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Tobacco toxicant exposure in cigarette smokers who use or do not use other tobacco products*

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Abstract

Background—Non-cigarette other tobacco products (OTP; e.g., cigarillos, little cigars) are typically used in combination with cigarettes, but limited data exists on the tobacco toxicant exposure profiles of dual cigarette-OTP (Cig-OTP) users. This study examined biomarkers of nicotine and carcinogen exposure in cigarette smokers who used or did not use OTP.

Methods—111 Cig-OTP and 111 cigarette only (Cig Only) users who smoked equivalent cigarettes per day were matched on age (< 40, ≥ 40), race (African American, White), and gender. Participants reported past 7-day daily use of cigarettes and OTP and provided urine for nicotine, cotinine, total nicotine equivalents (TNE) and total NNAL concentrations.

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Contributors

All authors have contributed to the preparation of this manuscript and have approved its final submission.

Conflicts of Interest

Benowitz is a consultant/advisory board member for Pfizer and GlaxoSmithKline, and has provided expert testimony for tobacco litigation. The other authors have no conflicts of interest to disclose.

Results—Cig-OTP users reported greater past 7-day tobacco use (15.9 versus 13.0 products/day, $p < 0.01$) but had significantly lower creatinine-normalized nicotine (606 versus 1,301 ng/mg), cotinine (1,063 versus 2,125 ng/mg), TNE (28 versus 57 nmol/mg) and NNAL (251 versus 343 pg/mg) than Cig Only users ($p < 0.001$).

Conclusions—Cig-OTP users had lower levels of nicotine and metabolites of a lung carcinogen relative to Cig-Only users, but concentrations of toxicants among Cig-OTP users were still at levels that place smokers at great risk from the detrimental health effects of smoking.

Impact—Our study finds that nicotine and carcinogen exposure in Cig-OTP users are lower compared to cigarette only users, but still likely to be associated with substantial harm. A better understanding of why toxicant levels may be lower in Cig-OTP is an important area for future study.

Keywords

Tobacco toxicants; biomarkers; non-cigarette tobacco products; cigarettes

1. Introduction

Use of non-cigarette other tobacco products (OTP) has grown exponentially in the United States over the last two decade (Federal Trade Commission, 2012; Giovenco et al., 2015; Hu et al., 2016; Kasza et al., 2017; Singh et al., 2016). While use of OTP varies by demographics, mostly race/ethnicity, age, and gender, current national prevalence estimates indicate that 40% of US adult tobacco users use multiple products (Kasza et al., 2017; Lee et al., 2014). Aside from cigarettes, the most commonly used products are little cigars or cigarillos (LCC; 57%), electronic cigarettes (45%), and regular/full-size cigars (33%) (Kasza et al., 2017). Cigars are a diverse market that contain three primary product types: little filtered cigars ('little cigars'), cigarillos, and regular/full-size cigars ('traditional cigars') (Corey et al., 2014). LCC users are more likely than traditional cigar users to report daily cigar smoking and, because of concurrent use of cigarettes, to report greater smoke inhalation compared to exclusive cigar users (National Cancer Institute, 1998). The combination of daily use of cigarettes and LCC plus greater depth of inhalation may put this group of OTP users at an increased risk for tobacco-related diseases.

OTP users cite harm reduction as a primary reason for use of these products (Jolly, 2008; Page and Evans, 2004; Zhou et al., 2015). Yet while OTP are typically used in combination with cigarettes, knowledge of the potentially harmful effects comes from studies of single-product OTP use (Cheng, 2014; Djordjevic and Doran, 2009; Federal Trade Commission, 2000; Goniewicz et al., 2014b; Janbaz et al., 2014; Shihadeh et al., 2015). The use of cigarettes in combination with one or more OTP likely influences toxicant exposure. Dual cigarette-OTP users may use OTP to replace or as a supplement to cigarettes, resulting in no net change, reduction, or possibly an increase in toxicant exposure. In a study that oversampled African American and Hispanic/Latino adult cigarette users, two groups with a high prevalence of OTP use (Cantrell et al., 2013; Corey et al., 2014; Corral et al., 2013), over half had used OTP, mostly cigars and cigarillos, in the past 30 days (Nollen et al., 2016a). Dual cigarette-OTP users in this study smoked fewer overall cigarettes per month

but, through supplementation with OTP, used more units of total tobacco products than respondents who exclusively smoked cigarettes. A separate study found a similar pattern with dual cigarette-cigar smokers using fewer cigarettes than cigarette only smokers but having equivalent or higher tobacco product use in the past 5 days due to supplementation with cigars (Chen et al., 2014).

Given the growing prevalence of dual cigarette-OTP users but the paucity of data on toxicant exposure associated with this pattern of use, the current study examined biomarkers of nicotine and carcinogen exposure in cigarette smokers who used or did not use OTP. Because of the overwhelming use of cigarettes in combination with LCC and the estimated health impacts of this pattern of use (Corey et al., 2014; Nonnemaker et al., 2014), this study sampled dual cigarette-LCC users, the majority of whom also use other forms of OTP. We hypothesized that dual cigarette-OTP users (Cig-OTP) would use more total tobacco products in the past 7 days and be exposed to higher levels of nicotine and the tobacco-specific nitrosamine, NNK (assessed by measurement of its metabolite 4-(methylnitrosamino)-1-(3) pyridyle-1-butanol[NNAL] in urine), compared to cigarette smokers (Cig-Only) who did not use OTP (Nollen et al., 2015).

2. Methods

2.1. Study Design

Cig-OTP and Cig Only users were drawn from two parent studies. The first parent study contained a sample of 141 Cig-OTP users and the second parent study contained a sample of 449 Cig Only users. To accurately isolate the impact of OTP on tobacco toxicant exposure, it was necessary for the cigarette smoking patterns of the samples to be as closely matched as possible. Participants in the Cig Only study (Nollen et al., 2016b) were all daily cigarette users who smoked 3–20 cigarettes per day (CPD). The same criteria were applied to the Cig-OTP sample, excluding 30 and leaving 111 Cig-OTP smokers. The 449 Cig Only smokers from the parent study were then frequency matched to the Cig-OTP sample on dichotomous age (< 40, > 40), race/ethnicity (African American, White) and gender. 111 Cig Only smokers were randomly selected from these pairings, leaving a final sample of 111 Cig-OTP and 111 Cig Only participants; all were African American or White adults (> 18 years of age) who were daily cigarette smokers (> 25 days/month) and who smoked 3–20 CPD. Per our a priori interest in LCC, all Cig-OTP used LCC in the past 7 days; 80.2% also used other OTP.

CPD criteria were selected because they mirror national trends, with the majority of US adults smoking daily (76%) and 20 or less CPD (66%) (Jamal et al., 2016). Absence of OTP use was a condition of eligibility of the Cig Only study, with absence of OTP use confirmed at eligibility screening and again at baseline. Males, younger individuals, and racial/ethnic minorities, especially African Americans, have among the highest rates of OTP use (Backinger et al., 2008; Bombard et al., 2009; Bombard et al., 2007; Kasza et al., 2014; Richardson et al., 2012). African Americans on average have a slower rate of nicotine metabolism, extract more nicotine per cigarette smoked, and have a different toxicant exposure profile per cigarette smoked, overall, relative to Whites (Benowitz et al., 2011b). Because these factors are known to impact tobacco use behaviors and toxicant exposure

profiles, participants were matched on age, gender, and race/ethnicity to ensure a balanced distribution across groups and minimize these factors as potential confounders in explaining differences in tobacco toxicant exposure. A flow diagram showing the selection of participants and the age, gender, and racial/ethnic breakdown of the final sample is shown in Figure 1. Study procedures were approved by the University of Kansas Medical Center Institutional Review Board.

2.2. Survey Measures

Trained research assistants assessed all participants using identical questions for each measure described below.

2.2.1. Tobacco Consumption—*Cigarette consumption* was assessed by asking participants, ‘During the past 7 days, how many cigarettes did you smoke?’ (Centers for Disease Control and Prevention and National Center for Health Statistics). Responses were divided by 7 to obtain cigarettes per day in the past 7 days. The number of days cigarettes were smoked in the last 30 days was also assessed. *OTP consumption* was assessed using the stem: ‘During the past 7 days, how many _____ did you smoke/use?’ This question was asked separately for full size cigars, little cigars, cigarillos, hand-rolled cigarettes, blunts (defined as marijuana wrapped in cigar paper/tobacco leaf), pipes, smokeless tobacco, hookah, and electronic cigarettes (Kasza et al., 2014). Clarification of the stem was added for pipes (number of bowls), smokeless tobacco (number of dips or chews), electronic cigarettes (number of cartridges), and hookah (number of sessions). Responses for each OTP were divided by 7 to obtain the amount of each product used per day in the past 7 days. For each form of tobacco used, participants were also asked to provide the number of days used in the past 30 and average amount on the days used. Analyses for the current paper were limited to past 7 day cigarette and OTP consumption because, with the exception of NNAL, the biomarkers assessed have short half-lives (2–16 hours) and are only able to detect nicotine intake within the last 3–4 days (Benowitz et al., 2002).

Several variables were computed from the cigarette and OTP consumption questions and used in subsequent analyses. *Total tobacco products per day* was computed by summing the number of cigarettes, LCC, blunts, hand-rolled cigarettes, pipes, smokeless tobacco, electronic cigarettes, full size cigars, and hookah used per day in the past 7 days. *Total OTP in the past 7 days* was computed by summing the number of each OTP used in the past 7 days. *Total cigarettes in the past 7 days* reflect the number of cigarettes used in the past 7 days and *Total cigarettes and OTP in the past 7 days* was computed by summing the total cigarettes and total OTP.

2.2.2. Demographics and Tobacco Use History—Matching variables included age, gender, and race/ethnicity (Dorsey and Graham, 2011). Demographic variables included educational attainment, employment status, relationship status, and estimated monthly household income (Centers for Disease Control and Prevention, 2012; Dorsey and Graham, 2011). Tobacco use variables included age of initiation of cigarettes and OTP, length of time as a cigarette and OTP user, use of mentholated cigarettes and nicotine dependence, assessed by using time to first cigarette of the day (Al-Delaimy WK et al., 2009; Fagerstrom et al.,

2012). The time to first cigarette single item from the Fagerström Test of Cigarette Dependence has been validated against the full measure and is considered a better marker of nicotine dependence in samples that include light smokers (< 10 CPD).

2.3. Biomarkers

Three biomarkers of nicotine intake (i.e., nicotine, cotinine, and total nicotine equivalents) and one biomarker of carcinogen exposure (NNAL) were assessed in urine. These biomarkers were selected because of their relevance to tobacco exposure and health outcomes. Nicotine is rapidly and extensively metabolized to nine primary metabolites. Total nicotine equivalents (TNE) represent the sum of nicotine and metabolites – nicotine glucuronide, cotinine, cotinine glucuronide, trans-3'-hydroxycotinine (3HC), trans-3'-hydroxycotinine glucuronide, nicotine N-oxide (NNO), cotinine N-oxide (CNO), nornicotine (NNic) and norcotinine (NCot) (Benowitz et al., 2010). Because it includes nicotine and its metabolites, TNE reflects nicotine intake independently of individual pathways of nicotine metabolism and provides a better estimate of total systemic nicotine intake than an individual metabolite such as cotinine alone. TNE, relative to nicotine or cotinine, also captures more of the variability in exposure that is due to racial differences in nicotine metabolism (Benowitz et al., 2010; Zhu et al., 2013). NNK is a tobacco-specific nitrosamine and is considered to be one of the most important causative agents in the development of lung cancer (Hecht, 2002). NNK is metabolized to NNAL, which can be measured in the urine and is widely used to indicate tobacco-specific exposure to this potent lung carcinogen.

2.3.1. Analytic Chemistry—Urine concentrations of TNE (i.e., nicotine, cotinine, 3HC, and their respective glucuronide metabolites, nicotine N-oxide, cotinine N-oxide, nornicotine and norcotinine) and total NNAL (free plus conjugated) were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS), as described previously (Benowitz et al., 2010; Benowitz et al., 1994; Jacob et al., 2008). All measures were normalized for creatinine concentration. Values below the assay's limit of quantitation for NNAL (1.0 pg/ml) and the metabolites in TNE [nicotine (10 ng/ml), cotinine (10 ng/ml), 3HC (10 ng/ml), nicotine N-oxide (10 ng/ml), cotinine N-oxide (1 ng/ml), nornicotine (1 ng/ml), norcotinine (1 ng/ml)] were imputed to the limit of quantitation/ 2. Only 4 participants out of 222 (1.8%) had values below the limit of quantitation that required imputation.

2.4. Data Analysis

Differences between Cig-OTP and Cig Only users were compared using a chi-square test for categorical variables and Wilcoxon rank-sum test for continuous variables. Spearman correlations were calculated to measure the association between creatinine-normalized TNE and NNAL and numbers of OTP, cigarettes, and total tobacco products per past 7 days. Post-hoc exploratory Spearman correlations were re-run with OTP that were used, on average, more than once per day to examine if excluding OTP that were used infrequently resulted in stronger associations between OTP consumption and TNE and NNAL. The data analysis for this paper was generated using SAS/STAT software, Version 9.4 of the SAS System for Windows (Copyright © 2015 SAS Institute Inc).

3. Results

3.1. Demographic and Tobacco Use History

Table 1 displays demographic and tobacco use history characteristics of Cig Only and Cig-OTP users. Cig-OTP and Cig Only participants were equivalent in terms of their cigarette use history; both groups had similar cigarette dependence, age of cigarette smoking initiation, length of time as a cigarette smoker, and preference for menthol cigarettes. The groups differed on several demographic characteristics: On average, Cig-OTP users were younger, less educated, less likely to be employed, had lower household income, and were less likely to be married or live with a partner than Cig Only users. Participants in the Cig-OTP group were established OTP users, having used OTP for an average of 19.7 years. Regular OTP use was initiated an average of 2.4 years after regular cigarette use.

3.2. Past 7 Day Tobacco Use

Past 7 day tobacco product use by group is displayed in Table 2. Cig-OTP and Cig Only participants used nearly equivalent CPD over the last 7 days [13.0 (5.4) versus 12.5 (5.9), $p=0.36$]. However, the Cig-OTP group used an average of 2.9 (1.5) OTP per day and, as a result, used significantly more units of total tobacco products per day than the Cig Only group [15.9 (8.0)/day versus 13.0 (5.4)/day, $p < 0.01$]. Among Cig-OTP users, 46.8% were daily OTP users (OTP used on > 25 days in last 30). All Cig-OTP users (100.0%) had used LCC in the past 7 days, 58.6% had also used blunts, 36.9% hand-rolled cigarettes, 19.8% full-size cigars, 19.8% electronic cigarettes, 9.0% smokeless tobacco, 8.1% hookah, and 8.1% had used pipes in the last 7 days.

3.3. Biomarkers of Exposure

Median urine concentrations of nicotine, cotinine, TNE, and NNAL, shown with and without normalization for creatinine, are presented in Table 3. Despite greater self-reported tobacco use over the last 7 days (15.9 products/day versus 13.0 products/day, $p < 0.01$), Cig-OTP users had significantly lower creatinine-normalized nicotine, cotinine, TNE, and NNAL relative to Cig Only users ($p < 0.001$). The same difference was seen when median urine concentrations of nicotine, cotinine, TNE, and NNAL was stratified by CPD (< 5 , 6–10, > 11 CPD), as shown in Supplementary Figure 1¹.

3.4. Relationship between Tobacco Use and Nicotine and Carcinogen Exposure

To further understand the relationship between tobacco use and toxicant exposure, correlations between TNE, NNAL and the total OTP, cigarettes, and cigarettes-OTP used in the past 7 days were examined (see Figure 2). The within-subject correlations between TNE and NNAL were strong in both groups: Cig Only, $r = 0.58$ and Cig-ATP, $r = 0.60$. Moderate correlations were found between cigarette consumption and TNE (Cig-OTP $r_s = 0.39$, Cig Only $r_s = 0.34$) and cigarette consumption and NNAL (Cig-OTP $r_s = 0.41$, Cig Only $r_s = 0.43$) in both groups. In the Cig-OTP group, OTP consumption had only small correlations with TNE ($r_s = 0.0003$) and NNAL ($r_s = -0.09$).

¹Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:...

Post-hoc exploratory analyses were conducted to see if excluding OTP used less than once per day (i.e., keeping LCC and blunts and excluding hand-rolled cigarettes, pipes, smokeless tobacco, electronic cigarettes, full-size cigars, and hookah) resulted in stronger correlations with TNE and NNAL. Results of these exploratory analyses improved the correlations of OTP consumption to TNE ($r_s = -0.14$) and NNAL ($r_s = -0.19$). However, the relationships were still weak with only 1%–3% of the variance in TNE or NNAL explained by OTP used once or more per day (see Supplementary Figure 2²).

4. Discussion

To the best of our knowledge, our study is only the second to compare biomarkers of nicotine and carcinogen exposure in cigarette smokers only versus cigarette smokers who also use multiple OTP. Contrary to what was hypothesized, the Cig-OTP group had lower levels of creatinine-normalized nicotine, cotinine, TNE, and NNAL despite use of a greater number of tobacco products than the Cig Only group. Findings are similar to those of Chen et al. (2014) in which NNAL and cotinine levels in dual cigarette-cigar users were 3%–28% lower than those of cigarette-only smokers (Chen et al., 2014). Comparatively, the current study included all cigars (i.e., full-size cigars, little cigars, and cigarillos) along with other forms of OTP and found NNAL and cotinine levels in Cig-OTP users that were 37%–200% lower than those of Cig-Only smokers.

The combined findings of the current study and Chen's lead to interesting questions about why cigarette only smokers have greater toxicant exposure than dual users despite consuming fewer total units of tobacco. Previous studies have found that dual cigarette-cigar users report greater inhalation of cigar smoke compared to exclusive cigar users (National Cancer Institute, 1998), which should lead to greater absorption of tobacco smoke and increased biomarker concentrations, but this does not seem to be the case in the current study. Conversely, dual users may have different motivations for tobacco use (e.g., harm reduction) and may be striving to reduce their nicotine consumption, which could influence how intensely tobacco is consumed.

The literature suggests other possible reasons for differences in biomarker concentrations, including cigarette type (menthol versus non-menthol), CPD, daily versus non-daily smoking status, nicotine dependence, and demographic and racial/ethnic differences in nicotine and NNK absorption (Benowitz et al., 2011a; Benowitz et al., 1999; Shiffman et al., 2014; St Helen et al., 2013), but these are unlikely to explain the differences in biomarker concentrations in the current study because Cig-OTP and Cig Only users were matched or equivalent on these factors. Cig Only smokers were interested in quitting smoking in the next two weeks as part of enrollment in a clinical trial. Smokers seeking smoking cessation treatment might be more highly dependent than dual users who are not, explaining the greater nicotine and toxicant exposure, although we did not find greater dependence among the Cig Only versus Cig-OTP users in the current study. Both groups were highly dependent as evidenced by 79% of Cig Only and 74% of Cig-OTP users smoking their first cigarette of the day within 30 minutes of waking.

²Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:...

Findings of the current study raise interesting questions about whether dual Cig-OTP use reduces harm from tobacco. While toxicant exposure levels were lower in dual Cig-OTP users, their levels are elevated and substantially higher than non-tobacco users. For example average urine NNAL ranged from 0.98–1.01 pg/mg creatinine in large, nationally representative cohorts of non-tobacco users (Chen et al., 2014; Rostron et al., 2015) compared to levels of 251 pg/mg creatinine for NNAL in the current study. Levels of exposure of this magnitude place dual Cig-OTP users at substantial risk from the health effects of smoking (Timofeeva et al., 2011; Yuan et al., 2014; Yuan et al., 2011; Yuan et al., 2009), and it is not clear to what extent, if any, the difference in exposure levels translates to differences in health outcomes.

Another interesting, but expected, finding of the current study is the low correlation between OTP use and urine TNE or NNAL. Nicotine and its metabolites comprising TNE and NNAL have different half-lives, with TNE reflecting exposure over a few days and NNAL reflecting average level of exposure over several weeks. Notably, the correlations between tobacco product use and these biomarkers were similar, suggesting consistency in the relationship between exposure and biomarkers in the short and longer term. The within-subject correlations between TNE and NNAL were strong and consistent with other studies (Benowitz et al., 2011b). Low correlations between OTP use and TNE or NNAL are likely a function of several factors. First, all dual users were primary cigarette smokers, meaning that their use of OTP was secondary to their use of cigarettes, which makes it difficult to isolate the impact of OTP on biomarkers over-and-above the toxicant exposure resulting from cigarettes. Second, delivery of nicotine and carcinogens varies by OTP type, with products like hookahs and electronic cigarettes delivering relatively little NNK and less nicotine than cigars (Goniewicz et al., 2014a; Goniewicz et al., 2014b; McRobbie et al., 2015; Primack et al., 2016). Removing these products resulted in higher but still weak associations between OTP and biomarkers that, again, is likely related to difficulty in isolating the impact of OTP on biomarkers above that contributed by cigarettes. It is important to note, however, that our sample selection criteria are generalizable to the majority of dual Cig-OTP users who, like the current sample, are primary cigarette-secondary OTP users and whose pattern of multiple tobacco product use is predominately cigarettes in combination with LCC (Corey et al., 2014; U.S. Department of Health and Human Services, 2014). The rate and frequency of tobacco product use also generalizes well to nationally representative samples of multi-tobacco products users, with our sample, on average, having equivalent or higher daily use of cigarettes and total tobacco products than similar studies in the literature (Chen et al., 2014; Nollen et al., 2016a), enhancing the external validity of the current findings.

The high rate of blunt use in this study was unexpected. Because blunts are marijuana wrapped in cigar paper, they also likely deliver less NNK and nicotine than cigarettes, which may also be confounding the associations with biomarkers in the current study. Finally, the possibility of reporting bias of tobacco product use cannot be ruled out, although the bias would likely be non-differential and equally influence the responses for both the Cig-Only and Cig-OTP groups. Given that the strength of the associations found between cigarette consumption and biomarkers are consistent with those found in the literature (Benowitz et al., 2011b; Khariwala et al., 2014), it is unlikely that misreporting alone explains the lack of association between OTPs and biomarkers in the current study.

Our findings should be considered in light of the following limitations: The current study was comprised of a convenience sample of middle-aged adult Cig-OTP and Cig-Only smokers and, therefore, the findings cannot be applied to youth or young adult smokers whose proportion of OTP to cigarettes might be higher. The study did not obtain information on depth of inhalation, which could provide a potential explanation for the lower tobacco toxicant levels of Cig-OTP users. Other biomarkers of toxicant exposure exist (e.g., N'-nitrosonornicotine [NNN], metabolites of polycyclic aromatic hydrocarbons and volatile organic compounds, carbon monoxide), and should be examined in future studies to better understand the relative harm of Cig-OTP versus Cig-Only use (Chang et al., 2017). The study was not designed to examine differences in biomarker concentrations between different types of OTP, although the product mix of the current sample generalizes well to the majority of multiple tobacco product users. Larger studies with wider variability in quantity of use and OTP type are needed to better understand toxicant exposure profiles by dual cigarette-OTP subtypes. Finally, the sample was comprised of primary cigarette smokers who supplemented with OTP and, therefore, the overall pattern of findings cannot be generalized to primary OTP users who supplement with cigarettes. More research is needed to examine toxicant exposure profiles and adverse health effects of primary cigarette-secondary OTP versus primary OTP-secondary cigarette users.

5. Conclusions

Cig-OTP users had lower exposure to nicotine and the lung carcinogen NNK relative to Cig-Only users. However, given that biomarker levels in dual users were still substantial, the harm reduction potential of dual cigarette-OTP use is questionable. A better understanding of why toxicant levels may be lower in Cig-OTP is an important area for future study. Exclusion of OTP users from most smoking cessation clinical trials has resulted in almost complete lack of knowledge about effective treatments for this growing population of tobacco users. As trends in non-cigarette OTP use continue to rise, research is needed to examine effective strategies for encouraging cessation from all tobacco products among dual Cig-OTP users.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Polytobacco use likely influences toxicant exposure relative to single product use
- Polytobacco users smoked more tobacco products per week than single product users
- Despite more tobacco use, polytobacco users had lower nicotine and carcinogen levels
- Nicotine and carcinogen levels in polytobacco users were still substantial

Figure 1.

Flow diagram showing selection of 111 Cigarette-OTP and 111 Cigarette Only Users along with the race, gender, and age breakdown of the study sample

Figure 2.

Scatterplots of the associations between urinary total nicotine equivalents, NNAL, and past 7 day consumption of (a) other tobacco products, (b) cigarettes, and (c) cigarettes plus other tobacco products in Cig Only versus Cig-OTP users.

Table 1

Demographic and Tobacco Use Characteristics of Cigarette Only and Dual Cigarette plus Other Tobacco Product (OTP) Smokers

	Cigarettes Only (n=111)	Cigarettes-OTP (n=111)	p value
Matching Variables			
> 40 years of age, %	53.2%	53.2%	–
Male, %	61.3%	61.3%	–
Non-Hispanic African American, %	82.0%	82.0%	–
Demographic Characteristics			
Age, mean (SD)	43.0 (11.2)	39.4 (13.0)	0.03
> High school education, %	59.5%	36.0%	< 0.01
Not currently employed, %	29.7%	54.1%	< 0.01
Married/living with partner, %	38.7%	24.3%	0.02
Household income, median (range)	\$22,000 (\$0–\$72,000)	\$12,000 (\$0–\$250,000)	0.01

Tobacco Use				
Days used cigarettes in the past 30 days, mean (SD)	29.9 (0.7)	29.8 (1.0)	0.35	
Menthol, % yes	75.7%	81.8%	0.26	
Time to first cigarette, % < 30 minutes	79.3%	73.9%	0.34	
Age started smoking cigarettes regularly, mean (SD)	17.8 (7.3)	17.4 (5.5)	0.97	
Length of time as a cigarette smoker in years, mean (SD)	25.1 (12.4)	22.1 (13.5)	0.09	
Age started smoking OTP regularly, mean (SD)	–	19.8 (9.3)	–	
Length of time as OTP smoker in years, mean (SD)	–	19.7 (12.2)	–	
Used one or more OTP on > 25 days/month, (%)	–	46.8%	–	

Table 2

Past 7 Day Tobacco Consumption among Cigarette Only and Dual Cigarette plus Other Tobacco Product (OTP) Smokers

Cigarettes Only (n=111)			Cigarettes-OTP (n=111) ^a				
			Among the subset using each product				
	n	mean (SD)	n	mean (SD)	p value	n	mean (SD)
Cigarette and Other Tobacco Product Use Per Day, Past 7 Days							
Total tobacco products per day, Past 7 Days ^b	111	13.0 (5.4)	111	15.9 (8.0)	<0.01	—	—
Cigarettes	111	13.0 (5.4)	111	12.5 (5.9)	0.36	—	—
Little cigars and/or cigarillos (LCC)	—	—	111	1.14 (1.7)	—	111	1.14 (1.7)
Blunts	—	—	111	1.02 (1.7)	—	65	1.73 (2.0)
Hand-rolled cigarettes	—	—	111	0.82 (2.2)	—	41	2.21 (3.2)
Pipes	—	—	111	0.09 (0.5)	—	9	1.13 (1.6)
Smokeless tobacco	—	—	111	0.08 (0.4)	—	10	0.86 (0.9)
Electronic cigarettes	—	—	111	0.06 (0.2)	—	22	0.31 (0.3)
Full size cigars	—	—	111	0.15 (0.7)	—	22	0.76 (1.3)
Hookah	—	—	111	0.02 (0.1)	—	9	0.29 (0.2)

^aThe mean (SD) of OTP use is reported among all Cig-OTP participants and among the subset of Cig-OTP participants who reported using the product

^bTotal products per day is the sum of the number of cigarettes, LCC, blunts, hand-rolled cigarettes, pipes (number of bowls), smokeless tobacco (number of dips or chews), electronic cigarettes (number of cartridges), full size cigars, and hookah (number of sessions) used per day in the past 7 days

Table 3

Biomarkers of Tobacco Toxicant Smoke Exposure in Cigarette Only versus Cigarette plus Other Tobacco Product (OTP) Users

	Cigarette Only Users (n=111)	Cigarette-OTP Users (n=111)	p value
	Median (IQR)^a	Median (IQR)	
Nicotine (ng/mL)	1343 (519–2,432)	758 (267–2,018)	0.01
Nicotine, creatinine normalized (ng/mg creatinine)	1301 (641–2,910)	606 (215–1,438)	<0.001
Cotinine, (ng/mL)	2062 (1,059–4,101)	1373 (720–2,566)	0.001
Cotinine, creatinine normalized (ng/mg creatinine)	2125 (1,053–4,121)	1063 (493–1,946)	<0.001
TNE, (nmol/mL) ^b	51 (23–102)	38 (18–71)	0.01
TNE, creatinine normalized (nmol/mg creatinine)	56 (30–98)	28 (13–52)	<0.001
NNAL _x (pg/mL) ^c	345 (133–819)	313 (141–631)	0.53
NNAL _x , creatinine normalized (pg/mg creatinine)	343 (186–634)	251 (109–413)	0.001

^a Median (interquartile range) reported due to non-normal distribution

^b TNE = Total Nicotine Equivalents computed as the sum of the molar concentrations of nicotine and its major metabolites

^c NNAL= 4-(Methylnitrosamino) -1-(3) pyridyl-1-butanol