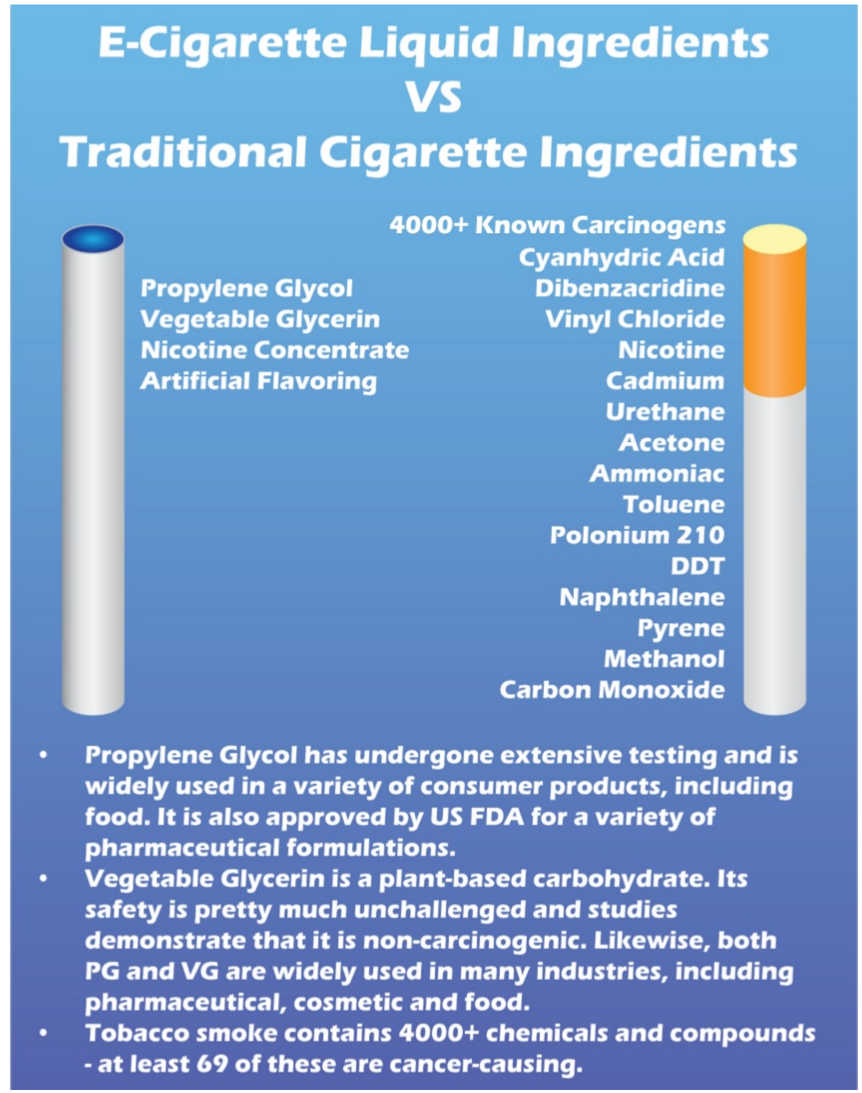
- Social influences and marketing strategies for these products have clearly had an effect on children.



Johnston, L. D., O'Malley, P. M., Miech, R. A., Bachman, J. G., & Schulenberg, J. E. (2016). Monitoring the Future national *survey* results on drug use*, 1975*-201*5:* Overview, *k*ey *f*indings on *a*dolescent *d*rug *u*se. Ann Arbor: Institute for Social Research, The University of Michigan.

Reasons for increased use

- Peer influence
- Enticing flavors
- Extensive marketing of e-cigarettes as safer.

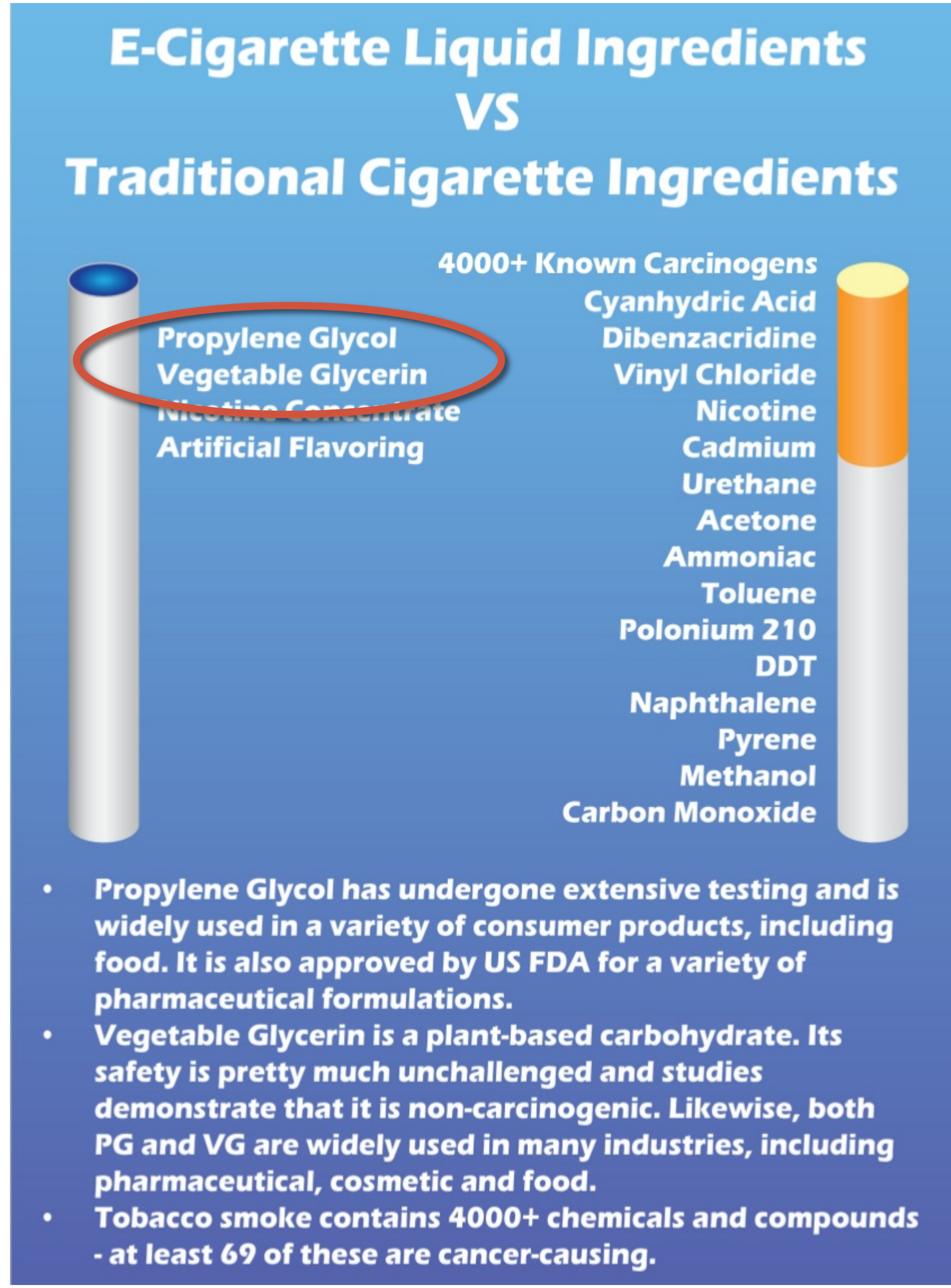


Safety

- Despite claims, there is uncertainty about the safety of e-cigarettes.
- By aerosolizing nicotine rather than combusting tobacco, e-cigarettes do produce fewer toxins.

Safety

- e-cigarettes contain additives and solvents, which can form carcinogenic compounds when heated.



Volatile Organic Compounds (VOC)

- When heated to vaporize:
  - **propylene glycol** can form the VOC **propylene oxide** (a carcinogen).[1]
  - **glycerol** forms **acrolein**,[2] which has been associated with lung cancer.[3]

[1] Laino T, Tuma C, Moor P, Martin E, Stolz S, Curioni A. Mechanisms of propylene glycol and triacetin pyrolysis. *J Phys Chem A.* May 10 2012;116(18):4602-4609.
[2] Henderson T, Clark C, Marshall T, Hanson R, Hobbs C. Heat degradation studies of solar heat transfer fluids. *Solar Energy.* 1981;27(2):121-128.
[3] Feng Z, Hu W, Hu Y, Tang MS. Acrolein is a major cigarette-related lung cancer agent: Preferential binding at p53 mutational hotspots and inhibition of DNA repair. *Proc Natl Acad Sci U S A.* Oct 17 2006;103(42):15404-15409.

Toxicants in adults

- There is some controversy on how usage patterns may affect exposure
- Data from adults show that these toxicants can be detected in the urine of ENDS users.*

*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.* Oct 21 2014.

Adolescent Use

- Currently no data on toxicant exposure in adolescent users.

Adolescence onset is riskier

- Exposure to toxicants during adolescence may result in greater harm given their **cumulative exposure** compared to adult onset users.

Goals

- Using a cross-sectional design, we sought to assess the presence of certain VOC toxicants linked to adolescent e-cigarette use and examine how specific patterns of use, may influence exposure.

METHODS

Participants

- Adolescent (aged 13-18) e-cigarette users (use in past 30 days and least 10 lifetime use episodes) were recruited from the San Francisco Bay area using fliers and online advertising.
- E-cigarette users who <u>only</u> use their devices to vaporize marijuana were excluded.

Baseline Visit

- Baseline appointments were scheduled within 24 hours from last use of their e-cigarettes.
- Surveys were completed including questions about use behaviors.
- Urine was collected for the measurement of the tobacco-specific nitrosamine NNAL and levels of metabolites of 8 volatile organic compounds (VOCs).
- Participants received $30.

Controls

- Specimens were also collected from 20 age-matched controls attending pediatric clinics at a Bay area public hospital with undetectable cotinine and NNAL confirming no e-cigarette or nicotine use.

Categories of Participants

- Three categories were developed based on a combination of reported e-cigarette and cigarette use and urine NNAL.

1) E-cigarette-Only users

- no traditional combustion cigarettes in past 30 days and NNAL <1 pg/mg creatinine

2) Dual Users

- use traditional cigarettes in the past 30 days in addition to e-cigarettes and NNAL > 30 pg/mg creatinine

3) Controls

- NNAL and cotinine below the limit of quantitation

Exclusion from Analyses

- We excluded from analyses participants who did not use e-cigarettes in the prior 24 hours.
- To create well-differentiated comparison groups, we also set an a priori exclusion from analyses participants with intermediate levels of NNAL (i.e., 1-29 pg/ml creatinine)

Measures to assess ENDS exposure

- Frequency of use:
  - days of use in past 30
  - number of sessions on each day in past week
- Flavor preferences
- Type of vape instrument (i.e. Mod, Juul, vape pen, or other)
- Nicotine content (if known)

Volatile Organic Compounds (VOCs)

- VOCs were measured in urine and expressed per mg of creatinine.
  1. Propylene oxide
  2. Acrolein
  3. Ethylene oxide
  4. Crotonadehyde
  5. Acrylonitrile
  6. Benzene
  7. Acrylamide
  8. 1,3, butadiene

RESULTS

Participants

- 386 adolescents were screened, 229 were found to be eligible and 180 agreed to participate.
- 29 admitted to not using an e-cigarette in the prior 24 hours and were excluded from analyses.
- 48 had levels of NNAL 1-29 ppm/mg creatinine, and per our a priori criteria, were excluded from analyses.
- The final sample consisted of 67 **E-cigarette-Only users**, 16 **Dual Users**, and 20 **Controls**.

Demographics

Characteristic	E-Cigarette-Only (n=67)	Dual Users (n=16)	Controls (n=20)	*p*
Age (years)[1]	16.3 (1.2)	17.1 (.96)	16.0 (1.8)	.06
% Male[2]	49 (73%)	12 (80%)	7 (35%)	<.01

1. Comparing 3 groups on age (Anova)
2. comparing 3 groups on sex (chi-square)

Demographics

Characteristic	E-Cigarette-Only (n=67)	**Dual Users (n=16)**	**Controls** (n=20)	*p*
Race/Ethnicity[1]				.06
White	36 (54%)	9 (67%)	0	
Asian/PI	12 (19%)	2 (12%)	2 (10%)	
Mixed race	10 (15%)	3 (19%)	0	
Hispanic	7 (10%)	2 (12%)	18 (90%)	

1. comparing 3 groups on sex (chi-square)

Flavors

E-cig characteristic	E-Cigarette-Only (n=67)	Dual Users (n=16)	*p*
Usual flavor			
fruit	37 (55%)	10 (67%)	.42
candy	11 (16%)	2 (13%)	.77
menthol	12 (18%)	2 (13%)	.67
tobacco	5 (8%)	2 (13%)	.46

Frequency of use

E-cig characteristic	E-Cigarette-Only (n=67)	Dual Users (n=16)	*p*
Hours from last use	1:58 (6:29)	2:02 (7:17)	.91
Days used in past 30	12.8 (8.9)	25.5 (6.6)	<.001
Sessions per day	2.0 (3.6)	8.4 (11.6)	<.05

Type of Device

E-cig characteristic	E-Cigarette-Only (n=67)	Dual Users (n=16)	*p*
Usual Device			
Vape pen	24 (36%)	6 (40%)	.82
Mod	17 (25%)	4 (27%)	
Juul	18 (27%)	4 (27%)	
Other/unsure	8 (12%)	1 (7%)	

Nicotine

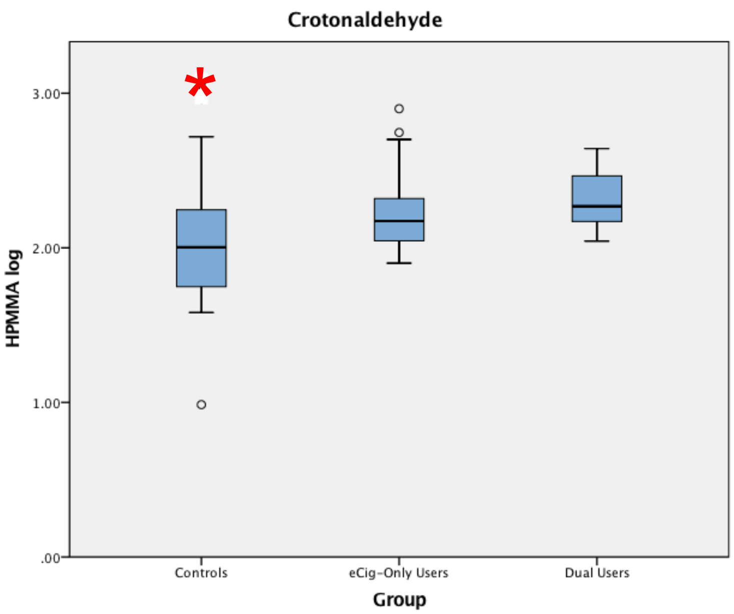
E-cig characteristic	E-Cigarette-Only (n=67)	Dual Users (n=16)	*p*
E-cigarettes contain nicotine			
Always	21 (31%)	9 (60%)	.06
Sometimes	26 (39%)	6 (40%)	
Unsure	10 (15%)	0 (0%)	
Never	10 (15%)	0 (0%)	

Toxicants (Median ng/mg of creatinine)

Toxin	Biomarker	control	e-cig only	Dual users
Benzene	PMA	0	0	.2**
1,3-Butadiene	MHBMA	0	0	0
Ethylene Oxide	HEMA	1.3	.5	1.0
Acrylonitrile	CNEMA	0**	1.3	59.4**
Acrolein	3-HPMA	192.8*	254.3	439.7*
Propylene Oxide	2-HPMA	15.2**	28.8	40.2
Acrylamide	AAMA	34.5**	67.3	235.6**
Crotonaldehyde	HPMMA	100.4*	148.7	185.4

*P<.05 ** p<.001 e-cig-only as comparison group using regression models of log-transformed values including planned covariates (sex, race/ethnicity)

Significant VOC exposure in E-cigarette Only vs. Controls and E-cigarette Only vs. Dual Users.

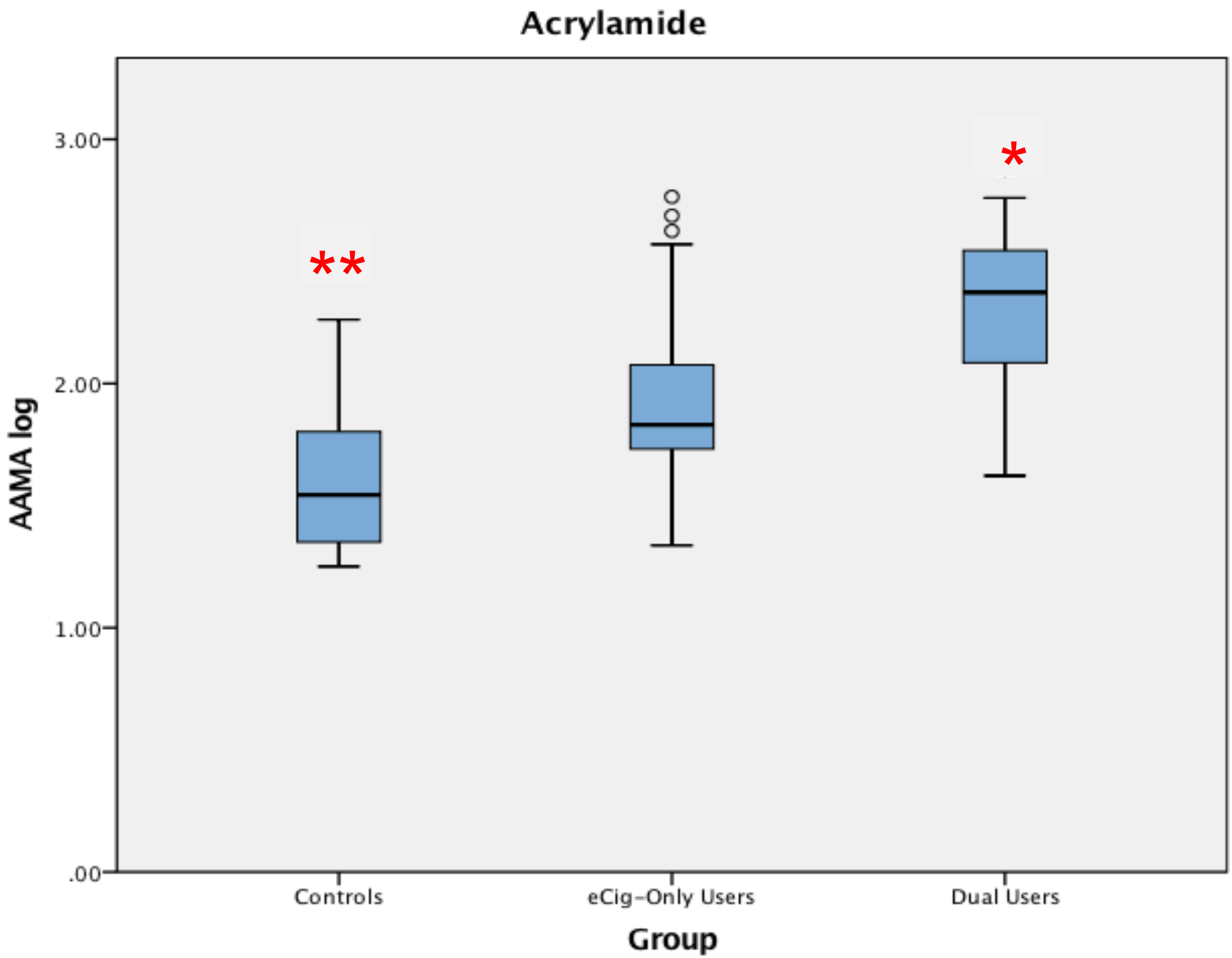


Tests based on regression models of shifted log-transformed values including planned covariates (sex, race/ethnicity) with contrasts between E-Cigarette-Only users versus Controls and E-Cigarette-Only users versus Dual Users.

Note: All comparisons are made with E-Cigarette-Only (eCig-Only) Users as comparison group.

* *p*<.05

** *p*<.001


Acrylamide
**
*
3.00
2.00
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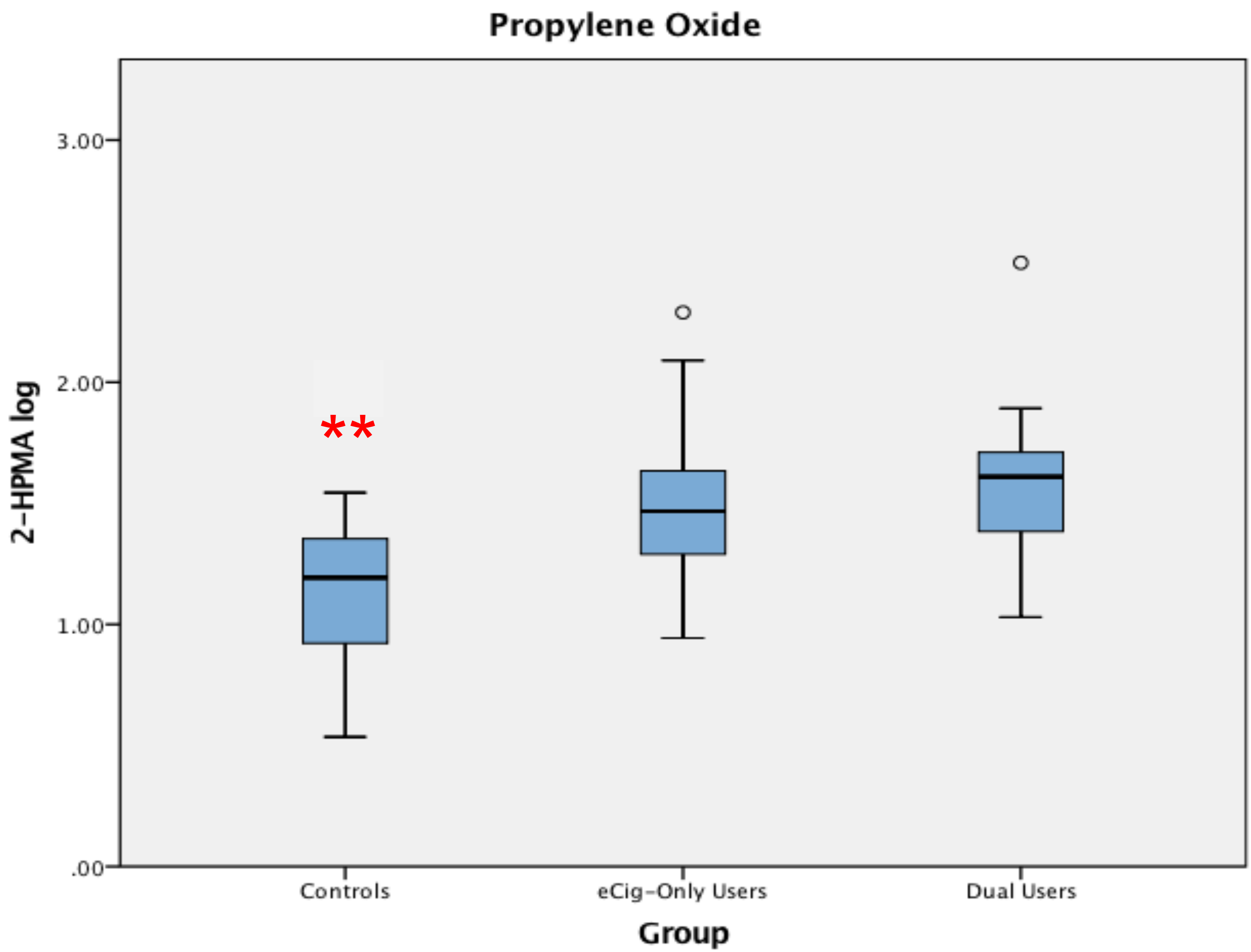
AAMA log
Controls
eCig-Only Users
Dual Users
Group

* $p<.05$ ** $p<.001$


Propylene Oxide
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2-HPMA log
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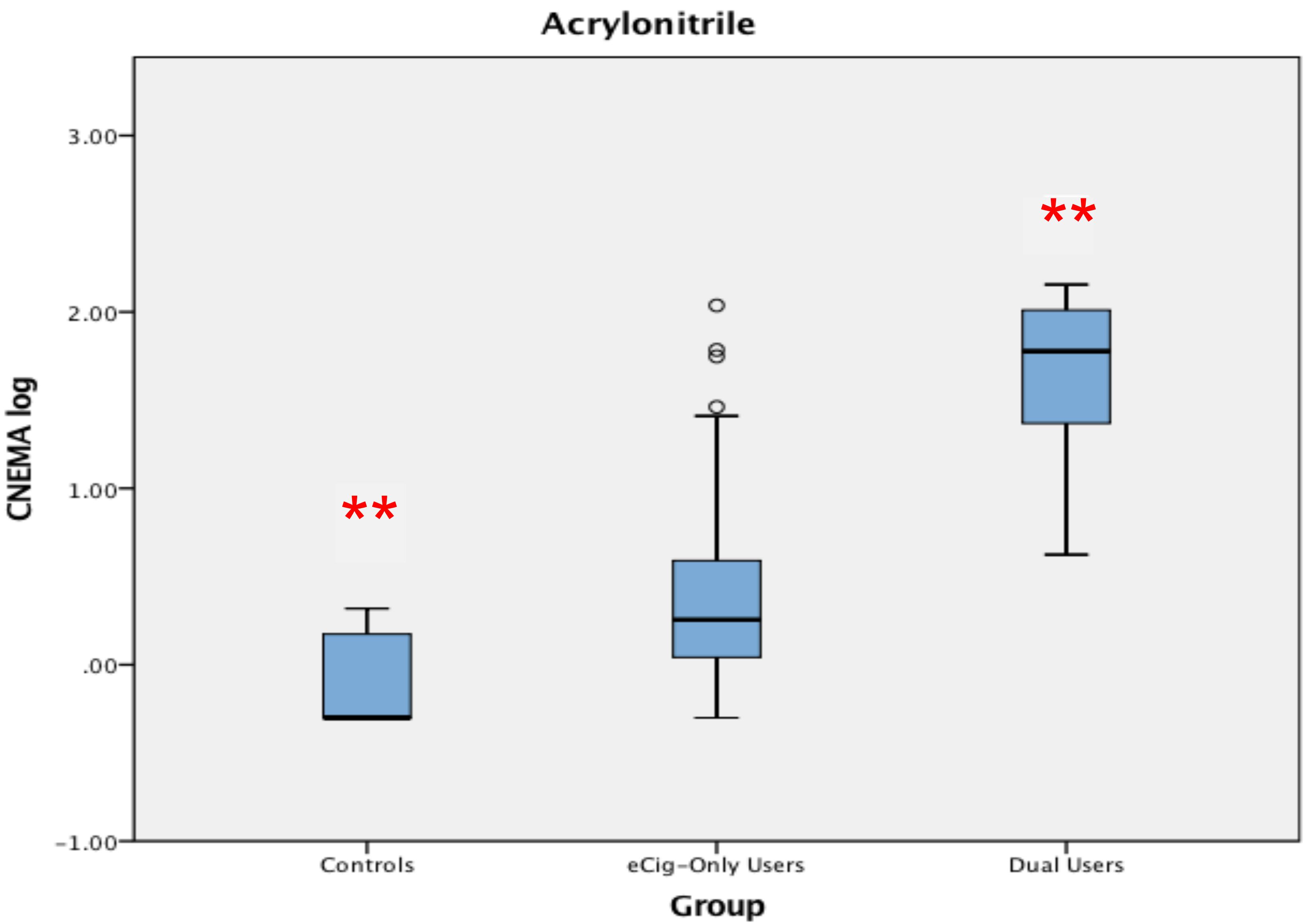
Controls
eCig-Only Users
Dual Users
Group

** *p*<.001


Acrylonitrile
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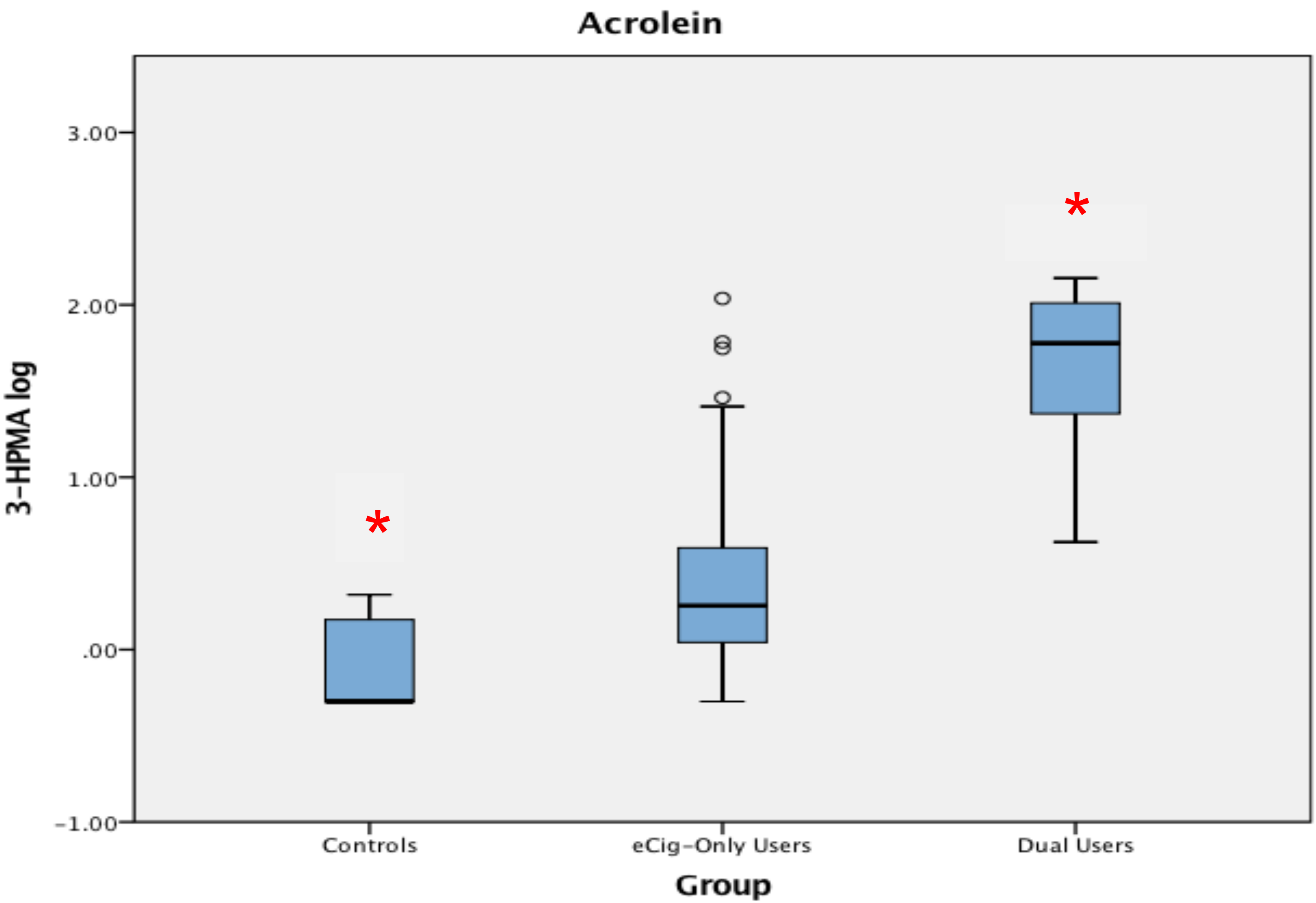
CNEMA log
Controls
eCig-Only Users
Dual Users
Group

** *p*<.001



Acrolein
3.00
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3-HPMA log
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Controls
eCig-Only Users
Dual Users
Group

* *p*<.05

ASSOCIATIONS BETWEEN VOCS AND E-CIGARETTE USE AMONG E-CIGARETTE ONLY USERS

Frequency

- The average number of sessions of e-cigarette use per day was associated with increased levels of:
- **CNEMA** (Acrylonitrile*; r=.36, *p*=.003).

*Class 2B carcinogen

Nicotine

- Compared to those who “never” used nicotine in their e-cigarettes, participants using nicotine “all” or “some” of the time had significantly higher median levels of:
  - **CNEMA** (Acrylonitrile;1.50 vs. .88 ng/ml creatinine, *p*=.05)
  - **AAMA** (Acrylamide*;71.5 vs. 60.4 ng/ml creatinine, *p*=.05).

*Studies in rodent models have found that acrylamide exposure increases the risk for several types of cancer.

Product type

- There were no differences in levels of the five significant VOCs based on type of product used.
  - F's ranged from .51 to 2.3; *p* values ranged from .09 to .67.

Flavors

- Participants who used fruit flavors had higher CNEMA (Acrylonitrile) levels.
  - 10.4 ng/ml vs. 2.1 ng/ml, p=.03
- There were no differences in VOC levels among those who used other flavors.

Summary

- Adolescent **E-Cigarette-Only users** had levels of five VOC toxicants detected in quantities up to 3 times greater than in **controls**.
- **Dual Users** had levels of VOCs up to 3 times higher than E-Cigarette-Only users.

Conclusions

- While e-cigarette vapor may be less dangerous than combustion cigarettes, with lower overall exposure to VOC toxicants, our findings challenge the idea that e-cigarette vapor is safe.
- Many of the VOCs we identified among e-cigarette users are carcinogenic and were present whether or not the product contained nicotine.
- As with traditional cigarettes, messaging to teens must include warnings about the potential risk from toxic exposure to carcinogenic compounds generated by these products.

THANKS

Marijuana

- In all models, group membership (e-Cig Only, Dual User, Control) remained a statically significant predictor of VOC value independent of marijuana use frequency.

Toxicants (Median ng/mg of creatinine)

Toxin	control	e-cig only	Dual users
Acrylonitrile	0**	1.3	59.4**
Acrolein	192.8*	254.3	439.7*
Propylene Oxide	15.2**	28.8	40.2
Acrylamide	34.5**	67.3	235.6**
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