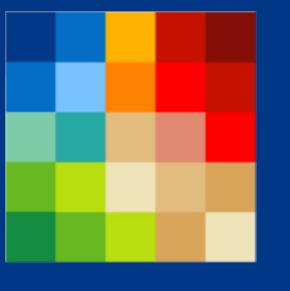
Cross-Sectional Study Comparing Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Inflammation and Oxidative Stress Between Adult E-vapor Users and Conventional Cigarette Smokers



Altria Altria Client Services



Abstract

Introduction: There are approximately 10 million past 30-day e-vapor users in the USA but limited data exist on the health effects of long term use of e-vapor products (EVPs). This study was designed to measure biomarkers of exposure and biomarkers of potential harm in a cross-section of current exclusive users of EVPs relative to current conventional cigarette (CC) smokers.

Method: 144 subjects with 6+ months of exclusive EVP use after 10+ years of CC use and 73 CC smokers with 10+ years of CC use history were recruited to participate in a cross-sectional study between January and March, 2017. Subjects were telephone screened then provided a log-in to an online portal where they were rescreened, provided informed consent, and completed quality of life and subjective measure questionnaires. Subjects then reported to one of 29 LabCorp Patient Service Centers (PSCs) in 9 states for collection of blood and urine samples.

Results: Overall, the biomarkers of exposure, total NNAL [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol] (NNK metabolite), 3-hydroxypropylmercapturic acid (acrolein metabolite), and carboxyhemoglobin (CO measure), were between 46% - 86% lower in EVP users as compared to CC smokers (p<0.0001 in all cases). Nicotine and 5 of its metabolites, expressed as Nicotine Equivalents, were 36% lower in EVP subjects as compared to CC smokers (p < 0.01). All the biomarkers of potential harm were directionally favorable in EVP users as compared to CC smokers with 29% lower 11-dehydrothromboxane B2 (p=0.04), 23% lower 8-epi-prostaglandin F2α (p=0.02), 16% lower soluble intercellular adhesion molecule-1 (p=0.02), 9% lower white blood cell counts (p>0.05) and 2% higher high-density lipoprotein cholesterol (p>0.05) in EVP subjects as compared to CC smokers (p>0.05).

Conclusions: Biomarkers of exposure to select HPHCs are significantly lower, accompanied by favorable changes in biomarkers of inflammation and oxidative stress, in exclusive users of EVP for 6+ months after 10+ years of cigarette smoking relative to cigarette smoking.

Objectives

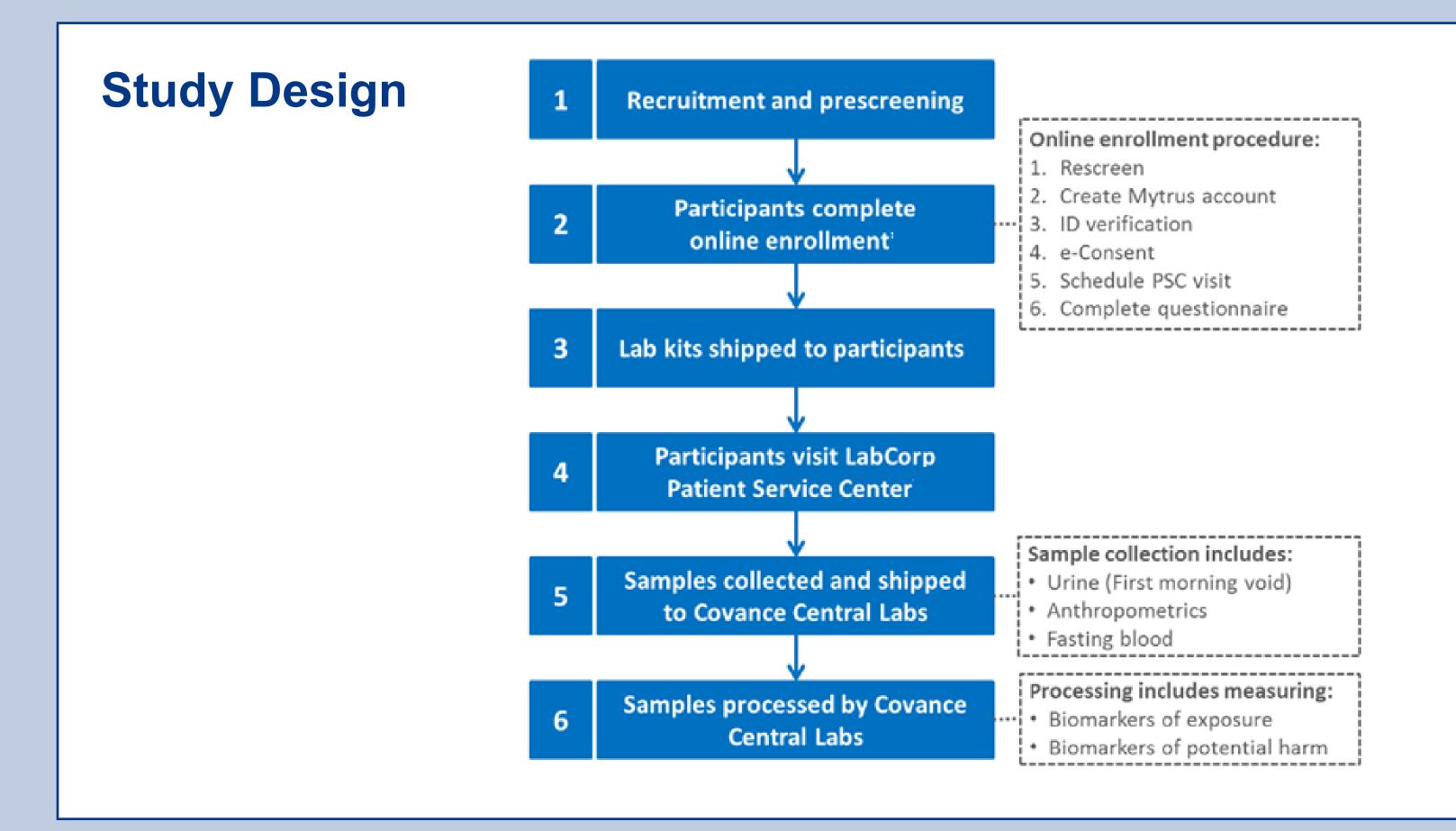
The objectives of this observational study are to measure and compare biomarkers of exposure (BOEs), biomarkers of potential harm (BOPHs), and responses to questionnaires in exclusive EVP users and CC smokers.

- BOEs* included total NNAL, urinary nicotine equivalents (nicotine and 5 of its metabolites), 3-HPMA, COHb
- BOPHs* included WBCs, HDL-C, 11-Dehydrothromboxane B2, 8-Epi-prostaglandin F2α, sICAM-1

• Questionnaire evaluations included General Quality of Life (QGEN®), Tobacco Quality of Life Impact Tool (TQOLIT™v1), Cough-related symptoms, Reasons for Vaping

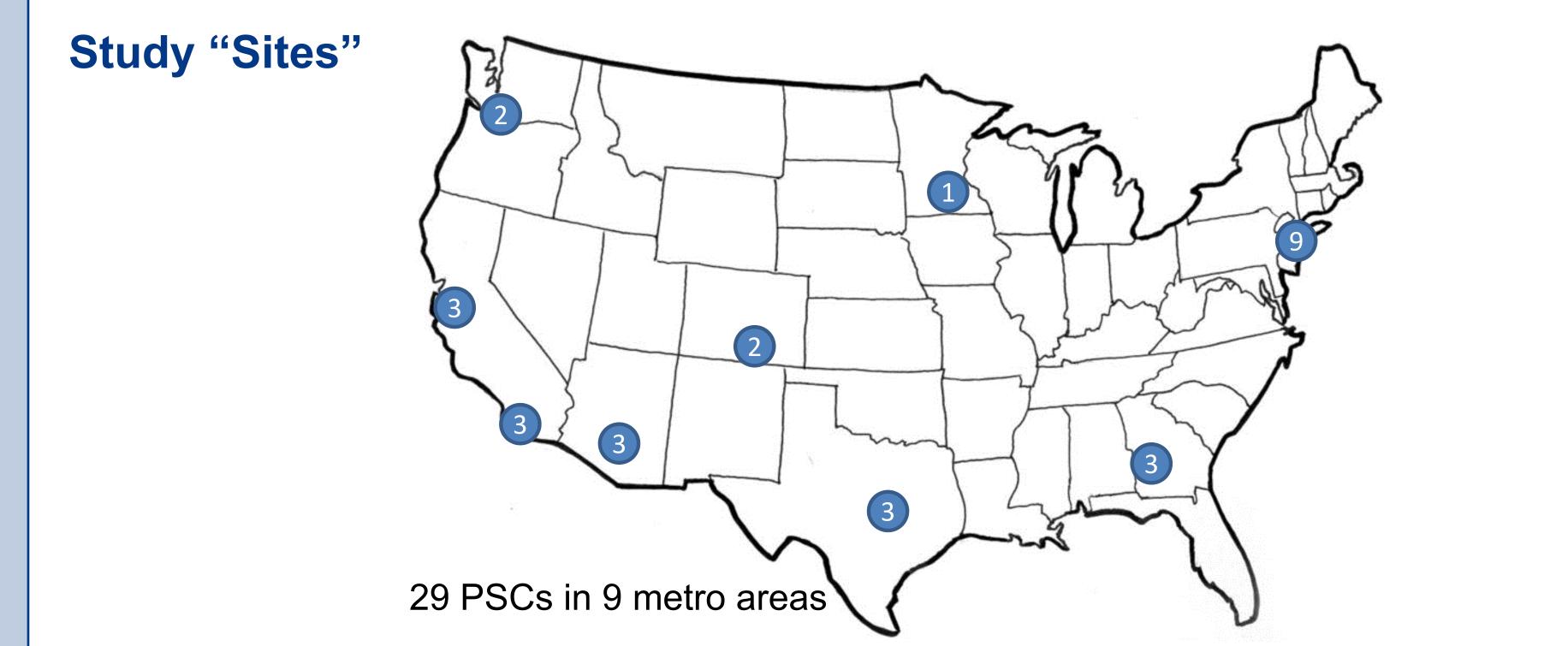
*focus of this poster

BOE Abbreviation	Biomarker	Cigarette Smoke Constituent
NNAL	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol	NNK
NE	Nicotine equivalents (nicotine + 5 metabolites)	Nicotine
3-HPMA	3-Hydroxypropylmercapturic acid	Acrolein
COHb	Carboxyhemoglobin	Carbon Monoxide
BOPH Abbreviation	Biomarker	Indication
WBC	White blood cells	Inflammation
HDL-C	High-density lipoprotein cholesterol	Cardiovascular Risk
8-epi	8-Epi-prostaglandin F2α	Oxidative Stress
11-dehydro	11-Dehydrothromboxane B2	Platelet Activation
sICAM	Soluble intercellular adhesion molecule-1	Endothelial Function



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Subjects: Male and Female Adults (30–65 years of age)

Group A: approximately 150 exclusive everyday EVP users

- Who have switched to EVP exclusive use (no other tobacco or nicotine containing products) for at least 6 months and be former smokers of at least 10 cigarettes per day for at least 10 years
- Users of cartridge-based products will be oversampled such that they represent at least 50% of Group A
- Users of tanks, mods, etc., will comprise the remainder of Group A
- **Group B:** approximately 75 exclusive CC smokers
- Will be current CC smokers and have smoked at least 10 cigarettes per day for at least the last 10 years and have not used any other tobacco or nicotine containing products for the past month before bio-sample collection

Subjects Demographics

			Conventional			
		Statistic	Cigarette Smokers	Exclusive EVP Users		
				All EVP	Tank-based (N=70)	Cartridge-based (N=62)
Assessment			(N=62)	(N=132)		
Age (years)		Mean	47.1	44.4	44.0	44.9
		SD	8.48	8.31	8.64	7.95
		Median	46.5	44.0	44.0	45.5
		Min	32	30	31	30
		Max	64	65	65	63
		N	62	132	70	62
Age Group	30 to <45 years	<u>n</u> (%)	28 (45.2)	67 (50.8)	37 (52.9)	30 (48.4)
	45 to <=65 years	n (%)	34 (54.8)	65 (49.2)	33 (47.1)	32 (51.6)
	45 to <55 years	<u>n</u> (%)	23 (37.1)	49 (37.1)	23 (32.9)	26 (41.9)
55	55 to <=65 years	<u>n</u> (%)	11 (17.7)	16 (12.1)	10 (14.3)	6 (9.7)
BMI (kg/m2)	Screening	Mean	26.50	27.54	27.71	27.36
		SD	4.807	5.047	5.400	4.654
		Median	25.99	26.59	26.60	26.36
		Min	18.8	18.1	18.1	18.6
		Max	36.9	39.5	39.5	38.4
		N	62	132	70	62
BMI (kg/m2)	PSC	Mean	27.40	29.25	29.74	28.70
		SD	5.909	6.375	6.851	5.797
		Median	26.60	27.95	27.70	28.15
		Min	18.4	17.0	17.7	17.0
		Max	40.9	49.0	49.0	40.9
		N	62	132	70	62

Analysis

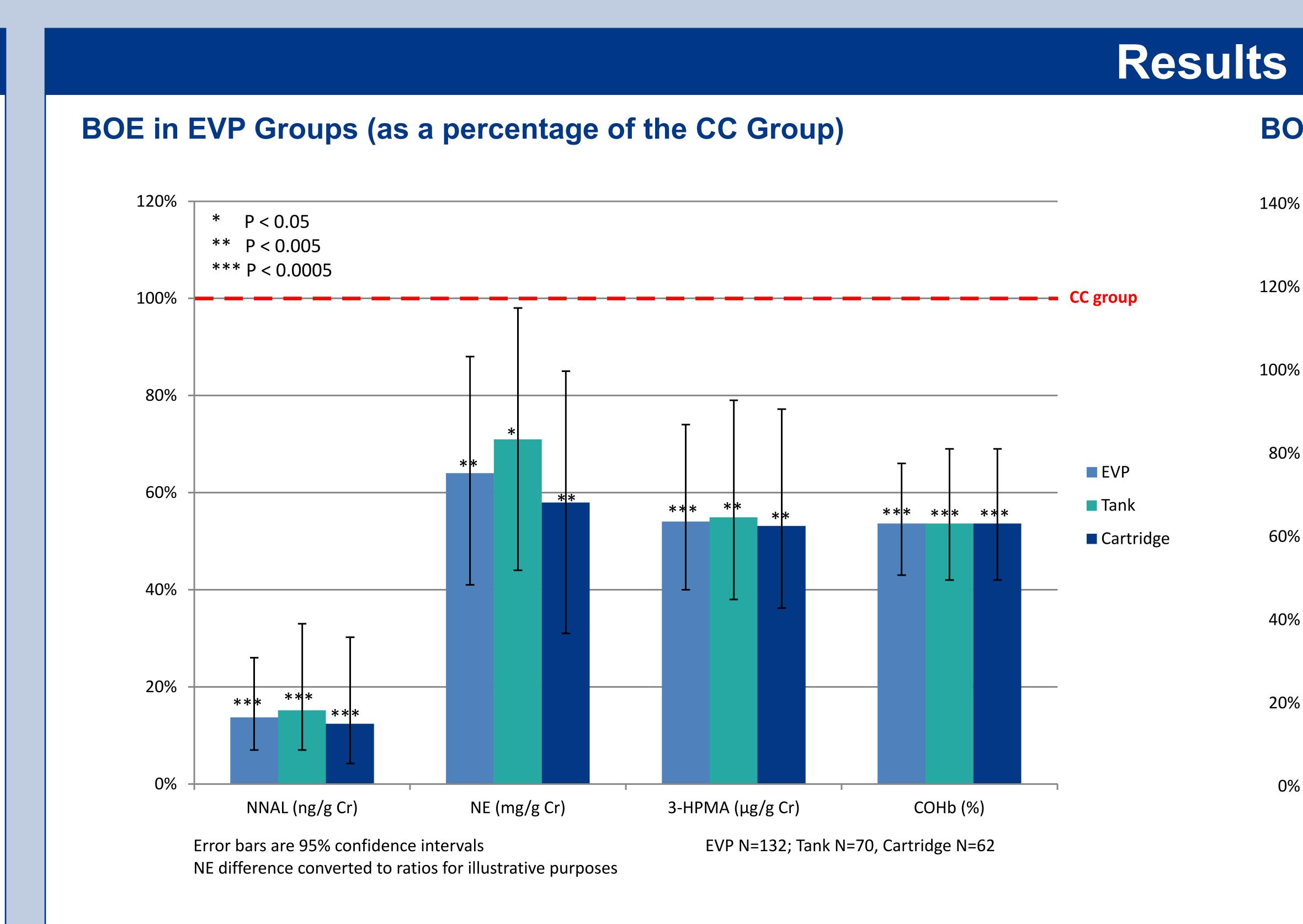
On the morning of the PSC visit, the subject was instructed to collect a first-void morning urine sample (at least 4 h of retention in the bladder overnight) and store at an ambient temperature. Upon completion of check-in, the PSC staff escorted the participant into an examination room for anthropometric measurements including height, weight, waist circumference, and sitting blood pressure. A phlebotomist then prepared the participant for the blood draw (8 h fasting).

- The outcomes for this cross-sectional observational study included the following: BOEs: total NNAL, urinary nicotine equivalents, 3-HPMA, COHb
- BOPHs: WBC, HDL-C, 11-dehydrothromboxane B2, 8-epi-prostaglandin F2α, sICAM-1

An analysis of variance (ANOVA) model with total NNAL level as the response variable and classification variables study group, study group × age group, study group × body mass index (BMI) group, age group, gender, and BMI group as model terms were used to examine the difference in total NNAL between CC smokers and exclusive EVP users. As the study groups being compared were not randomized, additional baseline covariates (e.g., biomarker measure) were added as appropriate (dealing with imbalance at baseline).

The ANOVA model for total NNAL was also used to examine the difference in all other biomarkers of exposures and biomarkers of effects between the study groups. Statistical comparison to assess the difference to the subgroups within EVP (tank and cartridge based) was also made using the same ANOVA model.

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Did the EVP Groups Use EVP Exclusively?

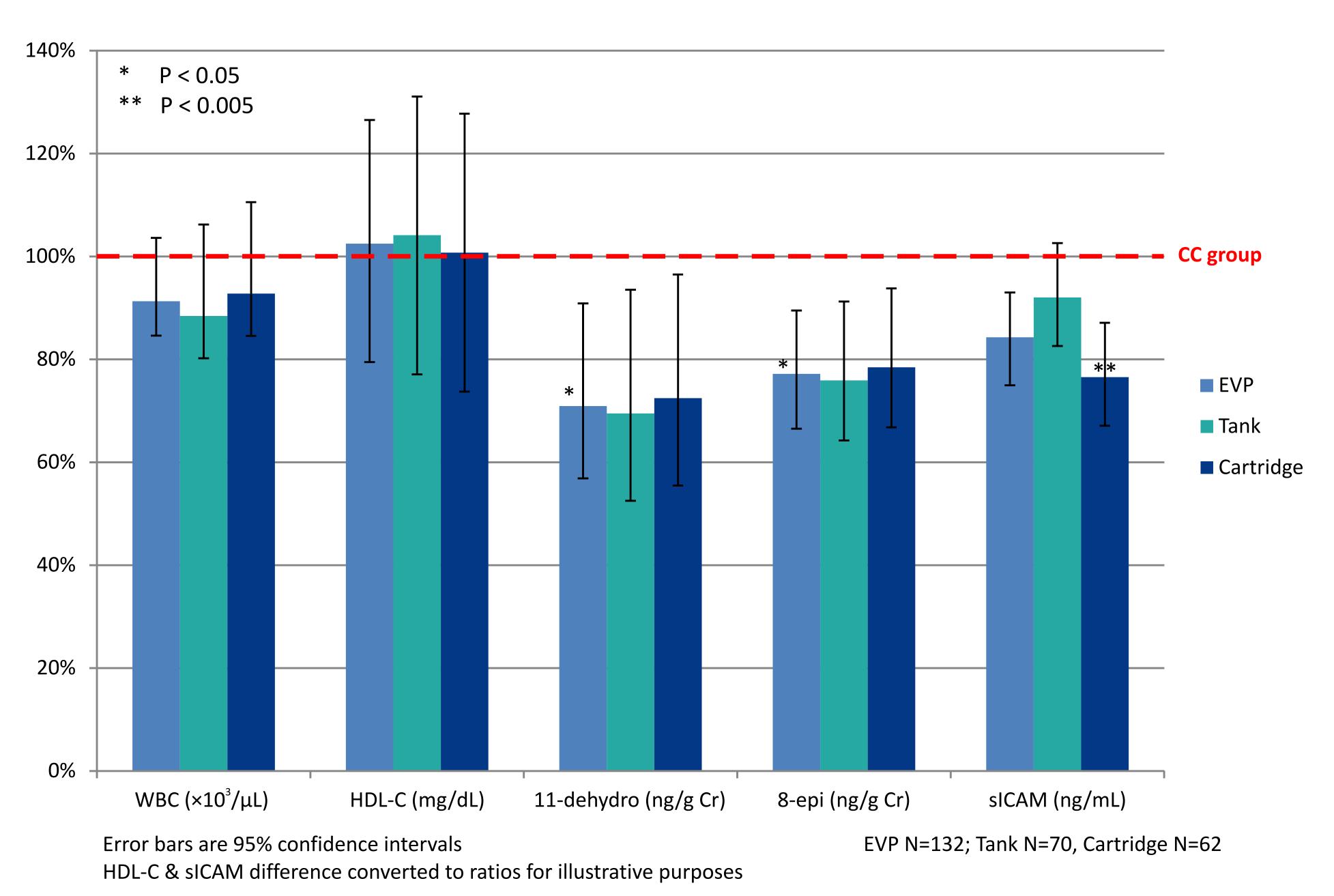
	Number of Subjects				
% COHb	Cigarette	Tank	Cartridge		
<u><</u> 2	8 (13%)	43 (62%)	33 (55%)		
<u>></u> 5	26 (43%)	12 (17%)	15 (25%)		

Summary

- Significantly lower levels of BOE were observed in exclusive EVP users compared to CC smokers
- Significantly lower levels of BOPH were found in exclusive EVP users compared to CC smokers, with the exception of WBC count and HDL-C
- Exclusion from analysis of subjects in the EVP groups with a COHb >5%, i.e., those subjects unlikely to be "exclusive" EVP users.
- All BOE, showed a greater difference between the EVP groups vs. CC group (reduced the p-values)
- WBC, 8-epi, and sICAM, showed a greater difference between the EVP groups vs. CC group (differences in WBC) now statistically significant)
- HDL-C and 11-dehydro, showed less difference between the EVP groups vs. CC group (differences in 11-dehydro now not statistically significant)
- The new clinical model paradigm was validated in this study.

This poster may be accessed at www.altria.com/ALCS-Science





BOE & BOPH in EVP Groups Excluding Subjects in EVP Group with COHb >5% (as a percentage of the CC Group)

