Not All Dual Tobacco Use Is the Same: Evidence From Tobacco Use Behavior, Biomarkers of Exposure, and Biomarkers of Potential Harm

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# Outline

- Introduction
- Characterization of Adult Dual User Subgroups
  - Differences in Tobacco Use Behaviors
  - Differences in Biomarkers of Exposure
  - Differences in Biomarkers of Potential Harm
- Key Takeaways



## **Risk Differential – Combustible vs. Smoke-Free Products**

#### **Risk Cliff Between Combustible & Smoke-Free Tobacco<sup>1</sup>**



<sup>1</sup>Adapted from Nutt, et. al Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach. Eur. Addict Res 2014; 20:218-225.



### Characterization of Dual Users Varies Across Studies Limiting Comparability

Any use of both products

Daily and non-daily use of both products

Frequent and infrequent use of both products

- Current cigarette and ever e-cigarette use (Christensen 2014, Cheng 2021)
- Everyday or some days use of both (Simonavicius 2017, Goniewicz 2018, Coleman 2019, Chang 2021, Strong 2021)
- Weekly use of both products (Levy 2017)
  - Daily cigarette use and everyday or some days e-cigarette use (Rostron 2019)
- Daily e-cigarette use with cigarette smoking (Biener 2014)
- Daily and non-daily use of both products (Smith 2021)

- Light, predominant, and heavy use of both products (Buu 2022)
- Frequent and infrequent use of both products (Lizhnyak 2022)

## Novel Approach to Evaluating Adult Dual User Subgroups

- The Population Assessment of Tobacco and Health (PATH) Study
  - Wave 1 Adult Questionnaire Restricted-Use Files and Biomarker Restricted-Use Files (2013-2014)
- Study Groups:
  - Dual User Subgroups
  - Exclusive Daily Cigarette Smokers
  - Exclusive Daily E-Cigarette Users
  - Never Tobacco Users
- Population:
  - Adults aged 18 or older<sup>1</sup>
- Outcomes
  - Demographics and tobacco use patterns
  - Biomarkers of exposure (BOE) and biomarkers of potential harm (BOPH)

		Cigarette Use Behavior		
	Frequency	≥20 days	<20 days	
E-Vapor Use Behavior	≥20 days	Frequent Duals	Vapers Who Smoke	
	<20 days	Smokers Who Vape	Infrequent Duals	

1- The analysis was not restricted to 21+ because, at the time data were collected, the federal minimum legal age to purchase tobacco products was 18.



### Key Differences in Demographics and Amount of Cigarette Smoking Among Adult Dual User Subgroups

- Greater proportion of females classified as Smokers who vape, Vapers who smoke, and Infrequent dual users.
- Higher proportion of non-Hispanic Whites classified as Frequent duals.
- Higher proportion of Hispanics and younger classified as Infrequent duals
- Vapers who smoke and Infrequent duals smoked fewer cigarettes per day.

	Exclusive daily cigarette smokers (n=2442)	Dual cigarette & e-vapor users (n=970)				Exclusive daily
Characteristics		Frequent duals (n=169)	Smokers who vape (n=678)	Vapers who smoke (n=57)	Infrequent duals (n=66)	e-vapor users (n=169)
Sex						
Male	47.6	43.0	36.6	37.9	34.5	43.1
Female	52.4	57.0	63.4	62.1	65.5	56.9
Age (mean)	46.0	46.2	43.5	43.1	38.5	43.9
Race/ethnicity						
NH-White	70.5	87.7	78.4	79.2	57.8	84.1
NH-Other	19.1	8.2	10.9	13.4	6.9	11.2
Hispanic	10.4	4.1	10.7	7.3	35.3	4.7
CPD (mean)	15.8	15.0	15.7	8.4	4.8	-



NH – Non-Hispanic

## Substantially Lower BOEs in Some Adult Dual User Subgroups

Biomarkers of Exposure Among Dual User Subgroups Relative to Exclusive Daily Cigarette Smokers



Abbreviations: TNE-7: Total Nicotine Equivalents -7; NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; NNN: N'-Nitrosonornicotine; 2-FLU: 2-hydroxyfluorene; 3-FLU: 3-hydroxyfluorene; 1-PYR: 1-hydroxyprene; AAMA: N-Acetyl-S-(2-carbamoylethyl)-L-cysteine; CEMA: N-Acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA: N-Acetyl-S-(2-cyanoethyl)-L-cysteine; 2HPMA: N-Acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA: N-Acetyl-S-(3-hydroxypropyl)-L-cysteine; HPMM: N-Acetyl-S-(3-hydroxypropyl)-L-cysteine; IPM3: N-Acetyl-S-(4-hydroxy-2-methyl-2-buten-1-yl)-L-cysteine; MADA - Mandelic acid; MHB3: N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine; PHGA - Phenylglyoxylic acid Note: \* - denotes statistically significant difference (p<0.05) when compared to exclusive cigarette smokers.

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# Evaluation of the Impact of Dual Use Should Consider Different Subgroups

Exposure to NNK Among Exclusive Daily Cigarette Smokers, Dual User Subgroups, Exclusive Daily E-cigarette Users, and Never Tobacco Users.



Abbreviation: NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.

Note: \* - denotes statistically significant difference (p<0.05) when compared to exclusive cigarette smokers.

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### Favorable Changes in BOPHs Among Some Adult Dual User Subgroups

Biomarkers of Potential Harm Among Dual User Subgroups Relative to Exclusive Daily Cigarette Smokers



Abbreviations:: hSCRP – High-sensitivity C-reactive protein; IL-6 – Interleukin 6; S-ICAM – Soluble intercellular adhesion molecule-1. Note: \* - denotes statistically significant difference (p<0.05) when compared to exclusive cigarette smokers.



# Evaluation of the Impact of Dual Use Should Consider Different Subgroups

Adult Dual User Subgroup	Biomarkers of Exposure	Biomarkers of Potential Harm	
Frequent Duals	Some Higher	No Change	
Smokers Who Vape	Some Higher	Some Higher	
Vapers Who Smoke	Substantially Lower	Favorable Changes	
Infrequent Duals	Substantially Lower	Favorable Changes	





- Adult Dual Users are Better Characterized as Subgroups Based on Frequency of Product Use.
- Differences in Demographics and Tobacco Use Patterns Exist Among Adult Dual User Subgroups.
- Differences in BOEs and BOPHs Are Driven by Frequency of Cigarette Smoking.
- We Conclude That Dual Users Should Not Be Treated as a Homogeneous Population. Lower Levels of BOEs and BOPHs in Some Dual User Subgroups Suggest Harm Reduction Potential.



# References

• Biener L, Hargraves JL. A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: association with smoking cessation and motivation to quit. *Nicotine Tob Res.* 2015;17:127-133.

• Buu A et al. Subtypes of dual users of combustible and electronic cigarettes: longitudinal changes in product use and dependence symptomatology. *Nicotine Tob Res.* 2022 Jun 23:ntac151. doi: 10.1093/ntr/ntac151. Epub ahead of print. PMID: 35738022.

• Chang JT et al. Biomarkers of Potential Harm among Adult Cigarette and Smokeless Tobacco Users in the PATH Study Wave 1 (2013-2014): A Cross-sectional Analysis. *Cancer Epidemiol Biomarkers Prev.* 2021 Jul;30(7):1320-1327. doi: 10.1158/1055-9965.EPI-20-1544. Epub 2021 May 4. PMID: 33947655; PMCID: PMC8254764.

• Cheng YW et al. Health risks of dual use of electronic and combustible cigarettes: exposure to acrylamide and glycidamide. *Pol Arch Intern Med.* 2022 Jan 28;132(1):16103. doi: 10.20452/pamw.16103. Epub 2021 Oct 6. PMID: 34612028.

• Christensen T et al. Profile of e-cigarette use and its relationship with cigarette quit attempts and abstinence in Kansas adults. *Prev Med.* 2014;69:90-94.

• Coleman B et al. Transitions in electronic cigarette use among adults in the Population Assessment of Tobacco and Health (PATH) Study, Waves 1 and 2 (2013–2015). *Tobacco Control.* 2019;28(1):50.

• Goniewicz ML et al. Comparison of Nicotine and Toxicant Exposure in Users of Electronic Cigarettes and Combustible Cigarettes. JAMA network open. 2018;1(8):e185937.

## References

• Levy DT et al. The Application of a Decision-Theoretic Model to Estimate the Public Health Impact of Vaporized Nicotine Product Initiation in the United States. *Nicotine Tob Res.* 2016.

• Lizhnyak, P.N., Noggle, B., Wei, L. et al. Understanding heterogeneity among individuals who smoke cigarettes and vape: assessment of biomarkers of exposure and potential harm among subpopulations from the PATH Wave 1 Data. *Harm Reduct J 19*, 90 (2022). https://doi.org/10.1186/s12954-022-00673-x

• Rostron BL et al. Associations of Cigarettes Smoked Per Day with Biomarkers of Exposure Among US Adult Cigarette Smokers in the Population Assessment of Tobacco and Health (PATH) Study Wave 1 (2013-2014). *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology.* 2019.

• Simonavicius E et al. What factors are associated with current smokers using or stopping e-cigarette use? *Drug and alcohol dependence*. 2017;173:139-143.

• Smith DM et al. Exposure to Nicotine and Toxicants Among Dual Users of Tobacco Cigarettes and E-Cigarettes: Population Assessment of Tobacco and Health (PATH) Study, 2013-2014. *Nicotine Tob Res.* 2021 May 4;23(5):790-797. doi: 10.1093/ntr/ntaa252. PMID: 33590857; PMCID: PMC8095240.

• Strong DR et al. Validation of the Wave 1 and Wave 2 Population Assessment of Tobacco and Health (PATH) Study Indicators of Tobacco Dependence Using Biomarkers of Nicotine Exposure Across Tobacco Products. *Nicotine Tob Res.* 2022 Jan 1;24(1):10-19. doi: 10.1093/ntr/ntab162. PMID: 34383052; PMCID: PMC8666120.



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