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### Title

RETRACTED: Changes in Tobacco Dependence and Association With Onset and Progression of Use by Product Type From Wave 1 to Wave 3 of the Population Assessment of Tobacco and Health (PATH) Study.

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1 Changes in Tobacco Dependence and Association with Onset and Progression of Use by Product Type  
2 from Wave 1 to Wave 3 of the Population Assessment of Tobacco and Health (PATH) Study  
3

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40 **Data Availability Statement:**

41 Data are available in a public, open-access repository, the National Addiction and HIV Data Archive:

42 <https://www.icpsr.umich.edu/web/NAHDAP/studies/36498>

43

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45

46

47 **ABSTRACT**

48 **Introduction.** This study examined trajectories of tobacco dependence (TD) in relationship to changes in  
49 tobacco product use, and explored the effects of product-specific adding, switching, or discontinued use  
50 on dependence over time.

51 **Methods.** Data were analyzed from the first three waves from the Population Assessment of Tobacco and  
52 Health (PATH) Study, a nationally representative, longitudinal study of adults and youth in the United  
53 States (U.S.). Data included 9556 Wave 1 (2013/2014) adult current established tobacco users who  
54 completed all three interviews and had established use at  $\geq 2$  assessments. Groups included: users of  
55 cigarettes only, e-cigarettes only, cigars only, hookah only, any smokeless only, cigarette + e-cigarette  
56 dual users, and multiple product users. A validated 16-item scale assessed TD across product users.

57 **Results.** Wave 1 e-cigarette only users' levels of TD increased, while multiple product users' TD  
58 decreased across waves. TD for all other user groups remained about the same. For cigarette only  
59 smokers, switching to another product or moving to a pattern of no established use was associated with  
60 lower levels of TD than smokers whose use stayed the same. Movement to no established use of any  
61 tobacco product was consistently associated with lower TD for all other product users. Daily tobacco  
62 users had higher baseline TD and demonstrated less change over time compared with non-daily users  
63 regardless of the type or combination of tobacco products used.

64 **Conclusions.** Except for e-cigarette only users, TD among U.S. tobacco product users was stable over  
65 time, with daily users less likely to vary from baseline.

66

67 **IMPLICATIONS**

68 The level of TD among most U.S. tobacco users was stable over the first three waves of the PATH Study  
69 and trends in levels of TD were predominantly unrelated to changes in patterns of continued product use.

70 Stable levels of TD suggest a population at persistent risk of health impacts from tobacco. Exclusive e-  
71 cigarette users experienced increasing levels of TD over time, perhaps due to increases in quantity or

- 72 frequency of tobacco product use, increasing efficiency of nicotine delivery, or users becoming more
- 73 adept at using these devices to extract nicotine more efficiently over time.

74 **INTRODUCTION**

75 Over the past 25 years, assessment of biological markers suggests that levels of nicotine exposure among  
76 persistent smokers in the United States (U.S.) have not changed.<sup>1,2</sup> Consistent with symptoms of tobacco  
77 dependence (TD) reflecting drive (e.g., craving) and sustained tobacco use have remained stable for more  
78 than a decade among U.S. adult smokers.<sup>3</sup> However, given the increasingly common use of non-cigarette  
79 tobacco products, it remains important to study the development and course of physiological and  
80 behavioral features used to characterize dependence at the population level.

81 The Population Assessment of Tobacco and Health (PATH) Study has enabled comprehensive  
82 examination of the reliability of multiple indicators of TD across a range of tobacco products. In our  
83 previous work,<sup>4</sup> Wave (W) 1 (2013/2014) and W2 (2014/2015) data were analyzed from a U.S. nationally  
84 representative sample of 32,320 W1 adult (18 years and older) participants who used any tobacco product  
85 in the past 12 months. We validated an instrument using 16 items borrowed from existing scales<sup>4-6</sup> that  
86 enables comparison of TD across users of cigarettes, e-cigarettes, cigars, hookah, smokeless, and multiple  
87 tobacco products.<sup>7</sup> The TD scale demonstrated strong relationships with urinary biomarkers of total  
88 nicotine equivalents, predictive associations with persistent tobacco use, and described associations with  
89 changes in patterns of product use.<sup>8,29</sup>

90 One study, using PATH Study data, examined associations between TD and transitions in tobacco  
91 product use across Waves 1 and 2. Adults with high TD were less likely to discontinue cigarette smoking  
92 and all tobacco than adults with low dependence.<sup>9</sup> More dependent tobacco users were also more likely to  
93 switch among products, and highly dependent cigarette smokers were more likely to add products  
94 compared to less dependent smokers. In the current study, we examine patterns of use into W3, which  
95 provides the opportunity to examine multiple transitions in use.

96 Study objectives are to 1) understand trajectories of TD scores in relationship to changes in  
97 tobacco use, and 2) explore associations of adding, switching product patterns, or discontinued use of  
98 products with TD across W1-W3. Groups of interest include exclusive users of cigarettes, e-cigarettes,  
99 cigars, hookah, smokeless tobacco, dual cigarette/e-cigarette users and multiple product users.

100

## 101 **METHODS**

### 102 **Study Participants**

103 Data come from the PATH Study, an ongoing, nationally-representative, longitudinal cohort study of  
104 adults in the U.S. The study uses audio computer-assisted self-interviews available in English and  
105 Spanish to collect self-reported information on tobacco-use patterns and associated behaviors.

106 Recruitment employed a stratified address-based, area-probability sampling design at W1 that  
107 oversampled adult tobacco users, young adults (18 to 24 years), and African-American adults.

108 Weighted response rates for W1 (2013/2014), W2 (2014/2015), and W3 (2015/2016) adult  
109 interviews were 74.0%, 83.2% and 78.4%, respectively. W2 and W3 data collection protocols followed  
110 procedures to interview each respondent close to the 1-year anniversary of their participation in the prior  
111 wave. Full-sample and replicate weights were created that adjust for the complex sample design (e.g.,  
112 oversampling at W1) and nonresponse at W1-W3. Combined with the use of a probability sample, the  
113 weights allow analyses of the PATH Study data to compute robust estimates for the U.S. population ages  
114 18 years and older.<sup>10</sup> Further details regarding the PATH Study design<sup>11</sup> and data are described in the  
115 *PATH Study Restricted Use Files (RUF) User Guide* at <https://doi.org/10.3886/Series606>. The study was  
116 conducted by Westat and approved by the Westat Institutional Review Board.

117 The current study analyzes data from 9,556 W1 adult current established tobacco users who  
118 completed all three interviews and had persistent established use at two or more interviews/waves. A  
119 current established cigarette user at W1 was defined as: An adult who has smoked at least 100 cigarettes  
120 in his/her lifetime and now smokes every day or some days. For all other tobacco products, a current  
121 established user was defined as an adult who has ever used the product “fairly regularly” and now uses it  
122 every day or some days. Mutually exclusive tobacco-user groups at W1 who also completed all three  
123 interviews include: cigarette only users (n=5,945), e-cigarette only users (n=287), cigar only (traditional,  
124 cigarillo, or filtered) users (n=387), hookah only users (n=248), smokeless tobacco only users (n=620),  
125 cigarette plus e-cigarette users (n=498), and users of multiple tobacco products (at least two or more

126 products above or pipe or dissolvable products in the past year other than cigarette plus e-cigarette users)  
127 (n=1571).

128

### 129 **Tobacco Use Outcome**

130 We defined tobacco product use outcomes at W2 and W3 accordingly: a) Same: Continued established  
131 use of same product(s) as in the previous wave, b) Switched: Change in the established use of product(s)  
132 from the previous wave, c) Added: Continued established use of the same product(s) and established use  
133 of an additional product(s) not reported in the previous wave, and d) No Established Use: No established  
134 use of any product in the examined wave. We also indexed use frequency among past 30 day product  
135 users and categorized these as: daily users (reported use during all 30 days), or non-daily users (used  
136 fewer than 30 days).

137

### 138 **Symptoms of TD at Waves 1-3**

139 The adult interview included 24 symptoms of TD, of which 16 TD symptoms were identified as a scale  
140 for use across tobacco products.<sup>7</sup> Single product users were asked TD items that referred to their specific  
141 product in the item/question stem. Dual users of cigarettes and e-cigarettes were offered parallel sets of  
142 TD items, one set for each product, but for this analysis, response to items for cigarettes were used to  
143 assess TD in the Cigarette+E-Cigarette user group. Users of multiple products were asked TD items that  
144 referred broadly to “tobacco” in the item stems and did not receive repeated assessments for each product  
145 they reported using. Selected items were derived from the Wisconsin Inventory of Smoking Dependence  
146 Motives (WISDM; 11 items),<sup>5</sup> Nicotine Dependence Syndrome Scale (NDSS; 4 items),<sup>4</sup> and Diagnostic  
147 and Statistical Manual (DSM) Criteria (1 item).<sup>6</sup> Item response options from original instruments were  
148 adapted for the PATH Study. Following scoring procedures<sup>7</sup>, WISDM and NDSS five-level categorical  
149 responses were assigned to three levels by converting options 1, 2-3, and 4-5 to 0, 1, and 2, respectively.  
150 The two-level DSM criteria was scored 0 if not present (‘No’) and 2 if present (‘Yes’). A raw sum score  
151 of item options will range from 0 to 32 with 2 as the max score for each of the 16 items. Item options also

152 were multiplied by 50 to allow each item to contribute equally to a total score by balancing the uneven  
153 number of categories across items in this rating scale and to produce an average TD item score ranging  
154 from 0-100, where higher scores represented higher levels of TD.

155

## 156 **Analysis**

157 The primary dependent variable was the TD score at W1-W3. The primary independent variables were  
158 W1 tobacco use group and changes in established pattern of tobacco use between W1-W2 and between  
159 W2-W3 (Same, Added, Switched, and No Established Use). Covariates included W1 daily tobacco use,  
160 age (18-24 years, 25-34 years, and 35 years+), sex (male vs. female), racial/ethnic groups (Non-Hispanic  
161 White vs. All other groups), daily use and former tobacco use prior to W1. Growth curve models were  
162 constructed to simultaneously evaluate within-person influences of change in patterns of use within each  
163 W1 tobacco user group (via time-varying covariates) and between-person influences of demographic  
164 characteristics, W1 daily use and former tobacco use prior to W1 on stability and change of TD over  
165 time.<sup>12</sup> Time-varying indicators of tobacco use patterns were related directly to TD assessed at the  
166 corresponding wave while controlling for the influence of levels of TD at W1 and average changes in TD  
167 over waves.<sup>13</sup> Thus, W2 and W3 measures of TD are jointly determined by the underlying intercept and  
168 slope growth factors and the impact of the pattern of tobacco use at that wave.

169 All-waves longitudinal weights with nonresponse adjustments were used with W1-W3 of the  
170 adult RUF. The Balanced Repeated Replication method with Fay's adjustment set to 0.3 was used for all  
171 analyses of weighted data as computed by the survey package<sup>14</sup> and lavaan.survey package<sup>15</sup> in R.<sup>16</sup>  
172 Missing data on age, sex, race, and Hispanic ethnicity were imputed at W1 as described in the PATH  
173 Study RUF User Guide. Due to an instrument error, W3 assessments of TD were not available for all  
174 respondents (n=1,117/9,556; 12% were imputed). We assumed that the data was missing at random and  
175 was unrelated to product use groupings. We used a multiple imputation (imputed data sets = 20) approach  
176 and the mice package<sup>17,18</sup> to incorporate sample weights as a covariate when estimating growth curve  
177 models of TD that include W3 assessments.



178

## 179 **RESULTS**

### 180 **Descriptive Analyses**

181 Weighted sample demographic characteristics are presented in Table 1. Population weighted average TD  
182 scores at W1 was 50.62 (se = 0.37) with a standard deviation ( $TD_{sd}$ ) of 29.24 (se=3.05). Population levels  
183 of TD for scores 0-18 were considered lower (<33<sup>rd</sup> percentile), TD scores 19-55 were considered  
184 medium (33<sup>rd</sup> – 65<sup>th</sup> percentile) and TD scores 56-100 were considered highest (66<sup>th</sup> percentile) levels of  
185 Wave 1 based on weighted terciles for TD scores for respondents who participated in all 3 surveys and  
186 had non-missing TD scores (n=13,262). The population standard deviation of TD was used throughout  
187 the results to compute standardized estimates (d) of the magnitude of differences in average levels of TD  
188 using standard deviation units.

189 Post-hoc analysis used a Signed Differential Test Functioning (sDTF) statistic to properly account  
190 for sampling variability in item parameter estimates<sup>27</sup> when quantifying the amount of any scoring bias in  
191 TD between W1 tobacco user groups who reported no current established use but only past year use at  
192 W2 (n=381) or W3 (n=580) suggested minimal bias in comparing expected TD scores to W2 (n=9131)  
193 and W3 (n=7901) current users. Very small positive values of sDTF at W2 (sDTF=0.02, 95%CI =0.020,  
194 0.022) and very small negative values at W3 (sDTF=-0.0286, 95%CI=-0.0294, -0.0280) indicated that  
195 current tobacco users (reference group) on average scored within one raw unit difference than past year  
196 users with the same level of TD (see Supplement Figure 1).

### 197 **TD Trajectories for Wave 1 Tobacco User Groups**

198 Figure 1 shows the weighted average level of TD (scaled 0-100) for W1 tobacco user groups across each  
199 wave. Weighted latent growth curve models with covariates at W1 were used to compare W1 levels of  
200 TD ( $TD_{Intercepts}$ ) and changes in TD ( $TD_{slopes}$ ) across the seven tobacco user groups. Sex, age group, and  
201 race-ethnicity each were associated with W1 levels of TD ( $TD_{Intercept}$ ) and changes in TD over the three  
202 waves ( $TD_{Slopes}$ ). In this model, being a daily user of tobacco product(s) was significantly associated with

203 higher W1 TD ( $TD_{Intercept}=0.328$ ,  $se=0.007$ ,  $p<0.001$ ;  $d=1.12$ ) and less change in TD ( $TD_{Slopes}=-0.030$ ,  
204  $se=0.004$ ,  $p<0.001$ ) than among non-daily tobacco users (Table 2).

205 Figure 1 shows a stable trajectory of high levels of TD for W1 Cigarette Only users that  
206 decreased only slightly through W3. When compared (Table 2) to W1 Cigarette Only users, W1 E-  
207 Cigarette Only users had lower levels of TD at W1 ( $TD_{Intercept}=-0.24$ ,  $se=0.02$ ,  $p<0.01$ ;  $d=0.82$ ) and had a  
208 greater increase ( $TD_{Slope}=0.07$ ,  $se=0.01$ ,  $p<0.01$ ) in TD reflecting a moderate increase from W1 to W3  
209 ( $d=0.41$ ). W1 Cigar Only ( $TD_{Intercept}=-0.16$ ,  $se=0.02$ ,  $p<0.01$ ;  $d=0.55$ ), W1 Hookah Only ( $TD_{Intercept}=-0.15$ ,  
210  $se=0.03$ ,  $p<0.001$ ;  $d=0.51$ ), and W1 Smokeless Only ( $TD_{Intercept}=-0.04$ ,  $se=0.02$ ,  $p=0.01$ ;  $d=0.14$ ) tobacco  
211 user groups also had lower levels of TD at W1 than W1 Cigarette Only users although rates of change in  
212 TD ( $TD_{slopes}$ ) among these user groups were not significantly different than rates of change among W1  
213 Cigarette Only users. When compared to W1 Cigarette Only users, W1 multiple product users including  
214 W1 Cigarette+E-Cigarette ( $TD_{Intercept}=0.03$ ,  $se=0.01$ ,  $p=0.02$ ;  $d=0.10$ ) and W1 Multiple Product users  
215 ( $TD_{Intercept}=0.04$ ,  $se=0.01$ ,  $p<0.01$ ;  $d=0.14$ ) had higher levels of TD at W1. W1 Cigarette+E-Cigarette  
216 users ( $TD_{Slopes}=-0.01$ ,  $se=0.007$ ,  $p=0.21$ ) had rates of change in TD ( $TD_{slopes}$ ) that were not significantly  
217 different than rates of change among W1 Cigarette Only users. W1 Multiple Product users ( $TD_{Slopes}=-$   
218  $0.02$ ,  $se=0.004$ ,  $p<0.001$ ) had significantly less change in TD than W1 Cigarette Only Users. W1 Hookah  
219 Only users reported mean of 8.54 ( $se=0.84$ ), a level that would fall in the bottom population tertile  
220 ( $<18.75$ ) and would correspond to endorsing less than three TD items (a raw sum score of  
221  $(8.54/50)*16=2.7$ ).

222

### 223 **Changes in Pattern of Use Over Waves 1-3 Among W1 Tobacco User Groups**

224 The percent of W1 tobacco user groups who added a product to those used in the previous wave varied  
225 across user groups (Supplemental Table 1). At W2, 4.6% of W1 Cigarette+E-Cigarette users and 19.3%  
226 of W1 E-Cigarette Only users added a product. At W3, 12.3% of W1 Cigarette+E-Cigarette and 22.6%  
227 of W1 Hookah Only users added a product. W1 Cigarette Only, W1 Smokeless Only, and W1 E-Cigarette  
228 Only users had the highest rates (range: 59.2%-85.8%) of stability at each subsequent wave. At W2 and

229 W3, having Switched product use patterns was most common among W1 Multiple Product (W2 = 50.9%;  
230 W3 =30.4%) and W1 Cigarette+E-Cigarette (W2 = 47.3%; W3 =28.8%) groups. Transitioning to No  
231 Established Use was most common among W1 Hookah Only users (W2 = 13.4%; W3 =29.3%).

232

### 233 **Changes in Patterns of Product Use and Trajectories of TD Among W1 Tobacco User Groups over** 234 **Waves 1-3**

235 To assess the impact of changes in tobacco use patterns on changes in TD, growth curves were fit to three  
236 longitudinal assessments of TD separately for each W1 tobacco user group (Table 3).

237

#### 238 *Between-Person Effects on TD Within W1 Tobacco User Groups*

239 Women had higher levels of W1 TD ( $TD_{Intercept}$ ) than men within W1 Cigarette Only, W1 E-Cigarette  
240 Only, and W1 Cigar Only user groups. Older tobacco users (ages 35 years and older) had higher W1  
241  $TD_{Intercept}$  than younger users (18-24) among W1 Cigarette Only, W1 Smokeless Only, W1 Cigarette+E-  
242 Cigarette and W1 Multiple Product user groups. Among W1 Cigarette+E-Cigarette and W1 Multiple  
243 Product users, adults ages 25-34 years and ages 35 years and older had higher levels of TD than adults 18-  
244 24 years old. Non-White W1 Cigarette Only and W1 Multiple Product users had lower levels of W1  
245  $TD_{Intercept}$  than White users from the same user groups. W1 daily users of tobacco had higher W1  $TD_{Intercept}$   
246 than non-daily users across all tobacco user groups. Former use of other tobacco products was associated  
247 with higher W1 TD within W1 Cigarette Only and W1 Multiple Product users. Former use of other  
248 tobacco products was associated with lower W1 TD among W1 Cigar Only users. Women had greater  
249 increases than men in  $TD_{slope}$  from W1 to W3 among W1 Multiple Product users. W1 E-Cigarette Only  
250 users aged 35+ had greater increases in  $TD_{slope}$  than 18-24 year old users. Non-White users had a slower  
251 increase in  $TD_{slope}$  over time than White users among W1 Cigarette Only and W1 E-Cigarette Only users.  
252 Daily use at W1 was associated with a lesser change in  $TD_{slope}$  among W1 Cigarette Only, W1 Smokeless  
253 Only, and W1 Multiple Product users.

254

255 *Associations Between Patterns of Use and TD Over Waves 1-3*

256 With adjustment for the levels of TD at W1 and a general increase in TD over time, we evaluated whether  
257 change in pattern of use at W2 and W3 were associated with changes in TD not predicted by expected  
258 trends in TD over time. Differences in levels of TD for W1 tobacco user groups who stayed the same,  
259 switched, or discontinued tobacco use were compared at each wave relative to users who added a product  
260 to their pattern of use at the previous wave.

261 W1 Cigarette Only users who either switched or had no established use at W2 had moderately lower  
262 levels of TD than those who added product(s) (Table 3). W1 Cigarette Only users whose product use  
263 pattern stayed the same at W2 had levels of TD that were not significantly different than those who added  
264 product(s). At W3, the majority (77.3%) of Cigarette Only users stayed the same as their W2 pattern of  
265 product use (Supplemental Table 1) and had slightly higher levels of TD at W3 than those who added a  
266 product between W2 and W3. Wave 1 Cigar Only and Hookah Only users who stayed the same at W2  
267 had slightly lower TD than similar W1 users who added products. Among W1 E-Cigarette Only, W1  
268 Smokeless Only, W1 Cigarette+E-Cigarette, and W1 Multiple Product users, those who stayed the same  
269 and those who Added product(s) at W2 or W3 did not have different levels of TD ( $p$ 's>0.11) at either W2  
270 or W3. In post-hoc analysis of changes between W1 and W2, among W1 E-Cigarette Only users ( $n=287$ ),  
271  $88\pm 6\%$  ( $n=34$  of 39) who switched products and  $83\pm 7\%$  ( $n=46$  of 56) who added products included new  
272 use of cigarettes at W2. We did not see a significant difference in W2 TD for W1 E-Cigarette Only users  
273 who stayed the same or switched product use patterns at W2 compared to those who added products at  
274 W2 (see Table 3). Mean TD trajectories increased for Wave 1 exclusive E-Cigarette Only users who  
275 remained exclusive users through Wave 2 and Wave 3 ( Supplement Figure 2).

276 W1 Cigarette Only, W1 Cigarette+E-Cigarette, and W1 Multiple Product users who switched  
277 patterns of product use at W2 had slightly lower levels of TD than those who added products at W2  
278 ( $p$ 's<0.01). Relative to W1 Multiple Product users who added products between W2 and W3, W1  
279 Multiple Product users switching patterns of products between W2 and W3 had lower TD at W3.  
280 Switching products between W1 and W2 or between W2 and W3 was not associated with corresponding

281 changes in levels of TD among W1 E-Cigarette Only, W1 Cigar Only, W1 Hookah Only or W1  
282 Smokeless Only user groups ( $p$ 's>0.13).

283 Post-hoc regressions explored if reductions in W2 TD for W1 user groups who switched  
284 patterns of products at W2 differed according to which products they reported using at W2. Models  
285 assessed W2 TD among the most common new patterns of use at W2 within W1 Cigarette Only, W1  
286 Cigarette+E-Cigarette, and W1 Multiple Product users. Models included W1 TD and covariates mirroring  
287 primary analyses. Among W1 Cigarette Only users who switched at W2 ( $n=90$ ), TD reductions at W2  
288 were not different ( $F(1,81)=1.4$ ,  $p=0.23$ ) among W1 Cigarette Only users switching to E-Cigarette Only  
289 ( $n=73$ ;  $84\pm 4\%$ ) or other patterns of use ( $n=17$ ;  $16\pm 4\%$ ) at W2. Among W1 Cigarette+E-Cigarette users  
290 who switched at W2 ( $n=230$ ), TD reductions ( $F(2,90)=100.3$ ,  $p < 0.001$ ) were larger among the  $15\pm 2\%$   
291 ( $n=32$ ) who switched to E-cigarette Only than among the  $79\pm 2\%$  ( $n=183$ ) who switched to Cigarette  
292 Only. Among W1 Multiple Product users ( $n=824$ ),  $51\pm 2\%$  ( $n=413$ ) switched to Cigarette Only,  $6\pm 1\%$   
293 ( $n=47$ ) switched to E-cigarette Only,  $9\pm 1\%$  ( $n=78$ ) switched to Cigarette+E-Cigarette, and  $34\pm 2\%$   
294 ( $n=286$ ) switched to another pattern of use. Reduction of W2 TD ( $F(3,89)=19.1$ ,  $p < 0.001$ ) were larger for  
295 those W1 Multiple Product users who switched to E-cigarettes Only than those who switched to Cigarette  
296 Only use.

297 Across all users, W1 tobacco users who had no established use at either W2 or W3 had  
298 significantly lower levels of TD ( $p$ 's $\leq 0.05$ ) than those who added products with standardized mean  
299 differences ranging from  $-0.05$  ( $se=0.02$ ;  $d=0.17$ ) for Hookah Only users to  $-0.42$  ( $se=0.05$ ;  $d=1.44$ )  
300 among Cigarette+E-Cigarette users.

## 301 302 **DISCUSSION**

303 The PATH Study enables continued monitoring of the impact of product use on addiction to  
304 tobacco in the U.S. Initial levels of TD differed between product user groups at the start of W1. W1  
305 Cigarette Only, W1 Smokeless Only, W1 Cigarette+E-Cigarette and W1 Multiple Product users showed  
306 higher levels of TD compared to W1 E-Cigarette Only, W1 Hookah Only or W1 Cigar Only users,

307 consistent with more frequent use patterns of products with high levels of nicotine.<sup>7</sup> Analysis of temporal  
308 changes across waves suggested W1 Multiple Product users' TD decreased and TD for other user groups  
309 remained roughly the same. W1 E-Cigarette Only users were distinguished by a moderate increase in TD  
310 from W1 to W3, an increase that was accelerated among older users. Exclusive W1 E-Cigarette users who  
311 remained exclusive users at W2 and W3 also increased TD from W1 to W3. Former use of other products  
312 and adding or switching to product use patterns that included cigarettes was common among W1 E-  
313 cigarette Only users, although these factors were not associated with increases in TD observed at  
314 subsequent waves. Factors that influence successful switching to non-cigarette products or initiation of E-  
315 Cigarette Only use such as susceptibility to rewarding effects of nicotine,<sup>19</sup> comorbid mental health,<sup>20</sup> or  
316 other influences can be explored to better understand the increase in TD relative to other tobacco user  
317 groups. Differential increases also may be attributed to such factors as increases in quantity or frequency  
318 of tobacco use and increasing efficiency of nicotine delivery, as these products continue to evolve their  
319 technology. It is also possible that W1 E-Cigarette Only users became more adept at using these devices  
320 to extract nicotine more efficiently over time. W1 Multiple Product users' decrease in TD was small  
321 although statistically significant. W1 Multiple Product users were more likely to switch to other products  
322 across waves. It is possible that switching to other products with lower associated TD (e.g., e-cigarettes,  
323 cigars, hookah), or falling into a pattern of less consistent use of any products, was responsible for the  
324 overall decrease in TD in this group.

325 For W1 Cigarette Only users, a switch to another product at W2 or discontinued use was  
326 associated with lower levels of TD. This makes sense insofar as discontinued use means that W1  
327 Cigarette only users were no longer smoking every day or on some days. While uncommon among W1  
328 Cigarette Only users, switching to non-cigarette tobacco products might lower TD and thus support  
329 efforts by users to replace cigarettes with products that potentially yield less nicotine or harmful  
330 constituents. Movement to the No Established Use category at W2 or W3 was also consistently associated  
331 with lower TD for all other product use groups, probably reflecting less use and nicotine intake. Overall,  
332 though, more than 3 of 4 W1 Cigarette Only users continued to use cigarettes only across each wave of

333 the study. Cigarette use and concomitant levels of TD were stable in this group. Recent studies of young  
334 adults in a large nationally representative sample (n=15,275) prospectively examined product use  
335 transitions over a period of 2.5 years and showed that short-term transitions ( $\leq 1$  year) between use of any  
336 product to subsequent use of any other product were equally likely, but affected only a small proportion of  
337 the population who were already product users.<sup>21,22</sup> After 2.5 years, the strongest transition probabilities  
338 were from initial use of cigarettes to continuing to smoke cigarettes, and from use of any other products  
339 including e-cigarettes to no current use. W1 Smokeless Only and W1 Cigarette Only users were also  
340 likely to persist in a consistent pattern of use across waves. W1 E-Cigarette Only and W1 Cigar Only  
341 users also reported high rates of persistent patterns of use. W1 Cigarette + E-cigarette users and W1  
342 Multiple Product users, however, were less likely to remain in these states over time. This relative  
343 instability suggests the possibility that these users are not completely satisfied with the products they are  
344 using. W1 Cigarette+E-Cigarette users who switched to E-Cigarettes Only at W2 saw a greater decrease  
345 in TD than W1 Cigarette+E-Cigarette users who switched to Cigarettes Only at W2. They may be  
346 considering cutting down, quitting, or transitioning to a favored product use pattern. W1 Cigarette+E-  
347 cigarette users and W1 Multiple Product users had higher W1 TD on average. The lower TD associated  
348 with switching patterns use may suggest success in efforts to reduce exposure though persistent high  
349 levels of TD also suggests risk of long-term tobacco use behaviors.

350 Limitations of collecting assessments approximately every 12-months include a decreased ability to link  
351 temporally between-interview changes in product use to TD assessments. We chose to focus on  
352 trajectories among continuing tobacco users when attempting to characterize the role of changes in  
353 product use patterns; therefore, we do not describe effects of product use changes among those who were  
354 able to quit successfully. W3 assessments of TD were not available for all respondents entering the study  
355 at W1 and multiple imputation methods were used to support inferences. We retained as a reference  
356 group, those who added products. This enabled direct comparisons between users who added or switched  
357 products, though we did not test all pairwise combinations (e.g., comparing those who switched to those  
358 who stayed the same). The TD scale was validated among current W1 product users. Post-hoc estimation

359 of differences in measurement of TD among past-year users reporting no established use at W2 or W3 did  
360 not suggest differences in test functioning and supported comparability of TD scores. The use of cigarette  
361 products to estimate TD among W1 Cigarette+E-Cigarette product users may limit precise assessment of  
362 dependence in this dual product using group. Other W1 Multiple Product users were asked globally about  
363 tobacco products and did not receive assessment of TD on any single product. Determining the utility of  
364 ascribing level of tobacco dependence to each product among multiple product users remains a challenge  
365 for assessing impacts of TD.<sup>23-26</sup> The relative difference in TD among product users may be useful for  
366 gauging population trends, the absence of a ‘gold standard’ criterion for dependence challenges  
367 development of clinical or diagnostic thresholds. Psychometric calibration of TD scores alongside  
368 clinically applied metrics such as the WISDM<sup>5</sup>, NDSS<sup>4</sup> and PROMIS<sup>30</sup> dependence instruments could  
369 advance development of meaningfully comparable scores.

370           The level of TD among U.S. tobacco users, except for W1 E-cigarette Only and W1 Multiple  
371 Product users, was stable over the first three waves of the PATH Study and trajectories in levels of TD  
372 were predominantly unrelated to changes in patterns of continued product use. Stable levels of TD  
373 suggest a population at persistent risk of health impacts from tobacco. We observed more change in TD  
374 among W1 E-cigarette Only and W1 Multiple Product users compared to W1 Cigarette Only users over  
375 time. Escalating TD among W1 E-cigarette Only users was not explained by changes in patterns of use,  
376 while decreases in TD among W1 Multiple Product users was associated with switching patterns of  
377 product use.

378

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383

## 384 **DECLARATION OF INTERESTS**



385 Wilson Compton reports long-term stock holdings in General Electric Company, 3M Company, and  
386 Pfizer Incorporated, unrelated to this manuscript. K. Michael Cummings provides expert testimony on the  
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394           The findings and conclusions in this report are those of the authors and do not necessarily  
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402

403

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405 None

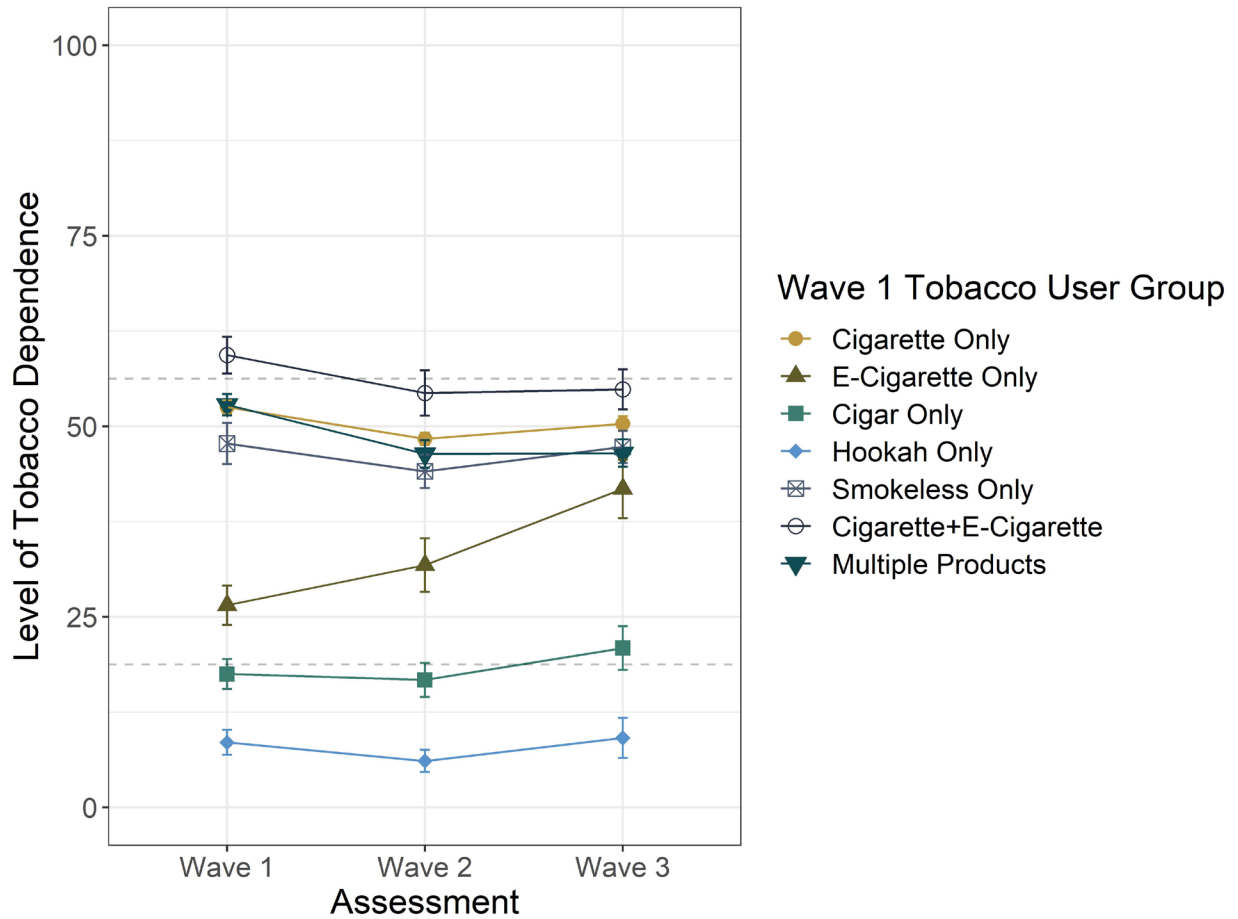
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**Table 1. Demographic and Tobacco Use Characteristics of Wave 1 Tobacco User Groups Who Had Established Tobacco Use at Two or More Assessments (n=9556).**

Demographic Factor	Cigarette Only (n=5945)		E-cigarette Only (n=287)		Cigar Only (n=387)		Hookah Only (n=248)		Smokeless Only (n=620)		Cigarette + E-cigarette (n=498)		Multiple Products (n=1571)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<b>Sex</b>														
Male	2708	50.8%	115	43.4%	297	81.9%	128	55.8%	590	95.6%	205	44.4%	1170	79.4%
se		0.7%		3.2%		2.2%		3.4%		1.1%		2.5%		1.0%
Female	3237	49.2%	172	56.6%	90	18.1%	120	44.2%	30	4.4%	293	55.6%	401	20.6%
se		0.7%		3.2%		2.2%		3.4%		1.1%		2.5%		1.0%
<b>Age Group</b>														
18-24	967	10.7%	64	15.3%	119	19.7%	198	72.9%	103	10.6%	93	13.1%	650	31.0%
se		0.4%		2.1%		1.8%		3.7%		1.1%		1.6%		1.3%
25-34	1305	23.2%	61	26.5%	69	19.7%	37	20.8%	107	19.5%	134	30.7%	368	28.4%
se		0.7%		3.0%		2.6%		3.5%		2.1%		2.4%		1.5%
35+	3673	66.0%	162	58.2%	199	60.6%	13	6.4%	410	69.9%	271	56.2%	553	40.5%
se		0.7%		3.5%		2.8%		1.9%		2.3%		2.7%		1.7%
<b>Racial/Ethnic Group</b>														
Non-Hispanic White	3911	69.5%	213	76.0%	206	61.2%	108	45.0%	534	89.4%	377	80.3%	1002	69.6%
se		0.7%		3.1%		2.5%		4.2%		1.4%		1.9%		1.3%
Other Groups	2034	30.5%	74	24.0%	181	38.8%	140	55.0%	86	10.6%	121	19.7%	569	30.4%
se		0.7%		3.1%		2.5%		4.2%		1.4%		1.9%		1.3%
<b>Tobacco Use</b>														
Non-Daily Use	999	16.9%	79	25.2%	279	72.4%	236	--	127	20.4%	54	9.0%	321	20.4%
se		0.6%		2.6%		2.5%		--		1.9%		1.4%		1.2%
Daily Use	4946	83.1%	208	74.8%	108	27.6%	12	--	493	79.6%	444	91.0%	1250	79.6%

se		0.6%		2.6%		2.5%		--		1.9%		1.4%		1.2%
<b>Former Use of Other Product</b>														
No Former Established Use	4953	83.8%	69	20.9%	214	50.8%	183	74.4%	336	52.2%	412	82.3%	1096	69.9%
se		0.5%		2.2%		3.0%		2.9%		2.2%		2.1%		1.2%
Former Established Use	992	16.2%	218	79.1%	173	49.2%	65	25.6%	284	47.8%	86	17.7%	475	30.1%
se		0.5%		2.2%		3.0%		2.9%		2.2%		2.1%		1.2%

**Note:** Includes tobacco users with established use at two or more waves of assessment. Values for numbers of cases (n) are unweighted. All percentages (%) are weighted estimates and include standard errors (se). Cells with '--' suppressed when the Relative Standard Error (RSE) was greater than 30% or RSE(1-proportion) is greater than 30%.



**Figure 1.** Survey weighted average level of tobacco dependence (scaled 0-100) for Wave 1 tobacco user groups who had established use at two or more waves of assessment. Dashed lines reflect lower (33<sup>rd</sup> percentile; TD <18.75) and higher (66<sup>th</sup> percentile; TD > 56.25) levels of Wave 1 weighted terciles for tobacco dependence for respondents who participated in all 3 surveys and had non-missing TD scores (n=13,262). A raw sum score of item options will range from 0 to 32 with 2 as the max score for each of the 16 items. Item options were multiplied by 50 to achieve a 0-100 scale for the total score. For example, a score of 18.75 on the 0-100 scale would be 6 as a raw sum score  $(18.75/50) * 16 = 6$ .

**Table 2.****Growth Model for Tobacco Dependence from Wave 1 to Wave 3 among Wave 1 Tobacco User**

**Groups. Survey weighted models estimate Wave 1 level (Intercept) and rate of change over waves (slopes) with adjustment for sex, age, race/ethnicity, daily use, and former product use.**

Status at Wave 1	Intercep			Slope	se	p
	t	se	p			
<i>Wave 1 Covariates</i>						
Female	0.039	0.007	0.000	0.005	0.003	0.070
Age 25-34	0.018	0.010	0.079	0.003	0.004	0.404
Age 35+	0.058	0.008	0.000	0.007	0.003	0.033
Non-White	-0.036	0.008	0.000	-0.015	0.003	0.000
Wave 1 Daily Use	0.327	0.010	0.000	-0.034	0.004	0.000
Formerly Used Other Products	0.009	0.007	0.204	0.001	0.003	0.675
<i>Wave 1 User Groups</i>						
Cigarette Only	–	–	–	–	–	–
E-Cigarette Only	-0.240	0.024	0.000	0.071	0.011	0.000
Cigar Only	-0.158	0.024	0.000	0.012	0.007	0.101
Hookah Only	-0.150	0.035	0.000	-0.001	0.007	0.904
Smokeless Only	-0.039	0.016	0.015	0.009	0.006	0.104
Cigarette+E-Cigarette	0.031	0.013	0.022	-0.008	0.007	0.207
Multiple Products	0.035	0.009	0.000	-0.021	0.004	0.000

Note: Measures of TD were rescaled during model estimation by dividing by 100. Estimates can be multiplied by 100 to recapture original metric of 0-100. All models included survey weights. ‘–’ indicates the reference group.

**Table 3.**

**Frequency of tobacco use patterns from Wave 1 to Wave 2, and Wave 2 to Wave 3 among Wave 1 Tobacco User Groups.**

	Added			Stayed Same			Switched			No Established Use		
	n	%	se	n	%	se	n	%	se	n	%	se
<b>Wave 1 User Group</b>	<b>Wave 1 -&gt; Wave 2</b>											
Cigarette Only	614	10.1%	0.5%	5039	85.0%	0.5%	90	1.5%	0.2%	202	3.4%	0.2%
E-Cigarette Only	56	19.3%	2.3%	176	61.9%	2.8%	39	13.4%	2.1%	16	5.3%	1.4%
Cigar Only	66	17.3%	2.2%	235	63.9%	2.8%	49	10.5%	1.8%	37	8.3%	1.1%
Hookah Only	33	14.9%	2.8%	142	56.0%	3.3%	38	15.8%	2.3%	35	13.4%	1.9%
Smokeless Only	44	6.7%	1.0%	527	85.8%	1.7%	16	2.3% <sup>a</sup>	0.7% <sup>a</sup>	33	5.3%	1.1%
Cigarette+E-Cigarette	28	4.6%	0.9%	226	45.4%	2.7%	230	47.3%	2.7%	14	2.7%	0.7%
Multiple Products	138	8.1%	0.7%	551	37.6%	1.5%	824	50.9%	1.4%	58	3.5%	0.5%
<b>Wave 1 User Group</b>	<b>Wave 2 -&gt; Wave 3</b>											
Cigarette Only	538	8.9%	0.4%	4578	77.3%	0.6%	440	7.2%	0.4%	389	6.5%	0.4%
E-Cigarette Only	39	12.5%	1.9%	171	59.2%	3.1%	47	17.8%	2.6%	30	10.4%	2.1%
Cigar Only	69	15.9%	1.8%	233	63.9%	2.9%	36	9.2%	1.6%	49	11.1%	1.8%
Hookah Only	56	22.6%	2.8%	97	39.6%	3.4%	19	8.5%	2.1%	76	29.3%	3.6%
Smokeless Only	69	9.9%	1.2%	475	78.5%	1.7%	27	3.9%	0.8%	49	7.6%	1.3%
Cigarette+E-Cigarette	59	12.3%	1.6%	257	51.6%	2.3%	147	28.8%	2.0%	35	7.3%	1.3%
Multiple Products	302	18.7%	1.1%	674	44.5%	1.4%	484	30.4%	1.2%	111	6.4%	0.7%

Note: Includes tobacco users with established use at two or more waves of assessment. Values for numbers of cases (N) are unweighted. All percentages (%) are weighted estimates and include standard errors (se). Cells with <sup>a</sup> flagged when the Relative Standard Error (RSE) was greater than 30% or RSE (1-proportion) is greater than 30%.

Table 4.

Growth model results describing trajectories of tobacco dependence (TD) scores among Wave 1 Tobacco User Groups across Waves 1, 2, and 3 and effect of time-varying changes in product use on levels of TD at Wave 2 and Wave 3.

	W1 Cigarette Only			W1 E-Cigarette Only			W1 Cigar Only			W1 Hookah Only			W1 Smokeless Only			W1 Cigarette+E-Cigarette			W1 Multiple Products		
	b	se	p	b	se	p	b	se	p	b	se	p	b	se	p	b	se	p	b	se	p
<i>Time Invariant Status at Wave 1</i>																					
<b>Intercept: W1 TD</b>																					
Female	0.04	0.01	0.00	0.06	0.02	0.01	0.11	0.04	0.01	-0.01	0.01	0.60	0.04	0.06	0.54	0.04	0.03	0.17	0.02	0.02	0.29
Age 25-34	0.00	0.01	0.74	0.01	0.04	0.84	-0.01	0.03	0.78	0.02	0.03	0.52	0.01	0.04	0.75	0.11	0.04	0.00	0.05	0.02	0.02
Age 35+	0.05	0.01	0.00	0.06	0.03	0.10	0.01	0.03	0.66	0.02	0.03	0.49	0.09	0.04	0.02	0.13	0.04	0.00	0.09	0.02	0.00
Non-White	-0.04	0.01	0.00	-0.03	0.04	0.34	-0.01	0.03	0.84	0.02	0.02	0.23	-0.04	0.04	0.22	-0.04	0.03	0.20	-0.03	0.02	0.05
W1 Daily Use	0.35	0.01	0.00	0.11	0.03	0.00	0.26	0.03	0.00	0.18	0.08	0.03	0.29	0.03	0.00	0.21	0.05	0.00	0.36	0.02	0.00
Formerly Used Other Products	0.03	0.01	0.01	-0.06	0.03	0.08	-0.05	0.03	0.15	0.02	0.02	0.40	-0.03	0.02	0.16	0.03	0.03	0.25	0.03	0.02	0.04
<b>Slope: W1 to W3 Change in TD</b>																					
Female	0.00	0.00	0.40	0.00	0.02	0.82	-0.01	0.02	0.62	-0.01	0.01	0.47	0.01	0.02	0.81	0.00	0.02	0.86	0.02	0.01	0.00
Age 25-34	0.00	0.00	0.76	0.05	0.03	0.07	0.01	0.01	0.49	-0.03	0.02	0.09	0.01	0.02	0.53	-0.01	0.02	0.52	0.00	0.01	0.76
Age 35+	0.00	0.00	0.76	0.06	0.03	0.03	0.02	0.02	0.22	0.01	0.02	0.78	0.02	0.02	0.29	-0.01	0.02	0.68	0.00	0.01	0.87
Non-White	-0.02	0.00	0.00	-0.05	0.02	0.03	-0.01	0.01	0.38	-0.02	0.01	0.13	0.00	0.01	0.77	0.01	0.02	0.70	-0.01	0.01	0.09
W1 Daily Use	-0.05	0.00	0.00	-0.02	0.02	0.32	-0.01	0.02	0.75	-0.06	0.05	0.26	-0.05	0.01	0.00	-0.03	0.03	0.30	-0.05	0.01	0.00
Formerly Used Other Products	0.00	0.01	0.83	0.01	0.02	0.69	0.01	0.01	0.44	0.01	0.01	0.35	0.02	0.01	0.11	-0.01	0.02	0.57	-0.01	0.01	0.30
<i>Time-Varying Status</i>																					
<b>Wave 2 Use Status</b>																					
Added	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stayed the Same	0.00	0.01	0.65	-0.02	0.03	0.55	-0.04	0.02	0.02	-0.03	0.01	0.01	-0.03	0.02	0.09	0.01	0.02	0.56	-0.01	0.01	0.26
Switched	-0.36	0.05	0.00	0.06	0.06	0.33	0.03	0.04	0.44	0.04	0.03	0.14	0.11	0.09	0.24	-0.05	0.02	0.01	-0.04	0.01	0.00
No Established Use	-0.19	0.02	0.00	-0.16	0.06	0.01	-0.08	0.04	0.04	-0.09	0.02	0.00	-0.14	0.04	0.00	-0.28	0.09	0.00	-0.18	0.04	0.00
<b>Wave 3 Use Status</b>																					
Added	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stayed the Same	0.03	0.01	0.00	-0.04	0.05	0.46	-0.05	0.03	0.07	-0.03	0.03	0.19	-0.01	0.03	0.80	0.03	0.02	0.18	0.01	0.01	0.60
Switched	0.02	0.01	0.28	0.03	0.07	0.66	-0.01	0.03	0.88	0.07	0.06	0.19	-0.04	0.04	0.35	-0.01	0.03	0.78	-0.03	0.02	0.03
No Established Use	-0.21	0.02	0.00	-0.20	0.07	0.00	-0.11	0.04	0.01	-0.05	0.02	0.03	-0.22	0.05	0.00	-0.42	0.08	0.00	-0.19	0.03	0.00

Note: Includes tobacco users with established use at two or more waves of assessment. Measures of TD were rescaled during model estimation by dividing by 100. Survey weighted estimates (b) can be multiplied by 100 to recapture original metric of 0-100. se = standard error. ‘-’ indicates the reference group. For example, W1 Cigarette + E-Cigarette users who reported No Established Use at W3 on average were 42 points lower (W3 Use Status<sub>No established Use</sub> = -0.42) on W3 TD than W1 Cigarette + E-Cigarette users who Added a product.

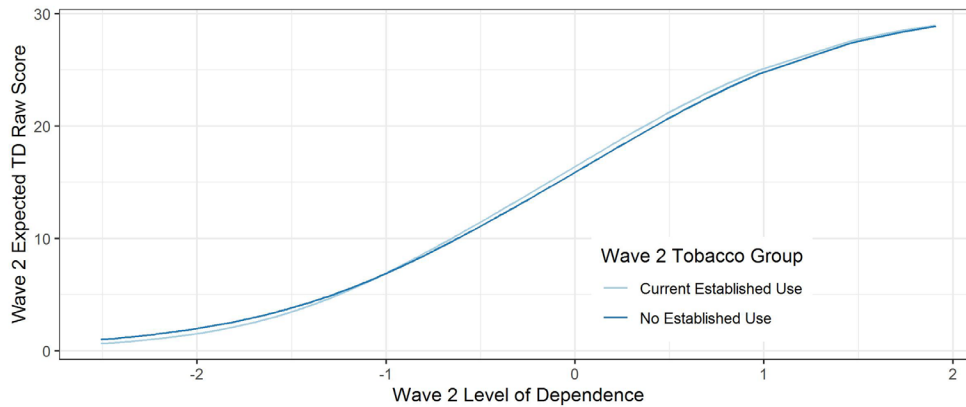
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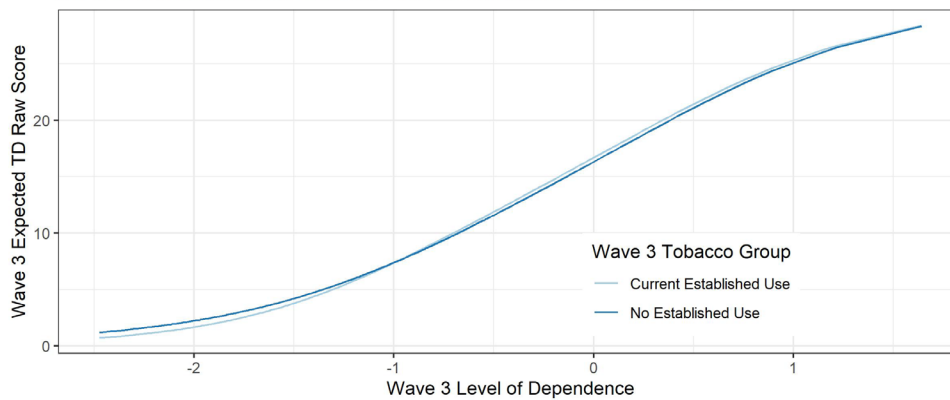
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Differential Test Functioning:  
 Wave 1 Tobacco User Groups Past-Year users with  
 No Current Established Use and Current Established Use at Wave 2



1

Differential Test Functioning:  
 Wave 1 Tobacco User Groups Past-Year users with  
 No Current Established Use and Current Established Use at Wave 3



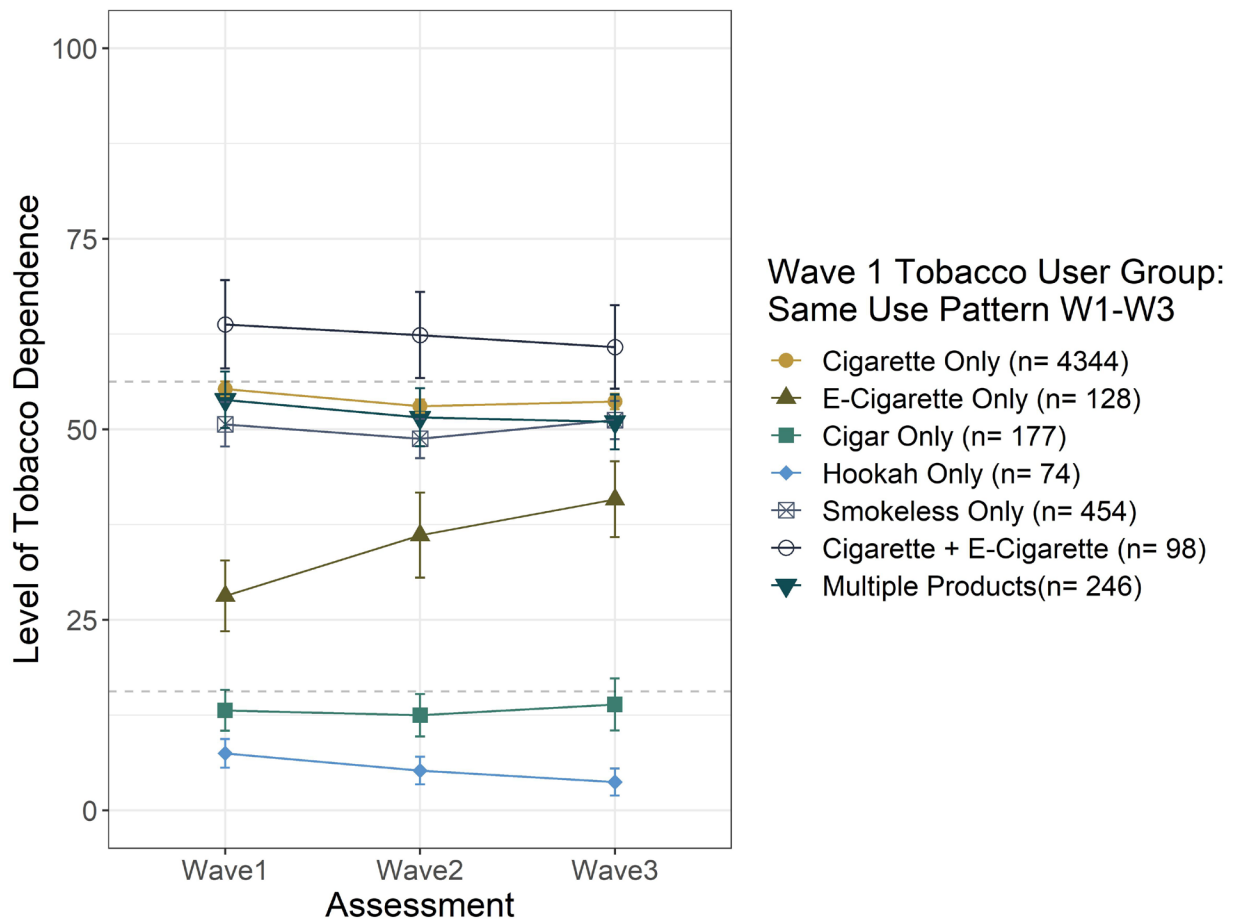
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3 **Supplement Figure 1.**

4 We used methods based on item response theory to assess the comparability of Tobacco Dependence  
 5 (TD) scores when assessed among past year users who reported No Current Established Use at follow-up  
 6 waves. We examined all W1 Tobacco User Groups with No Established Use at Wave 2 (n=395) or W3 (n  
 7 = 739) as the focal groups and examined Differential Test Functioning (DTF) using the remaining W2 (n  
 8 = 9161) and W3 (n = 8817) Current Established users as the reference group. DTF measures the  
 9 accumulation of individual item-level Differential Item Functioning across all items to quantify any bias  
 10 in test scores obtained from respondents who reported No Established Use at Wave 2 or Wave 3. We used  
 11 the differential test function from the 'mirt'<sup>28</sup> package within the R software environment with setting  
 12 zeroExtreme = TRUE to accommodate the expected presence of low levels of TD among those with No  
 13 Established Use. We observed acceptable fit of the graded response model at both W2 (RMSEA = 0.05,  
 14 95%CI = 0.049 – 0.052; Tucker Lewis Index = 0.96, Comparative Fit Index =0.96) and W3 (RMSEA =  
 15 0.051, 95%CI = 0.050 – 0.052; Tucker Lewis Index = 0.96, Comparative Fit Index =0.96). Signed DTF at  
 16 W2 (W2 sDTF = 0.02, 95%CI = 0.020, 0.022), and W3 sDTF (W3 sDTF = -0.0286, 95%CI = -0.0294 – -  
 17 0.0280) which are in units of raw TD scores suggest very small differences amounting to less than 1 point  
 18 between the No Established Use and Current Established user reports of TD. The plots above show  
 19 expected raw scores at W2 and W3 among W1 Tobacco User Groups reporting Current Established and  
 20 No Established Use at W2 and W3, respectively.

21

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### Supplement Figure 2.

27 Survey weighted average level of tobacco dependence (scaled 0-100) for Wave 1 tobacco user groups  
 28 who had established use at two or more waves of assessment and maintained established use of the same  
 29 pattern of products at Wave 1, Wave 2, and Wave 3. Dashed lines reflect lower (33<sup>rd</sup> percentile; TD  
 30 <18.75) and higher (66<sup>th</sup> percentile; TD > 56.25) levels of Wave 1 weighted terciles for tobacco  
 31 dependence for respondents who participated in all 3 surveys and had non-missing TD scores (n=13,262).  
 32 A raw sum score of item options will range from 0 to 32 with 2 as the max score for each of the 16 items.  
 33 Item options were multiplied by 50 to achieve a 0-100 scale for the total score. For example, a score of  
 34 18.75 on the 0-100 scale would be 6 as a raw sum score  $(18.75/50) * 16 = 6$ .

35