Characterization of Exposure to Cigarette Smoke Constituents in Adult Smokers Switching to E-vapor Products

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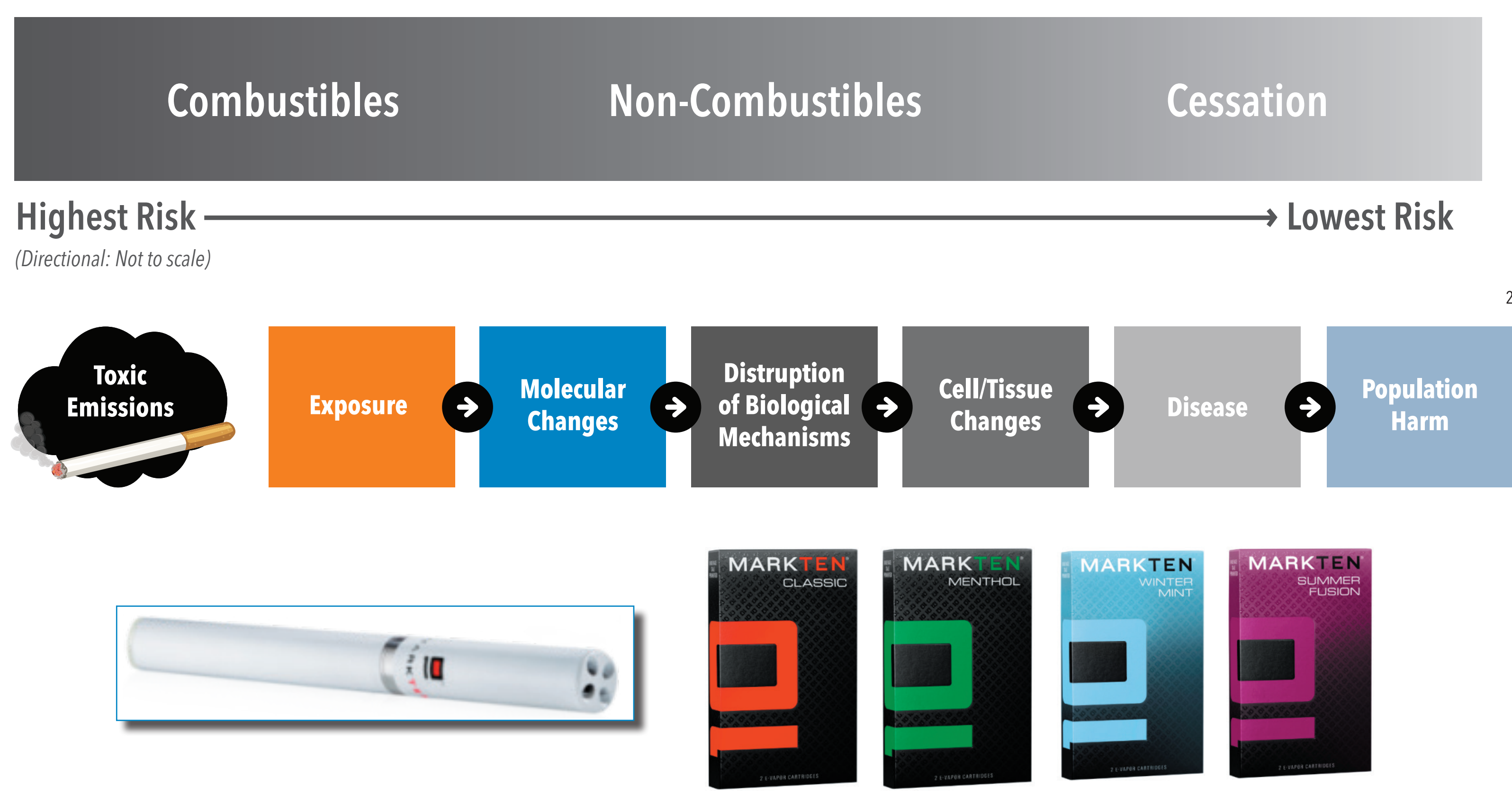**Altria Client Services LLC, Richmond, VA 23219**
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INTRODUCTION

"[P]olicies should account for changes that will move addicted smokers down that continuum of risk to…less harmful products." [1]

Tobacco Smoke Constituents	Urinary Biomarkers of Exposure (BOE)	Classification
2-Aminonaphthalene	2-AN (2-Aminonaphthalene)	CA
4-Aminobiphenyl	4-ABP (4-Aminobiphenyl)	CA
Acrylamide	AAMA (N-Acetyl-S-(2-carbamoylethyl)-l-cysteine) GAMA (N-(R,S)-Acetyl-S-(2-carbamoyl-2-hydroxyethyl)-l-cysteine)	CA
Acrylonitrile	CEMA (Cyanoethyl-mercapturic acid)	CA, RT
Ethylene oxide	HEMA (2-Hydroxy-ethyl-mercapturic acid)	CA, RT, RDT
Crotonaldehyde	3-HMPMA (3-Hydroxy-1-methylpropyl-mercapturic acid)	CA
1,3-Butadiene	2-MHBMA (2-Hydroxybutene-1-yl mercapturic acid)	CA, RT, RDT
Benzene	S-PMA (S-Phenyl-mercapturic acid)	CA, CT, RDT
Polycyclic Aromatic Hydrocarbons	2-OH-Fluorene, 1-OH-pyrene, 1-OH-phenanthrene	CA, CT
Naphthalene	2-OH-naphthalene	CA, RT
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	Total NNAL	CA
Acrolein	3-HPMA (3-Hydroxypropyl-mercapturic acid)	RT, CT
Carbon monoxide	COHb (Carboxyhemoglobin)	RDT
Nicotine	Nicotine Equivalents	RDT, AD

Classification: Carcinogen (CA), Respiratory Toxicant (RT), Cardiovascular Toxicant (CT), Reproductive or Developmental Toxicant (RDT), Addictive (AD)

CONCLUSIONS

► We observed significant reductions in exposure to the majority of smoke constituents after 7 days of complete switching.
► Other than Nicotine Equivalents (NE), the observed reductions in BOE are consistent with reductions associated with smoking cessation over a comparable length of time.
► The significant reductions in exposure to selected Harmful and Potentially Harmful Constituents (HPHCs) adds to the growing body of evidence regarding the harm reduction potential of e-vapor products (EVPs).
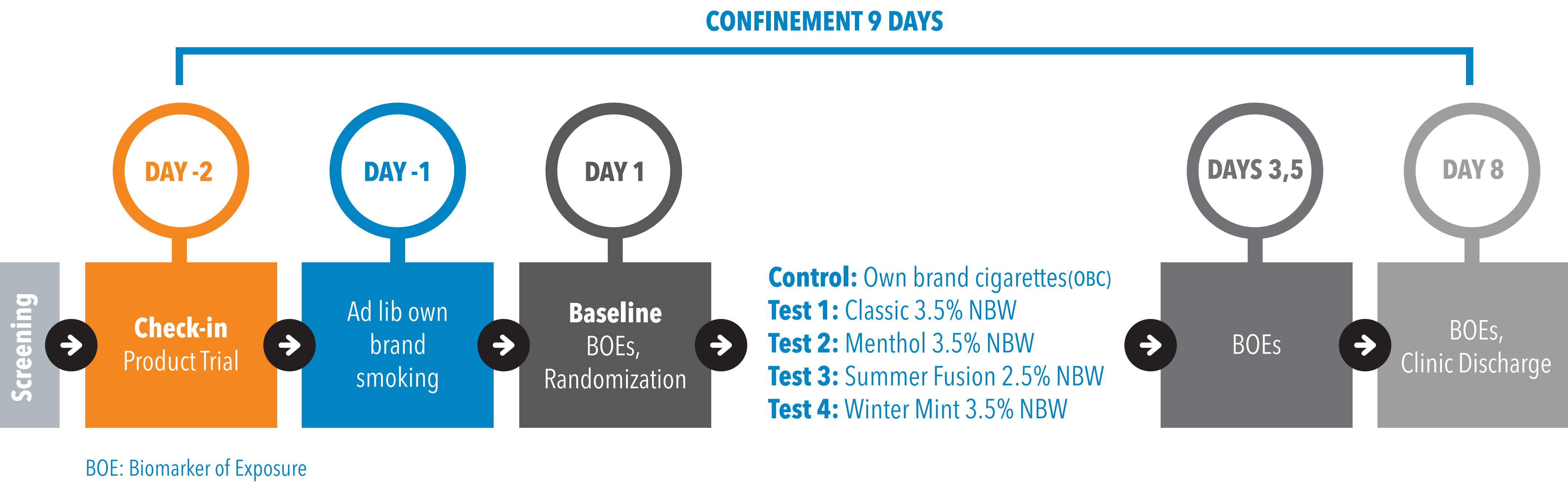
STRENGTHS & LIMITATIONS

► The study was conducted in a controlled clinical environment which allows characterization of the impact of EVP use on adult smokers without potential for use of other tobacco products.
► The study products were used under ad lib conditions giving adult smokers the opportunity to use the products unhindered which may mimic near real-world conditions.
► The study participants received the products free-of-charge, stayed within the clinic for the entire duration of the study and did not have open access to different flavor variants during the study.

REFERENCES & NOTES

1. "Protecting American Families: Comprehensive Approach to Nicotine and Tobacco," Remarks by Scott Gottlieb, M.D., Commissioner of Food and Drug Administration (June 28, 2017).
2. Adapted from National Research Council. 1987. Biological Markers in Environmental Health Research. Environmental Health Perspectives, 74:191.
3. U.S. Department of Health and Human Services (2012). Guidance for Industry: Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a) (3) of the Federal Food, Drug, and Cosmetic Act.
4. Adapted from Theophilus EH, Coggins CRE, Chen P, Schmidt E, Borgerding MF. 2015. Magnitudes of Biomarker Reductions in Response to Controlled Reductions in Cigarettes Smoked Per Day: A One-Week Clinical Confinement Study. Reg Tox Pharm 71, 225-34.

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DESIGN

CONFINEMENT 9 DAYS

Screening → **Check-in** Product Trial → Ad lib own brand smoking → **Baseline** BOEs, Randomization → BOEs → BOEs, Clinic Discharge

DAY -2 / DAY -1 / DAY 1 / DAYS 3,5 / DAY 8

Control: Own brand cigarettes(OBC)
Test 1: Classic 3.5% NBW
Test 2: Menthol 3.5% NBW
Test 3: Summer Fusion 2.5% NBW
Test 4: Winter Mint 3.5% NBW

BOE: Biomarker of Exposure

Demographic		Classic, 3.5% NBW (N = 30)	Summer Fusion, 2.5% NBW (N = 30)	Menthol, 3.5% NBW (N = 32)	Winter Mint, 3.5% NBW (N = 31)	Subject's Own Brand Cigarette (N = 30)	Overall (N = 153)
Age (years)	Mean	43	41	39	42	44	42
	SD	9.4	8.6	8.2	8.7	9.2	8.9
Sex	Male	18 (60.0%)	16 (53.3%)	21 (65.6%)	16 (51.6%)	13 (43.3%)	84 (54.9%)
	Female	12 (40.0%)	14 (46.7%)	11 (34.4%)	15 (48.4%)	17 (56.7%)	69 (45.1%)
Race	White	21 (70.0%)	21 (70.0%)	14 (43.8%)	18 (58.1%)	16 (53.3%)	90 (58.8%)
	Black or African American	9 (30.0%)	9 (30.0%)	14 (43.8%)	13 (41.9%)	13 (43.3%)	58 (37.9%)
	Other	---	---	4 (12.5%)	---	1 (3.3%)	5 (3.3%)
During the past 30 days, how many cigarettes did you smoke per day on average?	Mean	18	18.6	19.4	18.4	16.5	
	SD	5.3	5.62	7.94	5.94	5.93	

RESULTS

Completely Switching to E-vapor Products Substantially Reduces Exposure to Smoke Constituents

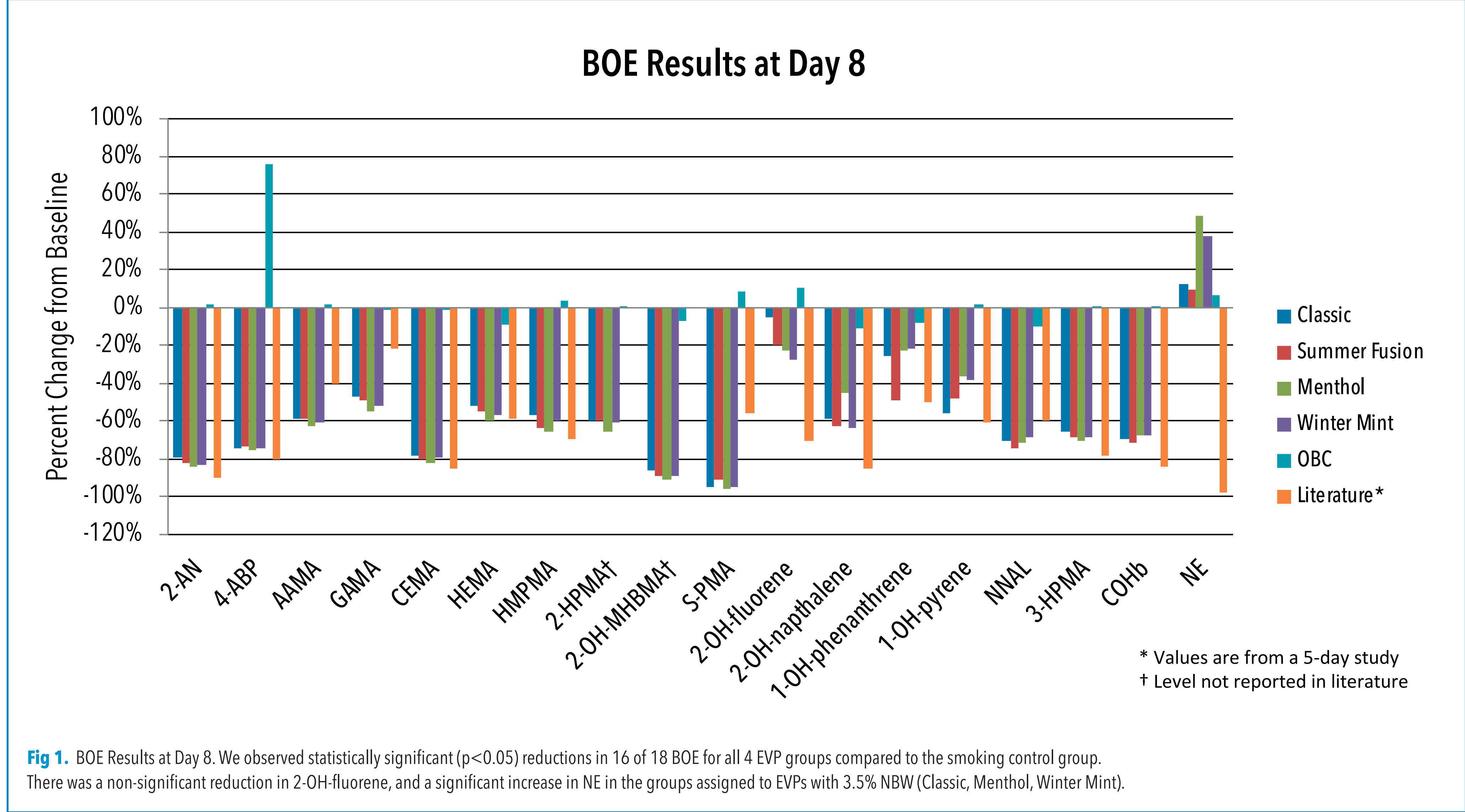#### Change from Baseline in Biomarkers at the End of the Study

Fig 1. BOE Results at Day 8. We observed statistically significant (p<0.05) reductions in 16 of 18 BOE for all 4 EVP groups compared to the smoking control group. There was a non-significant reduction in 2-OH-fluorene, and a significant increase in NE in the groups assigned to EVPs with 3.5% NBW (Classic, Menthol, Winter Mint).

* Values are from a 5-day study
† Level not reported in literature
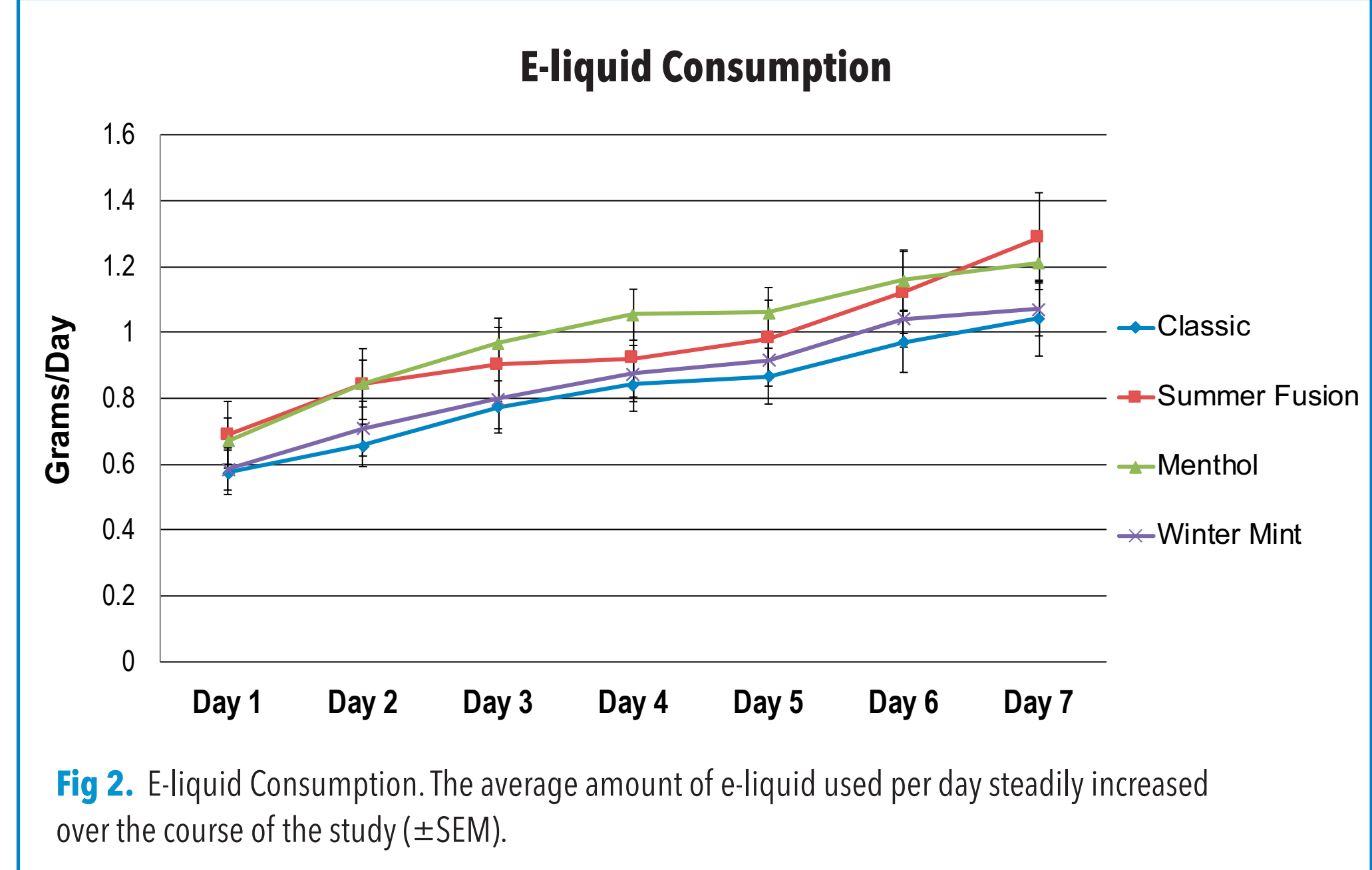
Product Consumption

Fig 2. E-liquid Consumption. The average amount of e-liquid used per day steadily increased over the course of the study (±SEM).
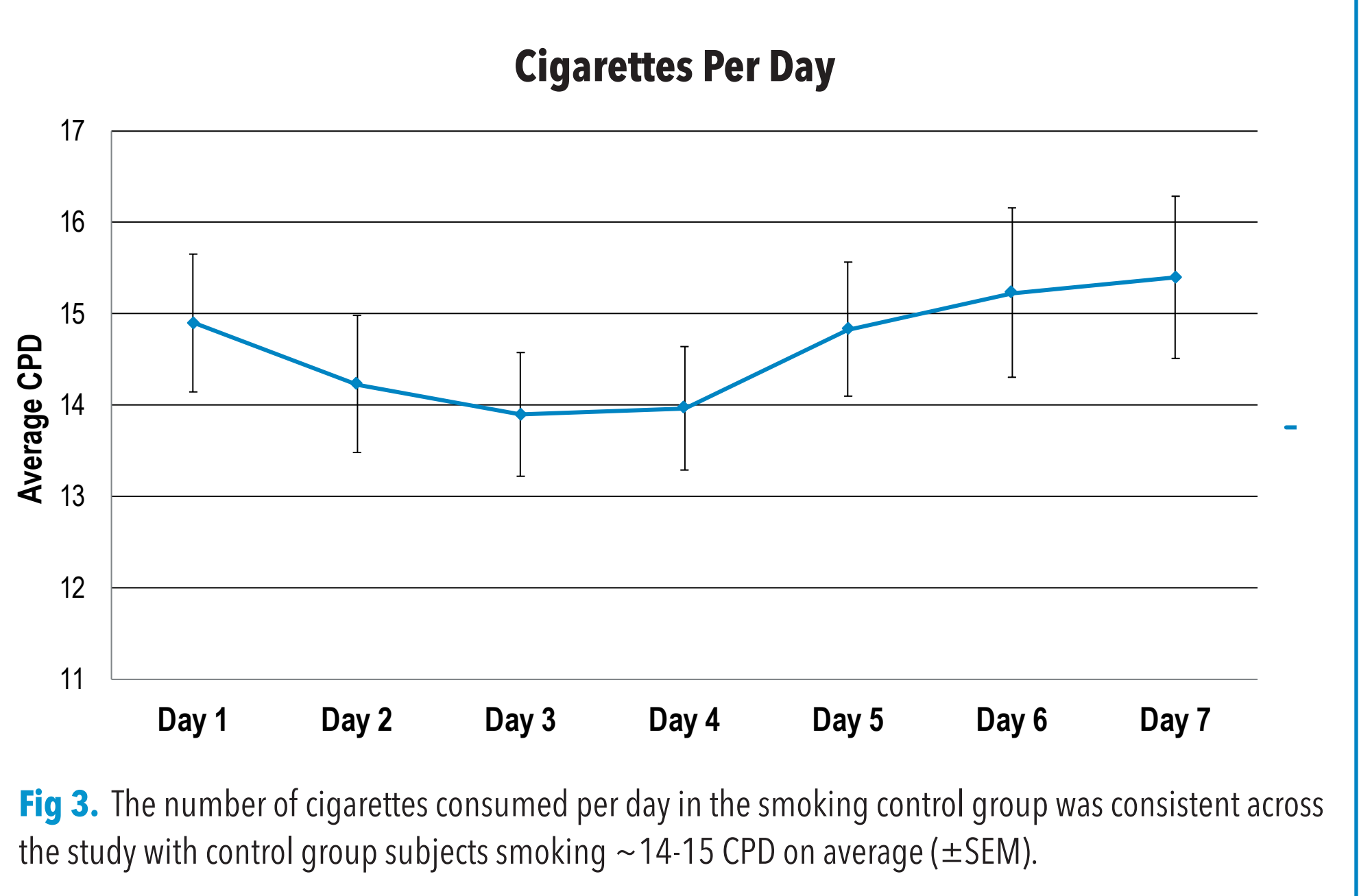

Fig 3. The number of cigarettes consumed per day in the smoking control group was consistent across the study with control group subjects smoking ~14-15 CPD on average (±SEM).

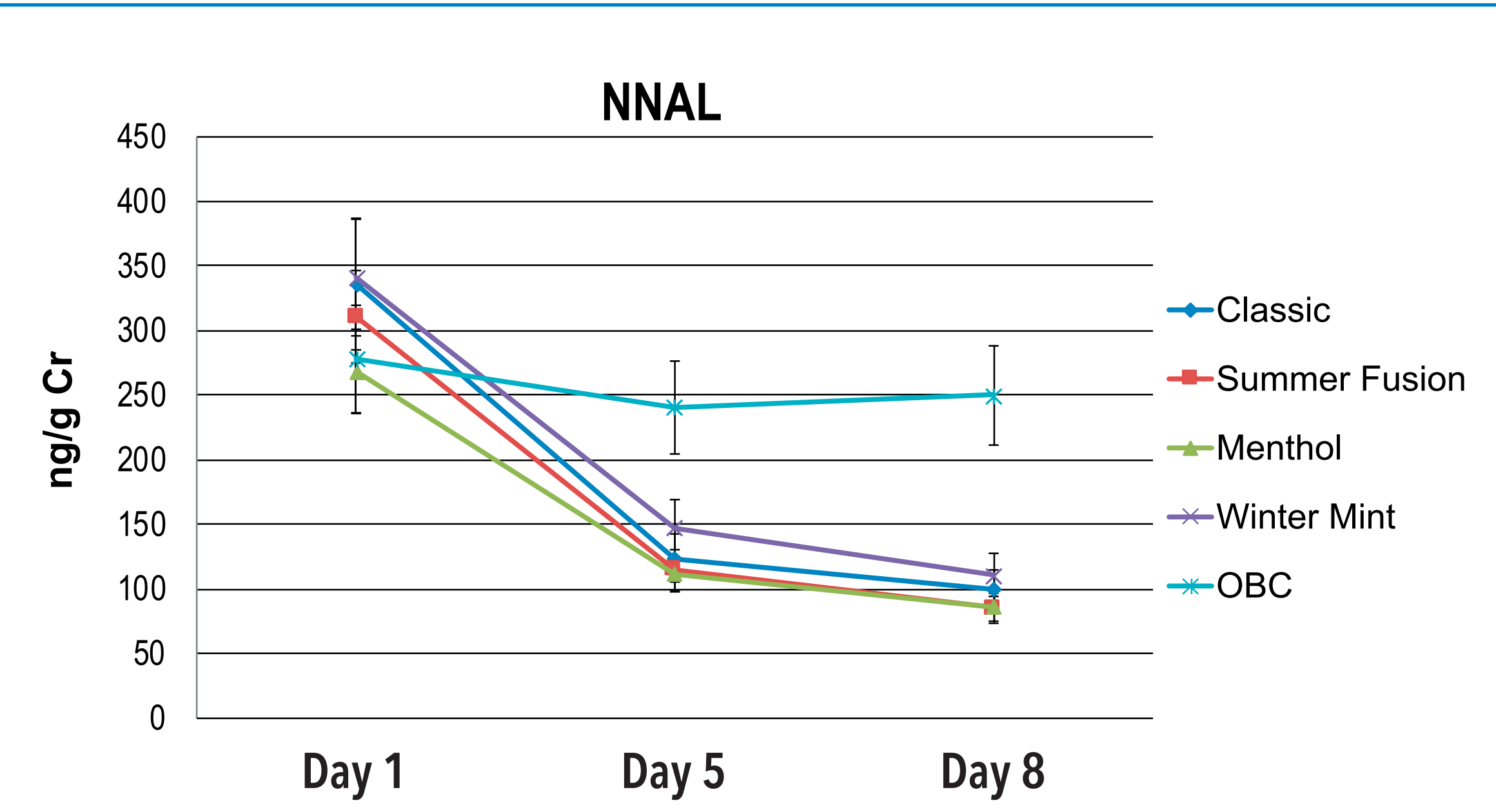### Primary Biomarkers Over Time

Fig 4. We observed a marked decrease in NNAL in all 4 EVP groups over the course of the study, while exposure remained consistent in the smoking control group (±SEM).
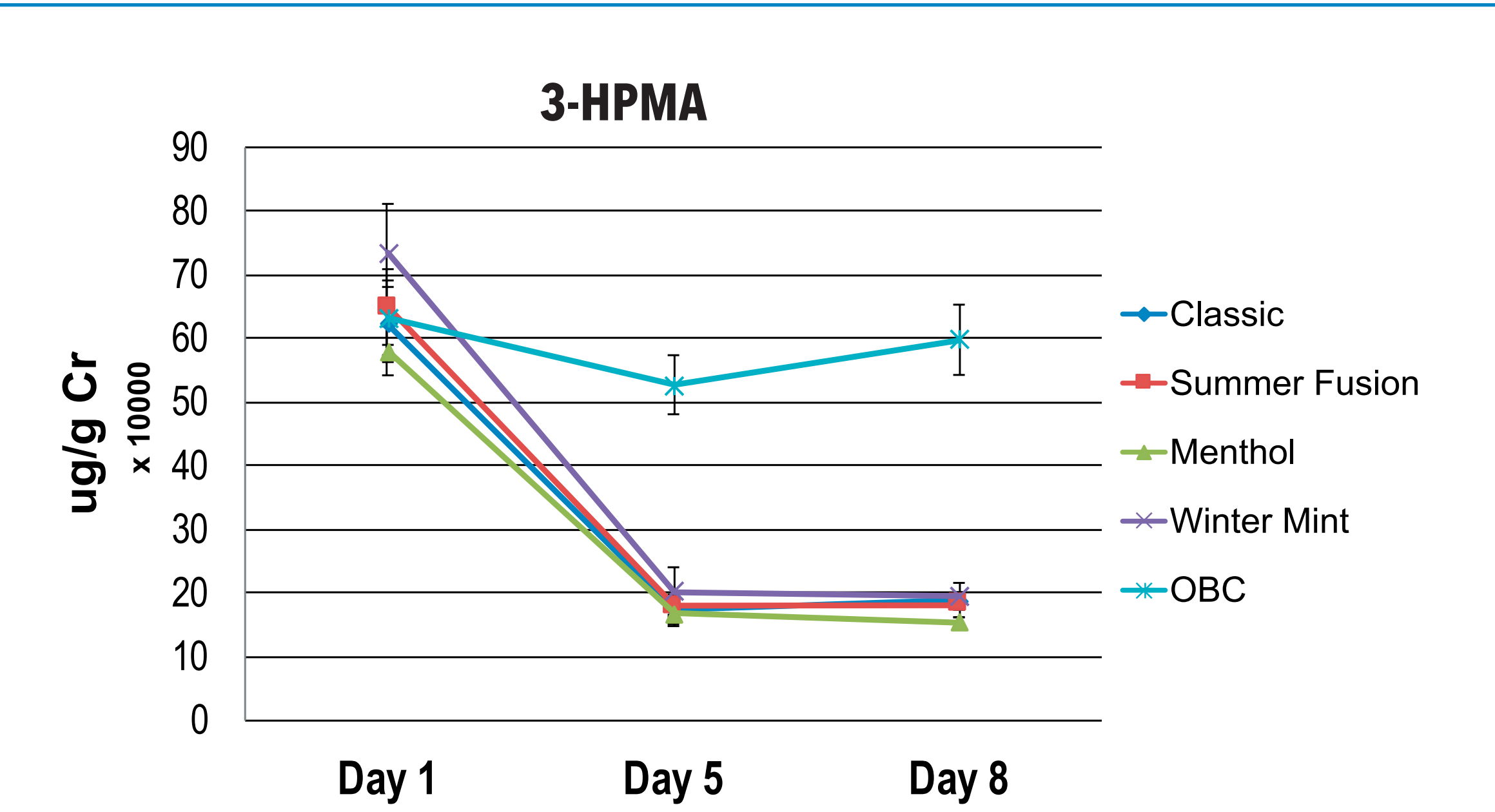

Fig 5. We observed a marked decrease in 3-HPMA in all 4 EVP groups over the course of the study, while exposure remained consistent in the smoking control group (±SEM).
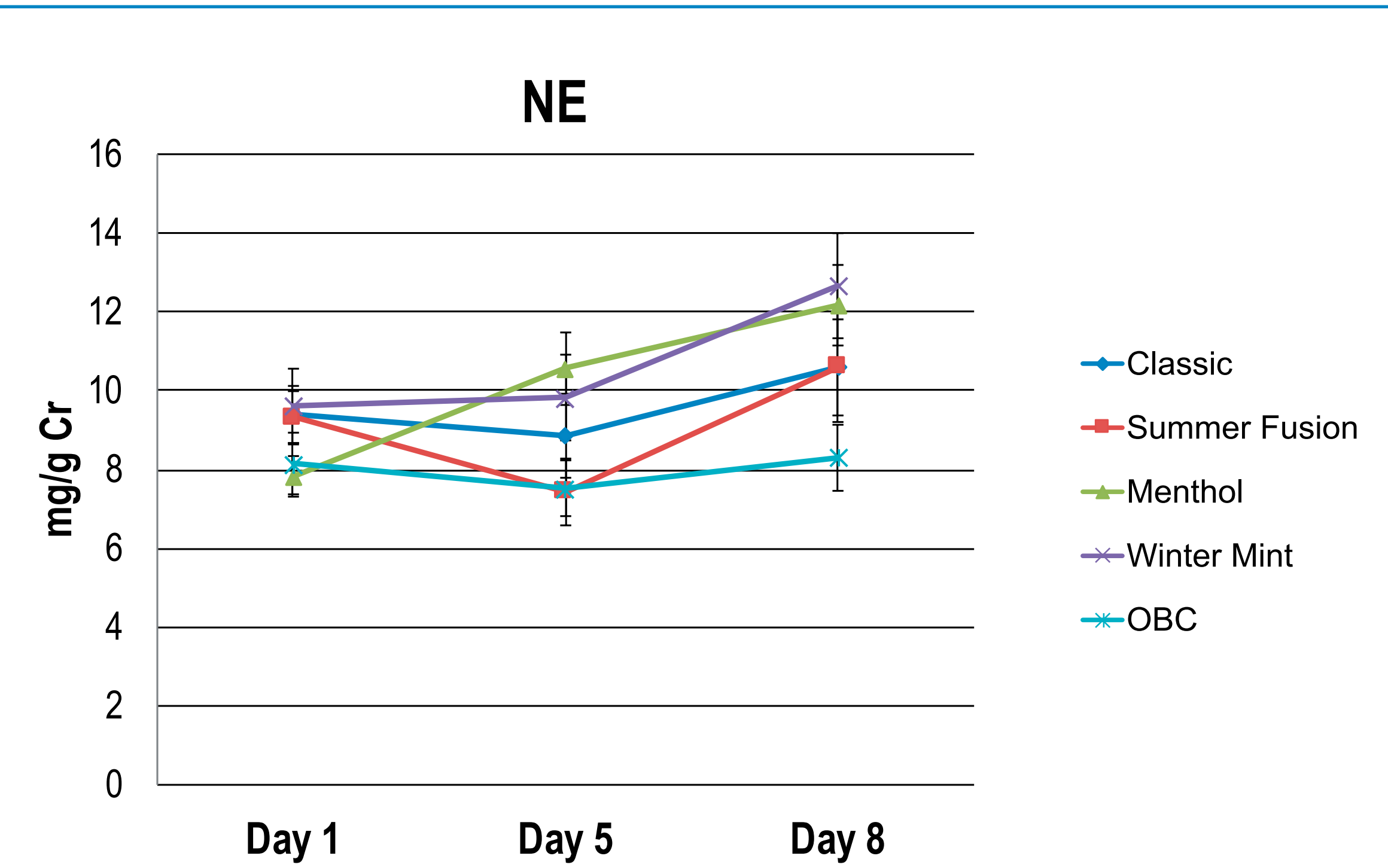

Fig 6. NE levels remained consistent in the smoking control group, and increased in all 4 EVP groups between Day 1 and Day 8 of the study (±SEM).
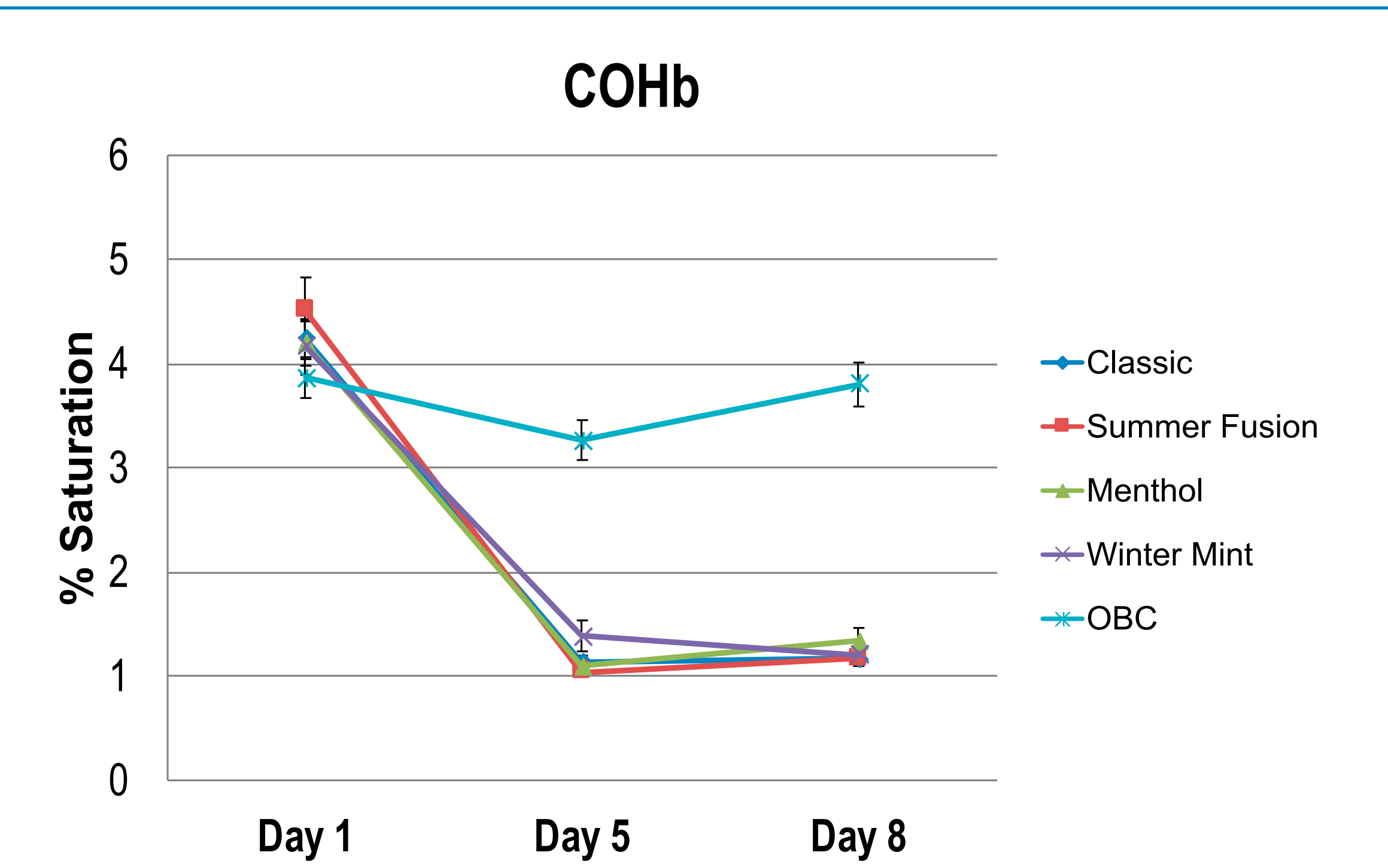

Fig 7. We observed a marked decrease in COHb in all 4 EVP groups over the course of the study, while exposure remained consistent in the smoking control group (±SEM).