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Switching and substantial reductions in cigarette consumption concurrent with use of a heated tobacco product among adults who smoke in Czechia: an actual use study

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Abstract

Background The potential for heated tobacco products (HTPs) to reduce smoking-related harm depends, in part, on how adults who smoke cigarettes use HTPs in their everyday lives, and the extent to which HTPs come to be used as a replacement for all or most of the cigarettes that a person smokes. This study assessed changes in cigarette smoking behaviour among adults who smoke when using HTPs in near-to-real world settings for six weeks.

Methods Participants were 332 adults aged 19 years and older who smoked between 5 and 30 cigarettes per day, on average, living in Prague or Brno, Czechia, who reported no intention to quit smoking within the next three months but reported a positive likelihood of using the PULZE + iD Heated Tobacco System ('the Study Product') on a regular basis following a brief trial use period. Participants were given a personal prepaid debit card to purchase packs of consumable heated tobacco sticks ('iD Sticks', the Study Sticks) in their choice of 12 commercially available flavours, directly from retailers in the community, to use as desired for six weeks. Participants recorded their daily consumption of cigarettes, Study Sticks, and other tobacco products in an electronic diary for 42 consecutive days. Data were collected between May-November 2023.

Results During Week-6 of *ad libitum* use of the Study Product, 16.0% of participants had completely switched from cigarettes to the Study Product (i.e., past 7-day use of the Study Product and zero cigarettes smoked) and 33.7% had reduced their daily cigarette consumption by 50–99% while continuing to use the Study Product. On average, weekly cigarette consumption reduced by 35.6% (1.9 fewer packs per participant) during Week-1 and 45.2% (2.4 fewer packs per participant) during Week-6, compared to the pre-study baseline week. Most Study Sticks consumed during the Observational Phase were flavoured to taste like fruit (40.1%), followed by tobacco (38.4%) and menthol/mint (21.5%). At Week-24, 63.6% continued to purchase Study Sticks with their own money and 50.9% were using the Study Product as a complete or majority replacement for cigarettes.

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Conclusions The Study Product has potential to help adults who smoke to completely switch away from cigarettes or substantially reduce cigarette consumption in the short- to medium-term in real-world settings.

Keywords Tobacco, Cigarette, Smoking, Actual use, Heated tobacco, Observational

Introduction

Tobacco smoking is a leading cause of premature death and disease, accounting for 7.69 million deaths (13.6% of all human deaths) and 200 million disability-adjusted life years (DALYs) (7.9% of all DALYs) globally in 2019 [1]. The vast majority (6.68 million; 86.9%) of all smoking-attributable deaths in 2019 were reportedly among adults who currently smoke. If current trends continue, the majority of the 300 million smoking-attributable deaths that are projected to occur globally between 2025 and 2049 will be among adults who currently smoke [2]. Most of the premature death and disease caused by smoking tobacco is attributable to the effects of inhaling combusted tobacco smoke, which contains over 7000 chemicals. Therefore, substituting combustible tobacco for products that deliver nicotine without smoke has the potential to reduce the number of premature deaths and disease cases that are caused by smoking [3, 4]. Making a range of less hazardous non-combustible tobacco and nicotine-containing products available to adults who smoke, in formulations they find satisfying and acceptable as marketplace alternatives to combustible cigarettes, may offer an additional effective means to increase cessation rates and reduce harm to the more than one billion adults who currently smoke tobacco globally [5–8].

Heated tobacco products (HTPs) are an emerging category of non-combustible tobacco products designed to replicate the behavioural rituals, sensorial experiences, and satisfaction of smoking a cigarette, but without burning tobacco or creating smoke [9]. Instead, HTPs heat specially-designed tobacco sticks in a controlled manner to temperatures below those at which tobacco combusts. Heating tobacco without burning produces an inhalable aerosol, not smoke, which contains nicotine and tobacco aromas. By avoiding combustion, the inhalable aerosol produced by HTPs typically contains fewer and substantially lower levels of harmful and potentially harmful constituents (HPHCs) compared to cigarette smoke.[9] HTPs therefore have potential to offer a harm reduction alternative to continued cigarette smoking.

Through their potential to deliver a satisfying dose of nicotine to the lung, in flavours that are liked by adult consumers, without burning tobacco or producing smoke, HTPs may appeal to some adults who smoke as a complete or partial substitute for cigarettes. Due to their relatively recent innovation and market introduction, however, real-world use of HTPs among adults who smoke and their impact on smoking behaviour over time are not well characterised. Useful information, however, comes from three actual use studies in which premarket HTPs were provided free of charge to adults who smoke for at-home use as desired. In a 2016 study 1,106 US adults who smoked cigarettes daily and had no intention to quit smoking were supplied with an early version of the IQOS heated tobacco product and choice of tobacco or menthol-flavoured consumable tobacco sticks (HeatSticks) to use ad libitum at home for 6 weeks. During Week-6, 33.8% of participants had adopted IQOS (i.e., used more than 100 HeatSticks in. the past six weeks) and 7.5% were using IQOS exclusively (i.e., complete switch from cigarettes to IQOS) [10]. Similarly, during Week-4 of a 4-week actual use study of 'Tobacco Heating System 3.0' (THS 3.0, an updated version of an IQOS device previously authorized by the US Food and Drug Administration for sale in the United States) and choice of tobacco or menthol-flavoured consumable tobacco sticks, 7.0% of adults who smoked with no intention to quit cigarettes reported having completely switched to THS 3.0, with close to half of participants having substantially reduced their daily cigarette consumption – defined as a 50% or greater reduction in daily cigarette consumption compared to pre-study levels – while continuing to use THS 3.0 [11]. A third actual use study of IQOS reported that 21.1% of all-enrolled participants had completely switched from cigarettes to IQOS during Week-6, with those who smoked menthol (versus non-menthol) cigarettes at baseline found to be significantly more likely to have switched [12].

Evidence from actual use studies of other non-combustible tobacco/nicotine products suggests rates of complete switching and cigarette reduction may be higher in contexts in which adults who smoke have access to alternative products in a larger, more diverse variety of flavour options than simply tobacco and menthol variants. For example, 1,147 US adults who smoked cigarettes and/or used smokeless tobacco (ST) with no intention to quit smoking/smokeless tobacco use were supplied with ON! nicotine pouches in choice of 7 flavours (5 nicotine strengths) to use ad libitum at home for 6 weeks following an initial 5-day trial [13]. During Week-6, 27% of participants who exclusively smoked cigarettes at baseline had completely switched to exclusive use of ON! nicotine pouches. Decreases in daily cigarette consumption were larger among those who used more nicotine pouches per day and those who used nicotine pouches in a higher number of flavour varieties. Similarly high rates of complete switching and substantial cigarette reduction over six weeks have also been observed among adults who

smoke when provided access to e-cigarettes in a larger portfolio of non-tobacco flavours [14].

This study examined how adults who smoke cigarettes use HTPs in their everyday lives, how their use of HTPs changes over time, and how cigarette smoking behaviour changes over time concurrent with use of HTPs. Through a focus on the extent to which adults who smoke use HTPs to completely switch or substantially reduce their cigarette consumption over six weeks when provided with means to purchase consumable heated tobacco sticks directly from retail outlets for use as desired, the results of this study can inform the real-world potential of HTPs to reduce smoking-related harm among adults when price is not a barrier to adoption.

Methods

Design

This was a single-arm, open-label, prospective observational cohort study—an 'actual use study'—conducted in three phases: an Enrolment Phase, a 6-week Observational Phase, and a Follow-Up Phase at 24 weeks (Fig. 1). Study enrolment was conducted at two sites, one each in the cities of Prague and Brno, Czechia. Field recruitment began on 13 April 2023 and ran through to 9 May 2023. On-site rescreening and enrolment began on 2 May 2023 and ended at the last site enrolment visit on 18 May 2023, with data collection for the intervening baseline week occurring from 3 May 2023 to 16 May 2023. Data collection for the Observational Phase ran from 16 May 2023 to 1 July 2023. Data collection for the Follow-Up Phase began on 31 October 2023 and closed on 5 November 2023. The study protocol and all study-related documents were submitted for ethical review to the Reading Independent Ethics Committee (RIEC). A favourable ethical opinion of the study was received from RIEC on 19 March 2023.

Study products

This study examined the PULZE + iD Heated Tobacco System, a product marketed by Imperial Brands PLC in several countries to adults who smoke as an alternative to cigarettes. The Study Product has two components: a handheld electronic heating device into which a specially designed consumable tobacco stick is inserted for heating. In Czechia, the electronic heating device and consumable heated tobacco sticks are commercialized under the brand names 'PULZE™' and 'iD™ Sticks', respectively. The PULZE device is intended to be exclusively used to consume iD Sticks, and vice versa, iD Sticks are intended to be exclusively used in the PULZE device. In this article, the term "Study Product" is used to refer to use of the PULZE device together with consumable iD Sticks; "Study Device" is used to refer to the PULZE heating device; and "Study Sticks" is used to refer to the consumable iD Sticks.

The PULZE device consists of a 1340 mAH rechargeable battery, a cylindrical ceramic heating rod, and a circuit board that controls the electrical components of the device, including the heating temperature and duration, encased in an aluminium shell. The consumable iD tobacco stick is a cylindrical rod that consists of four segments: (1) a mouthpiece filter; (2) a ventilated spacer; (3) a 3 mm hollow bore filter; and (4) a portion of reconstituted tobacco which is manufactured into a paper-like sheet and slit into strands. It contains raw tobacco leaf, glycerol, gum and pulp. Upon heating, the glycerol aerosolizes and mixes with the nicotine and tobacco aromas that are released from the tobacco leaf to create an inhalable aerosol. The tobacco portion of the stick is wrapped in aluminium foil to ensure the tobacco stick cannot be smoked like a conventional cigarette.

At the time of study, iD Sticks were commercially available in Czechia in 12 flavours, comprised of five tobacco flavours ('Balanced Blue'; 'Rich Bronze'; 'Velvet Copper; 'Bright Yellow'; and 'Warm Amber'); two menthol flavours ('Polar Green' and 'Capsule Polar Green'), one mint flavour ('Ice'); and four fruit flavours ('Capsule Summer Red', a watermelon flavour; 'Capsule Forest Purple', berry flavour'; 'Polar Capsule Yellow', yellow melon flavour; and 'Capsule Cosmic Blast', blueberry and orange flavours).

Participants

Participants were adults aged 19 years or older living in Prague or Brno, Czechia who currently smoked cigarettes

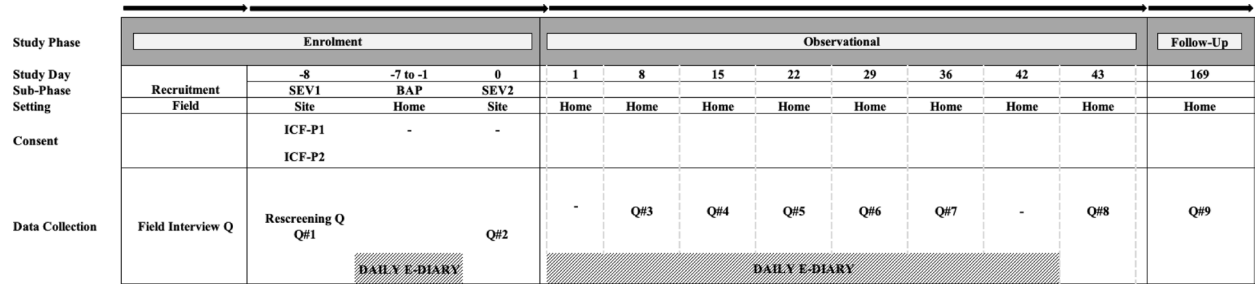

Fig. 1 Study design. Abbreviations: SEV = Site Enrolment Visit; Q = Questionnaire; ICF = Informed Consent Form; P1 = Part 1 of the study; P2 = Part 2 of the study; BAP = Baseline Week

and did not intend to quit within the next three months but expressed an interest in using the Study Product on a regular basis following a brief trial use period. A "current cigarette smoker" was defined in this study as a person who, at screening, had smoked ≥ 100 factory-made cigarettes in his/her lifetime, had smoked cigarettes on ≥ 10 of the past 30 days, and had smoked on ≥ 1 days in the past 7 days. No intention to quit smoking within the next three months was indicated by selection of response options 1–5 on the Motivation to Stop Smoking (MTSS) scale, a validated 7-level single-item instrument that measures the respondent's intention, desire, and self-efficacy to quit smoking [15]. Full inclusion/exclusion criteria are listed in the Supplementary File. The cities of Prague and Brno, Czechia were selected due to each city's relatively large population size within Czechia and to a widespread and dense retail availability of the Study Sticks throughout each city. The study sought to enrol a minimum of 308 participants, with quotas set to recruit approximately 50% of participants from Prague and Brno, respectively (i.e., 154 participants per city).

Recruitment

Study participants were selected using a three-stage, within-city, stratified design. In the first stage, the population of each city aged 18 years and older was stratified into several geographical regions called 'Primary Recruitment Units' (PRU), in which a PRU consisted of group of contiguous districts. The 22 districts of Prague were stratified into 7 PRUs and the 29 districts of Brno were stratified into 5 PRUs. The districts that were stratified into each PRU within each city, the estimated number of persons aged 18 years or older living within each PRU, and recruitment quotas set for each PRU are available in the Supplementary File (Table S1). Within each city, within-PRU quotas were set to ensure the proportion of the total participants recruited from each PRU approximately corresponded to the proportion of the city population who lived in each PRU. In the second stage, field interviewers selected residential housing unit addresses within each PRU. In the third stage, field interviewers selected adult occupants of selected households. One individual per household was eligible for recruitment.

Procedures

Enrolment phase

Individuals who satisfied eligibility criteria at the field interview were invited to attend a scheduled in-person Site Enrolment Visit (SEV-1). Once consented and confirmed as eligible at SEV-1, participants completed a web-based questionnaire that assessed demographic characteristics, dependence on cigarettes, attempts to quit smoking cigarettes, use of stop smoking products and methods as part of recent quit attempts, and historical use of other tobacco and nicotine products. Each participant was then given one pack of Study Sticks in each flavour variant and a Study Device to handle and inspect, but not turn on or use. Participants watched a 5-minute informational video about the Study Product on a laptop/tablet. This video, created by the manufacturer, described what the Study Product is, how the device and its features work, and how the Study Product differs from cigarettes. Written and spoken information about the Study Product were presented in Czech language in a manner designed to be comprehensible to potential consumers of all educational backgrounds by using minimal scientific terminology and by providing simple explanations of complex/scientific terminology, concepts, and processes. Following viewing of this video, participants rated their intentions to (i) try the Study Product at least once; and (ii) to use the Study Product on a regular basis (Response options: 1 = Definitely not; 2 = Very unlikely; 3 = Somewhat unlikely; 4 = Somewhat likely; 5 = Very likely; 6 = Definitely). Participants who reported a likelihood to try and use the Study Product on a regular basis (responses = 4 or higher for both items) were invited to give their consent to participate in a seven-week observational research study.

Consenting participants were asked to record their daily consumption of cigarettes and other tobacco and nicotine-containing products at home for one week in an electronic diary ('e-diary'). Site staff demonstrated how to record daily consumption of each product into the e-diary. During this baseline week, participants were free to smoke cigarettes and use other tobacco and nicotine products as they wished but were not given the Study Product to take home and were asked to refrain from purchasing/using the Study Product during this week. Participants who recorded the number of cigarettes smoked on all seven days of the baseline week, recorded smoking between 5–30 cigarettes per day, on average, and reported no use of the Study Product during the baseline week were invited to attend a second Site Enrolment Visit (SEV-2).

At SEV-2, participants tried using the Study Product with the Study Stick flavour variants of their choice (max. one stick per flavour). Each participant was given a charged Study Device, Study Sticks in the selected flavours, and the Study Product User Guide. Each participant was given 15 minutes to try using the Study Device to consume selected Study Sticks. Following trial of each selected Stick flavour, participants rated their liking of the flavour variant and likelihood of consuming Sticks in this flavour on a regular basis. Participants who indicated a positive likelihood of using the Study Product to consume at least one Study Product Stick flavour on a regular basis were enrolled in the 6-week Observational Phase and completed a questionnaire that assessed

tobacco product risk perceptions and reasons for interest in using the Study Product. Enrolled participants were given four items to take home from SEV-2, free of charge: (1) a Study Device; (2) one pack of Study Sticks (20 sticks) in the participant's flavour of choice; (3) a MasterCard® Prepaid Card (hereafter, the "Study Debit Card"; and (4) a Study Debit Card User Guide.

Observational phase

The Observational Phase lasted for 42 consecutive days, with each participant's 'Day-1' starting on the first full day following his/her SEV-2. For the duration of the Observational Phase, participants were free to use the Study Product, smoke cigarettes, and use any other tobacco or nicotine product if, as, and when they wished. Participants were given no guidance, instruction, or direction as to how they should or should not use the Study Product or any other tobacco product. Rather, participants decided if and when to start, continue, stop, and restart using the Study Product and any other tobacco product. Participants did not have to use the Study Product, smoke cigarettes, or use any other tobacco product if they did not want to, and participants were not required to use the Study Product or to continue or stop using any other product to remain part of the study.

Participants were given one pack of Study Sticks (20 sticks) in the flavour of their choice to take home from SEV-2 to ensure they had access to a sufficient supply of Study Sticks for the first 24 hours of the Observational Phase. During these first 24 hours, participants were encouraged to locate retail stores in their communities at which they could purchase additional packs of Study Sticks, if they so wished. If a participant wished to obtain more packs of Study Sticks for personal use at any time throughout the Observational Phase, the participant could use his/her Study Debit Card to purchase packs of Study Sticks from retailers. At the time of this study, Study Sticks were available to purchase in 12 flavour variants at a variety of convenience stores, supermarkets, tobacconists and other retail locations throughout Prague and Brno. Participants could use their Study Debit Card to purchase packs of Study Sticks in any flavour variant(s) they wished, from any retail outlet they wished. Participants did not have to continue purchasing Study Sticks with their Study Debit Card if they did not want to continue consuming them, and participants did not have to consume all the Study Sticks they had already purchased if they no longer wanted to continue consuming them. The procedures by which each participant's Study Debit Card was assigned, activated, and initially funded at SEV-2, funded weekly throughout the Observational Phase, and the procedures by which staff monitored participants' adherence to 'fair use rules' were manualised. Participants could telephone study staff between 09:00 and 17:00 Central European Time (CET), Monday to Sunday, throughout the Observational Phase to ask any questions they had about the Study Product or their Study Debit Card. Participants did not return to the site following SEV-2 except as necessary to collect a replacement Study Device or Study Debit Card in the event of a loss, breakage, or malfunction.

Beginning on Day-1, and on each day of the Observational Phase thereafter, participants were asked to record in an e-diary the number of cigarettes they had smoked, the number of Study Sticks they had consumed in each of the 12 commercially available flavour variants, and any use of a list of other tobacco and nicotine products in the past 24 hours. Participants accessed their e-diary each day by clicking or tapping a hyperlink in an email that was sent each day at 18:00 CET. Participants who did not respond to an e-diary invitation received up to two reminders by email or telephone prior to expiry of access to the day's e-diary, which occurred at 12:00 CET the following day (i.e., 18 hours after receipt of the first email invitation to complete the previous day's e-diary entry). The format of the e-diary was sufficiently simple that all participants were expected to be able to record their daily consumption of each product quickly, easily, and accurately. Each e-diary entry took around 2 minutes to complete, on average.

Participants were also invited by email to complete six web-based questionnaires at home, sent on Days-8, 15, 22, 29, 36, and 43 of the Observational Phase. Questionnaires assessed dependence, subjective effects, reasons for use, risk perceptions, and misuse in relation to the Study Product. Non-respondents to the first invitation to complete a questionnaire received two email reminders (after 8 and 24 hours), with access to each questionnaire closing 48 hours after receipt of the first invitation. Each questionnaire took 10–15 minutes to complete, on average.

At the end of the Observational Phase, participants were entitled to keep the Study Device and any Study Sticks they had purchased with their Study Debit Card, at no cost to participants. Participants who did not wish to keep these products were advised to dispose of them into waste or recycling bins as appropriate. Each participant's Study Debit Card was deactivated following expiry of access to the Day-42 e-diary.

Follow-up phase

The study concluded with administration of a web-based questionnaire at Week-24 (i.e., 18 weeks after the end of the Observational Phase). At the end of the Week-24 questionnaire, or upon premature withdrawal from the study, participants were debriefed to correct any misperceptions of the risks or safety of the Study Product that participants may have acquired during their participation

in this study. For example, participants were informed that, though the Study Products are authorised for sale in Czechia, this does not mean that using the Study Products is safe or without risk to health, and, because HTPs have been on sale for a relatively short time, little is known about the long-term health effects of using these products.

Compensation

Each participant could receive a maximum of 4,400 Kč (Czech Koruna) (approximately GBP £150, USD $190) for his/her time and contributions to this study according to the schedule presented in the Supplementary File (Table S2). 'Completion' of daily e-diaries in a given week was defined as having recorded an e-diary entry on at least five of the seven days in that week. Participants' level of compensation was wholly dependent on their completion of daily e-diaries and weekly online questionnaires and did not in any way depend on their level of use of the Study Product or any other tobacco product. To minimise the impact that increasing participants' disposable income via compensation payments could have had on participants' tobacco purchasing and use behaviours, participants were compensated for all contributions made during the Observational Phases after the end of the Observational Phase.

Data analysis

The primary analysis in this study described the proportion (and 95% confidence intervals (CI)) of participants who had completely switched from cigarettes to the Study Product during Week-6 (i.e., Day-36 to Day-42 inclusive) of the Observational Phase. The number of participants required for this study was calculated based on achieving sufficient precision in this primary analysis. On the assumption that a switch from cigarettes to the Study Product during Week-6 may be observed in as many as 20% of participants, 246 participants were required to detect a 20% switch rate with 5% absolute precision and 95% confidence. In anticipation that as many as 20% of all enrolled participants may be lost-to-follow-up at Day-43 of the Observational Phase, this study aimed to enrol a minimum 308 participants.

Data analyses were descriptive and inferential in nature; no hypotheses were tested. Descriptive statistics for outcome variables are presented in summary tables. Descriptive summary statistics for continuous variables include the number of participants in the population of interest (N), the number of participants in the population of interest with non-missing data on the outcome variable (n), and appropriate measures of central tendency (mean, median) and dispersion (standard deviation, standard error, range, interquartile range). All data analyses were conducted using IBM SPSS Statistics (version 27 or higher).

Study outcomes and their definitions are presented in Table 1. Patterns of use of cigarettes and the Study Product are described for each of the six weeks of the Observational Phase and for the Week-24 Follow-Up through descriptive statistics for past 7-day: (i) number of cigarette smoking days; (ii) total number of cigarettes smoked; (iii) mean number of cigarettes smoked per day; (iv) number of Study Stick consumption days; (v) total number of Study Sticks consumed; and (vi) mean number of Study Sticks consumed per day. Descriptive statistics on outcomes iv, v, and vi are reported for Study Sticks overall (i.e., all 12 flavour variants together), for each individual Study Stick flavour variant (×12), and for the groups of Study Sticks variants that come in tobacco flavours (×5), menthol/mint flavours (×3), and fruit flavours (×4). Tables also report the numbers and proportions (95% CI) of participants who met criteria for classification as having adopted the Study Products and as having used the Study Product on a regular basis during the Observational Phase.

Changes in participants' cigarette smoking behaviour concurrent with use/non-use of the Study Product are described by the number and proportion (95% CI) of participants who met criteria for classification into each of seven mutually exclusive product use groups (defined in Table 1) during each of the six weeks of the Observational Phase (via e-diary data) and at Week-24 (via questionnaire data): (i) switched from cigarettes to the Study Product; (ii) use of both cigarettes and the Study Product with a 50–99% reduction in mean daily cigarette consumption compared to the study's baseline week; (iii) use of both products with a 1–49% reduction in mean daily cigarette consumption; (iv) use of both products with no change in mean daily cigarette consumption; (v) use of both products with an increase in mean daily cigarette consumption; (vi) smoking cigarettes with no use of the Study Product; and (vii) no use of cigarettes or the Study Product. In this study, a 'substantial reduction' in cigarette consumption is defined as a 50–99% reduction in mean daily cigarette consumption compared to the study's baseline week.

This manuscript reports results of primary analyses of change in participants' cigarette smoking behaviour concurrent with use/non-use of the Study Product conducted in the Intention-to-Treat (ITT) population, which included all participants who satisfied all inclusion/exclusion criteria and enrolled in the Observational Phase of the study. Sensitivity analyses (reported in the Supplementary File) were conducted in four additional populations (defined in the Supplementary File) to test the robustness of the ITT results to different patterns and levels of e-diary completion. Data imputation was

Table 1 Outcomes, definitions, and measures used in the analysis of study objectives

Outcome	Definition/measure
Frequency of cigarette consumption	Number of cigarette smoking days
Intensity of cigarette consumption	Total number of cigarettes smoked
Mean daily cigarette consumption	Mean number of cigarettes smoked per day (CPD)
Frequency of Study Stick consumption	Number of Study Stick consumption days (overall and per flavour variant)
Intensity of Study Stick consumption	Total number of Study Sticks consumed (overall and per flavour variant)
Mean daily Study Stick consumption	Mean number of Study Sticks consumed per day (overall and per flavour variant)
Adoption of Study Product	Proportion of participants who consumed a total of ≥100 Study Sticks between Day-1 and Day-42 inclusive
Regular use of Study Product	Proportion of participants who consumed ≥1 Study Sticks on ≥ 3 days per week for a total of ≥ 3 weeks during the Observational Phase
Product Use Group (PUG) During Week 6	
1. Switched to Study Product	Proportion of participants who self-report consumption of ≥ 1 Study Sticks between Day-36 and Day-42 inclusive *and* zero cigarettes smoked between Day-36 and Day-42 inclusive
2. Dual use of cigarettes and Study Product (50–99% reduction in mean CPD)	Proportion of participants who self-report consumption of ≥ 1 Study Sticks between Day-36 and Day-42 inclusive *and* a 50–99% reduction in average CPD between Day-36 and Day-42 inclusive compared to the 1-week BAP
3. Dual use (1–49% reduction in average CPD)	Proportion of participants who self-report consumption of ≥ 1 Study Sticks between Day-36 and Day-42 inclusive *and* a 1–49% reduction in average CPD between Day-36 and Day-42 inclusive compared to the 1-week BAP
4. Dual use (no change in mean CPD)	Proportion of participants who self-report consumption of ≥ 1 Study Sticks between Day-36 and Day-42 inclusive *and* no change in average CPD between Day-36 and Day-42 inclusive compared to the 1-week BAP
5. Dual use (increase in mean CPD)	Proportion of participants who self-report consumption of ≥ 1 Study Sticks between Day-36 and Day-42 inclusive *and* an increase in average CPD between Day-36 and Day-42 inclusive compared to the 1-week BAP
6. Smoking cigarettes, no use of Study Product	Proportion of participants who self-report consumption of zero Study Sticks between Day-36 and Day-42 inclusive *and* ≥ 1 cigarette smoked between Day-36 and Day-42 inclusive
7. No use of cigarettes or Study Product	Proportion of participants who self-report consumption of zero Study Sticks between Day-36 and Day-42 inclusive *and* zero cigarettes smoked between Day-36 and Day-42 inclusive
PUG During Weeks 1–5 and Week 24	As defined above, with the time window set from the 1st to the 7th day of the study week inclusive

employed to account for missing data on the number of cigarettes smoked and Study Sticks consumed (per flavour variant). Procedures for handling missing cigarette and Study Stick consumption data in ITT analyses are fully described in the Supplementary File. Withdrawn participants were included in the ITT population with imputation of missing data as applicable.

Results

Participant disposition

Field interviewers visited a total of 3,257 households, from which 944 individuals (one per household) agreed to be interviewed. Of 944 interviewed individuals, 533 were determined to be ineligible. The 411 individuals who satisfied all inclusion/exclusion criteria were invited to a study site to undergo rescreening and enrolment procedures (SEV-1). Of the 411 individuals invited to SEV-1, 351 attended, passed rescreening, and started the baseline week. Following the baseline week, 332 individuals who continued to be eligible for the study attended a second site visit (SEV-2). From SEV-2, 332 individuals started the 6-week Observational Phase and were included in the ITT population. Participant disposition is summarised in Table 2.

Demographic and tobacco use characteristics

Most participants were female (56.6%); aged 25–44 years (54.2%); in full-time employment (70.5%); with a monthly household income of 10,000–49,999 CZK (64.8%) (Supplementary File, Table S3). At SEV-1, participants reported smoking a mean of 14.1 cigarettes per day in the past 7 days (SD = 5.02) in response to a 7-day retrospective question (Supplementary File, Table S4). During the baseline week, participants reported smoking a slightly higher number of cigarettes per day, on average (M = 15.0, SD = 5.11), in response to past 24-hour retrospective e-diary questions. Almost all participants (97.6%) reported smoking cigarettes 'every day' at SEV-1, and almost all (99.4%) started smoking cigarettes regularly more than 12 months ago. Most participants had not made any attempts within the past 12 months to completely quit smoking cigarettes (94.6%) or to quit by gradually cutting down cigarette smoking (89.5%) (Supplementary File, Table S5). Most participants had not used any tobacco or nicotine product other than cigarettes in the 7 days prior to SEV-1 (Supplementary File, Table S6). Other than cigarettes, the products most commonly used in the 7 days prior to SEV-1 were disposable e-cigarettes/vapes (5.7%), cigarillos or filtered cigars (5.1%), and heated tobacco products other than the Study Product (4.2%).

Table 2 Participant disposition

Study phase	N
Field interview questionnaire	
Number of households visited	3257
Individuals interviewed, screened for eligibility	944
Ineligible	533
Site Enrolment Visit #1 (SEV-1)	
Eligible, scheduled to attend SEV-1	411
Excluded, no show for SEV-1	26
Attended SEV-1, re-screened for eligibility	385
Excluded	34
Ineligible—failed rescreen	26
Ineligible—negative likelihood of using Test Products	8
1-Week Baseline Assessment Period (BAP)	
Eligible to start BAP	351
Excluded, did not start BAP	5
Started BAP	346
Excluded following BAP	12
Ineligible	12
Eligible from BAP but did not schedule SEV-2 visit	0
Site Enrolment Visit #2 (SEV-2)	
Eligible to Attend SEV-2	334
Excluded, no show for SEV-2	2
Attended SEV-2	332
Excluded	0
Ineligible	0
Enrolled, Started Observational Phase (OP)	332
OP Week 1	
Completed ≥ 4 of 7 daily e-diaries	331
Completed Questionnaire #3	330
OP Week 2	
Completed ≥ 4 of 7 daily e-diaries	326
Completed Questionnaire #4	326
OP Week 3	
Completed ≥ 4 of 7 daily e-diaries	323
Completed Questionnaire #5	324
OP Week 4	
Completed ≥ 4 of 7 daily e-diaries	326
Completed Questionnaire #6	317
OP Week 5	
Completed ≥ 4 of 7 daily e-diaries	318
Completed Questionnaire #7	303
OP Week 6	
Completed ≥ 4 of 7 daily e-diaries	309
Completed Questionnaire #8	310
Whole OP	
Completed ≥ 4 of 7 daily e-diaries in all six weeks of OP	302
Withdrawn during OP	1
FU Week 24	
Completed Questionnaire #9	279
Withdrawn during FU	0
Included in Intention-to-Treat (ITT) population	332

Abbreviations: N = number of participants in population of interest; SEV = Site Enrolment Visit; BAP = 1-Week Baseline Assessment Period; OP = Observational Phase; FU = Follow-Up Phase; ITT = Intention-To-Treat population

Study Product use patterns

Frequency and intensity of Study Product Stick consumption during the Observational Phase is summarised in Table 3 (all flavour variants together) and Table 4 (by flavour variant and flavour category). The Study Product was adopted by 95.8% (CI95: 93.2%, 97.6%) of participants during the Observational Phase; 98.8% (CI95: 97.2%, 99.6%) used the Study Product regularly throughout the Observational Phase. Participants consumed at least one Study Product Stick on a mean of 39.6 days (SD = 5.71; 94.3%) of the 42-day Observational Phase and consumed a mean total of 631.3 (SD = 396.31) Study Sticks during the Observational Phase, equivalent to 15.0 Study Sticks consumed by each participant on each day of the Observational Phase, on average (Table 3). Mean number of Study Product Stick consumption days per week ranged from a high of 6.8 days (SD = 0.85) during Week-1 to a low of 6.3 days (SD = 1.85) during Week-6, with mean number of Study Stick consumption days decreasing week-on-week between Week-1 and Week-6. Mean number of Study Sticks consumed per day ranged from a low of 13.2 (SD = 7.52) during Week-1 to a high of 15.8 (SD = 11.10) during Week 4. Participants consumed a mean total of 92.7 Study Sticks during Week-1 (SD = 52.62), which increased week-on-week to a high of 110.9 (SD = 77.71) during Week 4, and falling to 105.2 (SD = 78.45) during Week-6. The largest single-week increase in mean past 7-day total Study Stick consumption occurred between Week-1 (M = 92.7, SD = 52.62) and Week-2 (M = 105.8, SD = 63.57).

Participants self-reported consumption of a total of 209,583 Study Sticks (all flavour variants) during the Observational Phase (Table 4). Total weekly Study Stick consumption ranged from a low of 30,767 Study Sticks consumed during Week-1 to a high of 36,817 Study Sticks consumed during Week 4. Fruit-flavoured Study Sticks (Sum = 84,060; 40.1% of total) was the most consumed flavour category during the Observational Phase, followed closely by tobacco-flavoured Study Sticks (Sum = 80,429; 38.4% of total) and then by menthol/mint-flavoured Study Sticks (Sum = 45,093; 21.5% of total). Fruit- and menthol/mint-flavoured Study Sticks accounted for 40.3% and 20.5% of all Study Sticks consumed during Week-1, respectively, and 41.0% and 22.6% of all Study Sticks consumed during Week-6, respectively. In contrast, tobacco-flavoured Study Sticks accounted for 39.2% of all Study Sticks consumed during Week-1 and 36.4% of all Study Sticks consumed during Week-6.

Of all Study Sticks consumed during the Observational Phase, 30,728 (14.7%) and 27,129 (12.9%) were the 'Capsule Summer Red' (watermelon flavour) and 'Capsule Forest Purple' (berry flavour) variants, respectively. 'Rich Bronze' (Sum = 23,888; 11.4% of total) and 'Balanced Blue' (Sum = 22,747; 10.9% of total) were the third and

Table 3 Frequency and intensity of consumption of Study Sticks and combustible cigarettes

ITT population (N = 332)	BAP	Observational phase [a]							Follow-up phase[b]
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	WOP	Week 24
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
	Med. (IQR)	Med. (IQR)	Med. (IQR)	Med (IQR)	Med. (IQR)	Med. (IQR)	Med. (IQR)	Med. (IQR)	Med. (IQR)
N Study Stick Consumption Days	NA	6.8 (0.59)	6.8 (0.85)	6.7 (1.16)	6.6 (1.15)	6.4 (1.57)	6.3 (1.85)	39.6 (5.71)	-
	NA	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	42 (41.0–42.0)	-
Total N Study Sticks Consumed	NA	92.7 (52.62)	105.8 (63.57)	109.8 (74.28)	110.9 (77.71)	106.8 (77.15)	105.2 (78.45)	631.3 (396.31)	44.5 (67.73)
	NA	85.0 (50.0–124.5)	98.0 (57.0–142.0)	96.8 (57.0–147.5)	98.0 (51.7–151.0)	96.0 (51.6–147.0)	95.0 (47.0–144.0)	567.7 (332.1–846.3)	20.0 (0.0–70.0)
M N Study Sticks Consumed Per Day	NA	13.2 (7.52)	15.1 (9.08)	15.7 (10.61)	15.8 (11.10)	15.3 (11.02)	15.0 (11.21)	15.0 (9.44)	6.4 (9.68)
	NA	12.1 (7.1–17.8)	14.0 (8.1–20.3)	13.8 (8.1–21.1)	14.0 (7.4–21.6)	13.7 (7.4–21.0)	13.6 (6.7–20.6)	13.5 (7.9–20.2)	2.9 (0.0–10.0)
N Cigarette Smoking Days	7.0 (0.05)	6.3 (1.53)	5.7 (2.32)	5.5 (2.50)	5.4 (2.66)	5.3 (2.66)	5.3 (2.74)	33.5 (13.42)	4.1 (3.09)
	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	41.0 (30.5,40.2)	5.5 (0.0–7.0)
Total N Cigarettes Smoked	105.3 (35.75)	67.8 (45.77)	59.2 (51.22)	57.0 (52.49)	58.3 (55.13)	56.6 (54.39)	57.6 (53.92)	356.6 (300.04)	45.9 (49.12)
	104.0 (77.0–131.5)	57.5 (34.0–94.0)	48.5 (18.0–86.5)	44.2 (13.5–85.5)	44.6 (12.0–86.0)	40.0 (11.1–85.0)	44.5 (12.5–87.0)	292.0 (111.5–515.9)	33.5 (0.0–70.0)
M N Cigarettes Smoked Per Day	15.0 (5.11)	9.7 (6.54)	8.5 (7.32)	8.2 (7.50)	8.3 (7.88)	8.1 (7.77)	8.2 (7.70)	8.5 (7.14)	6.6 (7.02)
	14.9 (11.0–18.8)	8.2 (4.9–13.4)	6.9 (2.6–12.4)	6.3 (1.9–12.2)	6.4 (1.7–12.4)	5.7 (1.6–12.1)	6.4 (1.8–12.4)	7.0 (2.7–12.3)	4.8 (0.0–10.0)

Abbreviations: ITT = Intention-To-Treat population; BAP = Baseline Assessment Period; M = Mean; SD = Standard Deviation; Med. = Median; IQR = Interquartile Range; WOP = Whole Observational Phase; N = Number

[a] Cigarette and Study Stick consumption data collected during the observational phase were collected via the daily e-diary

[b] Cigarette and Study Stick consumption data collected at the Week 24 follow-up assessment were collected via a single questionnaire

fourth most consumed flavour variants, and the most consumed tobacco-flavoured variants. Together, two fruit flavour variants—'Capsule Summer Red' and 'Capsule Forest Purple'—and two tobacco flavours—'Rich Bronze' and 'Balanced Blue'—accounted for 49.9% of all Study Sticks consumed during the Observational Phase. 'Ice' (Sum = 19,113; 9.1% of total) was the fifth most consumed flavour variant overall, and the most consumed menthol/mint-flavoured variant. The least consumed flavour variants during the Observational Phase were 'Warm Amber' (Sum = 8,158; 3.9% of total) (tobacco flavour) and 'Polar Capsule Yellow' (Sum = 9,934; 4.7% of total) (yellow melon flavour).

Total weekly Study Stick consumption increased by 4,168 (+ 13.5%) between Week-1 (Sum = 30,767) and Week-6 (Sum = 34,935), equivalent to an additional 12.9 Study Sticks consumed per participant during Week-6 compared to Week-1. The largest absolute increase in total weekly Study Stick consumption between Week-1 and Week-6 was observed for fruit-flavoured variants (+ 1,930 Study Sticks consumed; + 15.6%; 12,384 to 14,314), followed by menthol/mint-flavoured variants (+ 1,590 Study Sticks consumed; + 25.2%; 6,312 to 7,902) and tobacco-flavoured variants (+ 649 Study Sticks consumed; + 5.4%; 12,070 to 12,719).

Cigarette consumption

Descriptive statistics summarising participants' frequency and intensity of cigarette consumption during the baseline week and 6-week Observational Phase are presented in Table 3. Each participant smoked a total of 356.6 cigarettes, on average (SD = 300.04) during the Observational Phase, giving a collective total of 118,379 cigarettes smoked by all participants during the Observational Phase. Participants smoked a mean of 15.0 cigarettes per day during the baseline week (SD = 5.11), with all participants except one having smoked at least one cigarette on all seven days of the baseline week (M = 7.0, SD = 0.05). A one-way repeated-measures ANOVA indicated that mean number of cigarettes smoked per day differed significantly across study weeks, $F(6, 1986) = 180.52$, $p < 0.001$. Post hoc Bonferroni-adjusted pairwise comparisons indicated that mean number of cigarettes smoked per day was significantly lower during each of the six weeks of the Observational Phase compared to the baseline week (all six comparisons, $p < 0.001$). Mean number of cigarettes smoked per day reduced from 15.0 during the baseline week to 9.7 during Week-1 and to 8.2 during Week-6. Similarly, mean number of smoking days reduced from 7.0 during the baseline week to 6.3 (SD = 1.53) during Week-1 and then steadily reduced each week thereafter to a low of 5.3 (SD = 2.74) during Week-6.

Table 4 Number of Study Sticks consumed per flavour variant and flavour category

	Observational phase [a]							Follow-up phase [b]
ITT population (N = 332)	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**WOP**	**Week 24**
N Study Sticks Consumed	**Sum**	**Sum**	**Sum**	**Sum**	**Sum**	**Sum**	**Sum**	**Sum**
All Flavours (n = 12)	30,767	35,141	36,462	36,817	35,462	34,935	209,583	14,773
All Tobacco Flavours (n = 5)	12,070	14,078	14,530	13,779	13,253	12,719	80,429	5,750
Balanced Blue	4,099	4,042	3,914	3,620	3,436	3,636	22,747	1,748
Rich Bronze	3,569	4,010	4,272	4,008	4,135	3,895	23,888	1,474
Velvet Copper	1,775	2,295	1,807	1,863	1,792	1,358	10,890	626
Bright Yellow	1,698	2,296	2,922	3,010	2,672	2,149	14,746	1,169
Warm Amber	930	1,436	1,615	1,279	1,217	1,681	8,158	733
All Menthol Flavours (n = 3)	6,312	7,154	7,445	8,493	7,787	7,902	45,094	3,401
Capsule Polar Green	2,078	2,306	2,366	2,763	2,445	2,272	14,231	1,147
Polar Green	1,947	1,998	2,116	2,136	1,790	1,762	11,749	770
Ice	2,287	2,850	2,963	3,594	3,551	3,869	19,113	1,484
All Fruit Flavours (n = 4)	12,384	13,908	14,486	14,545	14,422	14,314	84,060	5,622
Capsule Summer Red	5,168	5,370	5,268	5,328	4,915	4,680	30,728	2,168
Capsule Forest Purple	4,627	4,419	4,716	4,801	4,118	4,449	27,129	1,409
Polar Capsule Yellow	909	1,531	1,967	1,627	2,117	1,784	9,934	950
Capsule Cosmic Blast	1,680	2,589	2,536	2,789	3,272	3,402	16,269	1,095

Abbreviations: ITT = Intention-To-Treat population; BAP = Baseline Assessment Period; M = Mean; SD = Standard Deviation; Med. = Median; IQR = Interquartile Range; WOP = Whole Observational Phase; N = Number

[a] Study Stick consumption data collected during the observational phase were collected via the daily e-diary. Calculated from responses to the daily e-diary question for each Study Stick flavour variant: "How many [Flavour Name] iD™ Sticks have you consumed in your Pulze™ device in the past 24 h?"

[b] Study Stick consumption data collected at the Week 24 follow-up assessment were collected via a single questionnaire. Total number of Study Sticks consumed (all flavours) calculated in two steps. First, a total number of Study Sticks consumed in each of the 12 flavour variants was calculated by multiplying the reported "On how many of the past 7 days did you consume [Flavour Name] iD™ Sticks?" by "On average, on those days you consumed [Flavour Name] iD™ Sticks, how many [Flavour Name] iD™ Sticks did you usually consume each day?". Second, the total numbers of Study Sticks consumed in each of the 12 flavour variants were summed to give a total number of Study Sticks consumed in the past 7 days

Participants smoked cigarettes on a mean of 33.5 days (79.8%) of the 42-day Observational Phase and smoked a mean of 8.5 cigarettes per day during the Observational Phase (SD = 7.14).

Participants smoked a mean total of 105.3 cigarettes during the baseline week (SD = 33.75). Compared to the baseline week, mean past 7-day total cigarette consumption reduced by 35.6% during Week-1 (M = 67.8, SD = 45.77) and by 45.2% during Week-6 (M = 57.6, SD = 53.92) of the Observational Phase. The latter reduction equates to each participant smoking approximately 2.4 fewer packs of cigarettes ('pack' defined as '20 cigarettes') during Week-6 compared to the baseline week. Participants' past 7-day total cigarette consumption remained stable across the six weeks of the Observational Phase, ranging from a high of 67.8 cigarettes smoked per participant during Week-1 (SD = 45.77) to a low of 56.6 cigarettes smoked per participant during Week 5 (SD = 54.39).

At Week-24, 28.6% of participants had not smoked any cigarettes in the past 7 days. Each participant smoked on a mean of 4.1 of the past 7 days (SD = 3.09) and smoked a mean total of 45.9 cigarettes (SD = 45.12) during Week-24, a mean of 6.6 cigarettes smoked per day per participant (SD = 7.02) (Table 3). The ITT population is therefore estimated to have smoked a total of 15,239 cigarettes during Week-24, which is 19,721 fewer cigarettes than were reportedly smoked during the baseline week (total = 34,960).

Change in concurrent use of cigarettes and the Study Product

During Week-6, 16.0% (CI95: 12.3%, 20.2%) of participants had completely switched to the Study Product (i.e., past 7-day use of the Study Product and zero cigarettes smoked), while 33.7% (CI95: 28.8%, 38.9%) were smoking cigarettes and using the Study Product, but smoking 50–99% fewer cigarettes per day, on average, compared to during the baseline week (Table 5). The proportion of participants that had completely switched to the Study Product increased week-on-week from Week-1 through to Week-6, with the largest single-week increase in the rate of switching occurring between Week-1 and Week-2 (+ 9.6%). Use of both cigarettes and the Study Product while smoking 50–99% fewer cigarettes per day compared to the baseline week was the most common product use behaviour observed during every week of the Observational Phase, ranging from a high of 37.7% during Week 3 to a low of 33.4% during Week 4. This narrow range indicated that, at all times during the Observational Phase, around one-third of participants was using the Study Product and smoking 50–99% fewer cigarettes

Table 5 Concurrent cigarette smoking status and Study Product use status

ITT Population (N = 332)	Observational phase						Follow-up phase
	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 24
Product Use Group	**% (LB-UB)**	**% (LB-UB)**	**% (LB-UB)**	**% (LB-UB)**	**% (LB-UB)**	**% (LB-UB)**	**% (LB-UB)**
Switched to Study Product	0.3 (0.0, 1.4)	9.9 (7.1, 13.5)	12.3 (9.1, 16.2)	15.1 (11.5, 19.2)	15.4 (11.8, 19.5)	16.0 (12.3, 20.2)	24.7 (20.3, 29.5)
Dual use, 50–99% CPD reduction	36.1 (31.1, 41.4)	37.3 (32.3, 42.6)	37.7 (32.6, 43.0)	33.4 (28.5, 38.6)	35.2 (30.2, 40.5)	33.7 (28.8, 38.9)	26.2 (21.7, 31.1)
Dual use, 1–49% CPD reduction	46.4 (41.1, 51.8)	36.7 (31.7, 42.0)	32.8 (27.9, 38.0)	34.6 (29.7, 39.9)	31.3 (26.5, 36.5)	28.6 (24.0, 33.6)	10.5 (7.6, 14.2)
Dual use, no change in CPD	1.5 (0.6, 3.3)	0.3 (0.0, 1.4)	0.3 (0.0, 1.4)	0.6 (0.1, 1.9)	1.5 (0.6, 3.3)	1.2 (0.4, 2.8)	0.0 (0.0, 0.0)
Dual use, CPD increase	15.7 (12.1, 19.9)	15.7 (12.1, 19.9)	15.4 (11.8, 19.5)	15.1 (11.5, 19.2)	14.5 (11.0, 18.5)	16.3 (12.6, 20.5)	2.1 (0.9, 4.1)
Cigarette smoking only	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	1.5 (0.6, 3.3)	1.2 (0.4, 2.8)	1.8 (0.8, 3.7)	3.9 (2.2, 6.4)	32.5 (27.7, 37.7)
Cessation	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.3 (0.0, 1.4)	0.3 (0.0, 1.4)	3.9 (2.2, 6.4)

Abbreviations: N = number of participants in population of interest; ITT = Intention-To-Treat population; LB = lower bound 95% confidence interval; UB = upper bound 95% confidence interval; CPD = combustible cigarettes smoked per day; BAP = 1-Week Baseline Assessment Period

Week 1 = Day-1 to Day-7 inclusive; Week 2 = Day-8 to Day-14 inclusive; Week 3 = Day-15 to Day-21 inclusive; Week 4 = Day-22 to Day-28 inclusive; Week 5 = Day-29 to Day-35 inclusive; Week 6 = Day-36 to Day-42 inclusive. All cigarette and Study Stick consumption data collected during the observational phase were collected via the daily e-diary. Cigarette and Study Stick consumption data collected at the Week 24 follow-up assessment were collected via a single questionnaire

per day, on average, compared to during the baseline week. In contrast, the proportion of ITT participants who used the Study Product with a 1–49% reduction in daily cigarette consumption decreased across the Observational Phase, from a high of 46.4% during Week-1 to a low of 28.6% during Week-6.

Cigarette smoking without concurrent use of the Study Product was first observed during Week 3, with the proportion of participants only smoking cigarettes increasing from 1.5% during Week 3 to 3.9% during Week-6. For the three remaining product use categories—use of cigarettes and the Study Product with no change in mean daily cigarette consumption, use of both products with increased mean daily cigarette consumption, and cessation (i.e., use of neither product)—the proportion of ITT participants who met criteria for classification into each product use category remained relatively stable week-to-week between Week-1 and Week-6.

Approximately 16.3% of participants were using the Study Product and smoking more cigarettes per day, on average, during Week-6 compared to the baseline week. An exploratory analysis found that, of the 54 participants in this subgroup, 75.9% had smoked fewer than five additional cigarettes per day, on average, during Week-6 compared to during the baseline week. Lastly, 3.9% (CI95: 2.2%, 6.4%) of participants had smoked at least one cigarette but had not used the Study Product during Week-6, and 0.3% (CI95: 0.0%, 1.4%) had neither smoked any cigarettes nor used the Study Product.

Mean number of Study Sticks consumed per day during Week 6 and mean number of cigarettes smoked per day during Week 6 were significantly negatively correlated, $r(330) = -0.27$, $p < 0.001$ (Fig. 2). The trajectories of mean numbers of cigarettes smoked per day and Study Sticks consumed per day by each of five Week-6 Product Use Groups are presented in Fig. 3 and Fig. 4, respectively. Participants in the Week-6 'No Change in Cigarettes Smoke Per Day' group reported smoking a higher mean number of cigarettes smoked per day during the baseline week (M = 18.7) compared to the other four Week-6 groups (Ms = 14.5 to 15.4). Among participants who had switched completely to the Study Product during Week-6 ('Week-6 Switchers'), mean number of cigarettes smoked per day had reduced substantially between the baseline week (15.4) and Week-1 (4.5), had reduced to less than one cigarette per day (0.7) by Week 3, and remained below 1 cigarette per day during Weeks 4 and 5 before reaching 0 cigarettes per day during Week-6 (Fig. 3).

A similar trajectory of mean reduction in number of cigarettes smoked per day over the six weeks was observed among participants who had reduced their mean number of cigarettes smoked per day by 50–99% during Week-6 ('Week-6 Substantial Reducers'). Most notable was the finding that Week-6 Substantial Reducers had reduced their mean number of cigarettes smoked per day by 50–99% during all six weeks of the Observational Phase (M range = 7.5 (Week-1) to 3.7 (Week-6)) compared to the baseline week (M = 15.4). The same outcome was observed among participants who had reduced their mean number of cigarettes smoked per day by 1–49% during Week-6 compared to the baseline week, in that these participants had actually reduced their mean number of cigarettes smoked per day by 1–49% during all six weeks of the Observational Phase (M range = 10.2 (Week 3) to 11.2 (Week-1 and Week-6)) compared to the baseline week (M = 14.8). Lastly, Week-6 Switchers and Week-6 Substantial Reducers were observed to have both: (i) consumed more Study Sticks per day, on average,

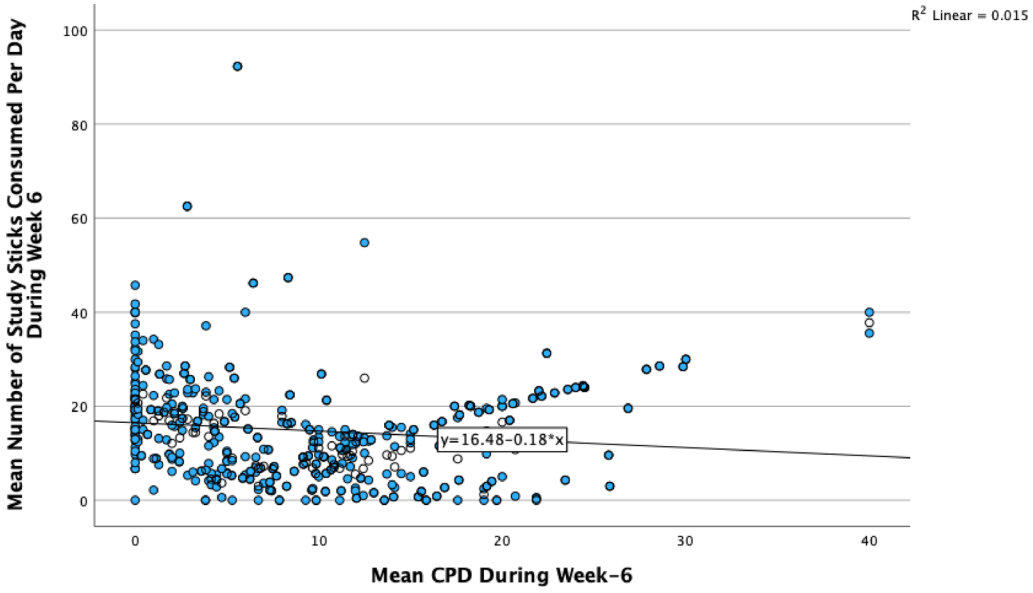

Fig. 2 Scatterplot of bivariate correlation between mean number of Study Sticks consumed per day during Week 6 and mean number of cigarettes smoked per day (CPD) during Week 6

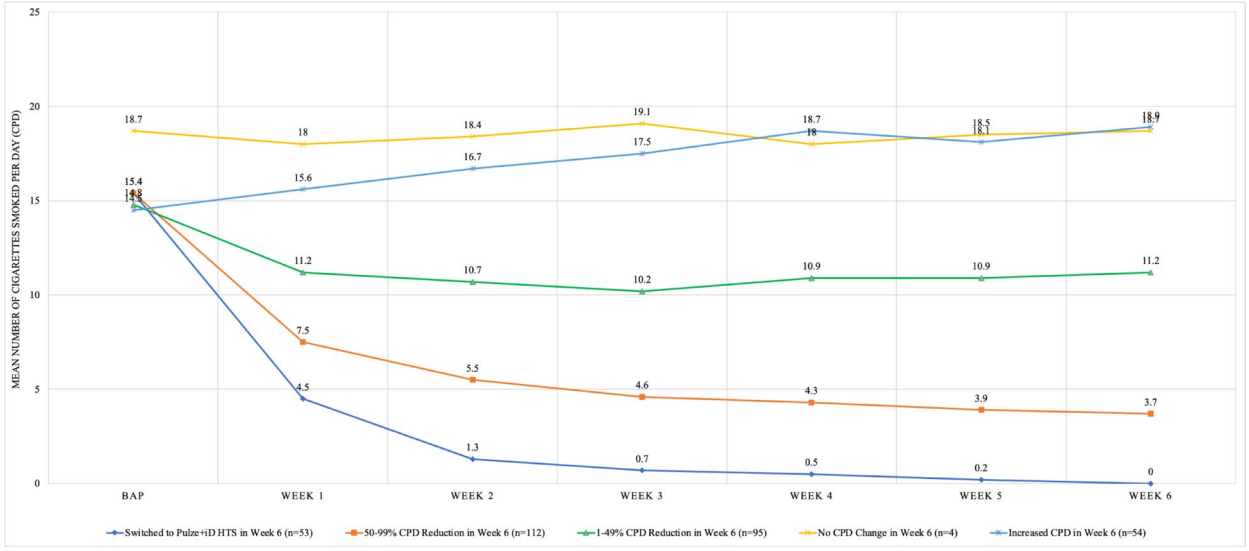

Fig. 3 Trajectories of mean number of cigarettes smoked per day (CPD) during each week of the Observational Phase, by Week-6 Product Use Group. Abbreviations: BAP = Baseline Week; CPD = Cigarettes Smoked Per Day; HTS = Heated Tobacco System

during all six weeks of Observational Phase, compared to other Product Use Groups; and (ii) reported larger increases in mean number of Study Sticks consumed per day between Week-1 and Week-6, compared to other Product Use Groups (Fig. 4).

At Week-24, 24.7% (CI95: 20.3%, 29.5%) of the ITT population had switched to the Study Product, while 26.2% were both smoking cigarettes and using the Study Product but smoking 50–99% fewer cigarettes per day (Table 5). A further 10.5% (CI95: 7.6%, 14.2%) were both smoking cigarettes and using the Study Product but smoking 1–49% fewer cigarettes per day, and 32.5% (CI95: 27.7%, 37.7%) had smoked at least one cigarette but had not consumed any Study Sticks (i.e., smoking cigarettes only). The remaining participants had neither smoked any cigarettes nor consumed any Study Sticks during Week-24 (i.e., cessation, 3.9%; CI95: 2.2, 6.4) or were both smoking cigarettes and using the Study Product and smoking more cigarettes per day, on average, compared to the baseline week (2.1%; CI95: 0.9, 4.1).

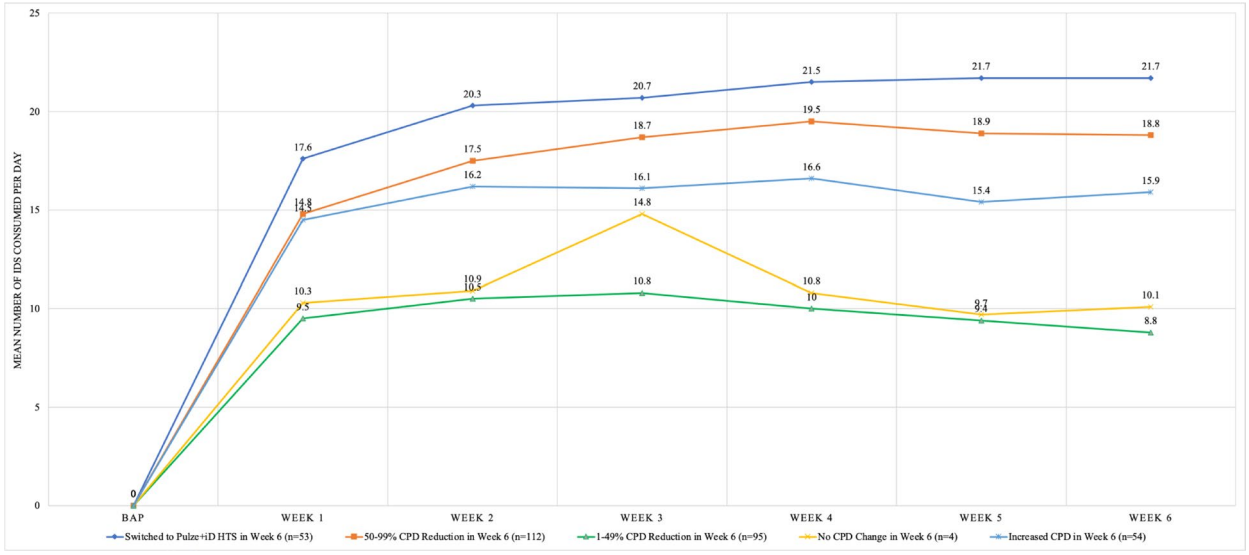

Fig. 4 Trajectories of mean number of Study Sticks consumed per day during each week of the Observational Phase, by Week-6 Product Use Group. Abbreviations: BAP = Baseline Week; CPD = Cigarettes Smoked Per Day; HTS = Heated Tobacco System

Discussion

Heated tobacco products (HTP) are an emerging category of non-combustible tobacco products that have potential to reduce individuals' risks for developing smoking-related diseases and associated healthcare costs when used in place of cigarettes [16]. To increase understanding of the real-world potential of HTPs to reduce smoking-related harm, this study assessed how a cohort of adults who smoke cigarettes in Czechia used HTPs in their everyday lives, and the extent to which HTPs were used to completely switch away from cigarettes or substantially reduce cigarette consumption when provided with a tobacco heating device and means to obtain consumable tobacco sticks in 12 flavour variants directly from retailers in the community, free of charge, for their own personal use as desired for six weeks.

Results demonstrate the potential for regular use of HTPs to help adults to completely stop smoking or substantially reduce their cigarette consumption in the short to medium-term. During the sixth week of ad libitum use of the Study Product, around half (49.7%) of participants—who at baseline were smoking around 15 cigarettes per day, on average—had either completely switched to the Study Product (16.0%) or had substantially reduced their daily cigarette consumption while continuing to use the Study Product (33.7%). An additional 28.6% had reduced their daily cigarette consumption by a non-substantial magnitude (i.e., 1–49% reduction) while continuing to use the Study Product during Week-6. This takes the total proportion of participants whose daily cigarette consumption reduced while using the Study Product in the context of this study to 78.3%, indicating that, by the end of Week-6, most participants had experienced *at least* a small reduction in daily cigarette consumption concurrent with use of the Study Product. Additionally, higher daily consumption of Study Sticks during Week 6 was significantly associated with lower mean daily cigarette consumption during Week 6, suggesting that Study Sticks were typically used in place of cigarettes, rather than in addition to cigarettes.

Rates of complete switching and substantial cigarette reduction—both individually and combined—observed for the Study Product during Week-6 of this study align with rates reported from three actual use studies conducted on other HTPs over similar time periods among individuals with similar baseline patterns of cigarette smoking and low levels of intention to quit cigarettes [12–14]. For example, Roulet et al. (2024) reported that close to half of participants had reduced their daily cigarette consumption by at least 50% while continuing to use the study HTP during the final week of a 4-week study. Similarities in study outcomes across different types of HTPs, study durations, times, and populations suggest that the use of HTPs in general may be helpful for stopping or reducing smoking.

Substantial reductions in cigarette consumption were evident as early as the first week of using the Study Product. Early reductions were typically sustained or grown for the remainder of the Observational Phase. Compared to the baseline week, participants smoked 35.6% fewer cigarettes during Week-1 and 45.2% fewer cigarettes during Week-6 of the Observational Phase. This latter reduction equates to each participant having smoked approximately 2.4 fewer packs of cigarettes during Week-6 compared to the study's baseline week. On the assumption that participants smoked cigarettes

as normal during the baseline week, and that participants would likely have continued to smoke cigarettes at the same intensity had they not enrolled in this study or been exposed to any smoking cessation intervention, it is estimated that each participant would have smoked approximately 631.8 cigarettes, on average, during a counterfactual 6-week period. Each participant's total six-week cigarette consumption is therefore estimated to have reduced by 43.6%, on average—equivalent to each participant having smoked approximately 13.8 fewer packs of cigarettes—during the six weeks of this study in which the Study Product was provided free of charge for ad libitum use compared to a counterfactual 6-week period during which participants would likely have smoked as normal.

High rates of use of the Study Product and substantial reductions in smoking prevalence and cigarette consumption continued to be observed up to four months after the end of the free provision of Study Sticks, during which time participants were required to purchase packs of Study Sticks from retailers with their own money, if they so wished. At Week-24, more than half of participants had either completely or substantially switched from cigarettes to the Study Product, with each participant having smoked approximately 3 fewer packs of cigarettes during Week-24 compared to during the baseline week (a 56.4% reduction), and approximately 0.6 fewer packs (12 fewer cigarettes) compared to Week-6 (a 20.3% reduction). Therefore, though it cannot be ruled out that some participants may have initially stopped or reduced smoking because they were obtaining an alternative tobacco product for free, the observation that more than half of participants continued to buy packs of Study Sticks with their own money and continued or began to use the Study Product as a complete or substantial replacement for cigarettes up to four months after their free supply of Study Sticks had ceased, suggests the Study Product represented an acceptable real-world marketplace alternative to cigarettes for most participants.

Participants' decisions to try and use the Study Product on a regular basis, and to continue obtaining packs of Study Sticks from retail outlets for use as a complete or substantial substitute for cigarettes, occurred without participants being required, directed, or encouraged to stop/reduce smoking, or to use the Study Product at all, let alone to use the Study Product to help to stop or reduce smoking, or for any other purpose. Additionally, participants who did completely stop or substantially reduce their cigarette consumption over six weeks did so despite having no intention of quitting cigarettes at the start of those six weeks. This suggests that even a brief period of use of the Study Product may be sufficient to increase motivation to switch from cigarettes. Results, therefore, provide useful estimates of the likelihood that adults who do not intend to quit cigarettes in the near-term will purchase, adopt and use the Study Product in post-marketing environments as a replacement for all or most of the cigarettes they would otherwise have likely continued to smoke.

Results indicate potential for high levels of adoption and regular use of the Study Product in place of cigarettes in contexts in which the Study Device and Sticks are commercially available and affordable in a variety of tobacco, menthol/mint, and fruit flavour variants. Consumption of Study Sticks was fairly well distributed across the 12 commercially available flavour variants. Two fruit-flavoured variants—'Capsule Summer Red' (watermelon flavour) and 'Capsule Forest Purple' (berry flavour)—were the two most consumed flavour variants during all six weeks of the Observational Phase. Together, four flavour variants—'Capsule Summer Red' (fruit: watermelon), 'Capsule Forest Purple' (fruit: berry), 'Rich Bronze' (tobacco), and 'Balanced Blue' (tobacco) accounted for close to half of all Study Sticks consumed during Week-6 and during Week-24, indicating little change between the short-term and long-term in participants' stronger preference for using these four flavour variants. For context, however, data collection for the Observational Phase of this study concluded prior to 23 October 2023, the date on which European Union (EU) Member States were required to have fully implemented a European Commission Directive (2022/2100/EU) that prohibits the marketing of HTPs with a characterising flavour (e.g., fruit, menthol, mint) in the EU [17]. This Directive, which withdrew the previous exemption of HTPs from a characterising flavour ban granted by a 2014 Directive (2014/40/EU), was proposed in 2022 in response to a reported increase in the sales volume of HTPs in several EU countries [18]. This means that seven of the twelve Study Stick flavour variants that were tested in this study—and which collectively accounted for the majority of Study Sticks consumed—were banned from sale in Czechia soon after the conclusion of this study's Follow-Up Phase. The results from the Follow-Up Phase therefore depict a picture of real-world use and purchasing of Study Sticks and concurrent changes in cigarette consumption that existed *before* consumers in Czechia lost legal retail access to seven of the twelve Study Stick flavour variants tested in this study.

This study had several strengths. First, the design enabled observation of how adults who smoke use the Study Product and other tobacco products in their everyday lives over time under conditions that closely reflected how real-world consumers obtain and use HTPs. Site enrolment visits were designed to give participants' similar information and experiences that potential consumers may receive when discovering the Study Product in a store or other retail location for the first time. For

example, at the first visit, participants were given all the information about the Study Product that a potential consumer in Czechia may reasonably expect to receive if they were to read the products' labelling or marketing materials in a store, ask the salesclerk questions about the products, or search the internet for information about the products (e.g., visiting the manufacturer's website). Following receipt of this information, participants decided whether the Study Product was a product they would like to try using, just as a consumer would use such information to decide whether to buy the Study Product from a retailer.

Second, participants' use or non-use of the Study Product and of any other tobacco product during this phase was entirely self-decided and not in any way assigned, guided, instructed, directed, dictated, scheduled, constrained, or otherwise controlled by the study protocol. Like real-world consumers, participants in this study were free to use their prepaid debit card to purchase packs of Study Sticks in any flavour they wished and free to change flavours at any time and as many times as they wished. With multiple flavour variants sold widely at convenience stores, shops, supermarkets, gas stations and other retail outlets throughout Prague and Brno, participants were free to choose where and when to purchase Study Sticks—subject to their preferred flavour variant(s) being in stock—and whether to purchase one or multiple packs of Study Sticks at a time. Results therefore give insight as to how and when adults who smoke chose to 'purchase' and use the Study Product and other tobacco products under near-to-real-world conditions.

Third, actual use studies of tobacco harm reduction products have traditionally required study participants to come to a study facility every week or every two weeks to collect a new supply of the investigational products. This method of product supply to can be (i) burdensome to participants, who need to travel to and from the facility; (ii) expensive to sponsors and investigators, who need to manufacture, transport, and store large quantities of products at each facility, much of which goes unused and so to waste; (iii) and unrepresentative of the places and processes by which participants would normally obtain tobacco/nicotine products in the real world. These three issues were avoided in the present study by giving each participant a prepaid debit card with which to purchase the Study Products directly from retailers in the community for the duration of the Observational Phase. Specifically, the novel 'debit card' method of product supply employed in this study allowed participants to 'buy' the Study Products they wished to use, whenever they wished to buy them, from the stores in which they would normally buy cigarettes and other tobacco and nicotine products. Additionally, this method enabled study investigators to monitor the content, times, and places of all purchases made with study debit cards in real-time. As a means to increase the real-world representativeness of how people 'purchase' tobacco harm reduction products, minimise study costs and product waste, minimise participants' contact with investigators, and minimize travel/time burden to participants, designers of future actual use studies of tobacco harm reduction products may wish to consider the feasibility of giving study participants a prepaid debit card with which they can 'purchase' products-of-interest directly from retail locations in the community as desired rather than coming to a study facility to collect products. This approach would require that the products-of-interest are widely commercially available throughout a geographical area-of-interest and that VISA/MasterCard are widely accepted as payment methods.

Study results must also be interpreted within the context of several limitations. First, participants were provided with a Study Device, free of charge, and money—in the form of a funded personal Study Debit Card—to be used for the sole purpose of purchasing packs of Study Sticks from retail outlets as desired for the duration of the Observational Phase. However, participants who wished to smoke cigarettes or use any other tobacco products were required to purchase those products with their own money. It is possible that some participants stopped smoking or smoked fewer cigarettes during the Observational Phase because they were receiving a supply of Study Sticks for free, and that their use of Study Sticks in place of cigarettes may not have continued once they were required to purchase Study Sticks with their own money during the Follow-up Phase.

Second, and relatedly, while the 6-week Observational Phase employed in this study is of sufficient duration to reliably detect meaningful short-to-medium-term changes in cigarette smoking behaviour, this period is not of sufficient duration to provide evidence of HTPs' longer-term impact on cigarette smoking. To examine whether rates of complete or substantial substitution of HTPs for cigarettes observed after six weeks are sustained, extended, or lost in the longer-term, future studies may wish to consider the feasibility of incorporating either a longer-term Observational Phase during which Test Products are provided free of change and/or a longer-term post-observation Follow-up Phase during which commercially available investigational products are purchased by participants with their own money.

Third, in an effort to minimise participants' contact with investigators throughout the Observational Phase and be minimally invasive upon participants' lives, all data collection during the Observational Phase was conducted remotely and limited to self-reported behavioural and perception outcomes. This study therefore did not collect any biospecimens from participants or any

self-report data on perceived changes in health, which creates two limitations (i) changes in participants' cigarette consumption were based on self-reported daily e-diary data that were not biochemically verified; and (ii) the extent to which the self-reported reductions in cigarette consumption subsequently translated into a reduced incidence of short and long-term smoking-related harms among this cohort was not addressed.

Fourth, study participants were smoking 5–30 cigarettes per day, on average, living in the cities of Prague and Brno, Czechia, and did not intend to quit cigarettes within the next three months at the time of study enrolment. Therefore, the study results may not be generalisable to adults whose daily cigarette consumption is very light or very heavy; adults who smoke who live in other cities, other countries, or in rural areas; or adults who smoke who are motivated to quit smoking in the near future. Additionally, by enrolling only individuals who expressed a positive intention to use the Study Products regularly, results may also be subject to a positive selection bias and are therefore unlikely to generalise to individuals who try the Study Products but do not like them enough to use on a regular basis.

Fifth, study results do not permit conclusions about the likelihood that adults who smoke will adopt the Study Product in a post-market retail environment in which a number of the alternative brands of HTPs compete with the Study Product on a range of factors that are known to influence consumers' purchasing decisions, such as retail availability, price/value for money, ease of device use, flavour options, and subjective effects of product use (e.g., nicotine delivery, taste, satisfaction, craving relief).

Lastly, given the lack of a comparison group in this study (e.g., a control group not using the Study Products), results do not permit the conclusion that observed reductions in cigarette consumption were caused by use of the Study Product. Readers are cautioned to interpret study results as evidence of changes in cigarette smoking behaviour that co-occurred with ad libitum use of a Study Product that was provided for free for six weeks.

Conclusions

HTPs offer adults who smoke a means to continue consuming nicotine in a potentially less harmful way than continuing to smoke cigarettes. This study demonstrated that use of HTPs in variety of tobacco and non-tobacco flavours can help adults who smoke to either completely switch away from cigarettes or substantially reduce their cigarette consumption. These harm reduction behaviours were observed both in the short-term when HTPs were provided free of charge, and in the long-term when participants purchased HTPs with their own money as desired from retailers in the community. The most popular heated tobacco sticks were those containing fruit flavours—watermelon and berry—that are now prohibited for sale in the EU.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12954-025-01293-x.

Supplementary Material 1

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Author contributions

CR was responsible for study conceptualisation and design, development of the methodology, analysis and interpretation of data, writing of study documents, writing and revision of the manuscript, and study supervision. GB was responsible for study conceptualisation and design, development of the methodology, project administration, and manuscript review and revision. VM was responsible for analysis and interpretation of data, and review and revision of the manuscript.SN managed activation, funding, and monitoring of study participants' prepaid debit cards. MF, LM, TN and MS assisted with project management and with manuscript draft review and revision.SW assisted with manuscript draft review and revision.NM was responsible for study conceptualisation and design, development of methodology, manuscript review and revision, and study supervision.

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Data availability

Beginning on publication and ending five years thereafter, de-identified datasets analysed in the current manuscript may be made available to researchers who submit a proposal that is accepted by the Study Sponsor. Requests should be sent to TN via email (Thomas.Nahde@impbrands.com) and will be reviewed on a case-by-case basis.

Declarations

Ethics approval and consent to participate

The study protocol and all studyrelated documents were submitted for ethical review to the Reading Independent Ethics Committee (RIEC). A favourable ethical opinion of the study was received from RIEC on 19 March 2023.

Consent for publication

Not applicable.

Competing interests

In the past three years, the employers of CR (Russell Burnett Research and Consultancy Ltd), and GB, VM, SN, and NM (Centre for Substance Use Research Ltd) have received funding from tobacco and nicotine product manufacturers to conduct research on tobacco and nicotine product use, use transitions, use intentions, and perceptions. TN, MF, LM, MS and SW are employed by Imperial Brands PLC, which markets the Study Products.

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