



## Full length article

## 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.

**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 1301 ng/mg), cotinine (1063 versus 2125 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.

## 1. Introduction

Use of non-cigarette other tobacco products (OTP) has grown exponentially in the United States over the last two decades (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

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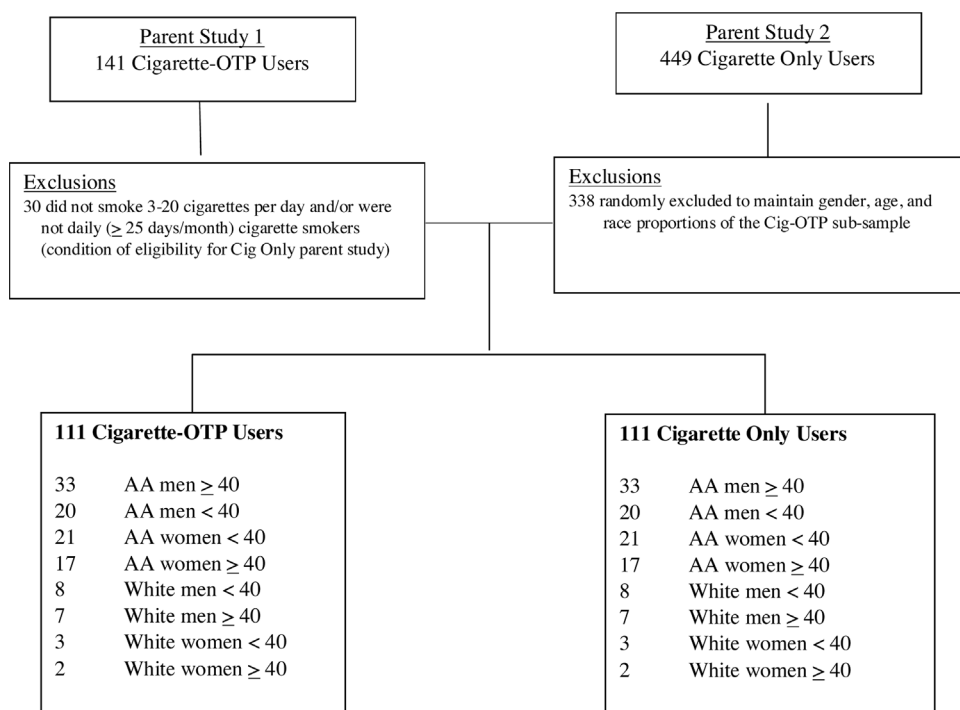


Fig. 1. Flow diagram showing selection of 111 Cigarette-OTP and 111 Cigarette Only Users along with the race, gender, and age breakdown of the study sample.

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., 2016) 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

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