

Use Patterns Assessment Of A Closed Electronic Nicotine Delivery System Among Adults In The United States Who Smoke Cigarettes Daily: An Actual Use Study

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Use Patterns Assessment Of A Closed Electronic Nicotine Delivery System Among Adults In The United States Who Smoke Cigarettes Daily: An Actual Use Study

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Abstract

Background: Adults who smoke cigarettes may reduce their exposure to cigarette smoke by switching completely or partially to an electronic nicotine delivery system (ENDS).

Objective: This study aimed to investigate the use patterns of a novel ENDS, over 8 weeks, among U.S. adults who smoke cigarettes daily. The objectives were to assess the proportion of participants who switched completely and any changes in cigarette consumption.

Methods: This actual use study assessed the use of a novel ENDS with two variants (tobacco and menthol) among exclusive cigarette smokers (n = 353) and dual users of cigarettes/ENDS (n = 367). Use of ENDS and cigarettes was reported daily during a 1-week baseline and during an 8-week observational period, during which participants could also use the novel ENDS. Use of, complete switching to, and sensory experience of both novel ENDS variants and cigarette consumption use patterns were assessed at the end of the observational period and compared to baseline.

Results: At the end of the observational period, over 85% of both study groups used the novel ENDS and 4% switched completely. Additionally, 25% of both study groups reduced their cigarette consumption by 50% or more. A higher proportion of participants used the menthol variant, which was also more positively evaluated in terms of taste, smell, and aftertaste than the tobacco variant.

Conclusions: This study indicates that adults who smoke cigarettes daily can switch to the novel ENDS, using it exclusively or substantially reducing their cigarette consumption. These results complement the scientific evidence suggesting that ENDS are an acceptable alternative to cigarette smoking among adults who would otherwise continue to smoke.

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Original Manuscript

Use Patterns Assessment Of A Closed Electronic Nicotine Delivery System Among Adults In The United States Who Smoke Cigarettes Daily: An Actual Use Study

ABSTRACT

Background: Adults who smoke cigarettes may reduce their exposure to cigarette smoke by switching completely or partially to an electronic nicotine delivery system (ENDS). This study aimed to investigate the use patterns of a novel ENDS, over 8 weeks, among U.S. adults who smoke cigarettes daily. The objectives were to assess the proportion of participants who switched completely and any changes in cigarette consumption.

Methods: This actual use study assessed the use of a novel ENDS with two variants (tobacco and menthol) among exclusive cigarette smokers ($n = 353$) and dual users of cigarettes/ENDS ($n = 367$). Use of ENDS and cigarettes was reported daily during a 1-week baseline and during an 8-week observational period, during which participants could also use the novel ENDS. Use of, complete switching to, and sensory experience of both novel ENDS variants and cigarette consumption use patterns were assessed at the end of the observational period and compared to baseline.

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Conclusions: This study indicates that adults who smoke cigarettes daily can switch to the novel ENDS, using it exclusively or substantially reducing their cigarette consumption. These results complement the scientific evidence suggesting that ENDS are an acceptable alternative to cigarette smoking among adults who would otherwise continue to smoke.

Keywords

E-Cigarettes; Electronic Nicotine Delivery Systems; Tobacco Use; Use Patterns; Smoking Reduction; Quitting Smoking

Introduction

Nearly 36 million adults in the United States (U.S.) smoked cigarettes or other combusted tobacco products in 2021 [1]. Exposure to cigarette smoke is harmful to both individual and public health, increasing the risks of developing many serious diseases [2-5].

The adverse health impacts of smoking can be mitigated by preventing smoking initiation and promoting smoking cessation among adults who smoke cigarettes (AS). Such adverse health impacts can also be reduced among adults who would otherwise continue to smoke by transitioning them away from cigarettes toward alternative tobacco and nicotine-containing products (TNP) that present lower risks to health, such as electronic nicotine delivery systems (ENDS) [6].

Estimates from population health modeling suggest that complete switching from cigarettes to ENDS among current AS in the U.S. could prevent approximately 6.6 million tobacco-related deaths over a 10-year period [7]. Switching to ENDS is the most common method used by AS in the U.S. when attempting to quit smoking [8-10]. Findings from cohort studies and randomized controlled trials (RCT) summarized in a recent Cochrane Review demonstrate higher rates of smoking reduction and quitting among AS who use ENDS than those who use other methods, such as nicotine replacement therapies (NRT). AS who completely or partially switch to ENDS are shown to smoke significantly fewer cigarettes per day (CPD) and have increased smoking abstinence compared to NRT, behavioral support, and no intervention [11].

AS who switch completely or partially from cigarettes to ENDS or substantially reduce cigarette consumption – often defined as $\geq 50\%$ fewer CPD [12, 13] – may reduce their exposure to the harmful and potentially harmful constituents present in tobacco smoke [14, 15]. In addition, a substantial reduction in cigarette consumption is associated with making more quit attempts [16, 17], reduced cigarette dependence [18-20], and increased likelihood of future smoking cessation [16, 17, 21-26]. Thus, among adults who would otherwise continue to smoke, switching completely or partially from cigarette smoking to ENDS use may reduce the adverse health impacts of smoking, given the known benefits of smoking cessation or substantial reductions in cigarette consumption [27-32].

The aim of this actual use study was to investigate use patterns of a novel closed-system ENDS (the study product [SP]), available with tobacco and menthol e-liquid cartridges, and changes in cigarette consumption among AS in the U.S. who smoked cigarettes daily in near real-world conditions over an 8-week period. The specific objectives were to assess: 1) the proportion of participants who became exclusive users of the SP; 2) changes in cigarette consumption; and 3) the proportion of participants who became exclusive users of the SP and changes in cigarette consumption stratified by SP variant(s) used.

Methods

The study was conducted from 24 May 2022 (first enrollment) to 03 October 2022 (last completion). All participants provided informed consent before participating in the study. The study was approved by the Sterling Institutional Review Board (Atlanta, GA). Oracle Life Sciences (Austin, TX) designed, managed, and oversaw the study in cooperation with the Sponsor.

Study design

This actual use study was conducted among AS in the U.S. who smoked cigarettes daily, including exclusive cigarette smokers and dual cigarette and ENDS users (hereafter, dual users). There were three phases: (1) a 1-week baseline phase to assess cigarette and other TNP use prior to the introduction of the SP; (2) an 8-week observational phase where participants were able to consume the provided SP and other TNP ad libitum, allowing assessment of SP use and changes in

cigarette and other TNP use; and (3) a 1-week closeout phase for continued surveillance of potential adverse events. Figure 1 presents the phases of the study design. The SP was available in two variants (tobacco and menthol), with one nicotine concentration (3.5%), for *ad libitum* use under near real-world conditions. The study design was based on previously conducted actual use studies [33-35].

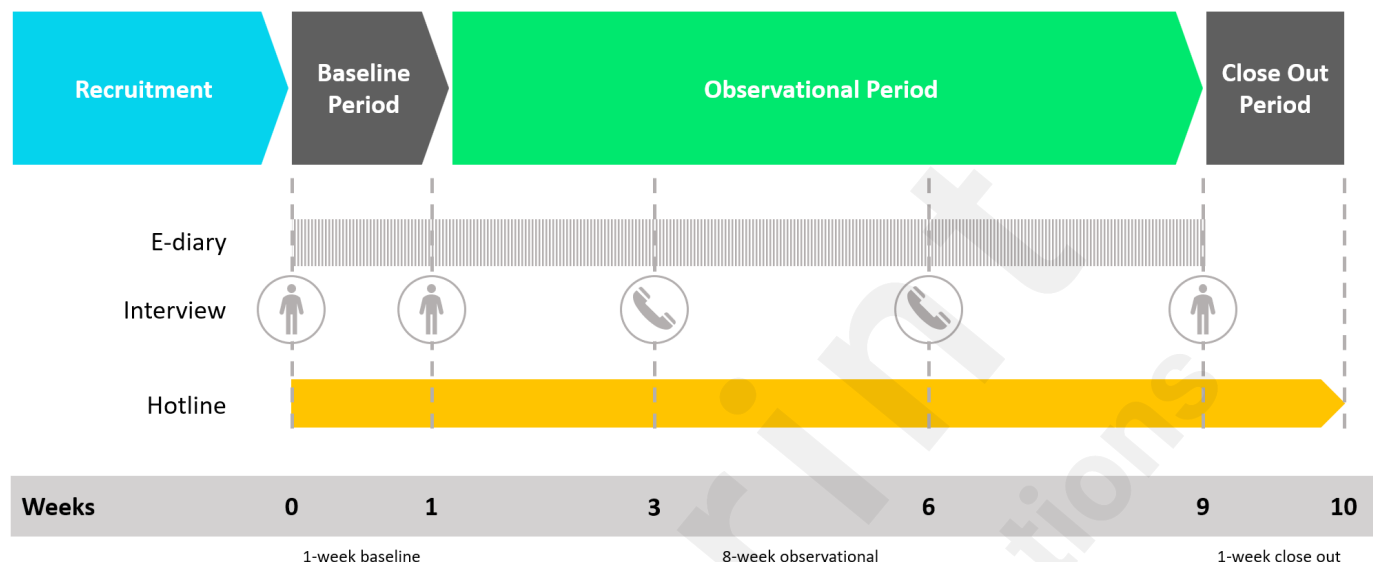


Figure 1. Study design

Participants

Participants were recruited from consumer databases of seven geographically distributed study sites in the U.S. (Atlanta, Baltimore, Miami, Nashville, Orlando, Phoenix, and St. Louis). Candidate participants were screened based on the inclusion and exclusion criteria presented in Table 1. Participants were required to be AS in the U.S. aged between 21 and 64 who had smoked 100+ cigarettes in their lifetime and currently smoked cigarettes daily.

Table 1.

Inclusion and Exclusion Criteria for Participation

Inclusion Criteria	Exclusion Criteria
Identify as male or female	No proof of age (e.g., photo identification, driver's license)
Age 21 to 64 years old	Self-reported currently being pregnant or breastfeeding
Current United States (U.S.) resident	Females of childbearing potential who were not using contraception
Able to read and understand English	Employed in journalism, market research, public relations, in the tobacco industry, or as a healthcare provider
Own a qualifying smartphone for daily electronic diary entries	Participated in a consumer or clinical study on tobacco and/or nicotine-containing products in the past 30 days
Smoked 100+ cigarettes in their lifetime ¹	Initiated cigarette or electronic nicotine delivery system (ENDS) use in the past 30 days
Currently smoke at least one cigarette daily ¹	
No intention to quit all tobacco and/or nicotine-containing products in the next 30 days ¹	
Report a positive intention to try, use, and buy the Study Products (after reviewing product information) ²	
Consent to participate	

¹ Behaviors and intentions were assessed at the time of the screening survey.

² Responded *somewhat likely*, *very likely*, or *definitely likely* when asked likelihood to try, use, and buy the Study Products.

Both, exclusive cigarette smokers and dual users could benefit from a reduction in cigarette smoking, therefore, they were considered as separate groups in this study. Qualifying daily AS who did not use ENDS at the time of enrollment, nor had used them 100+ times in their lifetime, were assigned as exclusive cigarette smokers. Qualifying daily AS who used ENDS daily or occasionally at the time of enrollment and had used them 100+ times in their lifetime were enrolled as dual users. Participant enrollment and recruitment aimed to represent the sociodemographic characteristics of AS in the U.S. who smoked daily, with marginal distributions of sex (male: 55%; female: 45%), age (21–24: 10%; 25–44: 50%; 45–64: 40%), and race (White: 70%; non-White: 30%) based on data from the National Health Interview Survey (NHIS).

Participants could voluntarily withdraw or be removed from the study if they did not report at least four e-diary entries during the baseline period, failed to comply with study procedures, misused the SP, or became pregnant. All participants were compensated fairly for their time at the end of the observational period.

Study procedures

Study products

The SP was the P4M3 Generation 2.0 System (Philip Morris Products S.A., Neuchâtel, Switzerland) ENDS device with non-refillable, replaceable cartridges containing e-liquid (3.5% nicotine concentration). Tobacco and menthol e-liquid cartridges were available for use during the observational period. Participants received the SP at no cost from study sites during the observational period but had to pay for any other TNP they chose to use, which is an approach that has been used in previous tobacco use studies [36, 37].

Participants obtained 10 cartridges at the beginning of the observational period and could select tobacco, menthol, or both variants; they were allowed to obtain additional cartridges during the study. A maximum number of SP cartridges available to each participant and was applied based on the participant's self-reported cigarette consumption at enrollment multiplied by a factor of two.

During the observational period, participants were repeatedly informed of a reduced exposure claim¹ and given the SP with all required safety warnings, labeling, and instructions for use. The SP device and any unused cartridges had to be returned to the study sites at the end of the observational period.

Data collection

Participants self-reported their daily use of cigarettes and other TNP (during the baseline and observational periods) and the SP (during the observational period only) in an app-based e-diary. Self-reported TNP use has been shown to be reliable for understanding actual TNP use [38]. Participants were also interviewed three times during the observational period (following Week 2, Week 5, and Week 8) to evaluate the SP's sensory attributes (taste, smell, aftertaste) and ease of use. Participants could report any potential adverse events or change in pregnancy status to a study-specific hotline number.

Outcomes

Study outcomes included the following and are based on results at the end of the observational period (i.e., Week 8) versus baseline: 1) the proportion of participants who exclusively used (i.e., switched completely to) the SP; 2) the absolute change in CPD; 3) the proportion of participants who reduced CPD by 50% or more; and 4) the proportion of participants who transitioned from daily to non-daily cigarette smoking. As continued SP use is associated with appealing product characteristics, 1) ratings of liking of sensory attributes (taste, smell, and aftertaste); and 2) ease of SP use were also assessed at the end of the observational period [39]. Each of the outcomes was assessed separately for exclusive cigarette smokers and dual users and were stratified by the variant(s) of SP (only tobacco, only menthol, or both variants) used in Week 8.

Measures and definitions

All measures and definitions were based on those commonly used in national surveys on TNP use (e.g., Population Assessment of Tobacco and Health [PATH]) [40] and from similar actual use studies [33, 34]. At enrollment, participants were asked to report the following sociodemographic characteristics: age in years, sex, race, ethnicity, level of education, and annual household income.

At enrollment, current TNP use was assessed using the following categories: cigarettes, ENDS, moist snuff/chewing tobacco/snus, nicotine pouches/oral tobacco-free nicotine products, cigars/cigarillos, pipe tobacco, and hookah/waterpipe tobacco (*What is your current [insert TNP category] use behavior?* [daily user, occasional user, nonuser]). Participants also reported the following: current CPD (*On average, how many cigarettes do you currently smoke per day?* [numerical response]); flavor of cigarette (*Is the brand of cigarettes you currently buy and smoke most often a menthol cigarette?* [yes, no]); and intention to quit smoking (*Are you seriously considering quitting smoking cigarettes in the next 6 months?* [yes, no, don't know]). Dual users were asked to report the flavor of e-liquid they used most often (*What flavor of ENDS with nicotine do you currently buy and you, yourself, use most often?*). The use of cigarettes and other TNP (as one overall category) was assessed each day during the baseline and observational periods, while SP/non-SP ENDS (dual users only) were assessed each day during the observational period. Participants self-reported the total number of times they used the TNPs each day in an app-based e-diary. Daily and occasional use and number of product uses per day were determined based on the number of entries for these products and were averaged across the specific week of the observational period. Participants also reported the SP variant(s) they used daily. *Exclusive SP users* (complete switchers) were defined as participants who reported using the SP but not smoking cigarettes or using other ENDS at Week 8. *Dual SP users with cigarettes* and *dual SP users with other ENDS only* were defined as those who reported using the respective products at Week 8.

Evaluation of SP sensory attributes (taste, smell, aftertaste) and ease of use of SP were

¹ The modified risk exposure claim stated that the *SP produces significantly fewer and lower levels of harmful chemicals compared to cigarettes. Scientific studies have shown that switching completely from cigarettes to SP significantly reduces your body's exposure to harmful chemicals. Important information: the SP is not risk-free.*

assessed via interviews. Each sensory attribute was evaluated using a 7-point Likert scale ranging from 1 (*I don't like it at all*) to 7 (*I like it very much*). Ease of use of SP was assessed using a 7-point Likert scale ranging from 1 (*not easy to use at all*) to 7 (*very easy to use*).

Sample size determination

The target sample sizes for exclusive cigarette smokers and dual users (study groups) were 500 and 375, respectively. Sample size calculations were based on an expected attrition rate of 40% for exclusive cigarette smokers and 20% for dual users, yielding a sample size of 300 participants in each study group at Week 8 of the observational period. A higher attrition among exclusive cigarette smokers was expected as they are less familiar with ENDS than dual users. The target sample sizes were also expected to provide reliable estimation of the proportion of exclusive SP users at Week 8, with a minimum predefined level of precision of $\pm 5\%$ if the proportion was within the expected range of 5%–20% for each study group.

Data analysis

Descriptive summary statistics were used to describe the study outcomes. Counts and percentages were calculated for categorical variables. Means, standard deviations (SD), and 95% confidence intervals (CI) were calculated for continuous and ordinal variables. Results were calculated for each outcome separately for exclusive cigarette smokers and dual users and stratified by the SP variant used at Week 8. Results for each week of the observational period were based on the number of daily e-diary entries reported for each participant. The average product use was calculated if there were at least 4 daily e-diary entries that week; otherwise, data for that week were considered missing. Data analysis was conducted using SAS 9.4 (SAS Institute; Cary, NC).

Results

Recruitment, enrollment, and participation

There were 10,493 candidate participants initially screened for eligibility, with 909 qualifying and able to attend a study site for rescreening. Of the 909 rescreened qualifying participants, 821 were enrolled in the study. There were 80 participants who discontinued or withdrew during the observational period, and 21 were excluded from the final analyses. Thus, 720 participants who completed the observational period and fulfilled the analysis criteria were included in the final analytical sample (353 exclusive cigarette smokers, 367 dual users). Figure 2 details the recruitment and enrollment.

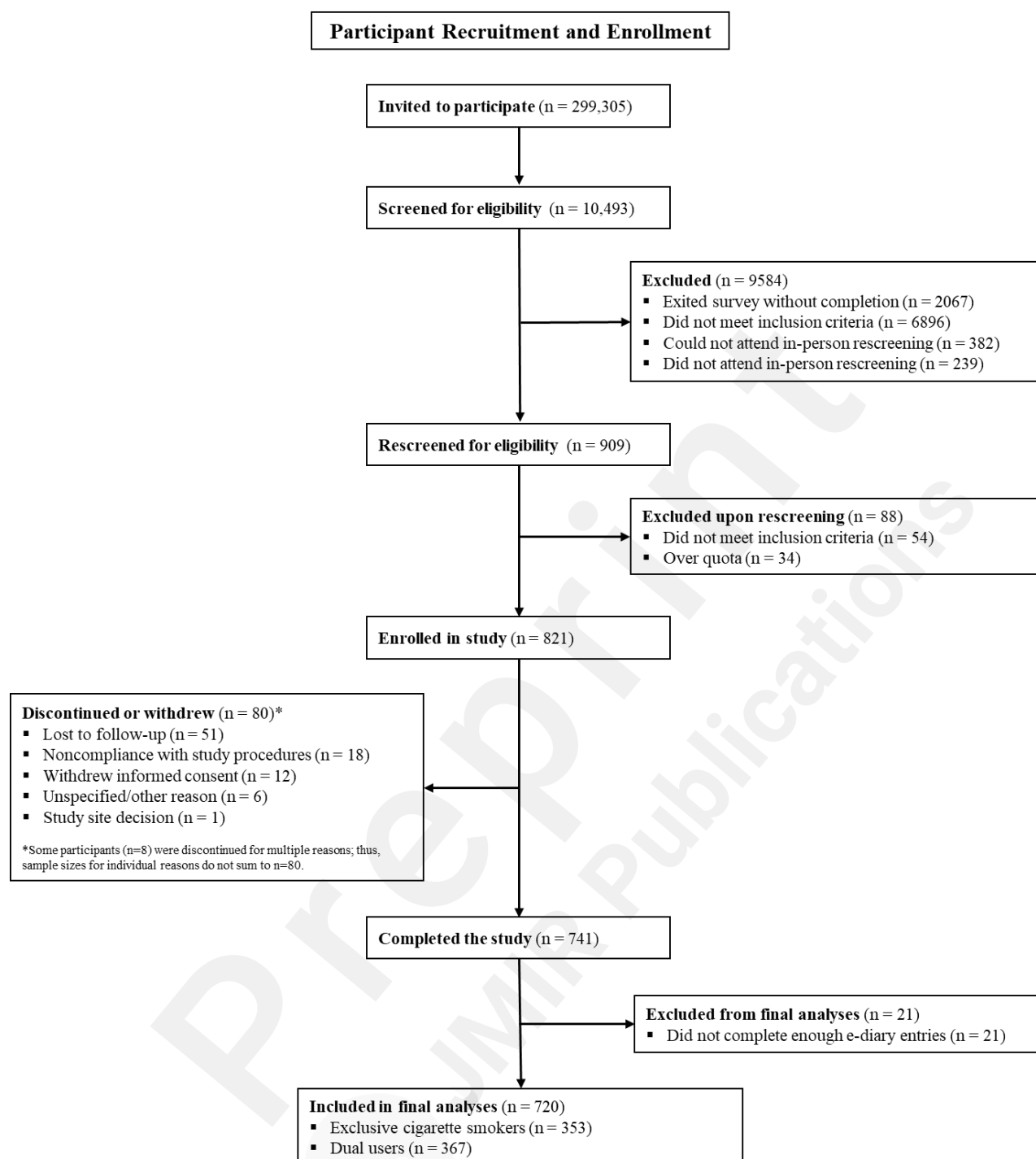


Figure 2. Participant recruitment and enrollment

Sociodemographic Characteristics of the Study Participants

Exclusive cigarette smokers were slightly older than dual users (mean ages: 47.0 versus 44.3 years) and contained fewer participants aged 21 – 34 years old (12.7% versus 17.2%) and males (males: 35.7% versus 49.3%). Results for other sociodemographic characteristics are presented in Table 2.

Table 2.

Sociodemographic Characteristics of the Study Participants

	Exclusive Cigarette Smokers n = 353	Dual Users n = 367
Sociodemographic Characteristics		
Age, mean (SD)	47.0 (10.4)	44.3 (9.6)
Age category, n (%)		
21–24 years	6 (1.7%)	5 (1.4%)
25–34 years	39 (11.0%)	58 (15.8%)
35–44 years	100 (28.3%)	122 (33.2%)
45–64 years	208 (58.9%)	182 (49.6%)
Sex, n (%)		
Male	126 (35.7%)	181 (49.3%)
Female	227 (64.3%)	186 (50.7%)
Ethnicity, n (%)		
Hispanic or Latino	54 (15.3%)	37 (10.1%)
Not Hispanic or Latino	299 (84.7%)	330 (89.9%)
Prefer not to answer	0 (0.0%)	0 (0.0%)
Race, n (%)		
White	226 (64.0%)	228 (62.1%)
Black	107 (30.3%)	111 (30.2%)
Another or multiple races	20 (5.7%)	28 (7.6%)
Prefer not to answer	0 (0.0%)	0 (0.0%)
Level of education, n (%) ¹		
Less than college graduate	242 (68.6%)	197 (53.7%)
College graduate or higher	111 (31.4%)	170 (46.3%)
Prefer not to answer	0 (0.0%)	0 (0.0%)
Annual household income, n (%) ²		
Less than \$75,000	217 (61.5%)	205 (55.9%)
\$75,000 or higher	135 (38.2%)	159 (43.3%)
Prefer not to answer	0 (0.0%)	2 (0.5%)
Don't know	1 (0.3%)	1 (0.3%)

Abbreviations: SD = Standard deviation.

¹ Level of education was collapsed based on the following response options: *Less than college graduate* [less than high school; some high school or general education diploma; high school graduate; some college]; *College graduate or higher* [college graduate; advanced degree]; *Prefer not to answer*.

² Annual household income was collapsed based on the following response options: *Less than \$75,000* [less than \$10,000; \$10,000 to \$29,999; \$30,000 to \$44,999; \$45,000 to \$59,999; \$60,000 to \$74,999]; *\$75,000 or higher* [\$75,000 to \$99,999; \$100,000 to \$149,999; \$150,000 or higher]; *Prefer not to answer*; *Don't know*.

Tobacco and nicotine product use at enrollment

Exclusive cigarette smokers and dual users smoked, on average, 13.3 and 12.1 CPD at enrollment, respectively. Nearly equal proportions reported they smoked menthol cigarettes (exclusive cigarette smokers: 55.8%; dual users: 54.8%). A higher proportion of exclusive cigarette smokers reported they planned to quit smoking in the next 6 months than dual users (planned quit attempt: 15.3% versus 9.3%) (Table).

Among dual users, there was nearly equal proportions who were daily (47.1%) or occasional (52.9%) ENDS users. Dual users reported using most often menthol (39.8%) and non-tobacco/nonmenthol (35.7%) ENDS variants. Information about other TNP used at enrollment can be found in Table .

Table 3.**Tobacco and Nicotine Product Use at Enrollment**

	Exclusive Cigarette Smokers n = 353	Dual Users n = 367
Characteristics of Cigarette Smoking at Enrollment		
Pattern of cigarette smoking, n (%)		
Daily smoker	353 (100.0%)	367 (100.0%)
Frequency of cigarette smoking, mean (SD)		
CPD	13.3 (7.3)	12.1 (7.2)
Type of cigarettes smoked, n (%)		
Menthol	197 (55.8%)	201 (54.8%)
Nonmenthol	156 (44.2%)	166 (45.2%)
Planned quit attempt in the next 6 months, n (%)		
Yes	54 (15.3%)	34 (9.3%)
No	261 (73.9%)	328 (89.4%)
Don't know	38 (10.8%)	5 (1.4%)
Characteristics of Other TNP Use at Enrollment		
Patterns of ENDS use, n (%)¹		
Daily user	0 (0.0%)	173 (47.1%)
Occasional user	55 (15.6%)	194 (52.9%)
Nonuser	298 (84.4%)	0 (0.0%)
Flavor of ENDS used most often, n (%)²		
Tobacco	-----	86 (23.4%)
Menthol	-----	146 (39.8%)
Non-tobacco/nonmenthol ³	-----	131 (35.7%)
Some other flavor	-----	4 (1.1%)
Don't know	-----	0 (0.0%)
Patterns of other TNP use, n (%)		
Moist snuff, chewing tobacco, or snus		
Daily user	1 (0.3%)	13 (3.5%)
Occasional user	16 (4.5%)	72 (19.6%)
Nonuser	336 (95.2%)	282 (76.8%)
Nicotine pouches		
Daily user	1 (0.3%)	11 (3.0%)
Occasional user	20 (5.7%)	84 (22.9%)
Nonuser	332 (94.1%)	272 (74.1%)
Cigars or cigarillos		
Daily user	23 (6.5%)	49 (13.4%)
Occasional user	118 (33.4%)	171 (46.6%)
Nonuser	212 (60.1%)	147 (40.1%)
Pipe tobacco		
Daily user	0 (0.0%)	1 (0.3%)
Occasional user	16 (4.5%)	47 (12.8%)
Nonuser	337 (95.5%)	319 (86.9%)
Hookah or waterpipe tobacco		
Daily user	0 (0.0%)	10 (2.7%)
Occasional user	87 (24.6%)	153 (41.7%)
Nonuser	266 (75.4%)	204 (55.6%)

Abbreviations: AS = adults who smoke cigarettes; CPD = cigarettes per day; ENDS = electronic nicotine delivery systems; SD = standard deviation; TNP = tobacco and nicotine-containing products

¹ AS who did not currently use ENDS daily nor had used them 100+ times in their lifetime were enrolled in the exclusive cigarette study group, whereas AS who currently used ENDS (daily or occasionally) and had used them 100+ times in their lifetime were enrolled in the dual study group.

² Exclusive cigarette smokers who neither currently used ENDS nor had used them 100+ times in their lifetime were not asked the flavor of ENDS they used most often.

³ Non-tobacco/nonmenthol ENDS flavor use included the following response options: fruit, chocolate, alcoholic/non-alcoholic drink, clove/spice, candy/desserts.

Study product use and assessment at Week 8

E-diary compliance was high, with 96% of participants in both study groups making four or more entries each week of the observational period.

At the end of the observational period (Week 8), 86.2% of exclusive cigarette smokers and 92.1% of dual users used the SP. Dual users reported using the SP more often than exclusive cigarette smokers (mean: 7.3 times per day versus 5.0 times per day). At Week 8, 4.0% of exclusive cigarette smokers and 4.1% of dual users having switched completely to the SP.

More participants in both groups used only the menthol variant (exclusive cigarette smokers: 54.6%; dual users: 49.4%) compared to those who used only the tobacco variant (exclusive cigarette smokers: 33.2%; dual users: 33.1%) and compared to those who used both variants (exclusive cigarette smokers: 12.2%; dual users: 17.5%).

The SP was liked by participants in both study groups, with mean ratings for liking the sensory attributes ranging between 4.6 and 6.2 on a 7-point Likert scale. Notably, they liked the smell, taste, and aftertaste of the menthol variant on average more than the tobacco variant. Participants evaluated the SP as easy to use (mean: 6.4 on a 7-point Likert scale) (Table 4).

Six adverse events were reported over the course of the study. None were related to the use of the SP.

Table 4.**Study Product Use and Assessment at Week 8**

	End of Observational Period (Week 8)	
	Exclusive Cigarette Smokers n = 353	Dual Users n = 367
SP Use at Week 8		
Patterns of SP use, n (%)¹		
Used SP (any SP use)	304 (86.2%)	338 (92.1%)
Exclusive use: SP (switched completely to SP)	14 (4.0%)	15 (4.1%)
Exclusive use: SP + other ENDS (switched completely to ENDS)	2 (0.6%)	4 (1.1%)
Dual use: SP and cigarettes	273 (77.3%)	218 (59.4%)
Dual use: SP+ other ENDS and cigarettes	15 (4.2%)	101 (27.5%)
Did not use SP (SP nonusers)	49 (13.8%)	29 (7.9%)
Frequency of SP use, mean (SD) [95% CI]²		
SP use, occasions per day	5.0 (8.2) [4.1, 5.9]	7.3 (12.3) [6.0, 8.5]
Patterns of SP use by variant used, n (%)		
Variant used overall (n = 304/n = 338)		
Tobacco	101 (33.2%)	112 (33.1%)
Menthol	166 (54.6%)	167 (49.4%)
Both	37 (12.2%)	59 (17.5%)
Variant used by exclusive SP users (n = 14/n = 15) ³		
Tobacco	5 (5.0%)	4 (3.6%)
Menthol	8 (4.8%)	8 (4.8%)
Both	1 (2.7%)	3 (5.1%)
SP variant(s) used by type of cigarettes smoked at enrollment, n (%)⁴		
Menthol cigarette smokers (n = 174/n = 187)		
Tobacco	12 (6.9%)	16 (8.6%)
Menthol	140 (80.5%)	134 (71.7%)
Both	22 (12.6%)	37 (19.8%)
Nonmenthol cigarette smokers (n = 130/n = 151)		
Tobacco	89 (68.5%)	96 (63.6%)
Menthol	26 (20.0%)	33 (21.9%)
Both	15 (11.5%)	22 (14.6%)
Assessment of SP Used at Final Follow-Up Interview		
Liking of sensory attributes, mean (SD) [95% CI]⁵		
Taste		
Tobacco (n = 101/n = 112)	4.8 (1.9) [4.5, 5.2]	4.6 (1.8) [4.3, 5.0]
Menthol (n = 166/n = 167)	5.4 (1.5) [5.2, 5.6]	5.3 (1.5) [5.1, 5.5]
Both (n = 37/n = 59)	5.2 (1.4) [4.7, 5.7]	5.6 (1.3) [5.3, 6.0]
Smell		
Tobacco (n = 100/n = 112)	5.9 (1.4) [5.6, 6.1]	5.5 (1.7) [5.2, 5.9]
Menthol (n = 162/n = 163)	6.2 (1.3) [6.0, 6.4]	5.9 (1.4) [5.7, 6.2]
Both (n = 37/n = 59)	5.9 (1.4) [5.5, 6.4]	6.2 (1.2) [5.9, 6.5]
Aftertaste		
Tobacco (n = 100/n = 112)	4.8 (1.9) [4.4, 5.2]	4.6 (1.9) [4.2, 4.9]
Menthol (n = 165/n = 165)	5.3 (1.7) [5.0, 5.6]	5.2 (1.7) [4.9, 5.4]
Both (n = 37/n = 58)	5.2 (1.5)	5.4 (1.6)

	[4.8, 5.7]	[4.9, 5.8]
Ease of use, mean (SD) [95% CI]⁶		
Ease of use	6.4 (1.2)	6.4 (1.1)
	[6.3, 6.5]	[6.3, 6.6]

Abbreviations: 95% CI = 95% confidence interval; ENDS = electronic nicotine delivery systems; SD = standard deviation; SP = study products.

¹ Pattern of SP use definitions are based on use at Week 8. Exclusive SP users were defined as exclusive cigarette smokers and/or dual users of cigarettes and other non-SP ENDS who switched completely to the SP at Week 8 (i.e., did not use cigarettes or other non-SP ENDS). Dual SP users were defined as participants who used the SP and cigarettes and/or other non-SP ENDS. SP nonusers were defined as participants who did not report using the SP.

² Calculated for participants who used the SP at Week 8.

³ Exclusive SP users stratified by using only tobacco, only menthol, or using both variants at Week 8.

⁴ SP nonusers are not included in these analyses.

⁵ Liking of each sensory attribute was assessed using a 7-point Likert scale ranging from 1 (*I don't like it at all*) to 7 (*I like it very much*); participants could also respond *don't know* (not shown) among users of the respective SP variant(s) at Week 8.

⁶ Ease of use was assessed using a 7-point Likert scale ranging from 1 (*Not easy to use at all*) to 7 (*Very easy to use*); participants could also respond *don't know* (not shown).

Changes in cigarette consumption at Week 8

Participants in both study groups reduced their daily cigarette consumption from baseline to Week 8 by −3.1 CPD among exclusive cigarette smokers and by −2.5 CPD among dual users. About one-quarter of exclusive cigarette smokers (25.6%) and dual users (28.1%) reduced CPD by 50% or more (Table 5).

Compared to baseline, more participants in both study groups did not smoke daily at Week 8 (exclusive cigarette smokers: 1.7% to 13.9%; dual users: 8.2% to 21.0%).

Table 5.
Changes in Cigarette Smoking from Baseline to Week 8

	Exclusive Cigarette Smokers		Dual Users	
	Baseline	Week 8	Baseline	Week 8
	n = 353		n = 367	
Characteristics of Cigarette Smoking at Week 8				
Frequency of cigarette smoking, mean (SD) [95% CI]¹				
Average CPD	12.4 (7.1) [11.6, 13.1]	9.3 (7.5) [8.5, 10.1]	10.7 (7.2) [10.0, 11.5]	8.3 (7.3) [7.5, 9.0]
<i>Absolute change from Baseline</i>	-----	-3.1 (4.5) [-3.5, -2.6]	-----	-2.5 (4.4) [-2.9, -2.0]
Days without cigarette smoking among non-daily smokers, mean (SD) [95% CI]²				
	n = 6	n = 64	n = 30	n = 98
Days per week	1.5 (0.8) [0.6, 2.4]	3.8 (2.4) [3.2, 4.4]	2.2 (1.5) [1.6, 2.8]	3.6 (2.3) [3.2, 4.1]
CPD reduction ≥ 50% from Baseline, n (%)				
Reduced CPD ≥ 50%	-----	91 (25.8%)	-----	103 (28.1%)
Cigarette Smoking by SP Variant Used at Week 8				
Patterns of cigarette smoking by SP variant used, n (%)²				
Tobacco (n = 101/n = 112)				
Daily smoker	101 (100.0%)	86 (85.1%)	104 (92.9%)	92 (82.1%)
Non-daily smoker	0 (0.0%)	10 (9.9%)	8 (7.1%)	15 (13.4%)
Non-smoker	-----	5 (5.0%)	-----	5 (4.5%)
Menthol (n = 166/n = 167)				
Daily smoker	163 (98.2%)	135 (81.3%)	151 (90.4%)	124 (74.3%)
Non-daily smoker	3 (1.8%)	25 (15.1%)	16 (9.6%)	35 (21.0%)
Non-smoker	-----	6 (3.6%)	-----	8 (4.8%)
Both (n = 37/n = 59)				
Daily smoker	37 (100.0%)	27 (73.0%)	56 (94.9%)	34 (57.6%)
Non-daily smoker	0 (0.0%)	9 (24.3%)	3 (5.1%)	20 (33.9%)
Non-smoker	-----	1 (2.7%)	-----	5 (8.5%)
Frequency of cigarette use (CPD) by SP variant used, mean (SD)[95% CI]¹				
Average CPD				
Tobacco (n = 101/n = 112)	13.4 (7.5) [12.0, 14.9]	10.0 (6.8) [8.7, 11.4]	12.0 (7.2) [10.7, 13.4]	9.7 (7.4) [8.3, 11.1]
<i>Absolute change from Baseline</i>	-----	-3.4 (4.7) [-4.3, -2.5]	-----	-2.3 (4.8) [-3.2, -1.4]
Menthol only (n = 166/n = 167)				
	12.1 (6.8) [11.1, 13.1]	8.7 (7.3) [7.6, 9.9]	10.4 (7.4) [9.3, 11.5]	7.7 (6.8) [6.7, 8.8]
<i>Absolute change from Baseline</i>	-----	-3.4 (4.6) [-4.1, -2.6]	-----	-2.7 (4.4) [-3.4, -2.0]
Both (n = 37/n = 59)				
	10.5 (5.8) [8.6, 12.4]	7.5 (6.9) [5.2, 9.8]	8.2 (5.2) [6.8, 9.6]	5.6 (5.5) [4.1, 7.0]
<i>Absolute change from Baseline</i>	-----	-3.0 (3.8) [-4.3, -1.8]	-----	-2.6 (3.6) [-3.5, -1.7]
CPD Reduction ≥ 50% from Baseline by SP variant used, n (%)				
Reduced CPD ≥ 50%				
Tobacco (n = 101/n = 112)	-----	18 (17.8%)	-----	24 (21.4%)
Menthol (n = 166/n = 167)	-----	52 (31.3%)	-----	48 (28.7%)
Both (n = 37/n = 39)	-----	11 (29.7%)	-----	23 (39.0%)
Patterns of cigarette smoking, n (%) ³				
Daily smoker	347 (98.3%)	289 (81.9%)	337 (91.8%)	269 (73.3%)

Non-daily smoker	6 (1.7%)	49 (13.9%)	30 (8.2%)	77 (21.0%)
Non-smoker	-----	15 (4.2%)	-----	21 (5.7%)

Abbreviations: 95% CI = 95% confidence interval; CPD = cigarettes per day; SD = standard deviation; SP = study products.

¹ CPD calculated only among participants who smoked cigarettes at Week 8.

² Results for daily and non-daily smoking when stratified by SP variant(s) used may not equal to the results for daily and non-daily smoking overall (see Footnote 2) given some participants did not use the SP at Week 8.

³ Daily cigarette smoking was an inclusion criterion for study enrollment and all (100%) participants in both study groups reported daily cigarette smoking. Results for use pattern of cigarette smoking were based on data at baseline, during which some exclusive cigarette smokers (n=6) and dual users (n=30) did not smoke daily.

Study results by SP variant(s) used at Week 8

The majority of participants used the same SP variant at Week 8 as the cigarette variants (menthol or nonmenthol) they smoked at enrollment. However, a higher proportion of nonmenthol cigarette smokers used the menthol SP variant than menthol cigarette smokers used the tobacco SP variant (Table 4).

Among *exclusive SP users*, the proportion of those who used only the tobacco variant (5.0% and 3.6% among exclusive cigarette smokers and dual users, respectively) and those who used only the menthol variant (4.8% among each group) were similar. The proportion of *exclusive SP users* who used both variants was 2.7% among exclusive cigarette smokers and 5.1% among dual users (Table 4).

Regarding changes in cigarette smoking, the absolute changes in CPD were similar by SP variant(s) used. The proportion of exclusive cigarette smokers and dual users who reduced CPD by 50% or more was higher among those who used both variants (29.7% and 39.0%, respectively) or only the menthol variant (31.3% and 28.7%, respectively) compared to those who used only the tobacco variant (17.8% and 21.4%, respectively) (Table 5).

Also, the proportion of participants who transitioned from daily to non-daily cigarette smoking, from baseline to Week 8, increased the most among those who used both variants of SP (exclusive cigarette smokers: 0.0% to 24.3%; dual users: 5.1% to 33.9%), followed by those who used only the menthol variant (exclusive cigarette smokers: 1.8% to 15.1%; dual users: 9.6% to 21.0%), then by those who used only the tobacco variant (exclusive cigarette smokers: 0.0% to 9.9%; dual users: 7.1% to 13.4%) (Table 5).

Discussion

AS who completely switch to ENDS or reduce cigarette consumption are exposed to far lower levels of inhaled toxicants [41] and report positive changes in their health compared to AS who continue to smoke cigarettes [42]. The ability for ENDS to help smokers to switch completely away from smoking or to reduce cigarette consumption is beneficial to population health if a sufficient number of AS switch to these products [7].

This study examined the use patterns of a novel ENDS among AS with no or limited experience using ENDS (exclusive cigarette smokers) and those using other ENDS (dual users). These tobacco users are the intended users of the SP, as both could benefit from switching completely from cigarette smoking [1]. Results showed high acceptance of the SP, as 86.2% of exclusive cigarette smokers and 92.1% of dual users used the SP at the end of the observational period (Week 8). Some exclusive cigarette smokers (4.0%) and dual users (4.1%) switched completely from cigarettes to the SP and over a quarter of all participants reduced CPD by $\geq 50\%$ (25.8% of exclusive cigarette smokers and 28.1% of dual users) by Week 8. The levels of reduction at Week 8 among all participants equated to smoking about 3 fewer CPD, corresponding to over one fewer pack of cigarettes per week (20 cigarettes/pack) than at baseline.

The findings of this study need to be considered in the context of other actual use studies on ENDS. Carpenter et al. (2023) found that after 4 weeks free supply of a commercially available ENDS about 70% of AS adopted the ENDS product, with 10% (after 12 weeks: 11%) completely switching to ENDS and 33% (after 12 weeks: 30%) reducing CPD by $\geq 50\%$ [43]. In other published actual use studies conducted over 6 weeks in a pre-market setting, one with an HTP and the other with oral nicotine products, the proportions of AS who switched completely to or substantially reduced their cigarette consumption using the investigational products were similar to the present study [33-35].

This study further supports existing evidence that ENDS are an alternative to cigarettes for AS. Cross-sectional studies on tobacco use transitions among adults in the U.S. have found that exclusive current ENDS users are more likely to be former cigarette smokers and that dual users smoked fewer cigarettes after initiating ENDS [44, 45]. Similar findings have been shown in other countries [46-48]. Cohort studies on tobacco use demonstrate that AS who use ENDS experience a reduction in CPD, transition from daily to non-daily smoking, have increased attempts to and successfully quit smoking, with stronger evidence for daily versus non-daily ENDS use [49-60]. Results from a recent systematic review of RCTs provide evidence of the increased efficacy of ENDS compared to conventional methods of quitting smoking, including NRT, behavioral support, and no intervention [11]. The more frequent use of menthol e-cigarettes, as seen in this study, has also been reported in previous studies [61-63].

Nicotine concentration, device type, and sensory attributes influence ENDS liking and use [64-73]. In this study, both groups liked the taste, smell, and aftertaste of the SP, with greater average liking for the menthol variant. This finding is likely to explain the higher proportions of participants, in both groups, who used only the menthol variant and who reduced cigarette consumption by $\geq 50\%$ at Week 8. The more frequent use of the menthol variant measured in this study has also been reported in previous studies [61-63]. These results suggest that the availability of menthol ENDS variants may increase exclusive use of ENDS or help further reduce cigarette consumption.

The study design was similar to previous actual use studies [33-35]. AS were allowed to use the SP *ad libitum* in near real-world conditions, allowing participants to establish their pattern of use over an extended period (8 weeks). Participants were recruited from seven geographically diverse metropolitan areas in the U.S., and the sample approximated that of the U.S. AS population with respect to sex, age, and race. The study included exclusive cigarette smokers and dual users, therefore providing estimates for two populations who might benefit from switching completely from cigarette smoking. Upon completion of the observational period, participants in the study continued

using their products according to their individual preferences.

The study was not without limitations. Participants did not have to pay for the SP but did have to pay for their cigarettes and other TNP. This might have affected their preference for the SP over other TNP during the observational period. Participants were compensated fairly for participation, but the impact on TNP use during the study was likely limited as payment was provided after study completion. Use of SP and all other TNP was self-reported and may be subject to recall bias, though self-reported TNP use is shown to reliably measure actual TNP use [38]. The SP was available in two variants (tobacco and menthol) and at one nicotine concentration (3.5%), which might have limited its use among dual users who may be familiar with a larger variety of variants and strengths of ENDS that are available [63].



Conclusions

Results of this actual use study show that exclusive cigarette smokers and dual users found the SP acceptable, leading some of them to switching completely to the SP or substantially reducing their cigarette consumption. Both groups liked the sensory experience of the tobacco and menthol variants and found the SP easy to use. These results complement existing scientific evidence that ENDS are an acceptable alternative to cigarette smoking among AS in the United States.

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Conflicts of Interest

SR and PM are employed by Philip Morris Products S.A. and hold stock in Philip Morris International Inc. CK was employed by Oracle Life Sciences, Oracle Corporation (formerly Cerner Enviza) while this study was conceptualized and conducted. Oracle Life Sciences was contracted by Philip Morris Products S.A. to conduct the study and draft this manuscript. GK was formerly employed by ARGUS GmbH and contracted by Philip Morris Products S.A. as the biostatistician for the study and contributed to writing the manuscript.

Abbreviations

AS: Adults Who Smoke Cigarettes

CI: Confidence Interval

CPD: Cigarettes Per Day

ENDS: Electronic Nicotine Delivery System

NHIS: National Health Interview Survey

NRT: Nicotine Replacement Therapies

PATH: Population Assessment of Tobacco and Health

RCT: Randomized Controlled Trials

SD: Standard Deviation

SP: Study Product

TNP: Tobacco and Nicotine-Containing Products

U.S.: United States

Data Availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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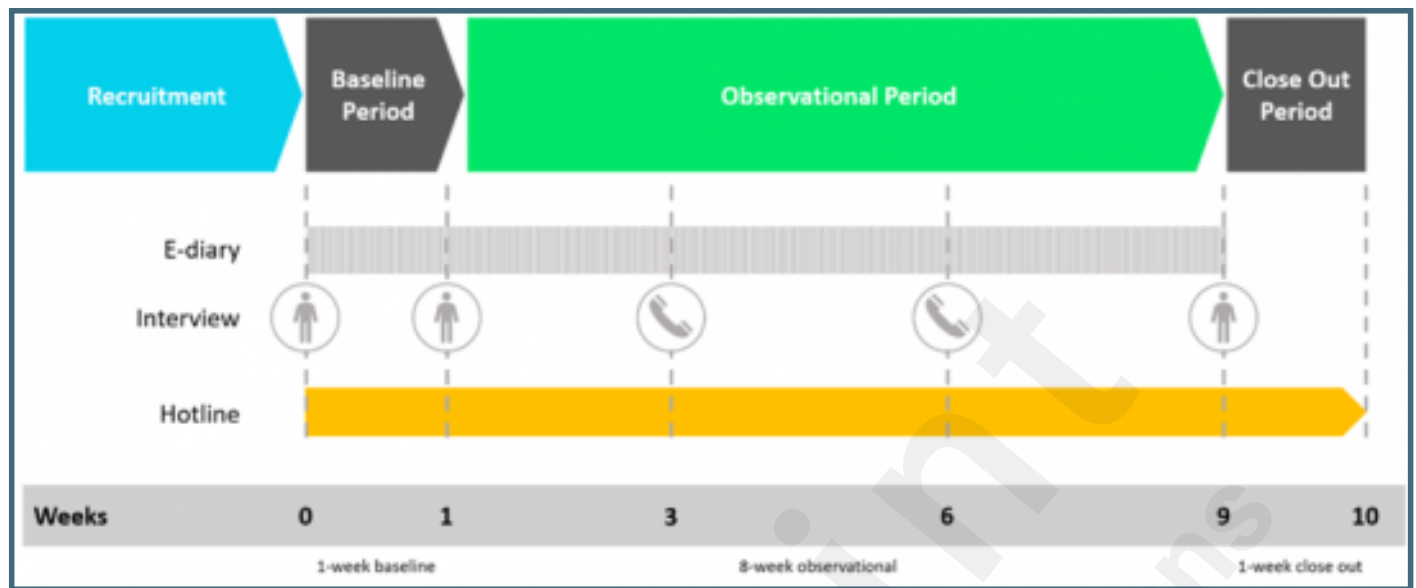
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Supplementary Files

Figures

Study design.



Participant recruitment and enrollment.

