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ABSTRACT

Background

Moist smokeless tobacco (MST) products expose people who use them to harmful and potentially harmful constituents—including FDA-classified carcinogens. Tobacco-free oral nicotine pouches substantially reduce or eliminate toxicant exposure compared to MST and cigarettes, offering a potentially lower-risk alternative for adults who use these products. We evaluated whether on! Plus™ nicotine pouches could reduce or replace MST and cigarettes among adults who use these products.

Methods

Adults aged 21–64 who reported MST use with or without cigarette smoking and were not planning to quit participated in this six-week actual use study (Dual Use Participants or MST Use Participants). All received free choice of research products—on! Plus™ nicotine pouch products—in mint, wintergreen, or tobacco flavors across three nicotine levels (6 mg, 9 mg, 12 mg) for ad libitum use. Daily tobacco and research product use were self-reported via smartphone application. Switching was defined on a seven-day point prevalence basis in Week 6. Descriptive statistics characterized switching behavior and changes in tobacco use among all enrolled and participants who completed the study.

Results

Overall, 333 MST Use Participants (54.4% of enrolled [n=612]; 72.2% of study-completing participants [n=461]) and 328 Dual Use Participants (54.0% of enrolled [n=607]; 71.9% of study-completing participants [n=456]) switched from MST to research products in Week 6. Among Dual Use Participants, 171 (28.2% of enrolled; 37.5% of study-completing participants) switched from cigarettes, and 156 (25.7% of enrolled; 34.2% of study-completing participants) switched from both MST and cigarettes. Most who switched used mint or wintergreen flavors and a single nicotine level, 6 mg. Among participants who did not completely switch, many reduced MST or cigarette use by ≥50%. Week 6 nicotine level use was similar across participants—most used 6 mg (36.8-40.7%), similar proportions used 9 or 12 mg (21.7-25.4%) and few used multiple levels (0.7-5.8%).

Conclusions

on! Plus™ nicotine pouches facilitated complete or partial switching from MST and/or cigarettes among adults not planning to quit. Availability of preferred flavors and multiple nicotine levels supported adoption and use, highlighting nicotine pouches as a potential harm reduction alternative for adults who use MST products or cigarettes.

BACKGROUND

Tobacco products span a continuum of harm, with combustible products posing the greatest health risks and smoke-free products with relatively lower risks (1-3). Among oral smoke-free products, risk levels likely vary based on manufacturing processes and whether tobacco leaf is present (1, 4). Moist smokeless tobacco (MST) products, such as moist snuff, contain harmful and potentially harmful constituents (HPHC)—including some classified as carcinogens by the United States (US) Food and Drug Administration (FDA)—though generally at substantially lower levels than combustible cigarette smoke (4, 5). Despite these risks, MST remains the most commonly used oral smokeless tobacco product in the US, accounting for 90% of the market (6). Moreover, over a third of adults who use MST also smoke cigarettes (7). While complete cessation is the most effective way to reduce tobacco-related harm, over 7 million US adults ages 21 or older reported using smokeless tobacco products within the past 30 days in 2023, 2.1 million of whom also reported cigarette use (7). For adults who use MST products—exclusively or dual use with combustible cigarettes—and are not planning to quit, switching entirely to tobacco-free oral nicotine products with low or undetectable HPHC levels may offer a viable harm reduction option (8).

Oral tobacco-derived nicotine pouches do not contain tobacco leaves and are not combusted. Instead, these products contain pharmaceutical-grade nicotine derived from tobacco, fillers, and flavorings. When used, they are placed between the lip and gum, then discarded after use. Accordingly, HPHC levels—including carcinogens and respiratory or cardiovascular toxicants found in tobacco—are either absent or markedly lower compared to cigarettes, snus, and MST (9-11). Oral tobacco-derived nicotine pouch products deliver nicotine at levels comparable to MST and cigarettes and have been shown to alleviate withdrawal symptoms in adults who smoke and those who use smokeless tobacco products, indicating their potential as substitutes for tobacco-containing products (12, 13). Actual use studies of oral tobacco-derived nicotine pouch products have shown that 3.1% to 27.3% of adults who smoked completely switched away from cigarettes to the nicotine pouch products by the end of the study (14-16). A recent randomized trial found that higher nicotine concentrations (6 mg vs. 3 mg) were more effective in promoting cigarette substitution (17). Additionally, Becker, McCaffrey (14) observed a 70.8% switching rate among exclusive MST users after six weeks of pouch use, suggesting that nicotine pouches may offer a promising, less harmful alternative for this subgroup of tobacco consumers.

Adults who use MST products are a diverse population of tobacco consumers with varying expectations for nicotine-containing products. Variation in pinch size and duration of use yields wide variability in nicotine exposure (13, 18-22). Biomarker data indicate that daily exclusive MST users have higher nicotine metabolite levels than daily exclusive cigarette smokers, consistent with greater systemic exposure (23). A recent randomized crossover study conducted among adults who used smokeless tobacco products found that higher nicotine content nicotine pouches (4 mg and 8 mg) delivered substantially more nicotine and more effectively reduced abstinence symptoms than 2 mg pouches, suggesting that higher-level products may better facilitate switching from smokeless tobacco (Eversole et al., 2025). Collectively, aligning product offerings with the preferences and nicotine needs of adults who use MST may facilitate switching and promote tobacco harm reduction.

The primary aim of the current six-week actual use study was to characterize switching behavior and changes in tobacco product use behavior among adults who use MST products (exclusively

or dual use with combustible cigarettes) when provided with free choice of on! Plus™ branded tobacco-derived nicotine pouch products for ad libitum use in their natural environment.

METHODS

Study Conduct

This multi-site, observational study was conducted from January 2023 to April 2023 across 28 research facilities in 14 US states (CA, CO, FL, GA, IL, MI, MO, NC, NV, NY, OH, OK, PA, VA). The Sterling Institutional Review Board (Atlanta, GA USA) reviewed and approved the study protocol and all related documents. The study protocol was not pre-registered.

Participant Recruitment and Enrollment

Adults aged 21-64 who self-reported using MST were eligible (i.e., used dip/snuff "every day" or "some days" within 30 days of screening). Individuals were further categorized into as MST Use Participants (no cigarette use in past 30 days and smoked <100 cigarettes in their lifetime;) and Dual Use Participants (smoked cigarettes "every day" or "some days" within 30 days of screening and smoked ≥100 cigarettes in their lifetime). All had to meet the lifetime MST product use threshold (≥20 uses), not plan to quit tobacco use within a month of screening and report being in generally in good health (i.e., no allergies to menthol, no periodontal disease, no gum disease or bleeding gums, no open mouth sores or ulcers, no cardiovascular disease, no diabetes, no high blood pressure, and no cancer). Exclusion criteria included inability to read, speak, or understand English, being employed by or in litigation with a tobacco company (self or close family member), pregnancy or nursing, participation in tobacco research lasting longer than two weeks in the past 12 months, or either experienced COVID-19 symptoms or exposure within 14 days of screening.

Potential participants were initially identified via third-party research suppliers' existing databases and pre-screened over the phone. Those who passed pre-screening were invited to the research facility to confirm eligibility. Soft quota targets were assigned for sex, age, race/ethnicity, education level, and region based on nationally representative data from the 2021 National Health Interview Survey (24).

Research Products

The research products were oral nicotine pouch products containing tobacco-derived nicotine, food-grade flavor ingredients, and soluble and insoluble fillers, branded as on! Plus™. Compared to the commercially available nicotine pouch products examined by Becker, McCaffrey (14), the on! Plus™ products were larger and in a moist pouch format. The on! Plus™ nicotine pouch products were available in mint, wintergreen, and tobacco flavors across three nicotine levels (6 mg, 9 mg, 12 mg), for a total of nine separate products. All products were packaged by the manufacturer in cans containing 14 pouches. At the time of study conduct, these products were not authorized for marketing by the US FDA. Since then, all flavors in the 6 mg and 9 mg nicotine levels have received marketing authorization, while the 12 mg products remain under review as of the time of writing (25). We will refer to these products collectively as the "research products"; otherwise, we will refer to specific flavors and/or nicotine levels.

Measures

Daily Tobacco Product Use

Daily tobacco product use was assessed via surveys administered through an application installed on participants' smartphones. Each day at 10:00 AM local time, participants received a notification prompting them to record their previous day's tobacco product use, including type and amount of tobacco product used (i.e., the research products, MST, cigarettes, and other tobacco products).

Procedures

The six-week study involved initial screening at the research facility, followed by two phases of ad libitum research product use in participants' natural environment. During study conduct, participants were required to attend weekly study site visits and complete at least four daily diary entries per week to be considered compliant with study procedures and remain in the study. Those who failed to attend a weekly study site visit or complete four or more daily diary entries per week were withdrawn from the study.

Screening Visit

During the initial screening visit, participants confirmed their age, provided informed consent, and completed a screening survey to confirm eligibility and gather additional information (e.g., demographics, current and past tobacco product use behaviors, etc.). Once eligibility was confirmed, participants downloaded and installed the smartphone application and received the research product for the Phase 1 Trial Period.

Phase 1: Six-Day Trial Period

The Phase 1 Trial Period lasted one week and was designed to help participants become familiar with using the research products and identify their preferred flavors and nicotine levels. Participants logged their use of the research products and other tobacco products each day via a survey on their smartphones.

At the end of the screening visit, participants received two bags of pre-portioned research products—labeled for use on Days 1-3 or Days 4-6—and detailed instructions for each day of the trial period. Participants were instructed to use the research products by placing a new pouch anywhere in their mouth (i.e., within the top or bottom lip, front or back) and to discard used nicotine pouches in the trash when finished. Instructions also indicated that there was no need to chew the nicotine pouches or spit while using them.

The bag labeled and intended for use during "Days 1-3" contained a total of twelve 6 mg nicotine pouches (four of each flavor). Each flavor was provided in its own smaller labeled bag. Participants were instructed to use up to four nicotine pouches per day and return any unused product at the end of the week using the provided bags.

The bag labeled "Days 4-6" included four nicotine pouches of each of the three flavors at three nicotine levels (6 mg, 9 mg, and 12 mg). Each flavor/nicotine level was packaged separately and labeled, for a total of nine bags. Participants were instructed to open only the bags of their two preferred flavors for Days 4-6 and return unused products.

At the end of the six-day trial period, participants returned to the study site to return unused research products and then began the next phase of the study.

Phase 2: Five-Week Extended Use Period

During the five-week Extended Use Period (Weeks 2-6), participants continued to complete the daily survey of research and tobacco product use on their smartphones. Participants returned to the study facility weekly to return unused research products and receive a new supply for the upcoming week. Participants received up to ten cans of research products each week in their choice of flavor and nicotine level; all were free to switch flavors and nicotine levels weekly. Participants were instructed to use products as much or as often as desired. At the end of Week 6, participants returned to the study facility to return any unused research products and were compensated upon completion of the study.

Study Product Outcome Definitions

We used a seven-day point prevalence measure of switching at Week 6 (26). For all participants, switching away from MST products was defined as having used ≥20 nicotine pouches during Weeks 2-6, self-reporting no MST product use in Week 6, and using the research products in Week 6. For adults who dual used MST products and combustible cigarettes, switching away from cigarettes was defined as having used ≥20 nicotine pouches during Weeks 2-6, reporting zero cigarettes smoked in Week 6, and using the research product in Week 6. Adults who dual used MST products and combustible cigarettes could also be classified as having switched away from both MST products and cigarettes if they met criteria for both.

Adverse Experience Reporting

Participants were instructed to call a toll-free phone number to report adverse experiences that occurred during the study. Additionally, study staff asked participants whether an adverse experience occurred within the past week during each research facility visit. Study staff were instructed to report any adverse experiences disclosed by participants via toll-free phone number, if not already reported by the participant. No adverse experiences were reported during the conduct of this study.

Data Preparation and Analysis

Data preparation and analyses were performed via IBM SPSS (Version 28) and SAS (Version 9.4).

Demographics (e.g., age, sex, etc.) and tobacco product use at screening are reported separately by product use categories (i.e., MST Use Participants or Dual Use Participants) via means and standard deviations or frequencies and proportions.

We used descriptive statistics to address our primary aim of characterizing switching behavior and changes in tobacco product use behavior. Results for these outcomes are described separately by product use categories via frequency distributions and proportions for categorical outcomes, and means and standard deviations for continuous outcomes. Additionally, 95% confidence intervals are provided to gauge the precision of point estimates.

For each derived tobacco product consumption value, we first computed a weekly mean using data from each participant, assuming they consumed the same amount on days when they did not complete a daily survey. To reduce potential bias due to attrition, switching behavior is reported by product use categories among all individuals enrolled into the study at Week 1 (MST Use Participants n=612; Dual Use Participants n=607) and among individuals who completed all six weeks of the study (MST Use Participants n=461; Dual Use Participants n=456).

Research product use behavior is reported overall, by flavor, and by nicotine level. We categorized Week 6 research product use by mutually exclusive combinations of flavors (Tobacco Only; Mint or Wintergreen; and Tobacco and Mint or Wintergreen) and nicotine level (6 mg, 9 mg, 12 mg, 6 mg and 9 mg, 6 mg and 12 mg, 9 mg and 12 mg, or 6 mg and 9 mg and 12 mg). Week 6 tobacco product use behavior among individuals who did not switch and continued to use the research products in Week 6 is reported by product use category based on change in MST or cigarette consumption relative to their self-reported consumption at screening: 50%-99% Reduction, 1%-49% Reduction, No Change, and Increase.

RESULTS

Participant Disposition

Among the 4905 individuals screened, 1219 were determined eligible at the screening visit and enrolled into the study (n=612 MST Use Participants; n=607 Dual Use Participants). During the six-day trial period, 30 participants (n=13 MST Use Participants; n=17 Dual Use Participants) did not use any research products and were removed from the study; additionally, three MST Use Participants withdrew due to personal reasons. During the five-week extended use period, 90 MST Use Participants and 100 Dual Use Participants were removed for non-compliance. Specifically, 55 MST Use Participants and 65 Dual Use Participants did not attend a weekly study site visit, and 35 in each study group did not complete at least 5 daily diaries in a given week. Overall, 506 MST Use Participants and 490 Dual Use Participants completed the study.

During the data validation process, data from 11 participants were removed because they failed attention check questions in the surveys. Another 66 participants reported using the research products during study site visits but did not record any use in the daily diaries, and were therefore excluded from the analyses. Data from two additional participants were removed due to invalid responding consisting of highly inconsistent, heavy usage across different combinations of tobacco products (e.g., using 80 pouches on day 39 after no use on days 1-38; using MST 60-80 times and 70-80 snus in the same day repeatedly; 50 premium cigars in one day, but no use on any others; 50 snus pouches per day on days 15-42; etc.). Analyses among all enrolled included 612 MST Use Participants and 607 Dual Use Participants. Analyses included only individuals who completed the study: 461 MST Use Participants and 456 Dual Use Participants.

Participant Demographics

Demographics by product use categories are presented in Table 1. Overall, individuals tended to be non-Hispanic, white, and male, corresponding to the proportions observed in the respective real-world populations of adults who use MST products or dual use MST products with cigarettes (27).

[INSERT TABLE 1 NEAR HERE]

Tobacco Product Use at Screening

Table 2 presents the proportions of participants in each product use category who used a given tobacco product within 30 days of screening, either every day or some days, or not at all. As per the inclusion criteria, all individuals used MST products (i.e., dip/snuff) every day or some days. All Dual Use Participants smoked cigarettes every/some days, as did 2.2% of MST Use Participants (but not within 30 days of screening, nor did they meet the criterion for established cigarette smoking of ≥100 lifetime cigarettes). Small proportions (<14%) of MST Use Participants used other tobacco products (i.e., snus, nicotine pouches, electronic nicotine delivery systems [ENDS], or cigars) every/some days at baseline. Among Dual Use Participants, just over a quarter used ENDS or cigars every/some days, 16.9% used snus, and 14.5% used white nicotine pouches.

[INSERT TABLE 2 NEAR HERE]

The mean (SD) number of times MST products were used per day was similar between MST Use Participants (5.9 [6.6]) and Dual Use Participants (5.5 [7.1]). Additionally, Dual Use Participants smoked an average of 10.5 (9.1) cigarettes per day at screening.

The majority of participants across product use categories reported using mint- or wintergreen-flavored MST products most often (63.8%), with nearly a quarter reporting using products that primarily have tobacco as a characterizing flavor (e.g., “Original”, “Natural”, “Straight”, etc.). The remaining individuals (12.8%) reported using MST products most often in other flavor categories.

Switching Behavior

MST Use Participants

Among MST Use Participants, 333 individuals completely switched from MST to the research products in Week 6—54.4% of all enrolled (n=612) and 72.2% of study-completing participants (n=461). In Week 6 among those who completely switched (n=333), 274 (82.3%) used mint or wintergreen, 35 (10.5%) used tobacco with either mint or wintergreen, and 24 (7.2%) exclusively used tobacco. Table 3 contains Week 6 nicotine level use among those who completely switched. Nearly 90% of those who switched used a single nicotine level in Week 6, with 42.9% switching to 6 mg, 24.0% switching to 9 mg, and 21.6% switching to 12 mg.

[INSERT TABLE 3 NEAR HERE]

Dual Use Participants

Among Dual Use Participants, 328 individuals completely switched from MST products to the research products in Week 6—representing 54.0% of all enrolled (n=607) and 71.9% of study-completing participants (n=456). In Week 6 among those who completely switched (n=328), 255 (77.7%) used mint or wintergreen, 43 (13.1%) used tobacco with either mint or wintergreen, and 30 (9.1%) exclusively used tobacco. As shown in Table 3, the majority of those who switched used a single nicotine level in Week 6 (38.7% used 6 mg, 22.6% used 9 mg, and 22.9% used 12 mg), and small proportions (i.e., 2.4%-6.4%) switched when using more than one nicotine level.

Within Dual Use Participants, 171 individuals (28.2% of all enrolled; 37.5% of study-completing participants) completely switched from cigarettes to the research products in Week 6 (i.e., continued using MST products). In Week 6 among those who completely switched from cigarettes (n=171), 137 (80.1%) used mint or wintergreen, 21 (12.3%) used tobacco with either mint or wintergreen, and 13 (7.6%) exclusively used tobacco-flavored research products. The majority of those who switched from cigarettes used a single nicotine level in Week 6 (81.3%; Table 3), with 38.6% using 6 mg, 23.4% using 9 mg, and 19.3% using 12 mg.

Among Dual Use Participants, 156 individuals (25.7% of all enrolled; 34.2% of study-completing participants) completely switched from both MST products and cigarettes to the research products in Week 6. In Week 6 among those who completely switched from MST products and cigarettes (n=156), 124 (79.5%) used mint or wintergreen, 19 (12.2%) used tobacco with either mint or wintergreen, and 13 (8.3%) exclusively used tobacco-flavored research products. Among these individuals, 81.4% completely switched from MST products and cigarettes when using a single nicotine level in Week 6. As shown in Table 3, over a third used 6 mg (35.9%), 25.0% used 9 mg, and 20.5% used 12 mg.

Week 6 Change in Tobacco Product Use Behavior

MST Use Participants

Table 4 displays the Week 6 categorical change in MST product use from screening among MST Use Participants who continued to use research products in Week 6 (n=452). Here, 13.1% of participants reduced MST product use from screening by 50-99% (n=59), and 6.9% reduced by 1-49% (n=31). Additionally, 1.8% had no change in their MST product usage (n=8) and 4.4% increased from screening (n=20).

As shown in Table 2, proportions of MST Use Participants using other tobacco products decreased from Baseline to Week 6 for all products measured.

[INSERT TABLE 4 NEAR HERE]

Dual Use Participants

Among Dual Use Participants who used research products in Week 6 (n=446; Table 4), 11.2% reduced MST product use by 50-99% (n=50), 4.7% reduced by 1-49% (n=21), 1.1% did not change their daily use (n=5), and 8.7% increased from screening (n=39). Further, 34.3% reduced cigarette consumption from screening by 50-99% (n=153), 15.0% reduced by 1-49% (n=67), 1.8% had no change (n=8), and 10.1% increased from screening (n=45).

Similar to the MST Use Participants, proportions of Dual Use Participants using other tobacco products decreased from Baseline to Week 6 for all products assessed (Table 2).

Extended Use Period Research Product Use Behavior

Frequency and Amount of Research Product Used

Across product use categories, participants tended to use the research products nearly every day per week. Regardless of flavor and nicotine level, the mean number of research product nicotine pouches used per day increased from Week 2 to Week 6 among both the MST Use Participants

(4.7 to 5.4) and the Dual Use Participants (5.2 to 5.9). Additional details on the frequency and amount of research product used per week, by product use category, are detailed in Table 5.

[INSERT TABLE 5 NEAR HERE]

Flavors Used

Overall, the majority of participants used mint- or wintergreen-flavored research products in Weeks 2 to 6 (≥56.2%), with ≤26.3% using the tobacco-flavored product (Figure 1). Across product use categories, participants tended to use more than one flavor per week, narrowing the number of flavors used from Week 2 to Week 6. Within the MST Use Participants, individuals used a mean (SD) of 1.6 (0.6) flavors in Week 2 and 1.4 (0.6) flavors in Week 6. Similarly, Dual Use Participants used 1.7 (0.7) flavors in Week 2 and 1.4 (0.6) flavors in Week 6. Among MST Use Participants who used the research products in Week 6 (n=456), 63.6% used mint or wintergreen, 28.5% used tobacco and mint or wintergreen, and 7.9% used tobacco. For the Dual Use Participants who used the research products in Week 6 (n=451), 57.4% used mint or wintergreen, 33.3% used tobacco and mint or wintergreen, and 9.3% used tobacco.

[INSERT FIGURE 1 NEAR HERE]

Nicotine Levels Used

Across the entire Extended Use Period, the 6 mg research products were used by the largest proportion of each product use category (66.8% of MST Use Participants; 68.9% of Dual Use Participants), followed by the 9 mg (56.0% of MST Use Participants; 64.7% of Dual Use Participants) and 12 mg products (46.2% of MST Use Participants; 51.5% of Dual Use Participants). Across product use categories, participants tended to use a single nicotine level each week. Among MST Use Participants, individuals reported using a mean (SD) of 1.3 (0.6) nicotine levels in Week 2, narrowing down to 1.1 (0.4) in Week 6. There was a similar pattern among the Dual Use Participants, who used 1.4 (0.7) nicotine levels in Week 2 and 1.2 (0.5) in Week 6.

Table 3 displays mutually exclusive nicotine level use by product use categories in Week 6 among those who used the research products. The largest proportions of each product use category exclusively used the 6 mg research products—40.7% of MST Use Participants and 36.8% of Dual Use Participants. In Week 6, small proportions of individuals within each product use category used two or more nicotine levels (i.e., ≤ 8.3%).

Duration of Use

Table 6 contains the mean duration of use (in minutes, averaged across Weeks 2-6) for each product use category, overall, by flavor, and by nicotine level. Overall, the mean duration of use was a few minutes longer among MST Use Participants than Dual Use Participants—16.6 and 13.1 minutes, respectively. Within MST Use Participants, mean duration of use ranged 16.1 to 17.5 minutes across flavors, shortest for mint and longest for tobacco. Within Dual Use Participants, the tobacco-flavored products were used for the shortest duration (12.1 minutes) and wintergreen for the longest (13.2 minutes). In both product use categories, the 6 mg nicotine level research products were used for shorter periods than the 9 mg or 12 mg products.

[INSERT TABLE 6 NEAR HERE]

DISCUSSION

This six-week actual use study evaluated switching behavior and changes in tobacco use among adults who used MST, either exclusively or in dual use with cigarettes, when provided with on! Plus™ nicotine pouch products for ad libitum use in their natural environment. To our knowledge, this is the first actual use study of moist nicotine pouch products in higher nicotine levels designed to appeal to adults who use MST. Notably, the majority of participants stopped using MST and transitioned to using the research products despite reporting no interest in quitting at enrollment. Among individuals who were still using MST during the last week of the study, the majority had reduced MST consumption by ≥50%. Among individuals who used both MST and smoked cigarettes at enrollment, more than a quarter stopped smoking by the end of the study; among those who continued smoking, the majority reduced cigarette consumption by ≥50%. These findings suggest that the research products may function as a complete or partial substitution of MST and/or cigarette use, highlighting their potential role in tobacco harm reduction.

Regarding the choice of research product varieties, by Week 6 participants predominantly used mint- or wintergreen-flavored pouches, most commonly at the 6 mg nicotine level, with smaller proportions using 9 mg or 12 mg products. Flavor and nicotine level preferences among individuals who switched were similar to preferences observed in participants overall.

The levels of switching in the current study are consistent with those previously reported in earlier actual use studies of nicotine pouch products conducted among adults who used smokeless tobacco products and combustible cigarettes. Becker, McCaffrey (14) reported that 71% of adults who used smokeless tobacco and 78% of adults who dual used smokeless tobacco products and cigarettes switched to nicotine pouch products, consistent with the 72.2% and 71.9% observed among the study-completing participants in the current study. Compared to the nicotine pouch products evaluated by Becker et al. (2023), the on! Plus™ products in this study were offered in higher nicotine levels (i.e., 6-12 mg vs 2-8 mg), in flavors commonly preferred by adults who use MST products (i.e., tobacco, mint, wintergreen; Delnevo et al., 2021), and in a moist, larger-pouch format designed with adults who use MST products in mind. Therefore, these results extend earlier findings by demonstrating robust switching among adults who use MST products when offered free choice of nicotine pouch products in a format designed to align with their preferences. Taken together, the on! Plus™ nicotine pouch products may serve as an adequate tobacco harm reduction option for adults who use MST products—exclusively or with cigarettes—and are not planning to stop consuming nicotine products.

Among those who did not switch in Week 6, a substantial proportion of participants in each product use category reduced MST use—or, among Dual Use Participants, cigarette consumption—by ≥50%, indicating that some individuals may require a longer transition period to fully switch from their usual tobacco products. Notably, the proportions of participants using other tobacco products decreased from Baseline to Week 6, suggesting they were not supplementing MST and/or cigarettes with these other products. Gradual reduction and co-use are common during the adoption of novel smoke-free alternatives, with the duration of this transition varying across individuals (28-31). According to the US FDA Center for Tobacco Products (32), partial substitution of MST products and/or cigarettes with nicotine pouches with lower HPHC levels (as in the research products) is expected to reduce overall HPHC exposure.

Regardless of product use categories, participants used mint- or wintergreen-flavored nicotine pouch products more than the tobacco flavor. Further, use of mint or wintergreen flavors was disproportionally higher among those who switched in Week 6 than those who continued using MST product and/or cigarettes. These results demonstrate both greater reach and greater efficacy (i.e., facilitating switching) of these flavored nicotine pouch products (relative to tobacco-flavored pouches) among adults who use MST products (exclusively or dual use with cigarettes). The impact of an intervention can be operationalized as the product of reach by efficacy (33), translating to a greater potential tobacco harm reduction impact for mint- and wintergreen-flavored nicotine pouch products for adults who use MST products.

By the end of the study, most participants used a single nicotine level. While the 6 mg nicotine level was exclusively used by the largest proportion of each product use category in Week 6 (i.e., 36-41%), 21-25% exclusively used 9 mg and 22-23% exclusively used 12 mg. In Week 6, the proportions of participants using each nicotine level matched the proportions who switched. These results indicate that participants were able to identify a nicotine level sufficient to meet their expectations and support complete switching. Results from a recent randomized clinical trial of 3 mg and 6 mg nicotine pouch products indicate that nicotine level is important for facilitating smoking reduction (17). The current study extends these findings by demonstrating that offering a variety of nicotine levels is important to support switching behavior among the diverse group of adults who use MST products (exclusively or dual use with cigarettes).

These findings should be interpreted in light of the study's limitations. Participants received on! Plus™ nicotine pouch products at no cost, which may have influenced product use behaviors (e.g., increased uptake, switching, or substitution of MST products or cigarettes). However, providing free research products is standard practice in actual use studies of pre-market tobacco products and is a valid method to demonstrate the potential impact of smoke-free tobacco products on switching/use behaviors in pre-market settings (34). Product use was self-reported, which may introduce bias; nonetheless, participants were neither instructed nor incentivized (other than the free research product) to switch or reduce their use of MST or cigarettes. Moreover, self-reported tobacco use has been validated (35) and is widely used in actual use studies (14, 15, 34, 36-38).

This study had several strengths that enhanced the validity and relevance of its findings. The nicotine pouch products were offered in flavors commonly available among MST products, providing participants with familiar options. Allowing participants to select their preferred flavors each week reflected real-world consumer behavior. Each product use category included a substantial number of individuals who, at enrollment, expressed no plans to quit using MST or cigarettes. Lastly, by presenting switching outcomes for all who enrolled and for those who completed the study, we provide a practical range of expected switching rates, bounded by conservative and optimistic estimates.

Conclusions

Results of this actual use study demonstrate that on! Plus™ nicotine pouch products can facilitate complete or partial switching from MST and/or cigarettes among adults not planning to quit. High levels of switching were observed among both adults who exclusively used MST and those who dual used MST and cigarettes. Across all participants, switching was supported by the use of mint and wintergreen flavors and the availability of a range of nicotine levels. These

findings underscore the potential of nicotine pouch products as a tobacco harm reduction tool for adults who use MST or cigarettes, particularly when offered in a range of flavors and nicotine levels.

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DECLARATIONS

Ethics approval and consent to participate

The Sterling Institutional Review Board (Atlanta, GA USA) reviewed and approved the study protocol and all related documents. All participants provided informed consent prior to engaging in study procedures.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors are/were employed by Altria Client Services LLC and declare that they have no additional competing interests.

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Authors' contributions

HGC and EB conceptualized the study; HGC oversaw preparation of the study protocol and questionnaire design; HGC oversaw statistical analysis plan development and data analysis; EB contributed to the interpretation of the analysis. JLK oversaw additional statistical analyses and interpretation of their results. JLK wrote the initial draft for submission and created data visualizations; BN, EB, and HGC made critical contributions and revisions to the paper; all authors agreed to the final version submitted for publication and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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TABLES

Table 1. Participant demographics by Product Use Category

	MST Use Participants (n=461)	Dual Use Participants (n=456)
Age	43.5 (11.7)	40.0 (11.8)
Sex		
Female	22 (4.77%)	36 (7.89%)
Male	439 (95.23%)	420 (92.11%)
Race/Ethnicity		
NH White	406 (88.1%)	391 (85.8%)
NH Black	31 (6.7%)	36 (7.9%)
Other	24 (5.2%)	29 (6.4%)
Education Level		
Less than College	14 (3.0%)	7 (1.5%)
Some College	191 (41.4%)	259 (56.8%)
College or Higher	256 (55.5%)	190 (41.7%)
Annual Income		
≤ $49,999	187 (40.6%)	202 (44.3%)
$50,000 to $74,999	109 (23.6%)	130 (28.5%)
$75,000 to $99,999	82 (17.8%)	58 (12.7%)
≥ $100,000	65 (14.1%)	47 (10.3%)
Did not Disclose	18 (3.9%)	19 (4.2%)

Note. NH=non-Hispanic. Values are means (standard deviation) or frequencies (proportion of column total). Proportions in columns may not add to 100% due to rounding.

Table 2. Other Tobacco Product Use at Baseline and Week 6 by Product Use Category

	MST Use Participants (n=461)		Dual Use Participants (n=456)	
	Baseline	Week 6	Baseline	Week 6
Snus				
Every/Some Days	6.9%	1.3%	16.9%	3.7%
Not at All	93.1%	98.7%	83.1%	96.3%
Nicotine Pouches (Excluding the Research Products)				
Every/Some Days	4.1%	0.9%	14.5%	2.0%
Not at All	95.9%	99.1%	85.5%	98.0%
ENDS				
Every/Some Days	10.4%	5.0%	27.0%	10.3%
Not at All	89.6%	95.0%	73.0%	89.7%
Cigars				
Every/Some Days	13.7%	1.7%	25.2%	6.4%
Not at All	86.3%	98.3%	74.8%	93.6%

Note. MST=moist smokeless tobacco; ENDS=Electronic Nicotine Delivery System. Values are proportion of column total. Week 6 values derived from daily dairies.

Table 3. Switching by Week 6 Nicotine Level Use by Product Use Category

	MST Use Participants		Dual Use Participants			
	Week 6 Use (n=452)	Switched from MST (n=333)	Week 6 Use (n=446)	Switched from MST (n=328)	Switched from Cigarettes (n=171)	Switched from MST & Cigarettes (n=156)
Nicotine Level	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
6 mg	184 (40.7%)	143 (42.9%)	164 (36.8%)	127 (38.7%)	66 (38.6%)	56 (35.9%)
9 mg	115 (25.4%)	80 (24.0%)	97 (21.7%)	74 (22.6%)	40 (23.4%)	39 (25.0%)
12 mg	101 (22.4%)	72 (21.6%)	103 (23.1%)	75 (22.9%)	33 (19.3%)	32 (20.5%)
6 mg & 9 mg	17 (3.8%)	16 (4.8%)	37 (8.3%)	21 (6.4%)	14 (8.2%)	13 (8.3%)
6 mg & 12 mg	6 (1.3%)	4 (1.2%)	10 (2.2%)	7 (2.1%)	5 (2.9%)	5 (3.2%)
9 mg & 12 mg	26 (5.8%)	16 (4.8%)	26 (5.8%)	16 (4.9%)	8 (4.7%)	7 (4.5%)
6 mg & 9 mg & 12 mg	3 (0.7%)	2 (0.6%)	9 (2.0%)	8 (2.4%)	5 (2.9%)	4 (2.6%)

Note. MST=moist smokeless tobacco; mg=milligram. Percentages represent proportions within each column.

Table 4. Categorical Change in MST and Cigarettes From Baseline to Week 6 by Product Use Category Among Participants Who Used Research Products in Week 6

	MST Use Participants (n=452)		Dual Use Participants (n=446)	
Change from Baseline Categories	n	%	n	%
50-99% Reduction in MST in Week 6	59	13.1	50	11.2
1-49% Reduction in MST in Week 6	31	6.9	21	4.7
No Change in MST in Week 6	8	1.8	5	1.1
Increase in MST in Week 6	20	4.4	39	8.7
50-99% Reduction in Cigarettes in Week 6	—	—	153	34.3
1-49% Reduction in Cigarettes in Week 6	—	—	67	15.0
No Change in Cigarettes in Week 6	—	—	8	1.8
Increase in Cigarettes in Week 6	—	—	45	10.1

Note. MST=moist smokeless tobacco. Sample sizes for each Study Group represent the number within each group who used a research product in Week 6. Within column percentages will not add to 100% as those who switched in Week 6 are not included in this table.

Table 5. Mean (SD) Research Product Use in Weeks 2-6 by Product Use Category Among Those Using Research Products in Each Week

	Week 2	Week 3	Week 4	Week 5	Week 6
MST Use Participants	n=448	n=454	n=453	n=452	n=452
Days Used Research Product	6.8 (0.8)	6.8 (0.8)	6.9 (0.6)	6.9 (0.5)	6.9 (0.5)
Research Product Used per Day on Days Used	4.7 (3.2)	5.2 (3.4)	5.3 (3.7)	5.4 (3.7)	5.4 (3.7)
Dual Use Participants	n=447	n=444	n=445	n=446	n=446
Days Used Research Product per Week	6.7 (1.0)	6.7 (0.9)	6.7 (0.9)	6.7 (0.9)	6.7 (0.9)
Research Product Used per Day on Days Used	5.2 (6.9)	5.6 (6.8)	5.8 (7.4)	5.7 (7.1)	5.9 (6.9)

Note. SD=standard deviation; MST=moist smokeless tobacco. Values are mean (SD).

Table 6. Mean (SD) Duration of Use (minutes) Across Weeks 2-6 Overall, by Flavor, and by Nicotine Level, per Product Use Category

			Flavor						Nicotine Level					
	Overall		Mint		Tobacco		Wintergreen		6 mg		9 mg		12 mg	
MST Use Participants	16.7 (13.0)	n=456 100%	16.1 (13.2)	n=379 83.1%	17.5 (13.8)	n=166 36.4%	16.9 (12.9)	n=349 76.5%	15.1 (12.1)	n=308 67.5%	17.4 (13.6)	n=258 56.6%	17.5 (14.2)	n=213 46.7%
Dual Use Participants	13.1 (10.9)	n=451 100%	13.1 (11.2)	n=379 84.0%	12.1 (10.3)	n=192 42.6%	13.2 (11.3)	n=362 80.3%	12.0 (9.9)	n=314 69.6%	12.4 (10.2)	n=295 65.4%	13.9 (12.4)	n=235 52.1%

Note. MST=moist smokes tobacco; SD=standard deviation; mg=milligram. Values are mean (SD) minutes. N's within Flavors and Nicotine Levels for each product use category are not mutually exclusive and represent the frequency (and proportion) of participants within each category who used a given product.

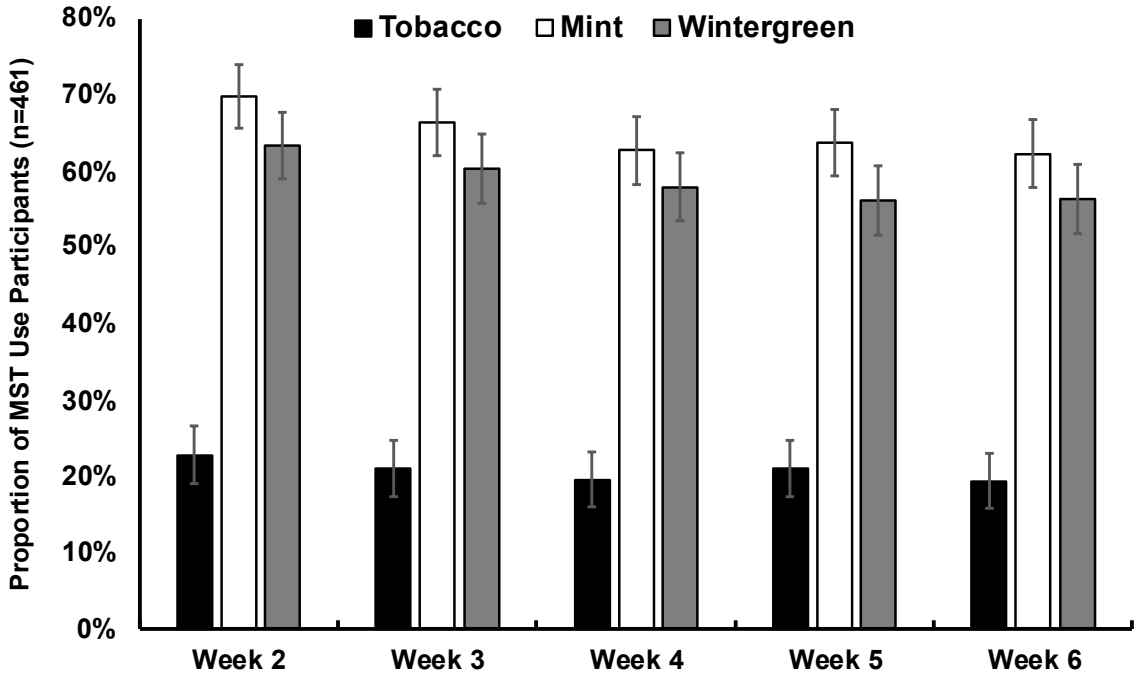
LIST OF ABBREVIATIONS

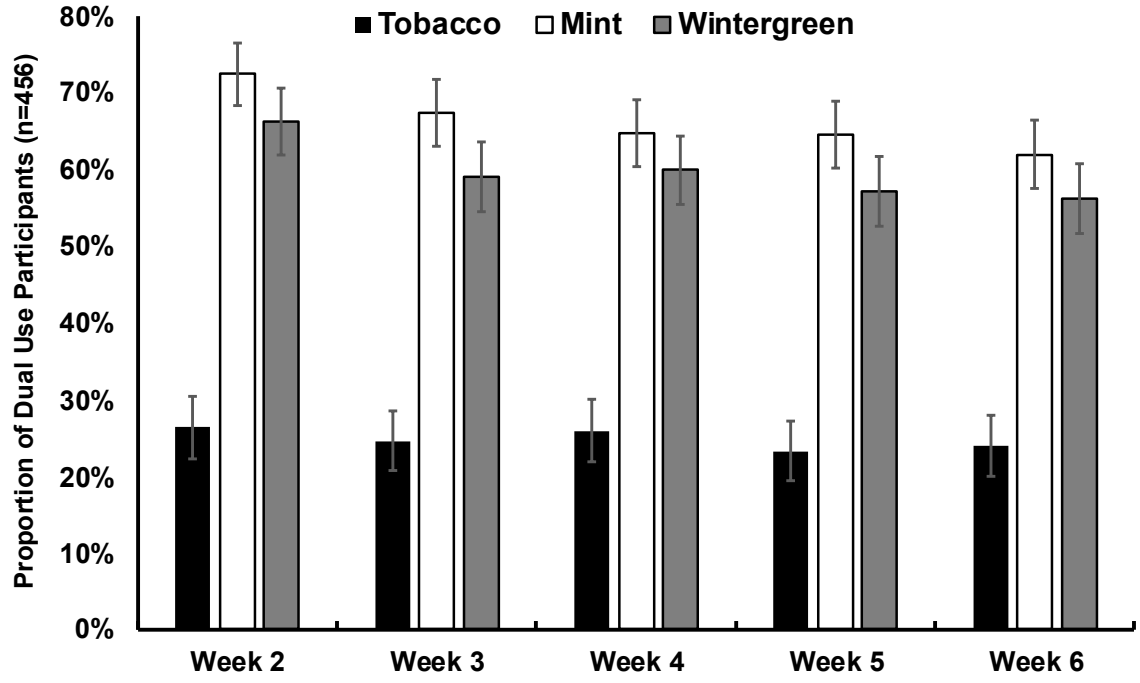
CA	California
CO	Colorado
ENDS	electronic nicotine delivery systems
FDA	Food and Drug Administration
FL	Florida
GA	Georgia
HPHC	harmful and potentially harmful constituents
IL	Illinois
mg	milligram
MI	Michigan
MO	Missouri
MST	moist smokeless tobacco
NC	North Carolina
NH	non-Hispanic
NV	Nevada
NY	New York
OH	Ohio
OK	Oklahoma
PA	Pennsylvania
SD	standard deviation
US	United States
USA	United States of America
VA	Virginia

FIGURE CAPTIONS

Figure 1. Proportion and 95% Confidence Interval of individuals using each flavor per week among the MST Use Participants (top) and Dual Use Participants (bottom).

Figure 1.


Tobacco
Mint
Wintergreen
Proportion of MST Use Participants (n=461)
80%
70%
60%
50%
40%
30%
20%
10%
0%
Week 2
Week 3
Week 4
Week 5
Week 6


Tobacco
Mint
Wintergreen
Proportion of Dual Use Participants (n=456)
80%
70%
60%
50%
40%
30%
20%
10%
0%
Week 2
Week 3
Week 4
Week 5
Week 6