Research Article

Population estimates of biomarkers of exposure to carbon monoxide, nicotine, and NNK in smokers and non-smokers

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Assessment of potentially reduced risk tobacco products (PRRPs) can be facilitated with availability of a single baseline population estimate for biomarkers of exposure (BOEs) for select constituents in cigarette smoke. The purpose of this analysis is to establish such a population estimate for BOEs to carbon monoxide (carboxyhemoglobin - COHb), nicotine (Nicotine Equivalents - NEQ), and nicotine-derived nitrosamine ketone (NNK; total urinary 4-[methylnitrosamino]-1-[3-pyridyl]-1-butanol [NNAL] - NNAL) based on pooled weighted average from published literature.

Four databases - PubMed®, ScienceDirect®, TOXNET®, and Google Scholar™ – were systematically searched for published literature between 2008-2020 based on a protocol for literature assessment to identify and select studies. A total of 217 scientific articles were identified and reviewed for potential inclusion, 87 studies met the pre-set criteria (reported clinical studies and/or observational studies with reportable original values), and 53 studies met the inclusion criteria for each BOE. We determined the pooled weighted average based on Epanechnikov kernel density curves. The NNAL levels were normalized to a unit (pmol/mg creatinine) commonly used in research studies and reported as geometric means.

Smokers had significantly ($p<0.05$) higher levels of NNAL (1.112 pmol/mg creatinine; 95% confidence interval [CI] 0.161, 2.047), COHb (5.21 % saturation; 95% CI 3.91, 6.00), and NEQ (13.81 mg/24 h; 95% CI 9.08, 21.19) compared to non-smokers (0.008 pmol/mg creatinine, 95% CI 0.001, 0.017 for NNAL; 1.05% saturation, 95% CI 0.04, 2.07 for COHb; and 0.058 mg/24 h, 95% CI 0.016, 0.112 for NEQ) This research addresses the existing gap in lack of population level estimates for BOEs by establishing population level estimates for COHb, NEQ, and NNAL that can be used to determine changes in exposure for smokers switching to PRRPs.

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Introduction

Cigarettes are the most harmful tobacco products, and adult smokers who are unable or unwilling to quit may benefit by switching to potentially reduced risk tobacco products (PRRPs). In recent years, the tobacco product landscape has changed dramatically with the introduction of non-combustible products (e.g., e-vapor, heated tobacco products, and oral tobacco derived nicotine products) that deliver nicotine without many of the harmful and potentially harmful constituents (HPHCs) associated with combustion and are therefore potentially less deleterious than cigarettes. Biomarkers of exposure (BOEs) to HPHCs inform the potential health risks from PRRPs as actually used by adult tobacco consumers. Establishing population level estimates of exposure among smokers and non-smokers can help determine changes in exposure from using a PRRP relative to cigarettes. Most clinical studies determine the impact of switching to a PRRP by either comparing to the baseline level of exposure among the study participants that switched or comparing to a control group that continues to smoke. The availability of a single, reliable, weighted-average estimate of BOEs can be useful in determining the relative changes in exposure in adult smokers switching to PRRPs at the population level.

While biomarkers of tobacco exposure can be measured in many different biological matrices, most are measured through the collection of blood or urine samples (Oliveri, Liang, & Sarkar, 2020; Sarkar et al., 2010). Historically, urinary or salivary cotinine have been the most common measure of nicotine exposure, but recent studies often report urinary total nicotine equivalents (NEQ) that can be measured in either urine collected over 24 hours or assessed from a spot-urine sample and are often creatinine adjusted (Sarkar et al., 2013). One of the challenges for comparison of levels for the same BOE across studies is the lack of standardization of units for the reporting of results. For example, Appleton et al.'s 2014 review found nine different units of 4-[methylnitrosamino]-1-[3-pyridyl]-1-butanol (NNAL) expression reported in the literature (Appleton, Olegario, & Lipowicz, 2014). At the population level, no reliable estimates of BOEs have been harmonized to a common unit of measurement. Given the wide and growing range of nicotine products, from heated tobacco products and e-cigarettes to snus and modern oral tobacco-derived nicotine products, developing standardized estimates of carboxyhemoglobin (COHb), NEQ, and NNAL will enable researchers to quantify the relative effects across these diverse products and equally diverse use patterns.

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Assessment of biomarkers for cigarette smoke constituents must be specific and not from other sources of exposure, as well as representative of the particulate phase and gas/vapor phase of cigarette smoke. Total urinary NNAL represents metabolites of a tobacco-specific nitrosamine (TSNA), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK, nicotine-derived nitrosamine ketone), which is found in the particulate-phase of the smoke aerosol and identified as a carcinogen (U.S. Food and Drug Administration, 2012). Since NNK is tobacco-specific, this biomarker differentiates between smokers and non-smokers (Roethig et al., 2009); correlates with cigarette consumption (Hecht, 2004); and provides a reasonable proxy for overall smoke exposure (Wang, Liang, Mendes, & Sarkar, 2011). Due to its long half-life (> 10 days), NNAL levels are not prone to the variability in measurement due to transient changes in smoking behavior (Goniewicz et al., 2009; Hecht et al., 1999). Exposure to nicotine provides a direct assessment of cigarette smoking as nicotine is rapidly metabolized to several metabolites that reflect ~80-90% of the daily nicotine uptake (Feng et al., 2007; Hatsukami, Benowitz, Rennard, Oncken, & Hecht, 2006; Kandel, Hu, Schaffran, Udry, & Benowitz, 2007; St Charles, Krautter, Dixon, & Mariner, 2006). The molar sum of nicotine and its five major metabolites, expressed as NEQ, provides an accurate assessment of total nicotine exposure. Exposure to carbon monoxide (CO) as a combustion product found in the gas phase of cigarette smoke can most accurately be measured as a percent of hemoglobin saturation (COHb) and helps differentiate between smokers and non-smokers (Hatsukami et al., 2007; Rodgman & Perfetti, 2009; Stratton, Shetty, Wallace, & Bondurant, 2001). Furthermore, COHb has been suggested as a biomarker of cardiovascular risk in never smokers (Hedblad, Engström, Janzon, Berglund, & Janzon, 2006). Thus, total NNAL, NEQ, and COHb provide a reasonably accurate and specific assessment of overall cigarette smoke exposure.

The aim of this analysis is to estimate a population level weighted average of total NNAL, NEQ, and COHb in smokers and non-smokers that can be used as a baseline for the comparison of changes in exposure for smokers switching to PRRPs. This analysis is based on a review of the published literature from 2008 through 2020. We estimate a single pooled weighted average representative of the population level exposure. A pooling of weighted observed values is an important statistical methodology that provides the opportunity to combine results of studies, allowing an increase in the number of observations and to improve estimates of the effect size across a diverse set of study participants that can reasonably represent the population (Hunter & Schmidt, 1990; Schmidt & Hunter, 2004).

This analysis was initiated by scientists from five global tobacco companies involved in the Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) Biomarker Sub-Group (BMSG). Founded in 1956 under French law and consisting of 158 member organizations across 37 countries, CORESTA is a non-profit organization whose mission is to promote international cooperation in scientific research relative to tobacco and its derived products. CORESTA seeks to develop standardized nomenclature, definitions, and methodologies as well as provide guidelines, reports, and training across four research domains: agronomy and leaf integrity, phytopathology and genetics, product technology, and smoke science. One of the objectives of the BMSG is to review present knowledge of tobacco and smoking related BOEs and effects. We share the findings from our pooling of weighted average-observed values in this manuscript.

Methods

The literature review was conducted based on inclusion criteria developed (described in Supplemental Appendix A), to determine eligibility of the studies and to ensure relevance. The major components of the inclusion criteria were: timeframe (2008-2020); publication type (e.g., relevance, country); study design (e.g., crossover/randomized controlled clinical study, sample size); analyte (e.g., biomarker analyzed, analytical method, biological fluid measurement); and demographics (e.g., gender, age, smoking history). The default publication language was English, and all studies included human subjects. Four databases (PubMed®, ScienceDirect®, TOXNET®, and Google Scholar™) were queried for each search to represent relevant publications in the field of cigarette smoking. The literature search strategy consisted of a core of three terms, "clinical studies," "observational studies," and "cigarette smoking," in conjunction with the specific BOEs of interest, COHb, NEQs, and NNAL, published worldwide between 2008 and 2020. An evidence table created based on the studies that met the inclusion criteria was processed by reviewing and filtering data by publication year, group (e.g., smokers), source of data, source of the publication (e.g., academia), and reported statistical parameters (e.g., mean, standard deviation, etc.). Finally, data analysis was separately conducted for each biomarker. For NNAL, a conversion table was developed based on two key assumptions: a median creatinine level of 122.665 mg/dL (Barr et al., 2005) equivalent to 2,208 mg creatinine/24 h (>20 years old adults) and an assumed urine volume of 1,800 mL excreted per day (Clark et al., 2011). The NNAL molecular weight of 209.24 g/mol was used to convert picogram levels to picomol levels.

Statistical Analysis

The database was organized by categories, filtered, and data-weighted according to the size of the groups. We pooled the aggregated data from different studies, taking into account the smoking status after weighting the studies by sample size. For each group, the density of the data was estimated using a kernel density estimator approach. In this study, the Epanechnikov kernel (Epanechnikov, 1969), has been used:

$$\text{Epanechnikov: } K(x) = \frac{3}{4}\max\{1 - x^2; 0\} \qquad \text{(Equation 1)}$$

Based on this density curve, the key statistical information such as the average, the standard deviation, and confidence interval (CI) have been estimated. A general linear model with Tukey's all-pair comparisons was used to compare the average biomarker levels obtained by group.

Results

Literature Search

A total of 195 publications were originally identified for this analysis. Four reviewers assessed the publications independently and excluded 111 publications. The following reasons for exclusion were documented in the evidence table: data reported in other than humans, no clinical or observation data reported, studies that constituted reviews with no original data, or the data was part of another publication. In addition, NNAL studies were excluded when data format (e.g., arithmetic means or median values) could not be converted to the unit of choice for the analysis. Overall, 84 publications were found to meet the initial criteria for inclusion (Table 1).

Table 1. Total scientific studies

Biomarker	Number of Publications		
	Total	Met Criteria	Pooling Analysis Inclusion
COHb	50	31	21
NEQs	69	11	10
NNAL	76	42	19
Total	**195**	**84**	**50**

COHb: Carboxyhemoglobin; NEQ: Nicotine Equivalents; NNAL: total urinary 4-[methylnitrosamino]-1-[3-pyridyl]-1-butanol

After a careful review of the reported analytical data, 50 published cross-sectional clinical or observational studies reporting biomarker data were included in the analysis. The relevant data were captured in an evidence table according to gender, race, age, and other demographics and grouped by smokers, non-smokers, and former smokers (Supplemental Appendix A). The rationale for data exclusion was documented.

Characteristics of the Included Studies

The main characteristics of the included studies are shown in the evidence table (Supplemental Appendix A). The studies included adult smokers from a diverse range of geographical regions, including USA, Brazil, Switzerland, Poland, Korea, Taiwan, Japan, South Africa, and Nepal for COHb; USA, Germany, UK and Japan for NEQ; and USA, Canada, Poland, Germany, Syria, Egypt, and China for NNAL.

A total of 33,882 smokers were included in the analysis with 3,238 non-smokers as control subjects. A total of 16,311 smokers, 278 former smokers, and 1,949 non-smokers were included in the COHb analysis from 14 clinical studies (Appleton, Liu, Lipowicz, & Sarkar, 2015; Haziza, de La Bourdonnaye, Merlet, et al., 2016; Haziza, de La Bourdonnaye, Skiada, et al., 2016; Haziza et al., 2017; Lüdicke, Baker, Magnette, Picavet, & Weitkunat, 2017; Lüdicke, Haziza, Weitkunat, & Magnette, 2016; Lüdicke et al., 2018; Round, Chen, Taylor, & Schmidt, 2018; Sarkar et al., 2010; Tran, Bosilkovska, de La Bourdonnaye, Blanc, & Haziza, 2020; Tricker, Jang, Martin Leroy, Lindner, & Dempsey, 2012; Tricker, Kanada, et al., 2012; Tricker, Stewart, et al., 2012; Unverdorben et al., 2010; van Staden, Groenewald, Engelbrecht, Becker, & Hazelhurst, 2013) and 7 observational studies (Kung, Wang, & Tseng, 2008; Mendes et al., 2009; Muhammad-Kah, Hayden, Liang, Frost-Pineda, & Sarkar, 2011; Oliveri et al., 2020; Rodgman & Perfetti, 2009; Theron, Schultz, Ker, & Falzone, 2010; Wang et al., 2010). A total of 5,353 smokers, 55 former smokers, and 129 non-smokers were included in the NEQ analysis from 8 clinical studies (D'Ruiz, Graff, & Robinson, 2016; Lowe, Gregg, & McEwan, 2009; Morin, Shepperd, Eldridge, Poirier, & Voisine, 2011; Prasad, Jones, Chen, & Gregg, 2016; Roethig et al., 2008; Round et al., 2018; Scherer, Newland, Papadopoulou, & Minet, 2014; Yuki, Takeshige, Nakaya, & Futamura, 2018) and 2

observational studies (Camacho, Sommarström, Prasad, & Cunningham, 2016; Roethig et al., 2009). Similarly, an aggregate of 12,218 smokers and 1,160 non-smokers were included in the NNAL analysis from 6 clinical studies (Benowitz et al., 2012; Benowitz, Goniewicz, et al., 2010; Hatsukami et al., 2010; Meier et al., 2020; St Helen et al., 2012; Yuan et al., 2016) and 14 observational studies (Al Ali et al., 2015; Ashley et al., 2010; Benowitz, Dains, et al., 2010; Benowitz, Goniewicz, et al., 2010; Branstetter & Muscat, 2013; Camacho et al., 2016; Czoli & Hammond, 2015; Derby et al., 2009; Radwan, Hecht, Carmella, & Loffredo, 2013; Rostron, 2013; Vogel, Carmella, Stepanov, Hatsukami, & Hecht, 2011; Wasserman et al., 2018; Wei, Blount, Xia, & Wang, 2016; Yuan et al., 2011). The data identified for the former smokers group (cessation group) consisted of mixed units, which was inconsistent with the criteria considered for statistical analysis and was therefore not included in this analysis.

Only total urinary NNAL (sum of NNAL and NNAL-glucuronide), reported as geometric means (excluding medians), were included in the analysis. Free NNAL data or total NNAL reported as the arithmetic mean was captured in the evidence table but was not included in the statistical analysis.

Summary of biomarker levels across groups

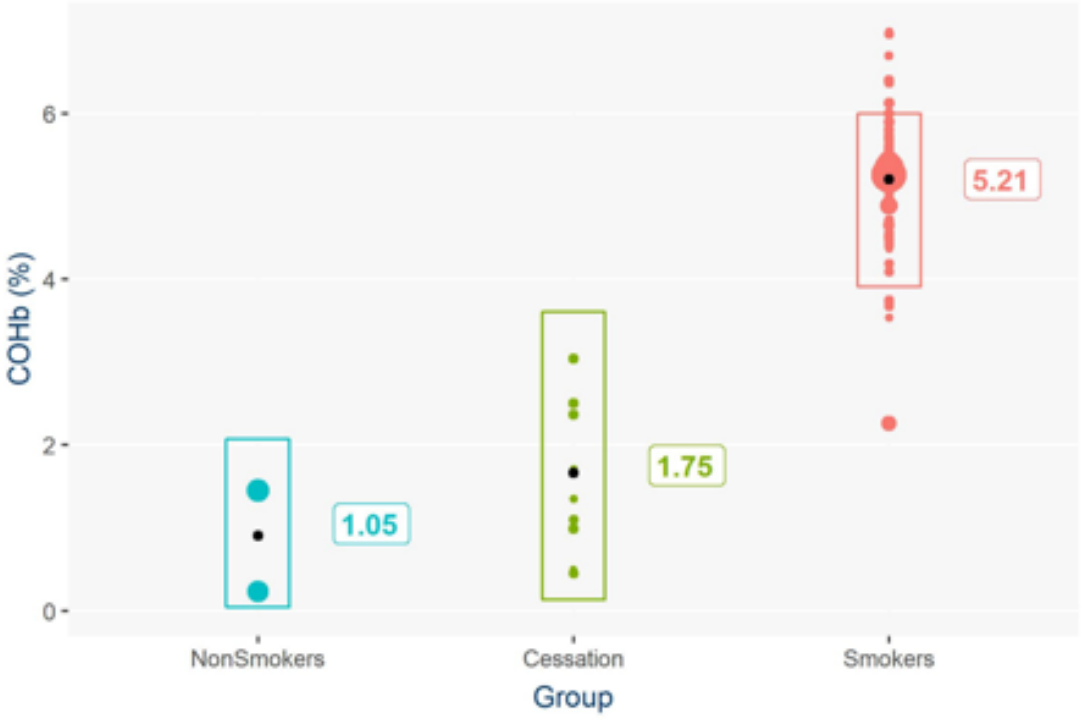
Carboxyhemoglobin. Not surprisingly, smokers had the highest percent COHb (5.21%) compared to former smokers (1.75%) and non-smokers (1.05%; Table 2a and Figure 1)

Table 2a. Percent Saturation Carboxyhemoglobin (% COHb)

Group	# Groups	Total Individuals	Average	Min	Max	S.D.	95% CI (LL)	95% CI (UL)
Non-smokers	2	1,949	1.05	0.23	1.45	0.61	0.04	2.07
Former Smokers	10	278	1.75	0.45	3.04	1.00	0.14	3.61
Smokers	61	16,311	5.21	2.26	6.99	0.56	3.91	6.00

SD: Standard Deviation; CI: Confidence Interval; LL: Lower Limit; UL: Upper Limit

Figure 1. Pooled weighted average estimates of COHb levels in non-smokers, former smokers, and current smokers



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Significant differences (p<0.0001) were observed for smokers compared to former smokers as well as to non-smokers. The former smokers group and non-smokers were not statistically different from each other (p=0.283; Table 3a).

Table 3a. Statistical Results for Carboxyhemoglobin

Group Comparison	Difference	P-value
Smokers vs. Non-smokers	4.30	< 0.0001
Smokers vs. Former Smokers	3.55	< 0.0001
Former Smokers vs. Non-smokers	0.76	0.283

P-values <0.05 were considered statistically significantly different.

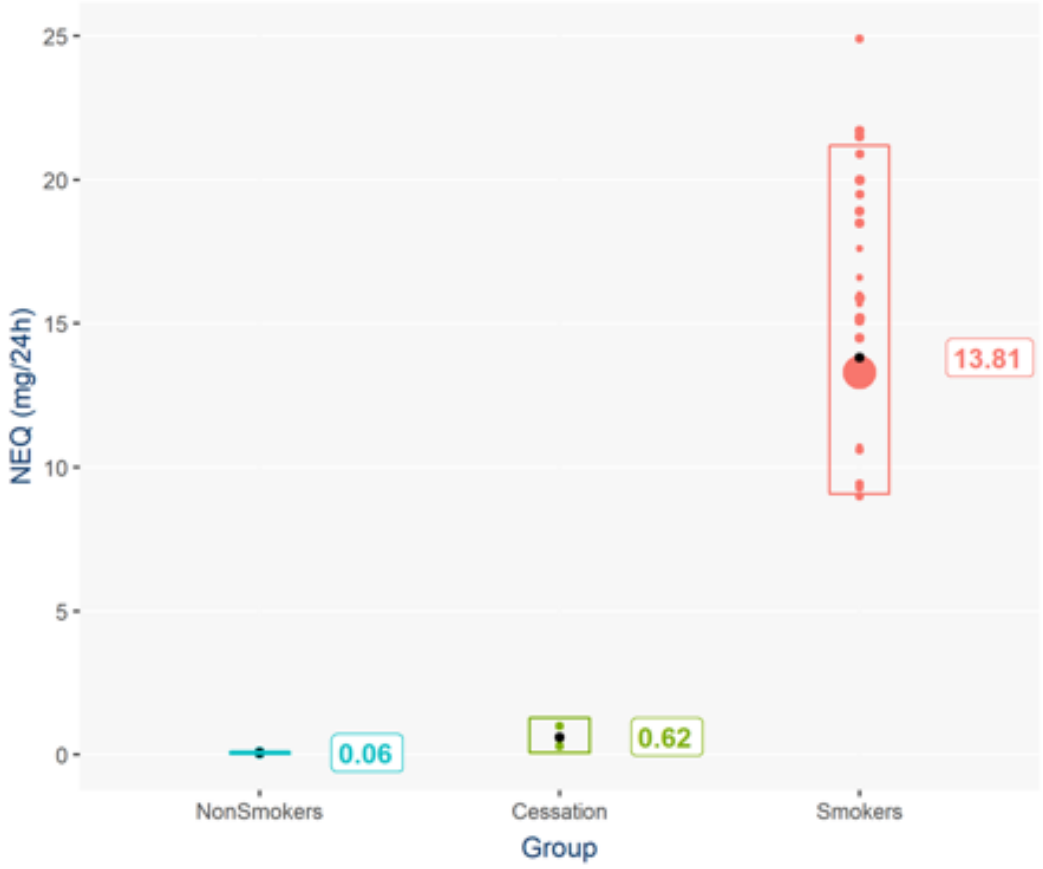
Nicotine Equivalents. The smokers group had the highest NEQ levels (13.81 mg/24 h) compared to former smokers (0.62 mg/24 h) and non-smokers (0.058 mg/24 h; Table 2b and Figure 2).

Table 2b. Nicotine Equivalents (mg/24 h)

Group	#Groups	Total Individuals	Average	Min	Max	S.D.	95% CI (LL)	95% CI (UL)
Non-smokers	4	129	0.058	0.03	0.10	0.031	0.016	0.112
Former Smokers	3	55	0.62	0.30	1.00	0.35	0.070	1.281
Smokers	26	5,353	13.81	9.00	24.91	2.82	9.081	21.190

SD: Standard Deviation; CI: Confidence Interval; LL: Lower Limit; UL: Upper Limit

Figure 2. Pooled weighted average estimates of NEQ levels in non-smokers, former smokers, and current smokers



Statistically significant differences (p<0.0001) were observed between smokers and non-smokers, and (p<0.001) between smokers and former smokers. The former smokers group and non-smokers were not statistically different from each other (p=0.99; Table 3b).

Table 3b. Statistical Results for Nicotine Equivalents (NEQ)

Group Comparison	Difference	P-value
Smokers vs. Non-smokers	13.75	< 0.0001
Smokers vs. Former Smokers	113.20	< 0.001
Former Smokers vs. Non-smokers	0.55	0.99

P-values <0.05 were considered statistically significantly different·

NNAL. Smokers had the highest level of NNAL (1.112 pmol/mg creatinine) compared to nonsmokers (0.008 pmol/mg creatinine; Table 2c and Figure 3).

Table 2c. NNAL (pmol/mg creatinine)

Group	# Groups	Total Individuals	Average	Min	Max	S.D.	95 % CI (LL)	95 % CI (UL)
Non-smokers	3	1,160	0.008	0.002	0.014	0.0038	0.001	0.017
Smokers	36	12,218	1.112	0.182	1.842	0.5505	0.161	2.047

SD: Standard Deviation; CI: Confidence Interval; LL: Lower Limit; UL: Upper Limit

Figure 3. Pooled weighted average estimates of NNAL levels in non-smokers and current smokers

Statistical analysis indicated that NNAL levels in smokers and nonsmokers were significantly different (p=0.0002; Table 3c). The former smokers group was not included in the analysis.

Table 3c. Statistical Results for NNAL

Group Comparison	Difference	P-value
Smokers vs. Non-smokers	1.09	0.0002

P-values <0.05 were considered statistically significantly different.

Discussion

We report here the population estimate of pooled weighted averages of key BOEs of cigarette smoke to establish baseline levels for smokers and non-smokers. While there are many studies of BOEs in tobacco research, and many tobacco exposure biomarkers can be measured, it may not always be practical to measure every available biomarker in every evaluation (Chang et al., 2017). The availability of a single population level estimate should allow for estimating changes in the levels of these biomarkers among those adult smokers switching to a PRRP. Additionally, the population estimate among former smokers and non-smokers provides data to support relative comparisons for evaluating reductions in HPHCs among those who completely switched to PRRPs. Characterization of changes in exposure to HPHCs through BOEs provides important information regarding the reduced risk potential of a tobacco product (Chang et al., 2017).

Exposure to CO, a product of incomplete combustion of all organic materials, can be measured in the blood as COHb (as percent saturation of hemoglobin). COHb is a well-established biomarker for CO due to correlation with exhaled CO, dose response with cigarette smoking, and its relationship with smoking cessation (Hatsukami et al., 2006). The results reported in our analysis align with values reported in literature. For example, in the Total Exposure Study (Roethig et al., 2009), which was a cross-sectional study of U.S. cigarette smokers (n = 3,585) and non-smokers (n = 1,077), COHb distinguished smokers from non-smokers with a 3.6-fold difference. In our analysis we observed a 4.96-fold difference between smokers and non-smokers and 1.67-fold

difference between smokers and former smokers. These observations provide useful information for designing studies on smoking cessation. COHb and CO are considered some of the most useful biomarkers for verifying smoking cessation in clinical trials. Additionally, COHb was not statistically different between former smokers (1.75%) and non-smokers (1.05%, Table 2a and Figure 1), demonstrating further, the utility of COHb as a marker of cessation.

Nicotine equivalents (NEQ) are the molar sum of urinary nicotine, cotinine, and several metabolites in the nicotine metabolic profile. NEQ is often considered the gold standard for daily nicotine intake. Unlike cotinine, NEQ accommodates factors that influence nicotine metabolism and exhibits a strong correlation with several tobacco BOEs, including hydroxy-PAHs and NNAL (Benowitz, Dains, Dempsey, Wilson, & Jacob, 2011). Similarly, 24 h urine NEQ has been suggested to be a surrogate measure for smoke exposure (Wang et al., 2011).

NNAL is the primary metabolite of NNK, a nicotine-derived nitrosamine ketone. NNAL is considered a good BOE because it is tobacco-specific and has a long half-life in biological fluids, around 10 to 45 days, making it less liable to variability in measurement due to transient changes in smoking behavior (Radwan et al., 2013; Roethig et al., 2009). In addition, NNAL correlates with other tobacco-specific markers, including cotinine and TNE (Goniewicz et al., 2009; Rostron et al., 2019). Several large epidemiologic studies, such as the National Health and Nutrition Examination Survey (NHANES), the Total Exposure Study, and the Multiethnic Cohort Study, report typical ranges of 1 to 2 pmol NNAL/mL of urine for smokers (Mendes et al., 2009; Roethig et al., 2008; Rostron, 2013; Round et al., 2018). Rostron et al., (2019) reported NNAL concentration by tobacco use status of the NHANES 1999 to 2012 data. The average value for exclusive cigarette smokers of 217.6 pg/mg creatinine (converted to 1.04 pmol/mg creatinine) was comparable to the pooled weighted average (1.11 pmol/mg creatinine) reported in our analysis. We note that the mean values for non-tobacco users (non-smokers) was 0.98 pg/mg creatinine (converted to 0.005 pmol/mg creatinine), which was lower than the value reported in our analysis (0.008 pmol/mg creatinine). Rostron et al., (2019) reported NNAL concentration by cigarettes per day from the Population Assessment of Tobacco and Health (PATH) Study Wave 1 (2013 – 2014). This study reported mean levels ranging between 155.26 and 295.76 ng/g creatinine (converted to 0.742 and 1.413 pmol /mg creatinine). In our analysis we report a mean value of 1.11 pmol/mg creatinine, which is within the range reported by Rostron et al., (2019).

The analyses presented here should be considered in light of several limitations. The analysis included data from different study populations across different geographical regions representing a range of different smoking behaviors and different cigarette types. However, estimating pooled weighted averages from a wide subset of study populations can provide a reasonable approximation of the overall population estimate. Additionally, the analytes were likely measured using different bioanalytic methodologies with possible differences in laboratory equipment, sensitivities, and calibration ranges. Nonetheless our analysis should be considered a general overall average as we pooled the aggregated data from different studies, taking into account the smoking status after weighting them by the sample size. In the case of NNAL, the analysis was limited to the largest body of data that either reported, or could be converted to, common units of NNAL excretion (pmol/mg creatinine). Also, due to data gaps in the reporting of demographic information, this analysis ignores characteristics of subgroups such as race, gender, population size of the country, etc. Therefore, observations reported may not be generalizable of the world population. Nonetheless, our pooled weighted averages should be considered reasonable population estimates that may be useful as baseline values for COHb, NEQ, and NNAL. The availability of a single reliable weighted average estimate of BOEs can be useful in determining the relative changes in exposure in adult smokers switching to PRRPs at the population level.

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Supplemental Appendix A

NNAL Conversion Table

Evidence Tables:

1. COHb: Complete list of studies included in the analysis; summary with study types

2. NEQ: Complete list of studies included in the analysis; summary with study types

3. NNAL: Complete list of studies included in the analysis; summary with study types

NNAL Conversion Table

								References:							
		NNAL Conversion						Urine 1.8 L/day (Median) (Clark et al., CJASN 6(11):2634-2641 (2011) Ref. 18.							
								0.8 -2 L/day (Medline Plus Medical Encyclopedia) https://medlineplus.gov/ency/article/003425.htm. Accessed 18-Nov. 2020.							
		1 pg	1E-12	g				Creatinine: 122.665 ± 24.025 mg/dL (1226.65 ± 240.25 mg/L)							
		1 L	1000	mL				From Barr et al 2005 (ALL adults > 20years old) Ref. 6.							
		NNAL MW	209.24	g/mol				Normal urine creatinine values generally range from 955 to 2,936							
		1 mol/L	1E-12	pmol/L				mg per 24 h for males, and 601 to 1,689 mg per 24 hs for							
		Total 24h Urine	1,800	mL				females, according to the Mayo Clinic. https://www.healthline.com/health/high-creatinine-symptoms#desired-range. Accessed 20-Nov. 2020.							
		Creatinine	2208	mg/24h				Min	601	mg/24 h					
		BW						Likely	1226.65x1.8L = 2208	mg/24 h					
								Max	2936	mg/24 h					
Study ID		pg/mL	pg/24h urine	ng/24h urine	pmol/L	Total pmol		Creatinine mg/24 h	pg NNAL/mg creatinine	ng NNAL/ mg creatinine	pmol NNAL/ mg creatinine	Reference	Published value	Published Units	
1											1.14	Meier et al 2020, Ref. 52	1.14	pmol/mg creat	
1											1.29	Meier et al 2020, Ref. 52	1.29		
1											1.38	Meier et al 2020, Ref. 52	1.38		
1											1.31	Meier et al 2020, Ref. 52	1.31		
1											1.15	Meier et al 2020, Ref. 52	1.15		
1											1.43	Meier et al 2020, Ref. 52	1.43		

2											0.008	Wasserman et al 2018, Ref. 94	0.008	pmol/mg creat
2											0.77	Wasserman et al 2018, Ref. 94	0.77	
2											1.474	Wasserman et al 2018, Ref. 94	1.474	
2											1.217	Wasserman et al 2018, Ref. 94	1.217	
3											N/A		N/A	N/A
4											N/A		N/A	N/A
5											N/A		N/A	N/A
6											N/A		N/A	N/A
7			307720	307.72		1470.655706		2208	139.365942	0.139365942	0.666	Camacho et al 2016, Ref. 12	307.72	ng/24 h
7			188000	188		898.4897725		2208	85.14492754	0.085144928	0.407	Camacho et al 2016, Ref. 12	188	
7			249000	249		1190.021028		2208	112.7717391	0.112771739	0.539	Camacho et al 2016, Ref. 12	249	
7			333000	333		1591.473906		2208	150.8152174	0.150815217	0.721	Camacho et al 2016, Ref. 12	333	
7			149000	149		712.1009367		2208	67.48188406	0.067481884	0.323	Camacho et al 2016, Ref. 12	149	
7			195000	195		931.9441789		2208	88.31521739	0.088315217	0.422	Camacho et al 2016, Ref. 12	195	
7			266000	266		1271.267444		2208	120.4710145	0.120471014	0.576	Camacho et al 2016, Ref. 12	266	
8											0.89	Yuan et al 2016, Ref. 99	0.89	pmol/mg creat
8											0.85	Yuan et al 2016, Ref. 99	0.85	
8											0.94	Yuan et al 2016, Ref. 99	0.94	

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9		200	360000	360	955.8401835	1720.51233		2208	163.0434783	0.163043478	0.779	Wei et al 2016, Ref. 95	200	pg/mL urine
9		1.08	1944	1.944	5.161536991	9.290766584		2208	0.880434783	0.000880435	0.004	Wei et al 2016, Ref. 95	1.08	
9		195	351000	351	931.9441789	1677.499522		2208	158.9673913	0.158967391	0.760	Wei et al 2016, Ref. 95	195	
9		205	369000	369	979.7361881	1763.525139		2208	167.1195652	0.167119565	0.799	Wei et al 2016, Ref. 95	205	
9			476928	476.928		2279.334735		2208	216	0.216	1.032	Wei et al 2016, Ref. 95	216	pg/mg creat
9			2627.52	2.62752		12.557446		2208	1.19	0.00119	0.006	Wei et al 2016, Ref. 95	1.19	
9			415104	415.104		1983.865418		2208	188	0.188	0.898	Wei et al 2016, Ref. 95	188	
9			565248	565.248		2701.43376		2208	256	0.256	1.223	Wei et al 2016, Ref. 95	256	
10		71.2	128160	128.16	340.2791053	612.5023896		2208	58.04347826	0.058043478	0.277	Czoli & Hammond, 2015, Ref. 20	71.2	pg/mL urine
10		82	181056	181.056		865.3030013		2208	82	0.082	0.392	Czoli & Hammond, 2015, Ref. 20	82	pg/mg creat
11											N/A			N/A
12											N/A			N/A
13		10.7	19260	19.26	51.13744982	92.04740967		2208	8.722826087	0.008722826	0.042	Ali et al 2015, Ref. 2	10.7	pg/mL urine
13		46.8	84240	84.24	223.6666029	402.5998853		2208	38.15217391	0.038152174	0.182	Ali et al 2015, Ref. 2	46.8	
13			19651.2	19.6512		93.91703307		2208	8.9	0.0089	0.043	Ali et al 2015, Ref. 2	8.9	ng/g creatinine
13			86332.8	86.3328		412.601797		2208	39.1	0.0391	0.187	Ali et al 2015, Ref. 2	39.1	
14											N/A			N/A
15		460	828000	828	2198.432422	3957.17836		2208	375	0.375	1.792	Branstetter, Muscat 2013, Ref. 11	0.46	ng/mL urine
15		470	846000	846	2246.224431	4043.203976		2208	383.1521739	0.383152174	1.831	Branstetter, Muscat 2013, Ref. 11	0.47	

15		450	810000	810	2150.640413	3871.152743		2208	366.8478261	0.366847826	1.753	Branstetter, Muscat 2013, Ref. 11	0.45	
16											1.22	Radwan et al 2013, Ref. 60	1.22	pmol/mg creat
17			584016	584.016		2791.129803		2208	264.5	0.2645	1.264	Rostron B. 2013, Ref. 64	264.5	pg/mg creat
17			850963.2	850.9632		4066.924106		2208	385.4	0.3854	1.842	Rostron B. 2013, Ref. 64	385.4	
18											N/A			N/A
19											N/A			N/A
20			461472	461.472		2205.467406		2208	209	0.209	1.00	Benowitz et al 2012, Ref. 10	0.209	ng/mg creatinine
20			415104	415.104		1983.865418		2208	188	0.188	0.90	Benowitz et al 2012, Ref. 10	0.188	
20			461472	461.472		2205.467406		2208	209	0.209	1.00	Benowitz et al 2012, Ref. 10	0.209	
20			646944	646.944		3091.875358		2208	293	0.293	1.40	Benowitz et al 2012, Ref. 10	0.293	
20			554208	554.208		2648.671382		2208	251	0.251	1.20	Benowitz et al 2012, Ref. 10	0.251	
20			368736	368.736		1762.26343		2208	167	0.167	0.80	Benowitz et al 2012, Ref. 10	0.167	
20			600576	600.576		2870.27337		2208	272	0.272	1.30	Benowitz et al 2012, Ref. 10	0.272	
20			554208	554.208		2648.671382		2208	251	0.251	1.20	Benowitz et al 2012, Ref. 10	0.251	
20			322368	322.368		1540.661441		2208	146	0.146	0.70	Benowitz et al 2012, Ref. 10	0.146	
21											0.014	St Helen et al 2012, Ref. 78	0.014	pmol/mg creat
21											0.0018	St Helen et al 2012, Ref. 78	0.0018	
21											0.88	St Helen et al 2012, Ref. 78	0.88	

doi.org/10.32388/ZJJ66O

21											1.05	St Helen et al 2012, Ref. 78	1.05	
22											0.28	Yuan et al 2011, Ref. 98	0.28	pmol/mg creat
22											0.2	Yuan et al 2011, Ref. 98	0.2	
23					1120	2016		2208			0.913	Vogel et al 2011, Ref. 91	1.12	pmol/mL urine
23					610	1098		2208			0.497	Vogel et al 2011, Ref. 91	0.61	
23					920	1656		2208			0.750	Vogel et al 2011, Ref. 91	0.92	
23					1250	2250		2208			1.019	Vogel et al 2011, Ref. 91	1.25	
23					810	1458		2208			0.660	Vogel et al 2011, Ref. 91	0.81	
23					1360	2448		2208			1.109	Vogel et al 2011, Ref. 91	1.36	
23					820	1476		2208			0.668	Vogel et al 2011, Ref. 91	0.82	
23					2950	5310		2208			2.405	Vogel et al 2011, Ref. 91	2.95	
23					2330	4194		2208			1.899	Vogel et al 2011, Ref. 91	2.33	
23					1180	2124		2208			0.962	Vogel et al 2011, Ref. 91	1.18	
23					2060	3708		2208			1.679	Vogel et al 2011, Ref. 91	2.06	
23					2140	3852		2208			1.745	Vogel et al 2011, Ref. 91	2.14	
24											N/A			N/A
25											N/A			N/A
26											N/A			N/A
27											N/A			N/A
28											N/A			N/A
29											0.9	Benowitz et al 2010, Ref. 7	0.9	pmol/mg creat
29											1.2	Benowitz et al 2010, Ref. 7	1.2	

30			492384	492.384		2353.202065		2208	223	0.223	1.07	Benowitz et al 2010, Ref. 8	223	pg/mg creat
30			264960	264.96		1266.297075		2208	120	0.12	0.57	Benowitz et al 2010, Ref. 8	120	
31			158976	158.976		759.7782451		2208	72	0.072	0.344	Ashley et al 2010, Ref. 5	0.072	ng/mg creatinine
31			640320	640.32		3060.217932		2208	290	0.29	1.386	Ashley et al 2010, Ref. 5	0.29	
31			479136	479.136		2289.887211		2208	217	0.217	1.037	Ashley et al 2010, Ref. 5	0.217	
31			240672	240.672		1150.219843		2208	109	0.109	0.521	Ashley et al 2010, Ref. 5	0.109	
31			306912	306.912		1466.794112		2208	139	0.139	0.664	Ashley et al 2010, Ref. 5	0.139	
32											N/A			N/A
33											0.96	Hatsukami et al 2010, Ref. 29	0.96	pmol/mg creat
33											0.92	Hatsukami et al 2010, Ref. 29	0.92	
33											1.06	Hatsukami et al 2010, Ref. 29	1.06	
34					640	1152		2208			0.522	Derby et al 2009, Ref. 22	0.64	pmol/mL urine
34					980	1764		2208			0.799	Derby et al 2009, Ref. 22	0.98	
34					850	1530		2208			0.693	Derby et al 2009, Ref. 22	0.85	
34					1130	2034		2208			0.921	Derby et al 2009, Ref. 22	1.13	
34					700	1260		2208			0.571	Derby et al 2009, Ref. 22	0.7	
34					600	1080		2208			0.489	Derby et al 2009, Ref. 22	0.6	
34					820	1476		2208			0.668	Derby et al 2009, Ref. 22	0.82	

35											N/A		N/A
36											N/A		N/A
37											N/A		N/A
38											N/A		N/A
39											N/A		N/A
40											N/A		N/A
41			960480	960.48		4590.326897	2208	435	0.435	2.08	Goniewicz et al 2009, Ref. 26	435	pg/mg creat
41			82137.6	82.1376		392.5520933	2208	37.2	0.0372	0.18	Goniewicz et al 2009, Ref. 26	37.2	
42											N/A		N/A
43											N/A		N/A

Evidence Tables:

Supplemental Table 1 COHb: Complete list of studies included in the analysis; summary with study types

Ref. ID	PUB_Yearso	PUB_Years	PUB_Type	PUB_Name	PUB_Country	PUB_Authors	PUB_Company	PUB_Code_comp	PUB_Title	PUB_r
71	2018	2017	Research article	Journal of Medical Toxicology	USA	Schimmel J., George N., Schwarz, N., Yousif S., Suner S., Hack J.B.	Academia	Other	Carboxyhemoglobin Levels Induced by Cigarette Smoking Outdoors in Smokers	N
71	2018	2017	Research article	Journal of Medical Toxicology	USA	Schimmel J., George N., Schwarz, N., Yousif S., Suner S., Hack J.B.	Academia	Other	Carboxyhemoglobin Levels Induced by Cigarette Smoking Outdoors in Smokers	N
71	2018	2017	Research article	Journal of Medical Toxicology	USA	Schimmel J., George N., Schwarz, N., Yousif S., Suner S., Hack J.B.	Academia	Other	Carboxyhemoglobin Levels Induced by Cigarette Smoking Outdoors in Smokers	N
49	2018	2018	Research article	Regulatory Toxicology and Pharmacology	Switzerland Poland	Florian Martin, Gregory Vuillaume, GizelleBaker, Zheng Sponsiello-Wang, Paolo F. Ricci, Frank Lüdicke, Rolf Weitkunat	Academia PMI	Mixed	Quantifying the risk-reduction potential of new Modified Risk Tobacco Products	N
49	2018	2018	Research article	Regulatory Toxicology and Pharmacology	Switzerland Poland	Florian Martin, Gregory Vuillaume, GizelleBaker, Zheng Sponsiello-Wang, Paolo F. Ricci, Frank Lüdicke, Rolf Weitkunat	Academia PMI	Mixed	Quantifying the risk-reduction potential of new Modified Risk Tobacco Products	N
49	2018	2018	Research article	Regulatory Toxicology and Pharmacology	Switzerland Poland	Florian Martin, Gregory Vuillaume, GizelleBaker, Zheng Sponsiello-Wang, Paolo F. Ricci, Frank Lüdicke, Rolf Weitkunat	Academia PMI	Mixed	Quantifying the risk-reduction potential of new Modified Risk Tobacco Products	N
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker,	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing	YI

						Patrick Picavet, Frank Lüdicke			smoking or abstaining from smoking for 5days	
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing smoking or abstaining from smoking for 5days	YI
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing smoking or abstaining from smoking for 5days	YI
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing smoking or abstaining from smoking for 5days	YI
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing smoking or abstaining from smoking for 5days	YI
33	2017	2017	Research article	Data in Brief	USA	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Biomarker of exposure level data set in smokers switching from conventional cigarettes to THS 2.2, continuing smoking or abstaining from smoking for 5days	YI
46	2017	2017	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Gizelle Baker, John Magnette, Patrick Picavet, Rolf Weitkunat	PMI	Tobacco	Reduced Exposure to Harmful and Potentially Harmful Smoke Constituents with the THS 2.1	YI

46	2017	2017	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Gizelle Baker, John Magnette, Patrick Picavet, Rolf Weitkunat	PMI	Tobacco	Reduced Exposure to Harmful and Potentially Harmful Smoke Constituents with the THS 2.1	YI
46	2017	2017	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Gizelle Baker, John Magnette, Patrick Picavet, Rolf Weitkunat	PMI	Tobacco	Reduced Exposure to Harmful and Potentially Harmful Smoke Constituents with the THS 2.1	YI
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46	2017	2017	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Gizelle Baker, John Magnette, Patrick Picavet, Rolf Weitkunat	PMI	Tobacco	Reduced Exposure to Harmful and Potentially Harmful Smoke Constituents with the THS 2.1	YI
46	2017	2017	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Gizelle Baker, John Magnette, Patrick Picavet, Rolf Weitkunat	PMI	Tobacco	Reduced Exposure to Harmful and Potentially Harmful Smoke Constituents with the THS 2.1	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux,	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure:	YI

						Nicola Lama, Rof Weitkunat			A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux,	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled,	YI

						Nicola Lama, Rof Weitkunat			Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	
48	2018	2018	Research article	Nicotine & Tobacco Research	Switzerland Japan	Frank Lüdicke, Patrick Picavet, Gizelle Baker, Christelle Haziza, Valerie Poux, Nicola Lama, Rof Weitkunat	PMI	Tobacco	Effects of Switching to the THS 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confiment and Ambulatory Settings (Part 1)	YI
32	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Evaluation of the Tobacco Heating System 2.2. Part8_5-Day randomized reduced exposure clinical study in Poland	N
32	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Evaluation of the Tobacco Heating System 2.2. Part8_5-Day randomized reduced exposure clinical study in Poland	N
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32	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz,	PMI	Tobacco	Evaluation of the Tobacco Heating System 2.2. Part8_5-Day randomized reduced exposure clinical study in Poland	N

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32	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Evaluation of the Tobacco Heating System 2.2. Part8_5-Day randomized reduced exposure clinical study in Poland	N
31	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland Japan	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Assessment of the reduction in levels of exposure to HPHCs in Japanese subjects using a novel THS compared to conventional cigarettes and smoking abstinence_A randomized controlled study in confinement	YI
31	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland Japan	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Assessment of the reduction in levels of exposure to HPHCs in Japanese subjects using a novel THS compared to conventional cigarettes and smoking abstinence_A randomized controlled study in confinement	YI
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31	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland Japan	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada,	PMI	Tobacco	Assessment of the reduction in levels of exposure to HPHCs in Japanese subjects using a	YI

						Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke			novel THS compared to conventional cigarettes and smoking abstinence_A randomized controlled study in confinement	
3	2016	2016	Research article	Regulatory Toxicology and Pharmacology	Switzerland Japan	Christelle Haziza, Guillaume de La Bourdonnaye, Dimitra Skiada, Jacek Ancerewicz, Gizelle Baker, Patrick Picavet, Frank Lüdicke	PMI	Tobacco	Assessment of the reduction in levels of exposure to HPHCs in Japanese subjects using a novel THS compared to conventional cigarettes and smoking abstinence_A randomized controlled study in confinement	YI
47	2016	2016	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Christelle Haziza, Rolf Weitkunat, John Magnette	PMI	Tobacco	Evaluation of biomarkers of exposure in Smokers Switching to a Carbon-Heated Tobacco Product: A Controlled, Randomized, Open-Label 5-Day Exposure Study	YI
47	2016	2016	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Christelle Haziza, Rolf Weitkunat, John Magnette	PMI	Tobacco	Evaluation of biomarkers of exposure in Smokers Switching to a Carbon-Heated Tobacco Product: A Controlled, Randomized, Open-Label 5-Day Exposure Study	YI
47	2016	2016	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Christelle Haziza, Rolf Weitkunat, John Magnette	PMI	Tobacco	Evaluation of biomarkers of exposure in Smokers Switching to a Carbon-Heated Tobacco Product: A Controlled, Randomized, Open-Label 5-Day Exposure Study	YI
47	2016	2016	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Christelle Haziza, Rolf Weitkunat, John Magnette	PMI	Tobacco	Evaluation of biomarkers of exposure in Smokers Switching to a Carbon-Heated Tobacco Product: A Controlled, Randomized, Open-Label 5-Day Exposure Study	YI
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									Open-Label 5-Day Exposure Study	
47	2016	2016	Research article	Nicotine & Tobacco Research	Switzerland	Frank Lüdicke, Christelle Haziza, Rolf Weitkunat, John Magnette	PMI	Tobacco	Evaluation of biomarkers of exposure in Smokers Switching to a Carbon-Heated Tobacco Product: A Controlled, Randomized, Open-Label 5-Day Exposure Study	YI
4	2015	2015	Research article	Inhalation Toxicology	USA	Appleton, S., Liu J., Lipowicz, P.J. and Mohamadi Sarkar	Altria	Tobacco	Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters	YI
4	2015	2015	Research article	Inhalation Toxicology	USA	Appleton, S., Liu J., Lipowicz, P.J. and Mohamadi Sarkar	Altria	Tobacco	Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters	YI
4	2015	2015	Research article	Inhalation Toxicology	USA	Appleton, S., Liu J., Lipowicz, P.J. and Mohamadi Sarkar	Altria	Tobacco	Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters	YI
4	2015	2015	Research article	Inhalation Toxicology	USA	Appleton, S., Liu J., Lipowicz, P.J. and Mohamadi Sarkar	Altria	Tobacco	Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters	N
4	2015	2015	Research article	Inhalation Toxicology	USA	Appleton, S., Liu J., Lipowicz, P.J. and Mohamadi Sarkar	Altria	Tobacco	Effect of cigarette design on biomarkers of exposure, puffing topography and respiratory parameters	N
82	2015	2015	Meeting abstract	Abstract EUROTOX -	USA	Eugenia Theophilus, Christopher Coggins, Peter Chen, Eckhardt Schmidt, Michael Borgerding	Academia	Other	Magnitudes of biomarker reductions in response to controlled reductions in cigarettes smoked per day: A one-week clinical confinement study	N
96	2013	2013	Research article	Respiration	Brazil	R. Fagundes Xavier, D. Ramos, J. Tiyaki Ito, F.M. Machado Rodrigues, G. Navarro Bertolini, M. Macchione, A. Choqueta de Toledo, E.M. Cipulo Ramos	Academia	Other	Effects of Cigarette Smoking Intensity on the Mucociliary Clearance of Active Smokers	N
96	2013	2013	Research article	Respiration	Brazil	R. Fagundes Xavier, D. Ramos,	Academia	Other	Effects of Cigarette Smoking Intensity on the	N

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						J. Tiyaki Ito, F.M. Machado Rodrigues, G. Navarro Bertolini, M. Macchione, A. Choqueta de Toledo, E.M. Cipulo Ramos			Mucociliary Clearance of Active Smokers	
96	2013	2013	Research article	Respiration	Brazil	R. Fagundes Xavier, D. Ramos, J. Tiyaki Ito, F.M. Machado Rodrigues, G. Navarro Bertolini, M. Macchione, A. Choqueta de Toledo, E.M. Cipulo Ramos	Academia	Other	Effects of Cigarette Smoking Intensity on the Mucociliary Clearance of Active Smokers	N
96	2013	2013	Research article	Respiration	Brazil	R. Fagundes Xavier, D. Ramos, J. Tiyaki Ito, F.M. Machado Rodrigues, G. Navarro Bertolini, M. Macchione, A. Choqueta de Toledo, E.M. Cipulo Ramos	Academia	Other	Effects of Cigarette Smoking Intensity on the Mucociliary Clearance of Active Smokers	N
90	2013	2013	Research article	South African Medical journal	South Africa	S R van Staden, M GroenewaldI, R Engelbrecht: P J Becker; L T Hazelhurst	Academia	Other	Carboxyhaemoglobin levels, health and lifestyle perceptions in smokers converting from tobacco cigarettes to electronic cigarettes	YE
90	2013	2013	Research article	South African Medical journal	South Africa	S R van Staden, M GroenewaldI, R Engelbrecht: P J Becker; L T Hazelhurst	Academia	Other	Carboxyhaemoglobin levels, health and lifestyle perceptions in smokers converting from tobacco cigarettes to electronic cigarettes	YE
90	2013	2013	Research article	South African Medical journal	South Africa	S R van Staden, M GroenewaldI, R Engelbrecht: P J Becker; L T Hazelhurst	Academia	Other	Carboxyhaemoglobin levels, health and lifestyle perceptions in smokers converting from tobacco cigarettes to electronic cigarettes	YE
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									cigarettes to electronic cigarettes	
62	2008	2008	Research article	The Journal of Clinical Pharmcacology	NA	Hans J. Roethig, Shixia Feng, Qiwei Liang, Jianmin Liu, William A. Rees, Barbara K. Zedler	Other	Other	A 12-Month, Randomized, Controlled Study to Evaluate Exposure and Cardiovascular Risk Factors in Adult Smokers Switching From Conventional Cigarettes to a Second-Generation Electrically Heated Cigarette Smoking System	YI
73	2012	2012	Research article	Sunsari Technical College Journal	Nepal	Shah BK, Nepal AK, Agrawal M, Sinha AK	Academia	Other	The effects of cigarette smoking on hemoglobin levels compared between smokers and non smokers	N
73	2012	2012	Research article	Sunsari Technical College Journal	Nepal	Shah BK, Nepal AK, Agrawal M, Sinha AK	Academia	Other	The effects of cigarette smoking on hemoglobin levels compared between smokers and non smokers	N
87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part3_8-Day randomized clinical trial in the UK	YI
87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part3_8-Day randomized clinical trial in the UK	YI
87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part3_8-Day randomized clinical trial in the UK	YI

87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part3_8-Day randomized clinical trial in the UK	YI
87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part3_8-Day randomized clinical trial in the UK	YI
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87	2012	2012	Research article	Regulatory Toxicology and Pharmacology	UK	Anthony R.Tricker, Adrian J. Stewart, Claire	Consulting PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking	YI

						Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey			System. Part3_8-Day randomized clinical trial in the UK	
85	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Korea	Anthony R.Tricker, In-Jin Jang, Claire Martin Leroy, Dirk Lindner, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part4_8-Day randomized clinical trial in Korea	YI
85	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Korea	Anthony R.Tricker, In-Jin Jang, Claire Martin Leroy, Dirk Lindner, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part4_8-Day randomized clinical trial in Korea	YI
85	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Korea	Anthony R.Tricker, In-Jin Jang, Claire Martin Leroy, Dirk Lindner, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part4_8-Day randomized clinical trial in Korea	YI
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85	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Korea	Anthony R.Tricker, In-Jin Jang, Claire Martin Leroy, Dirk Lindner, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part4_8-Day randomized clinical trial in Korea	YI
86	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Japan	Anthony R.Tricker, Shigeto Kanada, Kohji Takada, Claire	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part5_5-Day	YI

						Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey			randomized clinical trial in Japan	
86	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Japan	Anthony R.Tricker, Shigeto Kanada, Kohji Takada, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part5_5-Day randomized clinical trial in Japan	YI
86	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Japan	Anthony R.Tricker, Shigeto Kanada, Kohji Takada, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part5_5-Day randomized clinical trial in Japan	YI
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86	2012	2012	Research article	Regulatory Toxicology and Pharmacology	Japan	Anthony R.Tricker, Shigeto Kanada, Kohji Takada, Claire Martin Leroy, Dirk Lindner, Matthias K. Schorp, Ruth Dempsey	Academia PMI	Mixed	Reduced exposure evaluation of an Electrically Heated Cigarette Smoking System. Part5_5-Day randomized clinical trial in Japan	YI
55	2011	2011	Research article	Regulatory Toxicology and Pharmacology	USA	Muhammad-Kah, R.S., Hayden, A.D., Liang, Q., Frost-Pineda, K., and M. Sarkar	Altria	Tobacco	The relationship between nicotine dependence scores and biomarkers of exposure in adult cigarettes smokers	YI
19	2010	2011	Research article	Nicotine & Tobacco Research	USA/Lebanon	Caroline O. Cobb, Alan Shihadeh, Michael F. Weaver, Thomas Eissenberg	Academia	Other	Waterpipe Tobacco Smoking and Cigarette Smoking: A Direct Comparison of Toxicant Exposure and Subjective Effects	N
19	2010	2011	Research article	Nicotine & Tobacco	USA/Lebanon	Caroline O. Cobb, Alan	Academia	Other	Waterpipe Tobacco Smoking and Cigarette	N

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				Research		Shihadeh, Michael F. Weaver, Thomas Eissenberg			Smoking: A Direct Comparison of Toxicant Exposure and Subjective Effects	
19	2010	2011	Research article	Nicotine & Tobacco Research	USA/Lebanon	Caroline O. Cobb, Alan Shihadeh, Michael F. Weaver, Thomas Eissenberg	Academia	Other	Waterpipe Tobacco Smoking and Cigarette Smoking: A Direct Comparison of Toxicant Exposure and Subjective Effects	N
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng,	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI

						Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig				
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
68	2010	2010	Research article	Nicotine & Tobacco Research	USA	Mohamadi Sarkar, Jianmin Liu, Tamara Koval, Jingzhu Wang, Shixia Feng, Richard Serafin, Yan Jin, Yuli Xie, Kirk Newland, & Hans J. Roethig	Altria	Tobacco	Evaluation of biomarkers of exposure in adult cigarette smokers using Marlboro Snus	YI
89	2010	2010	Research article	Regulatory Toxicology and Pharmacology	South Africa	Unverdorben, M., Mostert, A., Munjal, S., vander Bijl, A., Potgieter, L., Venter, C., and Liang Q.	Consulting Altria	Mixed	Acute effects of cigarette smoking on pulmonary function	YI
89	2010	2010	Research article	Regulatory Toxicology and Pharmacology	South Africa	Unverdorben, M., Mostert, A., Munjal, S., vander Bijl, A., Potgieter, L., Venter, C., and Liang Q.	Consulting Altria	Mixed	Acute effects of cigarette smoking on pulmonary function	YI
89	2010	2010	Research article	Regulatory Toxicology and Pharmacology	South Africa	Unverdorben, M., Mostert, A., Munjal, S., vander Bijl, A., Potgieter, L., Venter, C., and Liang Q.	Consulting Altria	Mixed	Acute effects of cigarette smoking on pulmonary function	YI

93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
93	2010	2010	Research article	Regulatory Toxicology and Pharmacology	USA	Wang, J., Roethig, H.J., Appleton, S., Werley, M., Muhammad-Kah, R. and Paul Mendes	Altria	Tobacco	The effect of menthol containing cigarettes on adult smokerss exposue to nicotine and carbon monoxide	YI
83	2010	2010	Research article	South African Medical journal	South Africa	Ansa Theron, Cedric Schultz, James A Ker, Nadia Falzone	Academia	Other	Carboxyhaemoglobin levels in water-pipe and cigarette smokers	N
83	2010	2010	Research article	South African Medical journal	South Africa	Ansa Theron, Cedric Schultz,	Academia	Other	Carboxyhaemoglobin levels in water-pipe and cigarette smokers	N

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						James A Ker, Nadia Falzone				
83	2010	2010	Research article	South African Medical journal	South Africa	Ansa Theron, Cedric Schultz, James A Ker, Nadia Falzone	Academia	Other	Carboxyhaemoglobin levels in water-pipe and cigarette smokers	YI
83	2010	2010	Research article	South African Medical journal	South Africa	Ansa Theron, Cedric Schultz, James A Ker, Nadia Falzone	Academia	Other	Carboxyhaemoglobin levels in water-pipe and cigarette smokers	YI
76	2009	2009	Research article	Journal of Surgical research	Denmark	Lars Tue Sorensen, Stig Jorgensen, Lars J. Petersen, Ulla Hemmingsen, jens Bulow, Steffen Loft, Finn Gottrup	Academia	Other	Acute Effects of Nicotine and Smoking on Blood Flow, Tissue Oxygen, and Aerobe Metabolism of the Skin and Subcutis	N
76	2009	2009	Research article	Journal of Surgical research	Denmark	Lars Tue Sorensen, Stig Jorgensen, Lars J. Petersen, Ulla Hemmingsen, jens Bulow, Steffen Loft, Finn Gottrup	Academia	Other	Acute Effects of Nicotine and Smoking on Blood Flow, Tissue Oxygen, and Aerobe Metabolism of the Skin and Subcutis	N
76	2009	2009	Research article	Journal of Surgical research	Denmark	Lars Tue Sorensen, Stig Jorgensen, Lars J. Petersen, Ulla Hemmingsen, jens Bulow, Steffen Loft, Finn Gottrup	Academia	Other	Acute Effects of Nicotine and Smoking on Blood Flow, Tissue Oxygen, and Aerobe Metabolism of the Skin and Subcutis	N
76	2009	2009	Research article	Journal of Surgical research	Denmark	Lars Tue Sorensen, Stig Jorgensen, Lars J. Petersen, Ulla Hemmingsen, jens Bulow, Steffen Loft, Finn Gottrup	Academia	Other	Acute Effects of Nicotine and Smoking on Blood Flow, Tissue Oxygen, and Aerobe Metabolism of the Skin and Subcutis	N

1	2009	2009	Research article	Transfusion	Sweden	Anna-Maja Aberg, Birgitta Nilsson Sojka, Ola Winso, Pernilla Abrahamsson, Goran Johansson, Jan Erik Larsson	Academia	Other	Carbon monoxide concentration in donated blood: relation to cigarette smoking and other sources	N
53	2009	2009	Research article	Regulatory Toxicology and Pharmacology	USA	Paul Mendes, Qiwei Liang, Kimberly Frost-Pineda, Sagar Munjal, Ruediger-A. Walk, Hans J. Roethig	Altria	Tobacco	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US	YI
53	2009	2009	Research article	Regulatory Toxicology and Pharmacology	USA	Paul Mendes, Qiwei Liang, Kimberly Frost-Pineda, Sagar Munjal, Ruediger-A. Walk, Hans J. Roethig	Altria	Tobacco	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US	YI
53	2009	2009	Research article	Regulatory Toxicology and Pharmacology	USA	Paul Mendes, Qiwei Liang, Kimberly Frost-Pineda, Sagar Munjal, Ruediger-A. Walk, Hans J. Roethig	Altria	Tobacco	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US	YI
53	2009	2009	Research article	Regulatory Toxicology and Pharmacology	USA	Paul Mendes, Qiwei Liang, Kimberly Frost-Pineda, Sagar Munjal, Ruediger-A. Walk, Hans J. Roethig	Altria	Tobacco	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US	YI
53	2009	2009	Research article	Regulatory Toxicology and Pharmacology	USA	Paul Mendes, Qiwei Liang, Kimberly Frost-Pineda, Sagar Munjal, Ruediger-A. Walk, Hans J. Roethig	Altria	Tobacco	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US	YI
63	2009	2009	Research article	Nicotine & Tobacco Research	USA	Hans J Roethig, Sagar Munjal, Shixia Feng, Qiwei Liang, Mohamadi Sarkar, Ruediger-A Walk, Paul Mendes	Altria	Tobacco	Population estimates for biomarkers of exposure to cigarette smoke in adult US cigarette smokers	YI

63	2009	2009	Research article	Nicotine & Tobacco Research	USA	Hans J Roethig, Sagar Munjal, Shixia Feng, Qiwei Liang, Mohamadi Sarkar, Ruediger-A Walk, Paul Mendes	Altria	Tobacco	Population estimates for biomarkers of exposure to cigarette smoke in adult US cigarette smokers	YI
42	2008	2008	Research article	Clinical and Investigative Medicine	Taiwan	Chien-Min Kung, Hai-Lung Wang, Zu-Lin Tseng	Academia	Other	Cigarette smoking exacerbates health problems in young men	YI
42	2008	2008	Research article	Clinical and Investigative Medicine	Taiwan	Chien-Min Kung, Hai-Lung Wang, Zu-Lin Tseng	Academia	Other	Cigarette smoking exacerbates health problems in young men	YI
42	2008	2008	Research article	Clinical and Investigative Medicine	Taiwan	Chien-Min Kung, Hai-Lung Wang, Zu-Lin Tseng	Academia	Other	Cigarette smoking exacerbates health problems in young men	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI

66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
66	2018	2018	Research article	Nicotine & Tobacco Research	USA	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	YI
57	2020	2020	Research article	Nicotine & Tobacco Research	USA	Oliveri D, Liang Q, Sarkar M	Altria	Tobacco	Real-World Evidence of Differences in Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	YI
57	2020	2020	Research article	Nicotine & Tobacco Research	USA	Oliveri D, Liang Q, Sarkar M	Altria	Tobacco	Real-World Evidence of Differences in Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	YI
84	2020	2020	Research article	Sci Rep.	USA	Tran CT, Bosilkovska M, de La Bourdonnaye G, Blanc N, Haziza C	PMI	Tobacco	Reduced levels of biomarkers of exposure in smokers switching to the Carbon-Heated Tobacco Product 1.0: a controlled, randomized, open-label 5-day exposure trial Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	YI
84	2020	2020	Research article	Sci Rep.	USA	Tran CT, Bosilkovska M, de La Bourdonnaye	PMI	Tobacco	Reduced levels of biomarkers of exposure in smokers switching to the	YI

						G, Blanc N, Haziza C			Carbon-Heated Tobacco Product 1.0: a controlled, randomized, open-label 5-day exposure trial Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	
84	2020	2020	Research article	Sci Rep.	USA	Tran CT, Bosilkovska M, de La Bourdonnaye G, Blanc N, Haziza C	PMI	Tobacco	Reduced levels of biomarkers of exposure in smokers switching to the Carbon-Heated Tobacco Product 1.0: a controlled, randomized, open-label 5-day exposure trial Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	YI
84	2020	2020	Research article	Sci Rep.	USA	Tran CT, Bosilkovska M, de La Bourdonnaye G, Blanc N, Haziza C	PMI	Tobacco	Reduced levels of biomarkers of exposure in smokers switching to the Carbon-Heated Tobacco Product 1.0: a controlled, randomized, open-label 5-day exposure trial Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Potential Harm Between Adult E-Vapor Users and Adult Cigarette Smokers	YI

Evidence Tables:

Supplemental Table 2 NEQ: Complete list of studies included in the analysis; summary with study types

Ref. ID	PUB__Yearso	PUB__Years	PUB__Type	PUB__Name	PUB__Country	PUB__Authors	PUB__Company	PUB__Code__comp	PUB__Title	PUB__relevant	PUB__Ava
12	2016	2016	Article	Practical Laboratory Medicine	Germany	Camacho O.M., Sommarström J., Prasad K., Cunningham A	BAT	Tobacco	Reference change values in concentrations of urinary and salivery biomarkers of exposure	YES	YES
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes

100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
100	2018	2018	Article	Reg Toxicology and Pharmacology	Japan	Yuki D., Takeshige Y., Nakaya K., Futamura Y.	Japan Tobacco	Tobacco	Assessment of the exposure to harmful and potentially harmful constituents in healthy Japenese	Yes	Yes
37	2009	2009	Article	Cancer Epidemiol Biomarkers Prev	US	Heck, J. D	Lorillard Tobacco Company	Tobacco	Smokers of Menthol and Nonmenthol Cigarettes Exhibit Similar Levels of Biomarkers of Smoke Exposure	Yes	Yes
37	2009	2009	Article	Cancer Epidemiol Biomarkers Prev	US	Heck, J. D	Lorillard Tobacco Company	Tobacco	Smokers of Menthol and Nonmenthol Cigarettes Exhibit Similar Levels of Biomarkers of Smoke Exposure	Yes	Yes

58	2016	2016	Article	Clin Chem Lab Med	US	Prasad G.L., Jones B.A., Chen P., Gregg E.O.	Reynolds Tobacco	Tobacco	A cross-sectional study of biomarkers of exposure and effect in smokers and moist snuff consumers	Yes	Yes
58	2016	2016	Article	Clin Chem Lab Med	US	Prasad G.L., Jones B.A., Chen P., Gregg E.O.	Reynolds Tobacco	Tobacco	A cross-sectional study of biomarkers of exposure and effect in smokers and moist snuff consumers	Yes	Yes
58	2016	2016	Article	Clin Chem Lab Med	US	Prasad G.L., Jones B.A., Chen P., Gregg E.O.	Reynolds Tobacco	Tobacco	A cross-sectional study of biomarkers of exposure and effect in smokers and moist snuff consumers	Yes	Yes
45	2009	2009	Article	Clin Chem Lab Med	UK	Lowe F.J., Gregg E.O., McEwan M.	BAT	Tobacco	Evaluation of biomarkers of exposure and potential harm in smokers, former smokers and never-smokers	Yes	Yes
45	2009	2009	Article	Clin Chem Lab Med	UK	Lowe F.J., Gregg E.O., McEwan M.	BAT	Tobacco	Evaluation of biomarkers of exposure and potential harm in smokers, former smokers and never-smokers	Yes	Yes
45	2009	2009	Article	Clin Chem Lab Med	UK	Lowe F.J., Gregg E.O., McEwan M.	BAT	Tobacco	Evaluation of biomarkers of exposure and potential harm in smokers, former smokers and never-smokers	Yes	Yes

45	2009	2009	Article	Clin Chem Lab Med	UK	Lowe F.J., Gregg E.O., McEwan M.	BAT	Tobacco	Evaluation of biomarkers of exposure and potential harm in smokers, former smokers and never-smokers	Yes	Yes
62	2008	2008	Article	J clinical Pharmacology	US	Roethig H.J., Feng X., Liang Q., Liu J., Rees W.A., Zedler B.K	PMI	Tobacco	A 12-Month, Randomized, Controlled Study to Evaluate Exposure and Cardiovascular Risk Factors in Adult Smokers Switching From Conventional Cigarettes to a Second-Generation Electrically Heated Cigarette Smoking System	Yes	Yes
62	2008	2008	Article	J clinical Pharmacology	US	Roethig H.J., Feng X., Liang Q., Liu J., Rees W.A., Zedler B.K	PMI	Tobacco	A 12-Month, Randomized, Controlled Study to Evaluate Exposure and Cardiovascular Risk Factors in Adult Smokers Switching From Conventional Cigarettes to a Second-Generation Electrically Heated Cigarette Smoking System	Yes	Yes

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62	2008	2008	Article	J clinical Pharmacology	US	Roethig H.J., Feng X., Liang Q., Liu J., Rees W.A., Zedler B.K	PMI	Tobacco	A 12-Month, Randomized, Controlled Study to Evaluate Exposure and Cardiovascular Risk Factors in Adult Smokers Switching From Conventional Cigarettes to a Second-Generation Electrically Heated Cigarette Smoking System	Yes	Yes
62	2008	2008	Article	J clinical Pharmacology	US	Roethig H.J., Feng X., Liang Q., Liu J., Rees W.A., Zedler B.K	PMI	Tobacco	A 12-Month, Randomized, Controlled Study to Evaluate Exposure and Cardiovascular Risk Factors in Adult Smokers Switching From Conventional Cigarettes to a Second-Generation Electrically Heated Cigarette Smoking System	Yes	Yes
63	2009	2009	Article	Nicotine & Tobacco Research	US	Roethig H.J., Munjal S., Feng S., Liang O., Sarkar M., Walk R.A., Mendes P.E.	Altria	Tobacco	Population estimates for biomarkers of exposure to cigarette smoke in adult US cigarette smokers	Yes	Yes
63	2009	2009	Article	Nicotine & Tobacco Research	US	Roethig H.J., Munjal S., Feng S., Liang O., Sarkar M.,	Altria	Tobacco	Population estimates for biomarkers of exposure to	Yes	Yes

						Walk R.A., Mendes P.E.			cigarette smoke in adult US cigarette smokers		
70	2014	2014	Article	Biomarkers	UK	Scherer G., Newland K., Papadopoulau E., Minet E.	ABF/Celerion	Other	A correlation study applied to biomarkers of internal and effective dose for acrylonitrile and 4-aminobiphenyl in smokers	Yes	Yes
70	2014	2014	Article	Biomarkers	UK	Scherer G., Newland K., Papadopoulau E., Minet E.	ABF/Celerion	Other	A correlation study applied to biomarkers of internal and effective dose for acrylonitrile and 4-aminobiphenyl in smokers	Yes	Yes
70	2014	2014	Article	Biomarkers	UK	Scherer G., Newland K., Papadopoulau E., Minet E.	ABF/Celerion	Other	A correlation study applied to biomarkers of internal and effective dose for acrylonitrile and 4-aminobiphenyl in smokers	Yes	Yes
70	2014	2014	Article	Biomarkers	UK	Scherer G., Newland K., Papadopoulau E., Minet E.	ABF/Celerion	Other	A correlation study applied to biomarkers of internal and effective dose for acrylonitrile and 4-aminobiphenyl in smokers	Yes	Yes
54	2011	2011	Article	Regulatory Toxicology and Pharmacology	UK	Morin A., Shepperd C.J., Eldridge A.C., Poirier N., Voisine R.	Imperial	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian	Yes	Yes

									smokers as determined by filter analysis and biomarkers of exposure		
54	2011	2011	Article	Regulatory Toxicology and Pharmacology	UK	Morin A., Shepperd C.J., Eldridge A.C., Poirier N., Voisine R.	Imperial	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure	Yes	Yes
54	2011	2011	Article	Regulatory Toxicology and Pharmacology	UK	Morin A., Shepperd C.J., Eldridge A.C., Poirier N., Voisine R.	Imperial	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure	Yes	Yes
54	2011	2011	Article	Regulatory Toxicology and Pharmacology	UK	Morin A., Shepperd C.J., Eldridge A.C., Poirier N., Voisine R.	Imperial	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an	Yes	Yes

									E-Cigarette or Nicotine Gum		
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes

66	2018	2018	Article	Nicotine & Tobacco Research	US	Round E.K., Chen P., Taylor A.K., Schmidt E.	Raynolds Tobacco	Tobacco	Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E-Cigarette or Nicotine Gum	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use	Yes	Yes

									and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes		
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and	Yes	Yes

doi.org/10.32388/ZJJ66O

									assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes		
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on	Yes	Yes

									smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes		
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W.,	ITG Brands	Tobacco	Reductions in biomarkers of	Yes	Yes

						Robinson E.			exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes		
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes
21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes

doi.org/10.32388/ZJJ66O

21	2016	2016	Article	BMC Public Health	US	D'Ruiz C., Graff D.W., Robinson E.	ITG Brands	Tobacco	Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes	Yes	Yes

doi.org/10.32388/ZJJ66O

Evidence Tables:

Supplemental Table 3 NNAL: Complete list of studies included in the analysis; summary with study types

Ref. ID	PUB_Years	PUB_Type	PUB_Name	PUB_Country	PUB_Authors	PUB_Company	PUB_Code_comp	PUB_Title	PUB_relevant	PUB_Availa
52	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella, StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure	YES	YES
51	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella, StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure	YES	YES
51	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution	YES	YES

					A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella, StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami			on Smoking-Related Behaviors, and Biomarkers of Exposure		
51	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella, StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure	YES	YES
52	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella,		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure	YES	YES

					StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami					
52	2020	Research article	Nicotine Tob Res	USA	Ellen Meier,, Bruce R. Lindgren,, Amanda Anderson, Sarah A. Reisinger, Kaila J. Norton, Joni Jensen, LoriStrayer, LauraDick, Mei-KuenTang, MenglanChen, StevenG.Carmella, StephenS.Hecht, Sharon E. Murphy , Jing Yang, Irina Stepanov Richard J. O'Connor, Peter G. Shields, Dorothy K. Hatsukami		Other	A Randomized ClinicalTrial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure	YES	YES
94	2018		Cancer Epidemiol Biomarkers Prev.	USA	Wasserman EJ, Reilly SM, Goel R, Foulds J, Richie JP Jr, Muscat JE.		Other	Comparison of Biomarkers of Tobacco Exposure between Premium and Discount Brand Cigarette Smokers in the NHANES 2011-2012 Special Sample.	YES	YES
94	2018		Cancer Epidemiol Biomarkers Prev.	USA	Wasserman EJ, Reilly SM, Goel R, Foulds J, Richie JP Jr, Muscat JE.		Other	Comparison of Biomarkers of Tobacco Exposure between Premium and Discount Brand Cigarette Smokers in the NHANES 2011-2012 Special Sample.	YES	YES
59	2018		Nicotine Tob Res.	USA	Pulvers K, Emami AS, Nollen NL, Romero DR, Strong DR,	Academia, primarily CA Universities	Other	Tobacco Consumption and Toxicant Exposure of Cigarette Smokers	YES	Yes

					Benowitz NL, Ahluwalia JS.			Using Electronic Cigarettes.		
25	2017		Nicotine Tob Res	Poland	Goniewicz ML, Gawron M, Smith DM, Peng M, Jacob P 3rd, Benowitz NL.	Roswell Park Cancer Institute, U of Silesia, UCSF	Other	Exposure to Nicotine and Selected Toxicants in Cigarette Smokers Who Switched to Electronic Cigarettes: A Longitudinal Within-Subjects Observational Study.	YES	Yes
49	2016		Am J Physiol Lung Cell Mol Physiol.	USA	Martin EM, Clapp PW, Rebuli ME, Pawlak EA, Glista-Baker E, Benowitz NL, Fry RC, Jaspers I.	Academia, UNC, Chapel Hill, UCSF	Other	E-cigarette use results in suppression of immune and inflammatory-response genes in nasal epithelial cells similar to cigarette smoke.	YES	Yes
49	2016		Am J Physiol Lung Cell Mol Physiol.	USA	Martin EM, Clapp PW, Rebuli ME, Pawlak EA, Glista-Baker E, Benowitz NL, Fry RC, Jaspers I.	Academia, UNC, Chapel Hill, UCSF	Other	E-cigarette use results in suppression of immune and inflammatory-response genes in nasal epithelial cells similar to cigarette smoke.	YES	Yes
15	2016		Cancer Epidemiol Biomarkers Prev.	USA	Chen G, Luo S, Kozlovich S, Lazarus P.	Washington State University	Other	Association between Glucuronidation Genotypes and Urinary NNAL Metabolic Phenotypes in Smokers.	YES	Yes
15	2016		Cancer Epidemiol Biomarkers Prev.	USA	Chen G, Luo S, Kozlovich S, Lazarus P.	Washington State University	Other	Association between Glucuronidation Genotypes and Urinary NNAL Metabolic Phenotypes in Smokers.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an	YES	Yes

								ambulatory smoking study.		
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure	YES	Yes

								and mouth level exposure in individuals participating in an ambulatory smoking study.		
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes
12	2016		Pract Lab Med.	Germany	Camacho OM, Sommarström J, Prasad K, Cunningham A.	Industry BAT	Tobacco	Reference change values in concentrations of urinary and salivary biomarkers of exposure and mouth level exposure in individuals participating in an ambulatory smoking study.	YES	Yes

99	2016		Cancer Prev Res (Phila).	USA	Yuan JM, Stepanov I, Murphy SE, Wang R, Allen S, Jensen J, Strayer L, Adams-Haduch J, Upadhyaya P, Le C, Kurzer MS, Nelson HH, Yu MC, Hatsukami D, Hecht SS.	Academia, Universities of Pittsburgh, Minnesota and Southern California	Other	Clinical Trial of 2-Phenethyl Isothiocyanate as an Inhibitor of Metabolic Activation of a Tobacco-Specific Lung Carcinogen in Cigarette Smokers.	YES	Yes
99	2016		Cancer Prev Res (Phila).	USA	Yuan JM, Stepanov I, Murphy SE, Wang R, Allen S, Jensen J, Strayer L, Adams-Haduch J, Upadhyaya P, Le C, Kurzer MS, Nelson HH, Yu MC, Hatsukami D, Hecht SS.	Academia, Universities of Pittsburgh, Minnesota and Southern California	Other	Clinical Trial of 2-Phenethyl Isothiocyanate as an Inhibitor of Metabolic Activation of a Tobacco-Specific Lung Carcinogen in Cigarette Smokers.	YES	Yes
99	2016		Cancer Prev Res (Phila).	USA	Yuan JM, Stepanov I, Murphy SE, Wang R, Allen S, Jensen J, Strayer L, Adams-Haduch J, Upadhyaya P, Le C, Kurzer MS, Nelson HH, Yu MC, Hatsukami D, Hecht SS.	Academia, Universities of Pittsburgh, Minnesota and Southern California	Other	Clinical Trial of 2-Phenethyl Isothiocyanate as an Inhibitor of Metabolic Activation of a Tobacco-Specific Lung Carcinogen in Cigarette Smokers.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using	YES	Yes

								its urinary metabolite NNAL measured in US population: 2011-2012.		
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
95	2016		J Expo Sci Environ Epidemiol.	USA	Wei B, Blount BC, Xia B, Wang L.	Government, CDC	Other	Assessing exposure to tobacco-specific carcinogen NNK using its urinary metabolite NNAL measured in US population: 2011-2012.	YES	Yes
20	2015		Nicotine Tob Res.	Canada	Czoli CD, Hammond D.	Academia University of Waterloo	Other	TSNA Exposure: Levels of NNAL Among Canadian Tobacco Users.	YES	Yes
20	2015		Nicotine Tob Res.	Canada	Czoli CD, Hammond D.	Academia University of Waterloo	Other	TSNA Exposure: Levels of NNAL Among Canadian Tobacco Users.	YES	Yes
97	2015		Clin Chem Lab Med.	Not reported	Yang JY, Ahn HK, Lee SW, Han YJ, Oh YJ, Velázquez-Armenta EY, Nava-Ocampo AA.		Other	Simple high-throughput analytical method using ultra-performance liquid chromatography coupled with tandem	YES	YES

								mass spectrometry to quantify total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol in urine.		
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ,	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and	YES	Yes

					Fisher MT, Wang J, Gogova M, Kobal G.			levels of biomarkers of exposure in adult smokers.		
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
51	2014		Nicotine Tob Res.	USA	McKinney DL, Frost-Pineda K, Oldham MJ, Fisher MT, Wang J, Gogova M, Kobal G.	Industry ALCS	Tobacco	Cigarettes with different nicotine levels affect sensory perception and levels of biomarkers of exposure in adult smokers.	YES	Yes
2	2015		Tob Control.	Syria	Al Ali R, Rastam S, Ibrahim I, Bazzi A, Fayad S, Shihadeh AL, Zaatari GS, Maziak W.	Florida International University	Other	A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers.	Yes	Yes
2	2015		Tob Control.	Syria	Al Ali R, Rastam S, Ibrahim I, Bazzi A, Fayad S, Shihadeh AL, Zaatari GS, Maziak W.	Florida International University	Other	A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers.	Yes	Yes
2	2015		Tob Control.	Syria	Al Ali R, Rastam S, Ibrahim I, Bazzi A, Fayad S, Shihadeh AL, Zaatari GS, Maziak W.	Florida International University	Other	A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers.	Yes	Yes
2	2015		Tob Control.	Syria	Al Ali R, Rastam S, Ibrahim I, Bazzi A, Fayad S, Shihadeh AL,	Florida International University	Other	A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette	Yes	Yes

					Zaatari GS, Maziak W.			smokers and non-smokers.		
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
69	2013		Environ Toxicol Pharmacol.	USA	Sarkar M, Muhammad-Kah R, Liang Q, Kapur S, Feng S, Roethig H.	Industry ALCS	Tobacco	Evaluation of spot urine as an alternative to 24h urine collection for determination of biomarkers of exposure to cigarette smoke in adult smokers.	YES	Yes
11	2013		Cancer Epidemiol Biomarkers Prev.	USA	Branstetter SA, Muscat JE.	Academia Penn State	Other	Time to first cigarette and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels in adult smokers; National Health and Nutrition	YES	Yes

								Examination Survey (NHANES), 2007-2010.		
11	2013		Cancer Epidemiol Biomarkers Prev.	USA	Branstetter SA, Muscat JE.	Academia Penn State	Other	Time to first cigarette and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels in adult smokers; National Health and Nutrition Examination Survey (NHANES), 2007-2010.	YES	Yes
11	2013		Cancer Epidemiol Biomarkers Prev.	USA	Branstetter SA, Muscat JE.	Academia Penn State	Other	Time to first cigarette and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels in adult smokers; National Health and Nutrition Examination Survey (NHANES), 2007-2010.	YES	Yes
11	2013		Cancer Epidemiol Biomarkers Prev.	USA	Branstetter SA, Muscat JE.	Academia Penn State	Other	Time to first cigarette and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels in adult smokers; National Health and Nutrition Examination Survey (NHANES), 2007-2010.	YES	Yes
11	2013		Cancer Epidemiol Biomarkers Prev.	USA	Branstetter SA, Muscat JE.	Academia Penn State	Other	Time to first cigarette and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels in adult smokers; National Health and Nutrition Examination Survey (NHANES), 2007-2010.	YES	Yes
60	2013		Nicotine Tob Res.	Egypt	Radwan G, Hecht SS, Carmella SG, Loffredo CA.	Cairo Dept. of Health, U of Minnesota, Georgetown University	Other	Tobacco-specific nitrosamine exposures in smokers and nonsmokers exposed to cigarette or waterpipe tobacco smoke.	YES	Yes
64	2013			USA	Rostron B. 2013	Government, FDA	Other	NNAL exposure by race and Menthol Cigarette Use among U.S. smokers	YES	Yes
64	2013			USA	Rostron B. 2013	Government, FDA	Other	NNAL exposure by race and Menthol Cigarette Use among U.S. smokers	YES	Yes

41	2013		Head Neck	USA	Khariwala, S.S., Carmella, S.G., Stepanov, I., Fernandes, P., Lassig, A.A., Yueh, B., Hatsukami, D., Hecht, S.S..		Other	Elevated levels of 1-hydroxypyrene and N'-nitrosonornicotine in smokers with head and neck cancer: a matched control study.	YES	Yes
41	2013		Head Neck	USA	Khariwala, S.S., Carmella, S.G., Stepanov, I., Fernandes, P., Lassig, A.A., Yueh, B., Hatsukami, D., Hecht, S.S..		Other	Elevated levels of 1-hydroxypyrene and N'-nitrosonornicotine in smokers with head and neck cancer: a matched control study.	YES	Yes
81	2012		Int. J. Cancer 130, 1338–1346.	USA	Ter-Minassian, M., Asomaning, K., Zhao, Y., Chen, F., Su, L., Carmella, S.G., Lin, X., Hecht, S.S., Christiani, D.C., 2012.		Other	Genetic variability in the metabolism of the tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL).	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M,	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking	YES	Yes

					Dempsey D, Jacob P 3rd.			progressively reduced nicotine content cigarettes.		
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
10	2012	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P 3rd.	Academia UCSF	Other	Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes.	YES	Yes
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78	2012		Chem Res Toxicol.	USA, Poland	St Helen G, Goniewicz ML, Dempsey D,		Other	Exposure and kinetics of polycyclic aromatic	YES	YES

					Wilson M, Jacob P 3rd, Benowitz NL.			hydrocarbons (PAHs) in cigarette smokers.		
78	2012		Chem Res Toxicol.	USA, Poland	St Helen G, Goniewicz ML, Dempsey D, Wilson M, Jacob P 3rd, Benowitz NL.		Other	Exposure and kinetics of polycyclic aromatic hydrocarbons (PAHs) in cigarette smokers.	YES	YES
78	2012		Chem Res Toxicol.	USA, Poland	St Helen G, Goniewicz ML, Dempsey D, Wilson M, Jacob P 3rd, Benowitz NL.		Other	Exposure and kinetics of polycyclic aromatic hydrocarbons (PAHs) in cigarette smokers.	YES	YES
78	2012		Chem Res Toxicol.	USA, Poland	St Helen G, Goniewicz ML, Dempsey D, Wilson M, Jacob P 3rd, Benowitz NL.		Other	Exposure and kinetics of polycyclic aromatic hydrocarbons (PAHs) in cigarette smokers.	YES	YES
98	2011	Research article	Cancer Res.	Shanghai, China	Yuan JM, Gao YT, Murphy SE, Carmella SG, Wang R, Zhong Y, Moy KA, Davis AB, Tao L, Chen M, Han S, Nelson HH, Yu MC, Hecht SS.		Other	Urinary levels of cigarette smoke constituent metabolites are prospectively associated with lung cancer development in smokers.	YES	Yes
98	2011	Research article	Cancer Res.	Shanghai, China	Yuan JM, Gao YT, Murphy SE, Carmella SG, Wang R, Zhong Y, Moy KA, Davis AB, Tao L, Chen M, Han S, Nelson HH, Yu MC, Hecht SS.		Other	Urinary levels of cigarette smoke constituent metabolites are prospectively associated with lung cancer development in smokers.	YES	Yes
91	2011	Review	Biomarkers.	USA	Vogel RI, Carmella SG, Stepanov I, Hatsukami DK, Hecht SS.	Academia, University of Minnesota	Other	The ratio of a urinary tobacco-specific lung carcinogen metabolite to cotinine is significantly higher in passive than in active smokers.	YES	Yes
91	2011	Review	Biomarkers.	USA	Vogel RI, Carmella SG, Stepanov I, Hatsukami DK, Hecht SS.	Academia, University of Minnesota	Other	The ratio of a urinary tobacco-specific lung carcinogen metabolite to cotinine is significantly higher in passive than in active smokers.	YES?	Yes

91	2011	Review	Biomarkers.	USA	Vogel RI, Carmella SG, Stepanov I, Hatsukami DK, Hecht SS.	Academia, University of Minnesota	Other	The ratio of a urinary tobacco-specific lung carcinogen metabolite to cotinine is significantly higher in passive than in active smokers.	YES?	Yes
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44	2011	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Liu J, Liang Q, Frost-Pineda K, Muhammad-Kah R, Rimmer L, Roethig H, Mendes P, Sarkar M.	Industry ALCS	Tobacco	Relationship between biomarkers of cigarette smoke exposure and biomarkers of inflammation, oxidative stress, and platelet activation in adult cigarette smokers.	YES	Yes
74	2011	Research Article	Regul Toxicol Pharmacol.	Germany	Shepperd CJ, Eldridge AC, Errington G, Dixon M.	Industry BAT	Tobacco	A study to evaluate the effect on Mouth Level Exposure and biomarkers of exposure estimates of cigarette smoke exposure following a forced switch to a lower ISO tar yield cigarette.	YES	Yes
74	2011	Research Article	Regul Toxicol Pharmacol.	Germany	Shepperd CJ, Eldridge AC, Errington G, Dixon M.	Industry BAT	Tobacco	A study to evaluate the effect on Mouth Level Exposure and biomarkers of exposure estimates of cigarette smoke exposure following a forced switch to a lower ISO tar yield cigarette.	YES	Yes
74	2011	Research Article	Regul Toxicol Pharmacol.	Germany	Shepperd CJ, Eldridge AC, Errington G, Dixon M.	Industry BAT	Tobacco	A study to evaluate the effect on Mouth Level Exposure and biomarkers of exposure	YES	Yes

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9	2011	Research article	Nicotine Tob Res.	USA	Benowitz NL, Dains KM, Dempsey D, Wilson M, Jacob P.	Academia UCSF	Other	Racial differences in the relationship between number of cigarettes smoked and nicotine and carcinogen exposure.	YES	Yes
9	2011	Research article	Nicotine Tob Res.	USA	Benowitz NL, Dains KM, Dempsey D, Wilson M, Jacob P.	Academia UCSF	Other	Racial differences in the relationship between number of cigarettes smoked and nicotine and carcinogen exposure.	YES	Yes
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54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes

54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes
54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes
54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes
54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes
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doi.org/10.32388/ZJJ66O

54	2011	Research article	Regul Toxicol Pharmacol.	Canada	Morin A, Shepperd CJ, Eldridge AC, Poirier N, Voisine R.	Industry, Imperial Tobacco	Tobacco	Estimation and correlation of cigarette smoke exposure in Canadian smokers as determined by filter analysis and biomarkers of exposure.	YES	Yes
79	2011	Research article	Cancer Epidemiol. Biomarkers Prev. 20, 234–238.	USA	Strasser, A.A., Benowitz, N.L., Pinto, A.G., Tang, K.Z., Hecht, S.S., Carmella, S.G., Tyndale, R.F., Lerman, C.E.,		Other	Nicotine metabolite ratio predicts smoking topography and carcinogen biomarker level.	YES	Yes
8	2010	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Dempsey D, Havel C, Wilson M, Jacob P 3rd.	Academia UCSF	Other	Urine menthol as a biomarker of mentholated cigarette smoking.	YES	Yes
8	2010	Research article	Cancer Epidemiol Biomarkers Prev.	USA	Benowitz NL, Dains KM, Dempsey D, Havel C, Wilson M, Jacob P 3rd.	Academia UCSF	Other	Urine menthol as a biomarker of mentholated cigarette smoking.	YES	Yes
7	2010	Research article	Cancer Epidemiol. Biomarkers Prev. 19, 2795–2800.	USA	Benowitz, N., Goniewicz, M.L., Eisner., Lazcano-Ponce, E., Zielinska-Danch, W., Koszowski, B., Sobczak, A., Havel, C., Jacob III, P.	Academia UCSF	Other	Urine cotinine underestimates exposure to the tobacco-derived lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in passive compared with active smokers.	YES	Yes
7	2010	Research article	Cancer Epidemiol. Biomarkers Prev. 19, 2795–2800.	USA	Benowitz, N., Goniewicz, M.L., Eisner., Lazcano-Ponce, E., Zielinska-Danch, W., Koszowski, B., Sobczak, A., Havel, C., Jacob III, P.	Academia UCSF	Other	Urine cotinine underestimates exposure to the tobacco-derived lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in passive compared with active smokers.	YES	Yes
5	2010	Research Article	Cancer Epidemiol Biomarkers Prev.	Canada, United States, Australia, United Kingdom	Ashley DL, O'Connor RJ, Bernert JT, Watson CH, Polzin GM, Jain RB, Hammond D, Hatsukami DK, Giovino GA, Cummings KM,	CDC and Academia	Other	Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the levels of biomarkers in smokers.	YES	Yes

					McNeill A, Shahab L, King B, Fong GT, Zhang L, Xia Y, Yan X, McCraw JM.					
5	2010	Research Article	Cancer Epidemiol Biomarkers Prev.	Canada, United States, Australia, United Kingdom	Ashley DL, O'Connor RJ, Bernert JT, Watson CH, Polzin GM, Jain RB, Hammond D, Hatsukami DK, Giovino GA, Cummings KM, McNeill A, Shahab L, King B, Fong GT, Zhang L, Xia Y, Yan X, McCraw JM.	CDC and Academia	Other	Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the levels of biomarkers in smokers.	YES	Yes
5	2010	Research Article	Cancer Epidemiol Biomarkers Prev.	Canada, United States, Australia, United Kingdom	Ashley DL, O'Connor RJ, Bernert JT, Watson CH, Polzin GM, Jain RB, Hammond D, Hatsukami DK, Giovino GA, Cummings KM, McNeill A, Shahab L, King B, Fong GT, Zhang L, Xia Y, Yan X, McCraw JM.	CDC and Academia	Other	Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the levels of biomarkers in smokers.	YES	Yes
5	2010	Research Article	Cancer Epidemiol Biomarkers Prev.	Canada, United States, Australia, United Kingdom	Ashley DL, O'Connor RJ, Bernert JT, Watson CH, Polzin GM, Jain RB, Hammond D, Hatsukami DK, Giovino GA, Cummings KM, McNeill A, Shahab L, King B, Fong GT, Zhang L, Xia Y, Yan X, McCraw JM.	CDC and Academia	Other	Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the levels of biomarkers in smokers.	YES	Yes
5	2010	Research Article	Cancer Epidemiol Biomarkers Prev.	Canada, United States, Australia,	Ashley DL, O'Connor RJ, Bernert JT, Watson CH,	CDC and Academia	Other	Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the	YES	Yes

				United Kingdom	Polzin GM, Jain RB, Hammond D, Hatsukami DK, Giovino GA, Cummings KM, McNeill A, Shahab L, King B, Fong GT, Zhang L, Xia Y, Yan X, McCraw JM.			levels of biomarkers in smokers.		
17	2010	Research article	Biomarkers 15, 345–352.	USA	Church TR, Anderson KE, Le C, Zhang Y, Kampa DM, Benoit AR, Yoder AR, Carmella SG, Hecht SS.		Other	Temporal stability of urinary and plasma biomarkers of tobacco smoke exposure among cigarette smokers.	YES	Yes
17	2010	Research article	Biomarkers 15, 345–352.	USA	Church TR, Anderson KE, Le C, Zhang Y, Kampa DM, Benoit AR, Yoder AR, Carmella SG, Hecht SS.		Other	Temporal stability of urinary and plasma biomarkers of tobacco smoke exposure among cigarette smokers.	YES	Yes
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29	2010		Addiction 105, 343–355.	USA	Hatsukami, D.K., Kotlyar, M., Hertsgaard, L.A., Zhang, Y., Carmella, S.G., Jensen, J.A., Allen, S.S., Shields, P.G., Murphy, S.E., Stepanov, I., Hecht, S.S.	U of Minnesota Tob Use Res Cter	Other	Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation.	YES	Yes
29	2010		Addiction 105, 343–355.	USA	Hatsukami, D.K., Kotlyar, M., Hertsgaard, L.A., Zhang, Y., Carmella, S.G., Jensen, J.A., Allen, S.S., Shields, P.G., Murphy, S.E., Stepanov, I., Hecht, S.S.	U of Minnesota Tob Use Res Cter	Other	Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation.	YES	Yes
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					Stepanov, I., Hecht, S.S.					
22	2009	Research Article	Int J Cancer. 2009	USA	Derby KS, Cuthrell K, Caberto C, Carmella S, Murphy SE, Hecht SS, Le Marchand L.	Universities of Hawaii and Minnesota	Other	Exposure to the carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in smokers from 3 populations with different risks of lung cancer.	YES	Yes
22	2009	Research Article	Int J Cancer. 2009	USA	Derby KS, Cuthrell K, Caberto C, Carmella S, Murphy SE, Hecht SS, Le Marchand L.	Universities of Hawaii and Minnesota	Other	Exposure to the carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in smokers from 3 populations with different risks of lung cancer.	YES	Yes
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75	2009	Research article	Regul Toxicol Pharmacol	Germany	Shepperd CJ, Eldridge AC, Mariner DC, McEwan M, Errington G, Dixon M.		Other	A study to estimate and correlate cigarette smoke exposure in smokers in Germany as determined by filter analysis and biomarkers of exposure.	yes	yes
75	2009	Research article	Regul Toxicol Pharmacol	Germany	Shepperd CJ, Eldridge AC, Mariner DC, McEwan M, Errington G, Dixon M.		Other	A study to estimate and correlate cigarette smoke exposure in smokers in Germany as determined by filter analysis and biomarkers of exposure.	yes	yes
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								analysis and biomarkers of exposure.		
53	2009	Research article	Regul Toxicol Pharmacol	USA	Mendes P, Liang Q, Frost-Pineda K, Munjal S, Walk RA, Roethig HJ.		Other	The relationship between smoking machine derived tar yields and biomarkers of exposure in adult cigarette smokers in the US.	YES	yes
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13	2009	Research article	Chem Res Toxicol 22(4): 734-741	USA	Carmella SG, Chen M, Han S, Briggs A, Jensen J, Hatsukami DK, Hecht SS.		Other	Effects of smoking cessation on eight urinary tobacco carcinogen and toxicant biomarkers.	YES	YES
37	2009	Research article	Cancer Epidemiol. Biomarkers Prev. 18, 622–629.	USA	Heck JD.		Other	Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure.	YES	YES
37	2009	Research article	Cancer Epidemiol. Biomarkers Prev. 18, 622–629.	USA	Heck JD.		Other	Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure.	YES	YES
16	2009	Research article	Cancer Epidemiol. Biomarkers Prev.	USA	Church		Other	A prospectively measured serum biomarker for a tobacco-specific	Yes	yes

								carcinogen and lung cancer in smokers.		
16	2009	Research article	Cancer Epidemiol. Biomarkers Prev.	USA	Church		Other		YES	Yes
56	2009	Research article	Cancer Epidemiol Biomarkers Prev	USA	Muscat JE, Chen G, Knipe A, Stellman SD, Lazarus P, Richie JP Jr.		Other	Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation.	Yes	yes
56	2009	Research article	Cancer Epidemiol Biomarkers Prev	USA	Muscat JE, Chen G, Knipe A, Stellman SD, Lazarus P, Richie JP Jr.		Other	Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation.	YES	Yes
26	2009	Research article	Cancer Epidemiol. Biomarkers Prev. 18, 3421–3425.	USA, Poland	Goniewicz, M.L., Havel, C.M., Peng, M.W., Jacob III, P., Dempsey, D., Yu, L., Zielinska-Danch, W., Koszowski, B., Czogala, J., Sobczak, A., Benowitz, N.L.		Other	Elimination kinetics of the tobacco-specific biomarker and lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.	Yes	Yes
26	2009	Research article	Cancer Epidemiol. Biomarkers Prev. 18, 3421–3425.	USA, Poland	Goniewicz, M.L., Havel, C.M., Peng, M.W., Jacob III, P., Dempsey, D., Yu, L., Zielinska-Danch, W., Koszowski, B., Czogala, J., Sobczak, A., Benowitz, N.L.		Other	Elimination kinetics of the tobacco-specific biomarker and lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.	Yes	Yes
67	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes

67	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes
67	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes
66	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes
67	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes
67	2008	Research article	Nicotine Tob Res. 2008	USA	Sarkar M, Kapur S, Frost-Pineda K, Feng S, Wang J, Liang Q, Roethig H.	Industry Philip Morris USA	Tobacco	Evaluation of biomarkers of exposure to selected cigarette smoke constituents in adult smokers switched to carbon-filtered cigarettes in short-term and long-term clinical studies.	YES	Yes

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43	2008	Research article	Cancer Research	USA	LeMarchand L, Derby KS, Murphy SE, Hecht, SS, Hatsukami D, Carmella SG, Tirikaine M, and Wang H.	University of Hawaii	Other	Smokers with the CHRNA Lung Cancer–Associated Variants Are Exposed to Higher Levels of Nicotine Equivalents and a Carcinogenic Tobacco-Specific Nitrosamine	YES	Yes

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