Switching from cigarettes to IQOS: the relative importance of IQOS-associated reward, reinforcement and abstinence relief

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ABSTRACT

Introduction This study investigated whether IQOS, a heated tobacco product, can fully substitute for combustible cigarettes and the factors that promote substitution.

Methods Adults who smoked cigarettes daily (N=90; 21–65 years) completed a baseline ad-lib smoking period (days 1–5), two laboratory visits (days 6–7) and a 2-week period where they were instructed to switch from smoking cigarettes to using IQOS 3.0 (days 8–21). Mixed-effect modelling estimated the changes in cigarettes per day (CPD) and the percentage of baseline CPD substituted by HeatSticks during the switch period. Predictors included IQOS-associated subjective reward, relative reinforcing value, craving relief and withdrawal relief.

Results Participants reduced their CPD to about 30% of their baseline smoking rate by the end of the 14-day switch period (p<0001). A lower versus higher reinforcing value of smoking relative to IQOS (RRV; break point <5 vs ≥5) predicted greater reductions in CPD (β=−1.31 (95% CI −2.35 to −0.27) p=0.013). Initially, IQOS use was 72% of the baseline smoking rate (β=71.64 (95% CI 42.79 to 100.48) p<0.0001) and climbed by 0.8% per day (β=0.82 (95% CI 0.01 to 1.64) p=0.05), for an average substitution rate of 83%. The subjective reward of IQOS was the only predictor of a higher substitution rate (β=4.26 (95% CI 1.03 to 7.50) p=0.01).

Conclusions IQOS fully substituted for cigarettes in ~20% of people who were not immediately interested in quitting smoking while the remainder significantly reduced their smoking. Positive reinforcing effects of IQOS foster use and the transition away from combustible cigarettes.

Trial registration number NCT05076708.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Fully substituting a heated tobacco product for combustible cigarettes may offer a less harmful means of nicotine delivery for those who would not otherwise quit combustible cigarette smoking.

WHAT THIS STUDY ADDS

⇒ Clinical evidence of the substitutability of heated tobacco products, such as IQOS, for combustible cigarettes and the factors that promote substitution is limited.

⇒ Our findings indicate that IQOS can fully substitute for cigarette smoking among those who find IQOS and cigarettes similarly reinforcing. Among people who find cigarettes more reinforcing, significant reductions in smoking are achieved, but not complete switching.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Future research should determine if IQOS use and its rewarding and reinforcing effects result in the cessation of cigarette smoking among those seeking treatment and if harm exposure is reduced when substitution is not complete.

INTRODUCTION

Nearly, 70% of adults who smoke cigarettes want to quit,[1] and 55% report trying to quit at least once in the past year.[2] Yet over 90% fail[2] despite the use of smoking cessation medication.[1 3] Non-combustible tobacco products offer a potentially less harmful alternative means of nicotine delivery for those who would not otherwise quit smoking.

IQOS, a heated tobacco product (HTP), heats rather than combusts pressed leaf tobacco (HeatSticks) to produce a nicotine-containing aerosol for inhalation. Because IQOS heats rather than burns tobacco, there is less toxicant exposure than combustible cigarette smoking.[4] A systematic review documented that IQOS use results in significantly less exposure to 12 common biomarkers compared with combustible cigarette smoking.[5] However, four carcinogen-related biomarkers remained elevated compared with no tobacco use,[5] emphasising that IQOS use reduces harm but is not harmless. IQOS is designated as a reduced-exposure product,[6] and thus, its value as a harm reduction tool appears to rest on fully switching from combustible cigarettes to IQOS.[7] Survey studies have documented that the majority of people who use HTPs continue to smoke cigarettes[8–10] and that HTP use may not aid smoking cessation or prevent relapse.[11] Clinical evidence of the substitutability of IQOS for combustible cigarettes and the factors that promote switching is sparse.

In the only trial to date, Caponnetto *et al* found that 39% (43/110) of participants recruited from Catania, Italy, transitioned from combustible cigarette smoking to IQOS use (CO<10 ppm) after 12 weeks of IQOS provision and smoking cessation counselling.[12] Similarly, in the USA, a pilot study of 33 people who smoked daily showed that IQOS

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use resulted in a 75% reduction in cigarette smoking, with almost 20% completely switching to IQOS after 14 days without counselling.[13] These findings highlighted the potential impact of IQOS on cigarette smoking and suggested that for people to shift away from combustible cigarettes to IQOS, IQOS must have effects that make it substitutable.

Cross-sectional laboratory studies of the acute effects of IQOS have examined whether use is negatively reinforcing in that it reduces abstinence symptoms and whether it produces positive reinforcing effects that compete with cigarette smoking. Research has shown that IQOS use reduces abstinence-associated cigarette craving and, in some studies, withdrawal symptoms.[13–16] People who smoke do rate IQOS use as rewarding, although, in some studies, less rewarding than their brand of cigarettes.[14–17] When abstinent, individuals who smoke also show a preference for IQOS relative to cigarettes as the reinforcement schedule for earning cigarette puffs becomes increasingly lean.[17] Indeed, our pilot research documented that the reinforcing value of IQOS relative to cigarettes was the most important predictor of fully switching.[13]

This study sought to determine whether IQOS can fully substitute for combustible cigarettes among people who smoke. In addition, we investigated which IQOS-associated effects (ie, craving relief, withdrawal relief, subjective reward and relative reinforcing value), measured in the laboratory, predicted IQOS use and cigarette smoking in the natural environment. We anticipated that subjective reward and the relative reinforcing value of IQOS would be key determinants of IQOS use and cigarette smoking.

METHODS

Study sample

Participants were 90 adults 21–65 years who smoked at least 5 cigarettes per day (CPD) for the past 12 months and had no plans to quit smoking in the next 30 days but were interested in quitting within 6 months. An exhaled carbon monoxide (CO) >10 ppm was used to verify smoking status. Exclusion criteria included the regular use (>5 days/past 30 days) of non-cigarette nicotine products, current use of smoking cessation medication or use of specific medications (eg, stimulants, opiates), alcohol consumption exceeding 25 standard drinks a week, regular recreational substance use (except cannabis), serious or unstable medical condition (eg, cancer, asthma) within the past year, self-reported psychiatric conditions involving psychosis, pregnancy and lactation.[18 19] All participants provided written informed consent before enrolling in the 21-day study.

Recruitment was initiated in September 2021, and the first participant enrolled on 9 September 2021. The accrual was completed on 24 July 2023. Study screening, enrolment, retention and sample size for analyses are summarised in figure 1. The study is registered at ClinicalTrials.gov (NCT05076708).

Study procedures

Participants were recruited from the Philadelphia, Pennsylvania, metropolitan area via social media advertising. Ad respondents were prescreened over the telephone for inclusion and exclusion criteria. Those eligible at telephone screening provided in-person informed consent and completed eligibility screening to document a negative urine drug screen, a negative urine pregnancy test (females only), a breath alcohol test of 0.000, and a CO value >10 ppm. Participants eligible at the intake screening completed baseline measures and received instructions to smoke as usual for the next 5 days while collecting all spent filters each day (days 1–5). The average daily spent filters served as the baseline smoking rate.

On day 6, participants arrived at the lab at 9:00 hours after 10 hours of overnight cigarette smoking abstinence (CO verified <10 ppm).[20 21] Participants completed self-report measures of craving and withdrawal. Then, participants completed two 14-puff IQOS HeatStick exposures, one menthol-flavoured and the other tobacco flavoured, 45 min apart, with flavour order counterbalanced (ie, randomly determined via a computer programme) and stratified by sex. After each exposure, subjective reward, craving and withdrawal were measured.

On day 7, following overnight abstinence, participants were introduced to a validated behavioural choice task, which assessed the reinforcing value of IQOS (using the flavour with the highest rewarding value measured at the day six visit) relative to cigarettes.[13] Participants completed the task by moving a computer mouse to hit targets (IQOS image or a cigarette image) on one of two computer screens to earn points toward either IQOS puffs or cigarette puffs across 10 trials using a concurrent schedule. Consistent with relative reinforcement paradigms, earning puffs for IQOS required a fixed amount of work (FR-25, 25 target hits to earn each puff) while earning puffs for cigarettes required a progressively increasing amount of effort (PR-25x, 25, 50, 75, 100, 125, 150, 175, 200, 225 and 250 target hits to earn each puff).[21] The task was performed until a participant completed 10 trials and accumulated a total of 10 points from which they could have earned either one puff of IQOS (up to 10 puffs) or one puff of a cigarette (up to 10 puffs) for each point collected, or a combination thereof.

Next, participants were given the IQOS 3.0 system, a supply of Marlboro HeatSticks (regular and menthol based on preference) and date-stamped zipped baggies for the daily collection of used HeatSticks and spent cigarette filters. Participants were instructed to switch completely from using cigarettes to IQOS use for 14 days (days 8–21), beginning on the morning of day 8 and to collect any spent cigarette filters if they did smoke. Participants returned to the lab every 3 days to provide CO readings and return used HeatSticks and cigarette filters. Participants were compensated US$500 total.

Measures

Covariates and predictor variables

Covariates included age, biological sex, race and nicotine dependence as measured by the six-item Fagerström Test of Nicotine Dependence.[22]

Subjective reward

The subjective rewarding value of IQOS was measured by averaging the two-item satisfaction subscale ('Was it satisfying'? and 'Did it taste good'?) from the Cigarette Evaluation Scale (CES) adapted for IQOS use.[13 16 21]

Relative reinforcing value

The reinforcing value of IQOS use relative to cigarette smoking was measured with a validated choice task, evaluating the preference for IQOS versus cigarette puffs.[13 21] The relative reinforcing value of IQOS was determined by the break point, which is the highest trial completed across 10 trials to earn cigarette puffs.[23] Relative to IQOS, most participants (81%; n=73) worked predominately for cigarettes (375–1375 target hits for ≥5 cigarette puffs) while the remainder (19%; n=17) were far less willing to work (0–75 target hits for ≤2 cigarette puffs); thus a dichotomous indicator was used.[24]

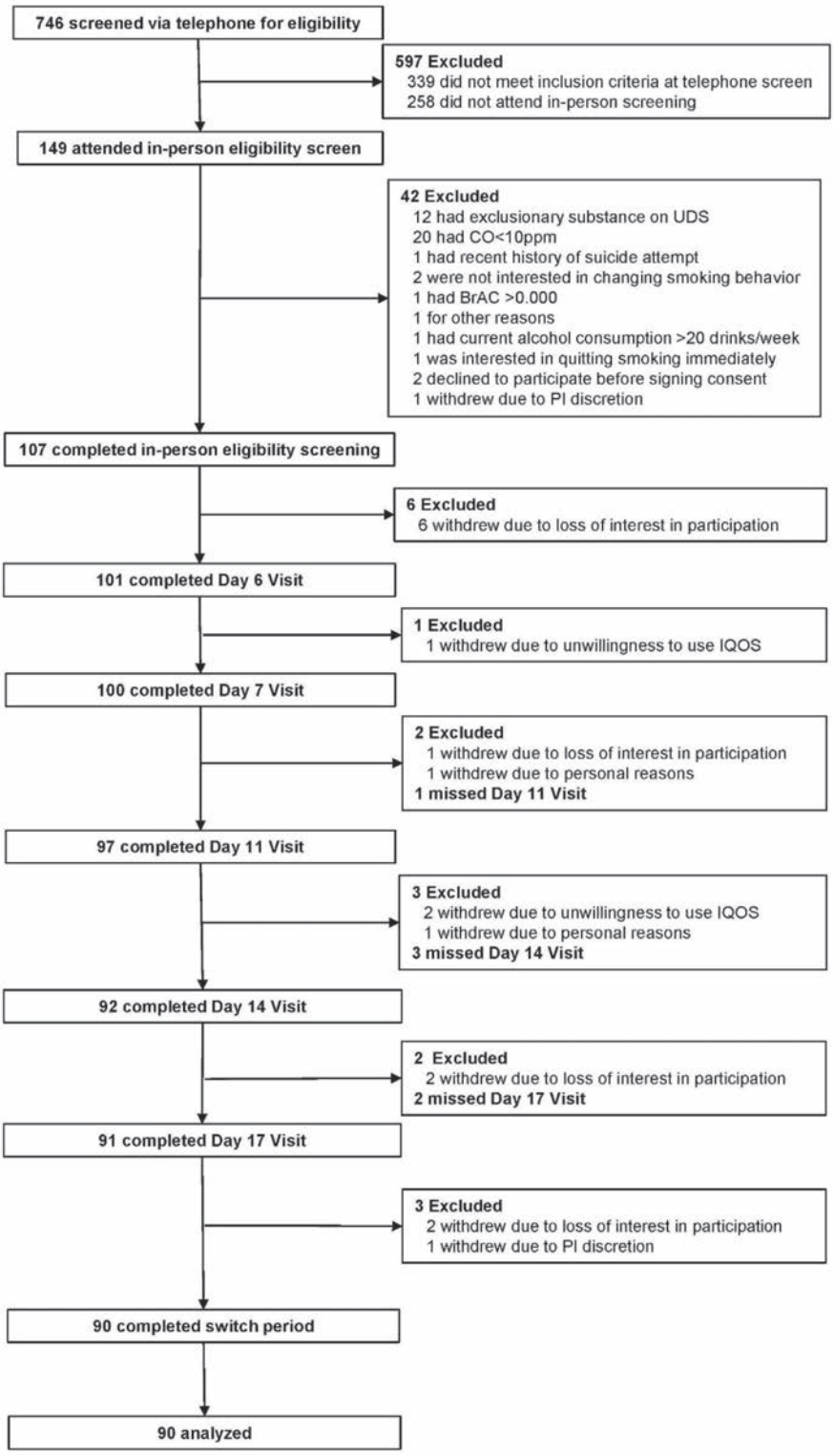

Figure 1 Flow diagram of study participation. BrAC, breath alcohol; CO, carbon monoxide; PI, Principal Investigator; UDS, urinary drug screen.

Craving and withdrawal relief

Withdrawal symptoms were measured by summating the eight-item Minnesota Nicotine Withdrawal Scale.[25 26] Craving was measured by summating the negative subscale (4-item anticipation of relief) from the 10-item Brief Questionnaire of Smoking Urges.[27] Relief scores were calculated as post-IQOS exposure responses minus abstinence-induced responses.

Outcome variables

Cigarette smoking

The primary outcome was the count of CPD across the 14-day switch period (days 8–21) compared with the average CPD at baseline (days 1–5). This outcome was determined by counting each daily spent cigarette filter returned and self-reported CPD.[13 28] The correlation between self-report and spent filter return was r=0.98. For the analysis, the daily counts were transformed to a percentage of the participant's average smoking rate from the baseline ad-lib smoking period.

IQOS use

Daily IQOS consumption during the 14-day switch period (days 8–21) was measured by counting each daily spent tobacco HeatSticks.[13 28] For the analysis, the daily HeatStick counts were transformed to a percentage of the participant's baseline smoking rate to quantify the percentage of cigarettes replaced by HeatSticks (ie, substitution rate).

Statistical analyses

Analyses were conducted by using Stata V.18. Longitudinal daily cigarettes and IQOS HeatStick use were analysed over the switch period, normalised to the mean smoking rate over the baseline period and expressed as a percentage. GEE regression methods were used, assuming an exchangeable correlation and a Gaussian distribution family. However, an examination of the normalised outcome values (ratios) revealed that they were bounded at zero and highly skewed. Thus, we relied on bootstrap-based bias-corrected and exact methods for inference. The bootstrap was based on 90 clusters (90 subjects) and 8000 replicates. The bootstrap provided variance estimates for each of the regressions. Hypotheses were tested at a type one error of 0.05, using z-scores generated using the bootstrap SEs. Exact p values and 95% CIs were determined using the bootstrap distributions of coefficient estimates to compare against the parametric values. The distributions of bootstrap replicated parameter estimates were examined and found to be symmetric and to have met assumptions of normality. The bias-corrected and accelerated confidence intervals for comparison are provided.

RESULTS

Sample characteristics

A total of 102 adults attended the baseline visit and enrolled in the study. Among these, 12 participants were excluded from the analysis; 4 withdrew from the study due to lack of interest and time commitment issues while 8 were lost at different time points during the switch phase, resulting in incomplete data. The analytical sample comprised 90 participants (figure 1 and table 1). The sample had slightly more males (57.8%) than females and had an average age of 51.2 years (SD=9.37), with most reporting their race as either white (35.6%) or black (58.9%). Participants predominately smoked menthol cigarettes (70%, n=63), were moderately nicotine dependent (M=5.1, SD=1.9) and smoked 13.4 CPD (SD=6.0) during the 5-day ad-lib baseline line smoking period.

Table 1 Sample characteristics (N=90)

Variable	N (%) or mean (SD)
Baseline smoking rate	13.40 (6.06)
Age	51.20 (9.37)
Race	
Black/African American	53 (59%)
White	32 (36%)
Other	5 (6%)
Sex	
Male	52 (58%)
Female	38 (42%)
Nicotine dependence (FTND)	5.11 (1.91)
Subjective reward (CES)	8.01 (3.16)
Relative reinforcing value	7.69 (3.21)
Break point	
Lower<5	17 (19%)
Higher>5	73 (81%)
Withdrawal symptom relief (MNWS)	−1.73 (3.74)
Craving relief (QSU negative)	−4.10 (6.11)

CES, Cigarette Evaluation Scale; FTND, Fagerstrom Test for Nicotine Dependence; MNWS, Minnesota Nicotine Withdrawal Scale; QSU, Questionnaire of Smoking Urges.

The effects of IQOS use on craving, withdrawal, subjective reward and relative reinforcement

Withdrawal symptoms (M=9.0, SD=5.5) and cigarette cravings (M=11.3, SD=6.5) were low and moderate, respectively, following the 10-hour overnight smoking abstinence. The use of IQOS significantly reduced cigarette craving (change=−3.27 (95% CI −4.42 to −2.11), p<0.0001) but did not significantly alleviate withdrawal symptoms (change=−0.63 (95% CI=−1.32 to 0.06), p=0.07). Participants rated IQOS use as moderately rewarding (M=8.01, average of the highest CES value from visit 1, SD=3.15). During the relative reinforcement task, participants worked on an average of 7.69 trials for cigarette puffs (SD=3.19). On closer inspection, 81.1% of participants found smoking more reinforcing than IQOS (mean break point=9.04, SD=1.53) while the remainder (18.9%) found IQOS similarly reinforcing (mean break point=1.88, SD=1.58).

The effects of IQOS use on CPD

Participants decreased their smoking rate from a baseline average of 13.39 CPD to an average of 5.43 CPD on day 8, decreasing to an average of 4.38 CPD on day 21. During the switch period, daily IQOS slightly increased over time (IRR 1.01, 95% CI 1.003 to 1.018, p=0.007) from an average of 7.74 HeatSticks (95% CI 6.23 to 9.25) per day at day 8 to 8.88 HeatSticks (95% CI 7.16 to 10.60) per day at day 21 (see figure 2). An unadjusted model of IQOS use predicting per cent reduction in CPD indicated that for every IQOS HeatStick used, there was an additional 1.41% reduction in cigarettes (β=−1.41, 95% CI −2.21 to −0.62, p<0.001).

17% of the sample fully switched to IQOS (defined as a reduction to 0 CPD throughout the last 7 days of the switch period, biochemically validated by a CO<5). CO decreased approximately 40% from an average of 15.6 ppm (SD=5.5) at intake to 9.4 ppm (SD=6.3) at day 21 (β=−6.20 (95% CI −7.41 to −4.91) p<0.0001). The average CO among those who fully switched was 4.99 ppm, and the average CO among those who did not was 10.44 ppm. A figure depicting these CO changes is located in online supplemental material.

IQOS-associated effects on cigarette smoking

In the covariate-adjusted model (table 2), smoking was approximately 32% of each subject's original level (intercept=31.68 (95% CI 7.82 to 55.54) p<0.0001 tested against 100%), followed by a negligible decline across days of 0.3% per day (ns). Withdrawal relief, craving relief and the subjective reward of

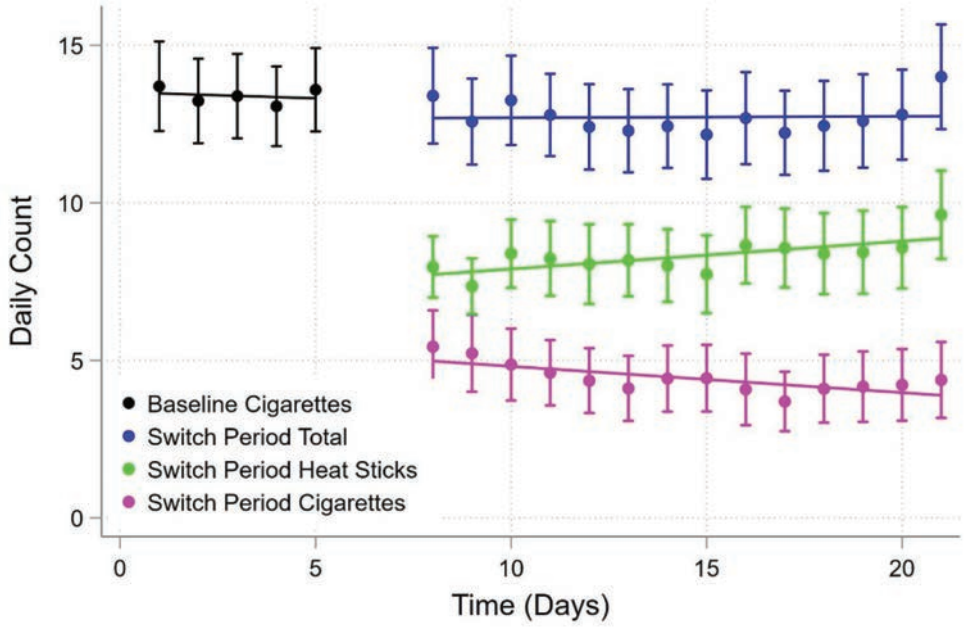

Figure 2 Cigarette Smoking and IQOS HeatStick use.

IQOS use had little impact on the per cent change in CPD. The reinforcing value of smoking relative to IQOS (RRV) was dichotomised at a break point of five (<5 vs ≥5), with higher RRV serving as the reference value. The main effect of lower RRV was nonsignificant, however, the effect increased in magnitude across the switch period at a rate of 1.3% per day (β=−1.31 (95% CI −2.35 to −0.27) p=0.013), an 18% difference in CPD at the end of the 14-day switch period.

Table 2 Positive and negative reinforcing effects of IQOS predicting cigarette smoking during 14-day switch period

					Bootstrap bias	Bootstrap	
Cigarette per cent of baseline	Coefficient	SE	P value	95% CI	Corrected estimates	Exact p values	Percentile CI
Phase							
Time in switch period (days)	−0.28	0.24	0.24	−0.76 to 0.19	−0.29	0.24	−0.77 to 0.19
Negative reinforcement							
Withdrawal Relief (MNWS)	−0.77	0.80	0.33	−2.34 to 0.80	−0.88	0.26	−2.52 to 0.63
Craving relief (QSU negative)	0.98	0.53	0.06	−0.05 to 2.01	0.98	0.07	−0.11 to 1.99
Positive reinforcement							
Subjective reward (CES)	−1.09	1.09	0.32	−3.23 to 1.04	−1.09	0.32	−3.21 to 1.05
Relative reinforcing value (RRV)							
Lower (break point <5)	−4.63	7.38	0.53	−19.10 to 9.83	−4.40	0.56	−19.31 to 10.04
Higher (break point >5)	*Ref*						
Lower RRV×day	−1.31	0.53	0.01	−2.35 to −0.27	−1.32	0.01	−2.38 to −0.28
Higher RRV×day	*Ref*						
Covariates							
Sex							
Male	Ref						
Female	−3.76	5.83	0.52	−15.19 to 7.67	−4.12	0.48	−15.88 to 7.06
Race							
Black/African American	8.15	5.64	0.15	−2.90 to 19.20	8.36	0.29	−2.79 to 19.43
White	Ref						
Other	18.79	18.43	0.31	−17.34 to 54.92	18.45	0.15	−18.49 to 57.54
FTND score	2.43	1.66	0.14	−0.83 to 5.68	2.47	0.15	−0.98 to 5.52
Intercept	31.68	12.18	<0.0001	7.82 to 55.54	31.17	<0.0001	8.26 to 55.47

MNWS (Likert response options: 0=none to 4=severe; range=0–32; α=0.87). Difference score reflects postexposure minus pre-exposure. QSU (Likert response options: 1=strongly disagree to 7=strongly agree; negative reinforcement range=4–28, α=0.81). Difference score reflects postexposure minus pre-exposure. CES (Likert response options: 1=strongly disagree to 7=strongly agree; range=2–14; α=0.87). FTND (range=0–9; α=0.61). MNWS, QSU, CES and FTND coefficients are estimated using raw point values, although significant relationships are translated to standardised values in the text to facilitate interpretation.
CES, Cigarette Evaluation Scale; FTND, Fagerstrom Test for Nicotine Dependence; MNWS, Minnesota Nicotine Withdrawal Scale; QSU, Questionnaire of Smoking Urges.

Table 3 Positive and negative reinforcing effects of IQOS predicting IQOS use during 14-day switch period

IQOS substitution rate	Coefficient	SE	P value	95% CI	Bootstrap bias Corrected estimates	Bootstrap Exact p values	Percentile CI
Phase							
Switch period (time in days)	0.82	0.42	0.049	0.004 to 1.64	0.82	0.04	0.04 to 1.66
Negative reinforcement							
Withdrawal relief (MNWS)	−0.54	1.26	0.67	−3.01 to 1.93	−0.41	0.73	−2.81 to 2.11
Craving relief (QSU negative)	0.65	0.81	0.43	−0.95 to 2.24	0.68	0.40	−0.90 to 2.30
Positive reinforcement							
Subjective reward (CES)	4.26	1.65	0.01	1.03 to 7.50	4.29	0.01	1.08 to 7.51
Relative reinforcing value (RRV)							
Lower (break point <5)	13.70	16.58	0.42	−18.79 to 46.19	13.33	0.42	−18.48 to 47.21
Higher (break point >5)	*Ref*						
Covariates							
Sex							
Male	*Ref*						
Female	−9.14	8.76	0.30	−26.32 to 8.04	−9.45	0.28	−26.13 to 8.66
Race							
Black/African American	1.67	8.50	0.84	−14.99 to 18.33	1.78	0.84	−14.63 to 18.62
White	*Ref*						
Other	−4.92	15.79	0.76	−35.87 to 26.02	−4.55	0.69	−32.58 to 30.47
FTND score	−7.59	2.22	0.001	−11.93 to −3.25	−7.64	0.001	−12.00 to −3.25
Intercept	71.64	14.72	0.000	42.79 to 100.49	72.07	0.000	44.16 to 102.06

MNWS (Likert response options: 0=none to 4=severe; range=0–32; α=0.87). Difference score reflects postexposure minus pre-exposure. QSU (Likert response options: 1=strongly disagree to 7=strongly agree; negative reinforcement range=4–28, α=0.81). Difference score reflects postexposure minus pre-exposure. CES (Likert response options: 1=strongly disagree to 7=strongly agree; range=2–14; α=0.87). FTND (range=0–9; α=0.61). MNWS, QSU, CES and FTND coefficients are estimated using raw point values, although significant relationships are translated to standardised values in the text to facilitate interpretation.
CES, Cigarette Evaluation Scale; FTND, Fagerstrom Test for Nicotine Dependence; MNWS, Minnesota Nicotine Withdrawal Scale; QSU, Questionnaire of Smoking Urges.

Subjective and objective effects of IQOS on HeatStick use

The IQOS substitution rate served as the outcome variable for this analysis. On the first day of the switch phase, IQOS use (table 3, adjusted model) was 72% of the baseline smoking rate (β=71.64 (95% CI 42.79 to 100.48) p<0.0001) and continued to climb by 0.8% per day (β=0.82 (95% CI 0.01 to 1.64) p=0.05). This corresponded to an average increase of 1.15 HeatSticks per day over the 14-day switch period. Neither withdrawal relief, craving relief or reinforcing value predicted IQOS substitution. The subjective reward of IQOS use increased the substitution rate by 4.3% for each one-point increase in subjective reward (β=4.26 (95% CI 1.03 to 7.50) p=0.01). This corresponds to a 13.4% increase in HeatStick use for each SD increase in subjective reward of IQOS use. Finally, higher nicotine dependence levels reduced IQOS use by 7.6 percentage points per one-point increase in the Fagerstrom Test for Nicotine Dependence (FTND) score (β=−7.59 (95% CI −11.93 to −3.25) p<0.001). This corresponds to a 14.4% drop in HeatStick use for an SD increase in the FTND score.

DISCUSSION

This study provides the first formal evaluation of whether adults who smoke cigarettes daily can fully transition from combustible cigarettes to IQOS and if IQOS-associated reward, relative reinforcement and abstinence symptom relief facilitate the transition. The results revealed that IQOS use was associated with a ∼70% reduction in smoking rate and that the level of substitution of HeatSticks for combustible cigarettes was high at 83%. Experiencing IQOS as rewarding (satisfying, liked the taste) fostered IQOS use and its substitution for cigarettes. Almost 20% fully switched to IQOS, and a comparable reinforcing value for IQOS relative to their cigarettes facilitated the transition away from combustible cigarettes. Four out of every five were unable to fully switch from cigarettes to IQOS, at least within a 2-week switch period. These findings emphasise that non-combustible nicotine delivery alternatives must be rewarding and reinforcing to replace combustible cigarettes, as the removal of craving and withdrawal is insufficient.

The current prospective findings document that 80% of people who use IQOS continued to smoke cigarettes, although at ∼30% of their baseline smoking rate. Survey studies conducted across continents have observed that approximately 80% of people who use HTPs also use cigarettes,[8 10] although fewer cigarettes per day than those who exclusively smoke cigarettes.[29] The harm reduction potential of HTP use, such as IQOS, is not likely realised without fully switching. Whether this is understood by those who dual use cigarettes and IQOS will rely heavily on public health communication and labelling efforts. While some research has reported positive effects of health warnings and claims on risk and harm reduction,[30] subgroups of the population, including those who dual use, are likely at greater risk of trying and using IQOS.[31] As such, there will be a need to monitor tobacco industry efforts to market the appeal and risk perceptions of HTPs[32–34] that could undermine public health efforts.

It is important to note that the sample was not seeking to quit smoking immediately and that smoking cessation counselling was not provided to mirror potential patterns of use in the real world. Yet almost 20% completely transitioned to IQOS. Indeed, our preliminary research revealed that switching to IQOS increased interest in quitting smoking among people who were not ready to quit smoking.[20] Similar findings have been documented among people who were initially uninterested in quitting smoking and who used e-cigarettes.[35 36] Those who

have failed to quit smoking with traditional smoking cessation medication are using alternative nicotine delivery products as cessation tools at increasing rates.[37 38] Behavioural counselling focused on aiding the transition to a less harmful product vs abstinence from all nicotine delivery products may translate to less dual use and greater numbers of people who fully transition from cigarette smoking. Given that the overwhelming majority of smoking-related harms are due to inhaling chemicals produced by combustion,[39] such shifts could reduce smoking-attributable morbidity and mortality.

Subjective reward and the relative reinforcing value of IQOS facilitated the substitution of IQOS HeatSticks for cigarettes and fully switching, respectively. The relief of abstinence symptoms did not affect IQOS use or change in cigarette smoking, although replication of these findings will be important as withdrawal symptoms were low. Nevertheless, the findings highlight the importance of product appeal and reinforcer efficacy for non-combustible nicotine products to compete with cigarette smoking. Individuals who were more dependent on nicotine tended to substitute fewer IQOS HeatSticks for their cigarettes. This likely reflects that IQOS nicotine delivery is less than that of combustible cigarettes[14 40] and why the HeatStick substitution rate in our preliminary study exceeded 100% for those who fully switched. As newer versions of IQOS enter the market,[41] assessing how product innovation affects nicotine delivery and use outcomes will be important.

As the first formal investigation of the impact of IQOS use and IQOS-associated effects on cigarette smoking, the study has strengths as well as potential weaknesses. Strengths include mapping validated laboratory tasks onto use behaviour in a natural setting, using a validated spent tobacco product collection protocol,[13 42–44] a 90% retention rate and recruiting a diverse sample. One potential limitation is that we only measured one biomarker of exposure to harmful chemicals—CO, which declined by 40% for the sample as a whole. Completely switching is associated with reduced exposure,[7] yet quantifying levels of harmful chemicals among the 80% of participants with various levels of smoking reduction may have allowed us to characterise toxicant exposure when switching is incomplete. While the design focused on characterising use patterns in the real world, we cannot determine how much cigarette reduction would have resulted from using a placebo device.

Another potential limitation is that the 2-week switch period may not have offered sufficient time for some who dual used to transition to exclusive IQOS use. However, studies of tobacco product switching among non-treatment seekers have shown little behaviour change after 12–14 days.[44–47] Similarly, the durability of smoking behaviour change is unknown without a follow-up period. A standard 6-month follow-up would allow a comparison of IQOS-associated switching and the smoking cessation rates of the three most widely used medications (eg, NRT=17.3%; bupropion=18.9% and varenicline=27.6%).[48] Finally, we recruited a sample not immediately interested in quitting smoking but instead planned to quit within the next 6 months. It is possible that enrolling participants who were interested in using IQOS as part of a smoking cessation attempt would have had greater success in fully transitioning to IQOS.

In conclusion, the study revealed that IQOS use resulted in significant reductions in smoking rate, but only one in five people who smoke were able to switch to IQOS fully. The positive reinforcing effects of IQOS fostered IQOS use and the transition away from combustible cigarettes among those who did completely switch. Future research should determine if IQOS use results in the eventual cessation of cigarette smoking among those seeking treatment and if harm exposure is reduced when switching is not complete.

Contributors JA-M was the principal investigator responsible for the study. JA-M conceptualised the study. JA-M wrote the majority of the manuscript with assistance from OK and FK, including critical review and revision. EPW conducted the analyses, interpreted the results and drafted the results section. AAS critically reviewed and revised the manuscript. JA-M is the guarantor. All authors approved the manuscript.

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