RESEARCH ARTICLE

REVISED Trends in prevalence and patterns of use of a heated tobacco product (*IQOS*™) in Japan: A three-year repeated cross-sectional study [version 2; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: Numerous smoke-free tobacco or nicotine-containing product (TNP) alternatives have been introduced to support individual- and population-level harm reduction relative to continued cigarette smoking. This article details the nationwide prevalence and patterns of TNP use between 2016 and 2019 in Japan following the commercialization of *IQOS*™, a smoke-free heated tobacco product (HTP).

Methods: Cross-sectional surveys were conducted over a period of three study years (2016/2017, 2017/2018, and 2018/2019) in representative samples of the Japanese general adult population and samples of Japanese adult *IQOS* users registered in the *IQOS* owner database of Philip Morris International's affiliate in Japan.

Results: Across the three study years (Y1-Y3), the prevalence of overall current TNP use (Y1-Y3: 18.5%, 18.9%, and 18.2%) and overall TNP use by age and sex remained similar. However, there was a growing shift from cigarette smoking to smoke-free TNP use across the three study years. While the cigarette smoking prevalence (Y1-Y3: 17.6%, 17.3%, and 16.0%) decreased, the use prevalence of smoke-free TNPs, including the HTP *IQOS*™ (Y1-Y3: 1.8%, 3.2%, and 3.3%) and e-cigarettes (Y1-Y3, 0.7%, 1.6%, and 2.0%) increased. At the same time, TNP initiation, TNP relapse, and TNP reinitiation with *IQOS* were all very low across the three study years. Across Y1-Y3, exclusive use of only one type of TNP (Y1-Y3: 82.3%, 75.0%, and 70.4%) decreased, while dual use of two types of TNPs (Y1-Y3: 14.3%, 17.2%, and 16.7%) increased, and poly-TNP use (Y1-Y3: 2.1%, 6.1%, and 10.0%) increased

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markedly. Moreover, the majority of adult *IQOS* users were exclusive *IQOS* users.
Conclusions: These trends in IQOS use behavior suggest that IQOS™ has the potential to switch adult smokers from cigarettes to smoke-free tobacco products, which presents a harm reduction opportunity, and that HTPs are effective tools for complementing current tobacco control measures.

Keywords
Tobacco harm reduction, heated tobacco, smoke-free, IQOS, use patterns, prevalence, smoking initiation, smoking reinitiation

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Competing interests: K.F., N.M., S.A., N.C., P.M., and S.R. are employees of Philip Morris International. M.S. and B.Z. are employees of ARGUS - Statistik und Informationssysteme in Umwelt und Gesundheit GmbH, a consulting statistics and information systems company commissioned by Philip Morris International. M.B. is an employee of Bajec Senseworks consulting, a consulting company commissioned by Philip Morris International.

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REVISED **Amendments from Version 1**

Abstract: The last sentence of the conclusion was rephrased.

Methods section: Links to existing standard questions to capture information on tobacco product use available in the literature were added.

Discussion section: An explanation of the rather large difference in total heated tobacco product (HTP) use prevalence between our study (>5%) and the study of Hori *et al.* (11%) was included. Literature information on *IQOS*/HTP prevalence data among youth was provided; the data show that in Japan uptake of HTPs by youth is rather low. An explanation for the decline in response rates observed for the JA*IQOS* samples across the three study years was provided.

Limitation section of the discussion:
The limitations of the cross-sectional and observational design that does not allow for cause-effect inference or investigation of switching/transition behaviors over time were highlighted. The limitations of the JA*IQOS* samples that were not representative of the *IQOS* users in the Japanese general adult population, but only of the *IQOS* users registered in PMI's Japanese *IQOS* owner database were highlighted. The information that because *IQOS* was the first HTP and had the highest use prevalence in Japan, *IQOS* use behavior may not have represented the use behavior of other HTPs available in Japan was included. The limitations that the study neither addresses quitting behavior, nor covers *IQOS*/HTP underage use, which are critical aspects for the impact of *IQOS*/HTP use on tobacco harm reduction were highlighted.

Conclusion section of the discussion:
The last sentence of the conclusion was rephrased.

Any further responses from the reviewers can be found at the end of the article

Introduction

It is well established that cigarette smoking can lead to numerous negative health outcomes, including premature and preventable death[1]. The burden of smoking on individual and population health has driven health authorities and regulatory bodies to recommend and implement various tobacco control policies[2]. Never initiating or quitting smoking are the most direct ways to alleviate the health burden of smoking[3]. However, strategies aimed at preventing smoking and promoting cessation continue to face numerous challenges, including smokers who are not motivated to quit or who relapse/reinitiate smoking after a period of abstinence[2,4,5]. While smoking prevalence has declined over the last decades, over 1 billion people globally continue to smoke combustible tobacco products today[1,6], and cigarette smoking continues to be responsible for the largest number of preventable deaths worldwide[7,8].

To complement tobacco control efforts[9], tobacco harm reduction strategies have been introduced around the world[10,11]. Tobacco harm reduction includes prevention of tobacco or nicotine-containing product (TNP) use initiation and reinitiation[2,11,12] while ensuring that adult smokers switch completely from combustible TNPs to less harmful smoke-free (i.e., non-combustible) TNPs[13,14].

Unlike cigarettes, which burn tobacco and produce a complex mixture of harmful and potentially harmful constituents (HPHC) through combustion, *IQOS*™, a smoke-free heated tobacco product (HTP) developed by Philip Morris International (PMI), heats a specifically engineered tobacco stick (i.e., *HEETS*™/*HeatSticks*™) to temperatures below the level of combustion[15]. As a consequence, smokers who switch completely to *IQOS* use are exposed to much lower levels of HPHCs than those who continue smoking cigarettes[16–20].

As part of PMI's commitment to a smoke-free future, *IQOS*™ was introduced in Japan in 2014 and is now available in more than 70 countries worldwide, with an estimated 21 million adult users globally[21]. The availability and demand for *IQOS* as an alternative to cigarettes has raised the need to monitor *IQOS* use prevalence and use patterns with the aim of informing public health authorities locally and worldwide. Such findings will further enable regulators to delineate the role of *IQOS* in harm reduction as a viable substitute for cigarettes[2,22].

Building on the reporting of Afolalu *et al.*[23], the aim of the current study was to analyze the temporal trends in TNP use in nationally representative samples of the Japanese general adult population (JGAP) and, separately, in samples of Japanese adult *IQOS* users (JA*IQOS*) from PMI's adult *IQOS* owner database in Japan across three recent years (2016/2017, 2017/2018, and 2018/2019).

Participants and methods

Setting

Cross-sectional surveys in representative samples of the Japanese general adult population (JGAP) and, separately, in samples of Japanese adult *IQOS* users (JA*IQOS*) registered in the *IQOS* owner database of Philip Morris International (PMI)'s affiliate in Japan were initiated in December 2016 and repeated annually over three full calendar years from 2016/2017 to 2018/2019 (Figure 1). Considering that *IQOS*™ was relatively new on the Japanese TNP market in 2016, the *IQOS* use prevalence in the JGAP was expected to be low. Therefore, additional surveys among JA*IQOS* samples were conducted alongside the JGAP surveys to obtain reliable estimates of *IQOS* use patterns among Japanese adult *IQOS* users[23].

Participants and study design

Study participants

To be included in the JGAP or JA*IQOS* samples, individuals had to be of legal age for purchasing TNPs in Japan (i.e., ≥20 years), current residents of Japan, and fluent in Japanese. Those included in the JA*IQOS* samples also had to have used >100 *HEETS*™/*HeatSticks*™ in their lifetime[24], be a current user of *IQOS*™ with *HEETS/HeatSticks*, have access to the internet, and not be currently employed by PMI or its affiliates.

JGAP — Sampling, sample size, and survey mode

The JGAP samples were obtained via a syndicated (Omnibus) survey overseen and coordinated by an independent global consumer research company. The fieldwork provider in Japan was Central Research Services Inc (Tokyo, Japan). The Omnibus surveys employed a three-stage stratified proportional random sampling strategy that included the whole country. In stage 1, sampling points in the 12 Japanese administrative regions

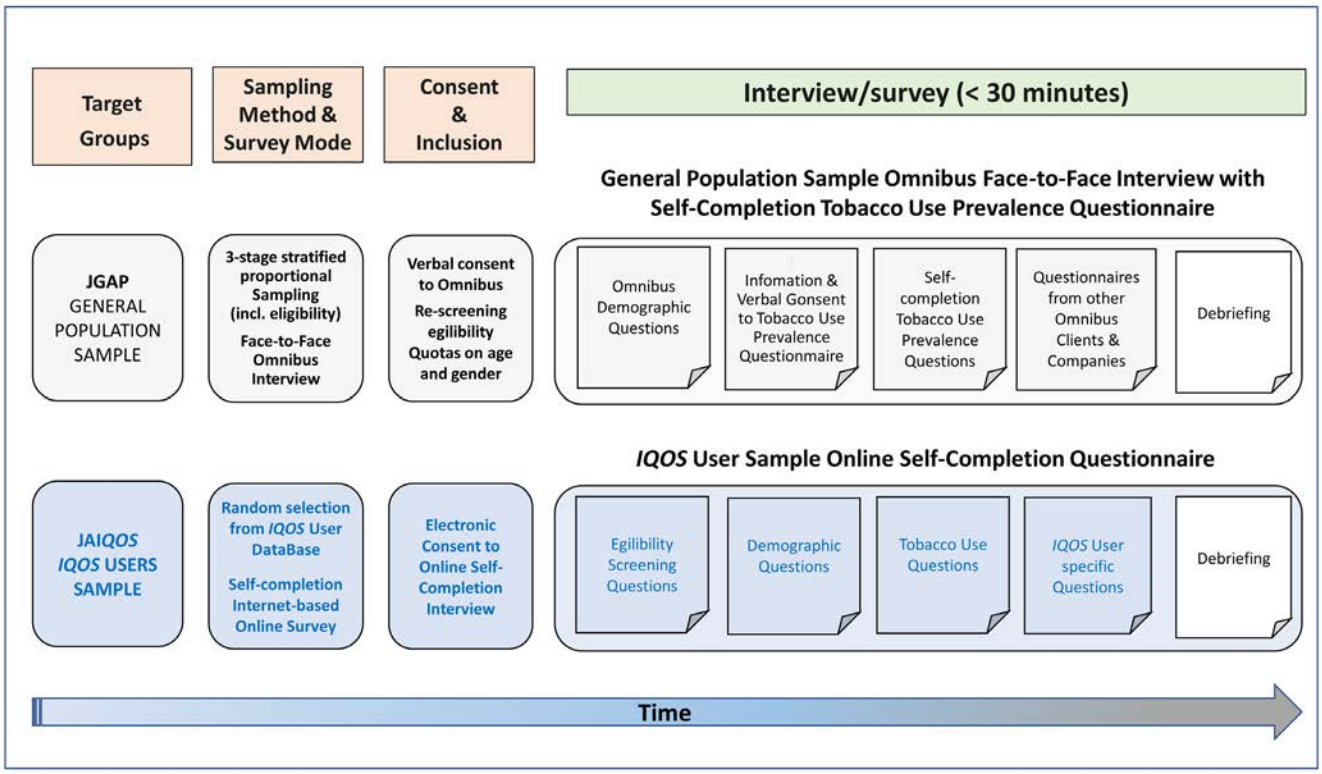

Figure 1. Overall survey study design for the JGAP and JA*IQOS* samples in each wave of the 3-year study period (2016/2017, 2017/2018, and 2018/2019) of the survey fielding. Abbreviations: ICF, informed consent form; *JAIQOS*, sample of adult Japanese *IQOS* users from PMI's *IQOS*™ owner database in Japan; JGAP, representative sample of the Japanese general adult population; PMI, Philip Morris International.

were allocated on the basis of their share of the population[25]. Households within each sampling point were identified in Stage 2 by using an electronic residential map, from which about 40 households were randomly selected. In the final stage 3, participants who met the inclusion criteria were selected from within the sampled households. Within each sampling point, quotas on age and sex were set to ensure the representativeness of the Japanese population.

The annual JGAP sampling consisted of four approximately equal-sized waves spaced throughout each study year to account for potential seasonal differences (Figure 2). A sample size of 5,000 participants per year was sufficient to estimate an *IQOS*™ use prevalence of 5.0% with 95% confidence and a precision of ±0.6% units. In the third year, six survey waves (7,000 participants) were conducted to increase the sample size and improve the accuracy of the estimates.

The JGAP surveys were conducted at participants' homes through in-person face-to-face pen-and-paper interviews. However, to avoid any bias on basis of social desirability of their response regarding their personal TNP use, the participants were handed the "Tobacco Use Prevalence" questionnaire section for self-completion. For completing the Omnibus questionnaires, each participant was given a coupon for JPY 500 (approximately USD 4).

JAIQOS — Sampling, sample size, and survey mode

Upon purchasing an *IQOS*™ device, users were invited to register in the PMI Japan *IQOS* owner database, which included about 350,000 adult *IQOS* owners in July 2017 and reached close to six million in 2019. Considering the demographic age-sex distribution of the database, individuals were randomly selected from the database and invited by email to participate in the survey for each wave.

A sample size of 2,000 participants per year was sufficient to estimate a 50% proportion of exclusive *IQOS*™ use with 95% confidence and a precision of ±2.19% units. Each annual *IQOS* user sample consisted of four approximately equal-sized waves spaced throughout each study year to account for potential seasonal differences (Figure 2), with the aim of recruiting 500 adult participants per wave. The JA*IQOS* surveys were conducted entirely online through computer-assisted self-interviewing. For completing the online survey, participants were given a gift code valued at JPY 500 (about USD 4). The existing standard TNP use questions are available in the literature.

Survey questionnaires

For the present study, the "Tobacco Use Prevalence" questionnaire was developed on the basis of several existing standard TNP use questions available in the literature to capture information

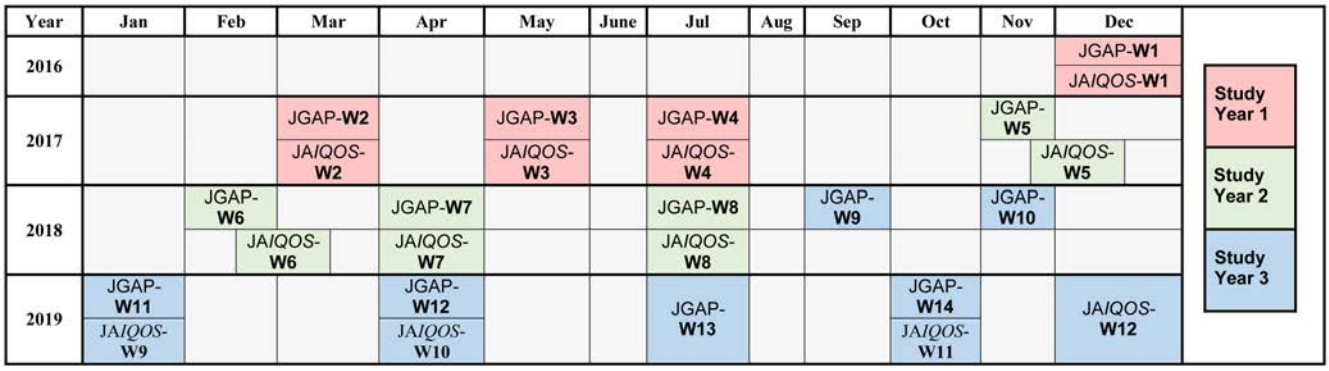

Figure 2. Allocation of the JGAP and JA*IQOS* survey waves over the 3-year study period (2016/2017, 2017/2018, and 2018/2019). Abbreviations: JA*IQOS*, sample of adult Japanese *IQOS*™ users from PMI's *IQOS* owner database in Japan; JGAP, representative sample of the Japanese general adult population; PMI, Philip Morris International; W, survey wave.

about TNP use such as the (i) CDC Adult Tobacco Use Questions of the National Health Interview Survey (NHIS), (ii) WHO/CDC/CPHA Questions of the Global Adult Tobacco Survey (GATS), (iii) NIH/FDA PATH Study questionnaires, and (iv) MHLW Tobacco Use Questions of the Japan National Health and Nutrition Survey. The questionnaire was not specifically validated. In both the JGAP and JA*IQOS* samples, the same questionnaire was used. However, while for the JGAP samples a pen-and-paper self-completion survey mode was used, for the JA*IQOS* samples an online mode was applied. The survey questions can be found in the Extended data.

Ethical conduct of the study

All subjects gave informed consent for inclusion in the study prior to participation. The participants of the JGAP samples gave verbal consent that was recorded by the interviewers as part of the Omnibus interviews, while the participants of the JA*IQOS* samples provided written consent. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and were consistent with Good Epidemiological Practice (GEP)[26]. The study protocol, including the procedures of providing informed consent, were approved by the Hakata Clinic Institutional Review Board (Reference ID: J-186) in Fukuoka, Japan.

Analytical methods

Analyses were conducted using SAS v9.4 (or higher; SAS Inc., Cary, North Carolina, USA). For both the JGAP and JA*IQOS* samples, data were analyzed and summarized descriptively for each study year. For participant characteristics and outcome measures, continuous data are presented as mean and standard deviation (SD) or 95% confidence intervals (CI) and categorical data as number and percentage (95% CI) for the total samples and/or stratified by age and sex. Missing data were not included in the statistical analyses.

The following definitions were applied: "Use/never use" of cigarettes or *IQOS*™ with *HEETS*™*/HeatSticks*™: having/not having used 100 cigarettes or 100 *HEETS/HeatSticks* in the lifetime, to differentiate established cigarette or *IQOS* users from triers or experimenters[24]. "Current use": daily or non-daily use of a TNP at the time of the survey. "Exclusive", "dual", and "poly" use: current use of only one type, two types, or three or more types of TNPs, respectively. "Initiation": the time point at which a participant started established use/smoking of a TNP. "Initiation rate": proportion of initiation in the last 12 months among never TNP users. "Relapse" and "reinitiation": restarting TNP use following a period of quitting all TNPs for ≤12 months and >12 months, respectively.

Prevalence of current TNP use for overall TNPs or by TNP category (cigarettes, *IQOS*™, e-cigarettes, etc.) was calculated in the JGAP samples. For both JGAP and JA*IQOS* samples, the following was calculated: response rates, sample characteristics, and patterns of TNP use (JGAP: exclusive, dual, and poly use; JA*IQOS*: exclusive *IQOS* use and *IQOS* use with combustible or smoke-free TNP) as well as frequency (past 30-day use), intensity (average daily consumption), and history (JGAP: initiation, relapse, and reinitiation with *IQOS*; JA*IQOS*: previous cigarette smoking history before starting *IQOS* use) of TNP use.

Results

Survey dispositions and outcome rates

Regarding survey dispositions and outcome rates (Figure 3), the JGAP samples had a response rate of >30% in each of the three study years (Y1-Y3), which resulted in sample sizes of 4,878, 4,791, and 7,236 for Y1-Y3 of the Omnibus survey, respectively. In the Y1-Y3 JA*IQOS* samples, response rates of 19.4%, 4.7%, and 2.0% yielded sample sizes of 2,000, 2,044, and 2,013, respectively.

Sample characteristics

JGAP samples

Overall, the demographic characteristics of the JGAP samples were similar across Y1-Y3 (Table 1) and comparable with those of the Japanese adult population[25]. The mean (±SD) ages of the Y1-Y3 samples were 53.8 (±17.9), 54.5 (±17.6), and

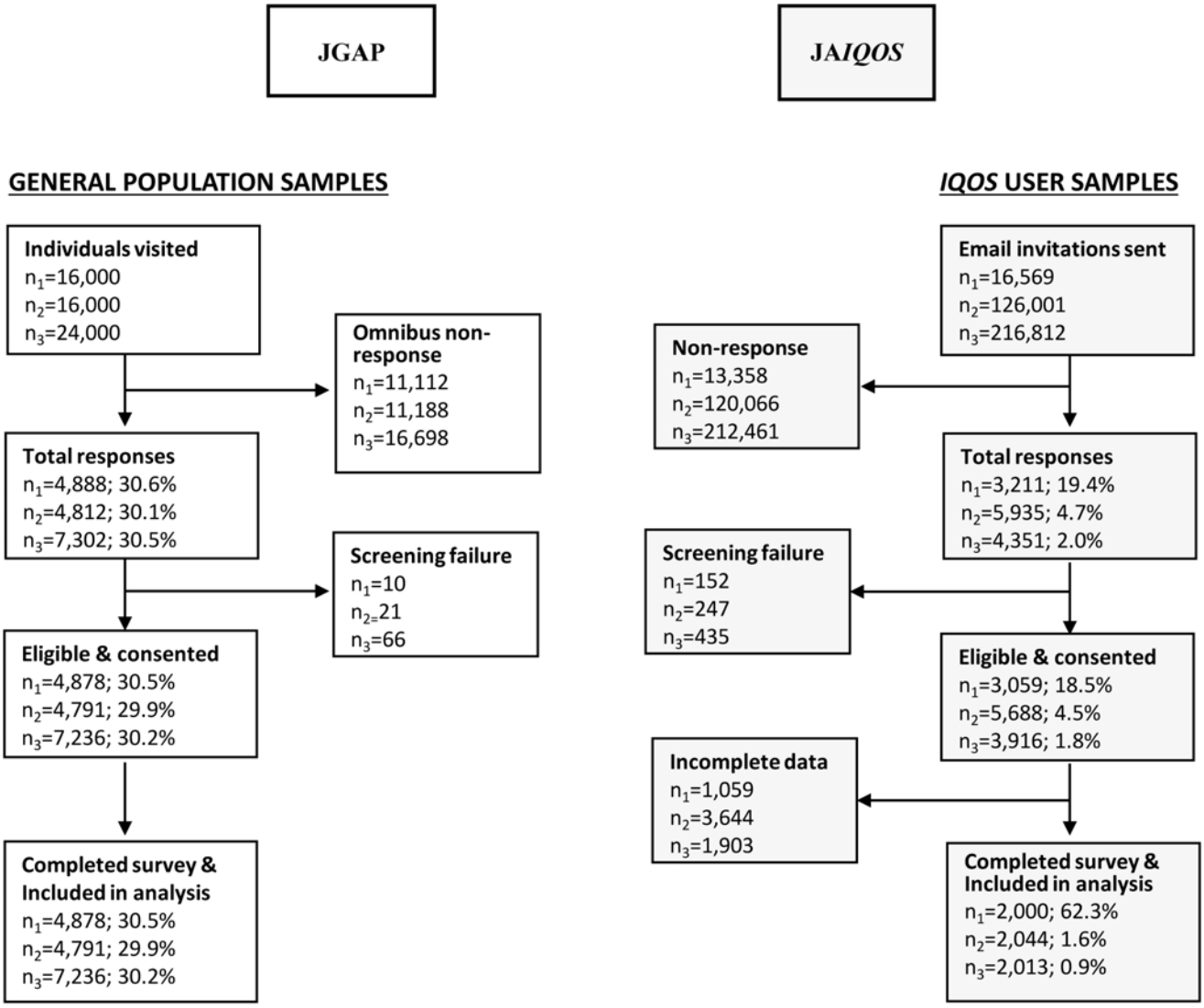

Figure 3. Flow diagram of study samples and survey dispositions in the JGAP and JA*IQOS* samples. Abbreviations: *JAIQOS*, sample of adult Japanese *IQOS*™ users from PMI's *IQOS* owner database in Japan; JGAP, representative sample of the Japanese general adult population; n1-n3, sample sizes for study years 1–3, respectively; PMI, Philip Morris International.

54.8 (±17.8) years, respectively, and each of the samples included slightly more women (Y1-Y3: 51.9%, 53.3% and 53.2%) than men (Y1-Y3: 48.1%, 46.7%, and 46.8%), mirroring the female skew in the actual Japanese population[25].

In each of Y1-Y3, a larger proportion of the sample was based in a major city (Y1-Y3: 27.4%, 28.1%, and 28.6%) than in rural areas (Y1-Y3: 10.0%, 9.3%, and 8.8%). Across Y1-Y3 (Table 1), most of the samples reported high school (Y1-Y3: 49.1%, 50.8%, and 49.8%) or college/university (Y1-Y3: 40.6%, 40.0%, and 41.0%) as the highest level of education, and the most common occupations were homemaker (Y1-Y3: 24.8%, 24.5%, and 24.8%), manual employee (Y1-Y3: 21.8%, 22.8%, and 21.6%), and clerical employee (Y1-Y3: 19.0%, 17.6%, and 17.8%).

JAIQOS samples

Overall, the demographic characteristics of the JA*IQOS* samples were similar across Y1-Y3 (Table 1). The mean (±SD) ages of the Y1-Y3 samples were 38.5 (±9.7), 39.7 (±10.1), and 39.9 (±9.9) years, respectively, and in each of the samples there were more men (Y1-Y3: 81.6%, 80.3%, and 79.9%) than women (Y1-Y3: 18.4%, 19.7%, and 20.1%).

Across Y1-Y3 (Table 1), most of the participants reported completing college/university (Y1-Y3: 56.8%, 54.4%, and 53.9%)

Table 1. Sample characteristics of the JGAP and JA*IQOS* samples.

	Japanese population (2016)* (%)	Number (n) and percentage (% [95% CI])					
		Year 1 (2016/2017)		Year 2 (2017/2018)		Year 3 (2018/2019)	
		JGAP (N=4,878)	JA*IQOS* (N=2,000)	JGAP (N=4,791)	JA*IQOS* (N=2,044)	JGAP (N=7,236)	JA*IQOS* (N=2,013)
Sex							
Men	48.3	2,345 48.1 [46.6–49.5]	1,632 81.6 [79.8–83.3]	2,238 46.7 [45.2–48.2]	1,641 80.3 [78.4–82.0]	3,385 46.8 [45.6–48.0]	1,609 79.9 [78.1–81.7]
Women	51.7	2,533 51.9 [50.5–53.4]	368 18.4 [16.7–20.2]	2,553 53.3 [51.8–54.8]	403 19.7 [18.0–21.6]	3,851 53.2; [52.0–54.4]	404 20.1 [18.3–21.9]
Age (years)							
20–29	12	528 10.8 [9.9–11. 8]	420 21.0 [19.2–22.9]	464 9.7 [8.8–10.6]	346 16.9 [15.3–18.7]	704 9.7 [9–10.5]	330 16.4 [14.8–18.1]
30–39	15.1	723 14.8 [13.8–15.9]	736 36.8 [34.6–39.0]	668 13.9 [12.9–15.0]	710 34.7 [32.6–36.9]	978 13.5 [12.7–14.4]	710 35.3 [33.1–37.5]
40–49	17.8	873 17.9 [16.8–19.1]	568 28.4 [26.4–30.5]	886 18.5 [17.4–19.7]	642 31.4 [29.4–35.5]	1,336 18.5 [17.5–19.4]	644 32.0 [29.9–34.1]
50+	55.2	2,754 56.5 [55.0–57.9]	276 13.8 [12.3–15.4]	2,773 57.9 [56.4–59.3]	346 16.9 [15.3–18.7]	4,218 58.3 [57.1–59.5]	329 16.3 [14.7–18.1]
Mean [±SD]	-	53.8 [±17.9]	38.5 [±9.7]	54.5 [±17.6]	39.7 [±10.1]	54.8 [±17.8]	39.9 [±9.9]
Education							
Junior high school	8.6	454 9.3 [8.5–10.2]	124 6.2 [5.1–7.4]	417 8.7 [7.9–9.6]	139 6.8 [5.7–8.0]	619 8.6 [7.9–9.3]	151 7.5 [6.3–8.8]
High school	40.1	2,395 49.1 [47.6–50.6]	726 36.3 [34.1–38.5]	2,433 50.8 [49.3–52.3]	753 36.8 [34.7–39.0]	3,603 49.8 [48.6–51]	744 37.0 [34.8–39.2]
College/University	41.8	1,980 40.6 [39.2–42.0]	1,135 56.8 [54.5–59.0]	1,917 40.0 [38.6–41.5]	1,114 54.4 [52.3–56.7]	2,967 41.0 [39.8–42.2]	1,085 53.9 [51.6–56.1]
Don't know/NA	9.5	49 1.0 [0.7–1.4]	15 0.8 [0.4–1.3]	24 0.5 [0.3–0.8]	38 1.9 [1.3–2.6]	47 0.6 [0.4–0.9]	33 1.6 [1.1–2.3]
Occupation							
Farming/Agriculture/Fishery	-	80 1.6 [1.3–2.1]	8 0.4 [0.1–0.8]	89 1.9 [1.4–2.3]	15 0.7 [0.4–1.3]	165 2.3 [1.9–2.7]	18 0.9 [0.5–1.5]
Self-employed/Small private business	12.1	538 11.0 [10.1–12.0]	329 16.5 [14.8–18.2]	511 10.7 [9.8–11.6]	347 17.0 [15.3–18.7]	848 11.7 [10.9–12.5]	354 17.6 [15.9–19.4]
Clerical employee	-	927 19.0 [17.9–20.2]	284 14.2 [12.6–15.9]	845 17.6 [16.5–18.8]	228 11.2 [9.8–12.6]	1,289 17.8 [16.9–18.8]	271 13.5 [12–19.4]

	Japanese population (2016)* (%)	Number (n) and percentage (% [95% CI])					
		Year 1 (2016/2017)		Year 2 (2017/2018)		Year 3 (2018/2019)	
		JGAP (N=4,878)	JA*IQOS* (N=2,000)	JGAP (N=4,791)	JA*IQOS* (N=2,044)	JGAP (N=7,236)	JA*IQOS* (N=2,013)
Manual employee	-	1,063 21.8 [20.6–23.0]	268 13.4 [11.9–15.0]	1,094 22.8 [21.6–24.1]	272 13.3 [11.8–14.9]	1,560 21.6 [20.6–22.6]	253 12.6 [11.1–14.1]
Managing profession	46.9	118 2.4 [2.0–2.9]	414 20.7 [18.9–22.6]	108 2.3 [1.8–2.8]	432 21.1 [19.3–23.0]	197 2.7 [2.3–3.2]	398 19.8 [18.0–21.6]
Housewife	19.9	1,211 24.8 [23.6–26.1]	84 4.2 [3.3–5.2]	1,175 24.5 [23.3–25.8]	115 5.6 [4.6–6.8]	1,791 24.8 [23.7–25.8]	95 4.7 [3.8–5.8]
Student	2	106 2.2 [1.7–2.7]	37 1.9 [1.3–2.6]	82 1.7 [1.3–2.2]	34 1.7 [1.1–2.4]	160 2.2 [1.8–2.6]	28 1.4 [0.9–2.1]
Retired/Unemployed	19.1	835 17.1 [16.0–18.3]	26 1.3 [0.8–1.9]	887 18.5 [17.3–19.7]	69 3.4 [2.6–4.3]	1,226 16.9 [16–17.9]	43 2.1 [1.5–2.9]
Don't know/NA	-	NA	550 27.5 [25.5–29.6]	NA	532 26.0 [24.1–28.0]	NA	553 27.5 [25.5–29.5]
Region							
Chubu	-	964 19.8 [18.6–21.0]	310 15.5 [13.9–17.2]	908 19.0 [17.8–20.1]	288 14.1 [12.6–15.7]	964 19.8 [18.6–21.0]	285 14.2 [12.6–15.8]
Chugoku	-	294 6.0 [5.3–6.8]	94 4.7 [3.8–5.8]	281 5.9 [5.2–6.6]	95 4.6 [3.7–5.7]	294 6.0 [5.3–6.8]	87 4.3 [3.4–5.4]
Hokkaido	-	219 4.5 [3.9–5.2]	58 2.9 [2.2–3.8]	214 4.5 [3.8–5.1]	93 4.5 [3.6–5.6]	219 4.5 [3.9–5.2]	93 4.6 [3.7–5.7]
Kanto	-	1,585 32.5 [31.1–33.9]	871 43.6 [41.3–45.8]	1,610 33.6 [32.2–35.0]	827 40.5 [38.3–42.7]	1,585 32.5 [31.1–33.9]	833 41.4 [39.2–43.6]
Kinki	-	757 15.5 [14.5–16.6]	342 17.1 [15.4–18.9]	728 15.2 [14.1–16.3]	349 17.7 [15.4–18.8]	757 15.5 [14.5–16.6]	333 16.5 [14.9–18.3]
Kyusyu	-	549 11.3 [10.3–12.2]	148 7.4 [6.2–8.7]	553 11.5 [10.6–12.5]	190 9.3 [8.0–10.7]	549 11.3 [10.3–12.2]	177 8.8 [7.5–10.2]
Shikoku	-	161 3.3 [2.8–3.9]	41 2.1 [1.4–2.8]	142 3.0 [2.5–3.5]	38 1.9 [1.3–2.6]	161 3.3 [2.8–3.9]	37 1.8 [1.2–2.6]
Tohoku	-	349 7.2 [6.4–8.0]	136 6.8 [5.7–8.0]	355 7.4 [6.6–8.2]	164 8.0 [6.8–9.3]	349 7.2 [6.4–8.0]	168 8.3 [7.1–9.7]

Abbreviations: CI, confidence interval; JA*IQOS*, sample of adult Japanese *IQOS* users from PMI's *IQOS* owner database in Japan; JGAP, representative sample of the Japanese general adult population; NA, not applicable; PMI, Philip Morris International; SD, standard deviation.

*Source: Statistics Bureau of Japan (2015) Source on Education: Statistics Bureau of Japan (2010) Source on Occupation: Public Opinion Survey on the Life of the People (23 June - 10 July 2016).

or high school (Y1-Y3: 36.3%, 36.8%, and 37.0%), and the most common occupations were manager (Y1-Y3: 20.7%, 21.1%, and 19.8%) and self-employed/small business owner (Y1-Y3: 16.5%, 17.0%, and 17.6%).

TNP use in JGAP samples

Prevalence of overall TNP use

Across Y1-Y3, the prevalence of overall current (Y1-Y3: 18.5%, 18.9%, 18.2%) former (Y1-Y3: 18.7%, 16.3%, 16.9%), and never (Y1-Y3: 62.9%, 64.8%, 64.9%) TNP use as well as of TNP use by age and sex were similar (Table 2).

Prevalence of individual TNP use

Cigarette smoking prevalence decreased from 17.6% in Y1 to 16.0% in Y3, while the use prevalence of other TNPs, including HTPs and e-cigarettes, increased (Table 3). The use prevalence of all HTP brands (i.e., *IQOS*™, Ploom/Ploom Tech, and glo) increased across Y1-Y3, and, of all HTP brands surveyed, *IQOS* had the highest use prevalence (Y1-Y3: 1.8%, 3.2%, 3.3%). The use prevalence of e-cigarettes increased from 0.7% to 1.6% to 2.0% during Y1-Y3.

In each of Y1-Y3, cigarette smoking was more prevalent among men (Y1-Y3: 28.2%, 28.4%, and 26.3%) than women (Y1-Y3: 7.9%, 7.7%, and 7.0%) and was highest among 40–49-year-olds (Y1-Y3: 24.6%, 22.2%, and 20.4%). The *IQOS*™ use prevalence in each of Y1-Y3 was higher among men (Y1-Y3: 3.0%, 5.1%, and 5.4%) than women (Y1-Y3: 0.6%, 1.5%, and 1.5%) and was highest among 20–29-year-olds (3.8%) in Y1, but shifted to be highest among 30–39-year-olds in Y2 (8.7%) and Y3 (9.0%). In both Y1 (1.7%) and Y2 (3.0%), e-cigarette use prevalence was highest among 20–29-year-olds, but in Y3 shifted to be highest among 30–39-year-olds (3.9%; Table 3).

Patterns of TNP use

Across Y1-Y3 (Table 4), exclusive use of only one type of TNP decreased (Y1-Y3: 82.3%, 75.0%, and 70.4%), while dual use of two types of TNPs increased (Y1-Y3: 14.3%, 17.2%, and 16.7%) and poly-TNP use increased markedly (Y1-Y3: 2.1%, 6.1%, and 10.0%).

Across Y1-Y3 (Table 4), the greatest proportion, although declining, of participants who reported TNP use were exclusive cigarette smokers (Y1-Y3: 79.5%, 68.1%, and 63.0%), while conversely, the proportion of exclusive *IQOS* users increased (Y1-Y3: 2.5%, 4.8%, and 5.3%), and that of exclusive e-cigarette users remained low (Y1-Y3: 0.3%, 1.1%, and 0.5%).

Frequency and Intensity of TNP use

Among the participants in the JGAP samples in Y1-Y3 who were currently using cigarettes (Y1-Y3: n=852; n=825; and n=1,150), the average number of cigarettes smoked per day (over the last 30 days) appeared to be stable (Y1-Y3: 16.0, 15.7, and 15.5) (Table 5).

TNP initiation/relapse/reinitiation

Among the participants who were never TNP users 12 months prior to the survey (Y1-Y3: n=3,066; n=3,109; and n=4,685), TNP use initiation with cigarettes in the preceding 12 months was considerably higher (Y1-Y3: 0.2%, 0.3%, and 0.2%) than initiation with *IQOS*™ (Y1-Y3: 0.03%, 0.1%, and 0.1%) (Table 6).

Among current TNP users in Y1-Y3 (Y1-Y3: n=894; n=900; and n=1,304), in each year only one participant reinitiated TNP use with *IQOS*™ (Y1-Y3: 0.1%, 0.1%, and 0.07%). No relapse to *IQOS* use was reported in any of the three study years (Table 7).

TNP use in the JA*IQOS* samples

Patterns of TNP Use

Across Y1-Y3, a decreasing majority of participants in the samples used *IQOS*™ exclusively (Y1-Y3: 63.4%, 52.3%, and 49.4%), while the proportion who used *IQOS* together with other smoke-free TNPs increased (Y1-Y3: 7.6%, 17.7%, and 27.0%) and the proportion who used *IQOS* together with combustible TNPs decreased (Y1-Y3: 28.4%, 25.4%, and 23.6%). Consequently, by Y3, a greater proportion of participants used *IQOS* together with other smoke-free TNPs than *IQOS* together with combustible TNPs (Table 8).

Frequency and intensity of TNP use

In each of Y1-Y3 (Table 5), the average number of days of *IQOS*™ use in the last 30 days (Y1-Y3: 29.1, 28.9, and 28.8) and the average number of *HEETS*™*/HeatSticks*™ used on the days of *IQOS* use in the last 30 days (Y1-Y3: 16.2, 16.5, and 15.9) were relatively stable. Thus, the average daily *HEETS/HeatSticks* consumption (over the last 30 days) across Y1-Y3 was similarly stable (Y1-Y3: 15.9, 16.1, and 15.5).

History of TNP use

In each of Y1-Y3, the majority of the JA*IQOS* sample participants had a smoking history before starting *IQOS*™ use (Y1-Y3: 98.0%, 98.7%, and 99.3%), while only a few were never smokers (Y1-Y3: 2.0%, 1.3%, and 0.7%) before starting *IQOS* use.

Discussion

The present study is the first to report data on the prevalence and patterns of TNP use in samples of the Japanese general adult population (JGAP) and samples of Japanese adult *IQOS* users (JA*IQOS*) from a large *IQOS* user database over the same three consecutive years (2016/2017, 2017/2018, and 2018/2019). The findings of this study are consistent with the trends observed by other surveys that have examined the prevalence and patterns of TNP use since the introduction of the HTP *IQOS*™ in Japan in 2014[27–31].

In the JGAP samples, the prevalence of overall TNP use was stable (~18%) across the study years. However, there was a trend towards a declining prevalence of cigarette smoking concurrent with an increase in smoke-free TNP and total HTP use, especially in the case of *IQOS*™ use (from 1.8% in 2016/2017 to 3.3% in 2018/2019).

Although the cross-sectional data of the present study does not allow to draw cause-effect conclusions, given the trends observed, it can be hypothesized that the introduction of

Table 2. **Prevalence of overall current, former, and never TNP use in the JGAP samples overall and by sex and age group.**

		Number (n) and percentage (% [95% CI])								
		Current TNP users			Former TNP users			Never TNP users		
	Age Group (years)	Year 1 (2016/2017)	Year 2 (2017/2018)	Year 3 (2018/2019)	Year 1 (2016/2017)	Year 2 (2017/2018)	Year 3 (2018/2019)	Year 1 (2016/2017)	Year 2 2017/2018)	Year 3 (2018/2019)
All	All	894 18.5 [17.3–19.6]	900 18.9 [17.7–20.1]	1,304 18.2 [17.2–19.1]	905 18.7 [17.5–19.9]	777 16.3 [15.2–17.4]	1,211 16.9 [16.0–17.8]	3,044 62.9 [61.4–64.3]	3,086 64.8 [63.4–66.2]	4,656 64.9 [63.8–66.1]
	20–29	110 20.8 [17.4–24.6]	84 18.1 [14.7–22]	129 18.4 [17.2–19.1]	30 5.7 [3.8–8.1]	25 5.4 [3.5–7.9]	40 5.7 [4.1–7.8]	388 73.5 [69.5–77.3]	354 76.5 [72.3–80.3]	531 75.9 [72.5–79]
	30–39	180 25.0 [21.8–28.4]	173 26.0 [22.6–29.5]	244 25.2 [15.6–21.6]	115 16.0 [13.3–18.9]	92 13.8 [11.2–16.7]	143 14.8 [12.5–17.2]	425 59.0 [55.3–62.7]	401 60.2 [56.3–64]	581 60.0 [56.8–63.2]
	40–49	222 25.5 [22.6–28.6]	213 24.2 [21.3–27.2]	314 23.7 [22.4–28.1]	145 16.7 [14.2–19.4]	136 15.4 [13.1–18]	200 15.1 [13.2–17.2]	502 57.8 [54.4–61.1]	532 60.4 [57–63.7]	809 61.1 [58.4–63.8]
	50+	382 14.0 [12.7–15.4]	430 15.6 [14.2–17.1]	617 14.8 [13.6–15.9]	615 22.6 [21–24.2]	524 19.0 [17.5–20.6]	828 19.8 [18.6–21.1]	1729 63.4 [61.5–65.3]	1,799 65.3 [63.5–67.2]	2,735 65.4 [63.9–66.9]
Men	All	683 29.4 [27.5–31.4]	686 30.9 [29–33]	994 29.7 [28.1–31.3]	723 31.1 [29.2–33.1]	620 28.0 [26.1–29.9]	965 28.8 [27.2–30.4]	916 39.4 [37.4–41.5]	911 41.1 [39–43.2]	1,389 41.5 [39.8–43.2]
	20–29	74 27.6 [22.3–33.4]	62 27.7 [21.9–34.1]	86 24.0 [19.6–28.8]	19 7.1 [4.3–10.9]	12 5.4 [2.7–9.2]	24 6.7 [4.3–9.9]	175 65.3 [59.2–71]	150 67.0 [60.3–73.1]	248 69.3 [64.2–74.1]
	30–39	142 36.0 [31.2–41]	139 40.3 [35–45.7]	189 37.3 [33–41.7]	68 17.3 [13.6–21.4]	55 15.9 [12.2–20.3]	90 17.8 [14.5–21.4]	184 46.7 [41.6–51.8]	151 43.8 [38.4–49.2]	228 45.0 [40.5–49.5]
	40–49	162 38.9 [34.2–43.9]	155 37.0 [32.3–41.9]	241 37.4 [33.6–41.3]	102 24.5 [20.4–29]	96 22.9 [18.9–27.3]	143 22.2 [19–25.7]	152 36.5 [31.9–41.4]	168 40.1 [35.3–45]	260 40.4 [36.5–44.3]
	50+	305 24.5 [22.1–27.1]	330 26.9 [24.3–29.5]	478 26.0 [24–28.1]	534 42.9 [40.1–45.8]	457 37.2 [34.4–40]	708 38.5 [36.2–40.8]	405 32.6 [29.9–35.3]	442 36.0 [33.2–38.8]	653 35.5 [33.3–37.8]
Women	All	211 8.4 [7.3–9.6]	214 8.4 [7.3–9.6]	310 8.1 [7.2–9.1]	182 7.2 [6.2–8.4]	157 6.2 [5.2–7.2]	246 6.4 [5.6–7.3]	2,128 84.4 [82.9–85.9]	2175 85.4 [83.9–86.8]	3,267 85.5 [84.2–86.6]
	20–29	36 13.8 [9.8–18.7]	22 9.2 [5.8–13.7]	43 12.6 [9.2–16.6]	11 4.2 [2.1–7.5]	13 5.4 [2.9–9.2]	16 4.7 [2.6–7.5]	213 81.9 [76.6–86.5]	204 85.4 [80.2–89.6]	283 82.7 [78.3–86.7]
	30–39	38 11.7 [8.3–15.7]	34 10.6 [7.4–14.5]	55 11.9 [9.1–15.3]	47 14.4 [10.7–18.8]	37 11.5 [8.2–15.6]	53 11.5 [8.7–14.8]	241 73.9 [68.8–78.7]	250 77.9 [72.9–82.4]	353 76.6 [72.4–80.4]
	40–49	60 13.2 [10.2–16.8]	58 12.6 [9.6–16]	73 10.8 [8.5–13.4]	43 9.5 [6.9–12.6]	40 8.7 [6.2–11.7]	57 8.4 [6.4–10.8]	350 77.3 [73.1–81.1]	364 78.8 [74.7–82.5]	549 80.9 [77.6–83.8]
	50+	77 5.2 [4.1–6.5]	100 6.6 [5.3–8.0]	139 5.9 [5.0–7.0]	81 5.5 [4.3–6.8]	67 4.4 [3.4–5.6]	120 5.1 [4.2–6.1]	1,324 89.3 [87.6–90.9]	1,357 89.0 [87.3–90.6]	2,082 88.9 [87.5–90.2]

Abbreviations: CI, confidence interval; JGAP, representative sample of the Japanese general adult population.

Table 3. Prevalence of individual TNP use in the JGAP samples overall and by sex and age group.

		Number (n) and percentage (% [95% CI])		
	Study year*	Cigarettes**	*IQOS*™	E-cigarettes
Overall				
	1	852 17.6 [16.5–18.7]	86 1.8 [1.4–2.2]	35 0.7 [0.5–1.1]
	2	825 17.3 [16.2–18.5]	152 3.2 [2.7–3.8]	76 1.6 [1.2–2.0]
	3	1150 16.0 [15.1–17.0]	240 3.3 [2.9–3.8]	146 2.0 [1.7–2.4]
Sex				
	1	654 28.2 [26.3–30.1]	70 3.0 [2.3–3.8]	25 1.1 [0.6–1.6]
Men	2	630 28.4 [26.5–30.4]	114 5.1 [4.2–6.2]	59 2.7 [2.0–3.5]
	3	882 26.3 [24.8–27.9]	181 5.4 [4.6– 6.3]	104 3.1 [2.5–3.8]
	1	198 7.9 [6.8–9.0]	16 0.6 [0.3–1.1]	10 0.4 [0.1–0.8]
Women	2	195 7.7 [6.6–8.8]	38 1.5 [1.0–2.1]	17 1.1 [0.3–1.1]
	3	268 7.0 [6.2–7.9]	59 1.5 [1.1–2.0]	42 1.1 [0.7–1.5]
Age group (years)				
	1	98 18.6 [15.3–22.2]	20 3.8 [2.3–5.8]	9 1.7 [0.7–3.3]
20–29	2	70 15.1 [11.9–18.8]	23 5.0 [3.1–7.4]	14 3.0 [1.6–5.1]
	3	108 15.4 [12.8–18.4]	37 5.3 [3.7–7.3]	22 3.1 [1.9–4.8]
	1	172 23.9 [20.8–27.2]	23 3.2 [2.0–4.8]	6 0.8 [0.3–1.9]
30–39	2	145 21.8 [18.625.2]	58 8.7 [6.6–11.2]	16 2.4 [1.3–3.9]
	3	196 20.2 [17.7–23.0]	87 9.0 [7.2–11.0]	38 3.9 [2.7–5.4]
	1	214 24.6 [21.7–27.7]	25 2.9 [1.8–4.3]	9 1.0 [0.4–2.0]
40–49	2	196 22.2 [19.5–25.2]	36 4.1 [2.8–5.7]	23 2.6 [1.6–3.9]
	3	270 20.4 [18.2–22.7]	62 4.7 [3.6–6.0]	37 2.8 [1.9–3.9]
	1	368 13.5 [12.2–14.9]	18 0.7 [0.3–1.1]	11 0.4 [0.2–0.8]
50+	2	414 15.0 [13.7–16.5]	35 1.3 [0.8–1.8]	23 0.8 [0.5–1.3]
	3	576 13.8 [12.7–14.9]	54 1.3 [0.9–1.7]	49 1.2 [0.8–1.6]

Abbreviations: CI, confidence interval; JGAP, representative sample of the Japanese general adult population; TNP, tobacco or nicotine-containing product.

*Year 1 (2016/2017), Year 2 (2017/2018), and Year 3 (2018/2019)

**Cigarettes include hand-rolled cigarettes

Table 4. TNP use patterns in the JGAP samples.

	Number (n) and percentage (% [95% CI])		
	Year 1 (2016/2017) (n=887)	**Year 2 (2017/2018) (n=900)**	**Year 3 (2018/2019) (n=1,304)**
Exclusive use	730 82.3 [79.6–84.8]	675 75.0 [72.0–77.8]	918 70.4 [67.8–72.9]
Cigarettes*	705 79.5 [76.6–82.1]	613 68.1 [64.9–71.2]	822 63.0 [60.3–65.7]
IQOS™	22 2.5 [1.5–3.8]	43 4.8 [3.4–6.4]	69 5.3 [4.1–6.7]
E-cigarettes	3 0.3 [0.0–1.0]	10 1.1 [0.5–2.1]	6 0.5 [0.1–1.0]
One other TNP	-	9 1.0 [0.4–1.9]	21 1.6 [0.9–2.5]
Dual use	127 14.3 [12.0–16.8]	155 17.2 [14.8–19.9]	218 16.7 [14.7–18.9]
Cigarettes + other product	64 7.2 [5.6–9.2]	72 8.0 [6.3–10.0]	110 8.4 [6.9–10.1]
Cigarettes + *IQOS*	40 4.5 [3.2–6.1]	62 6.9 [5.3–8.8]	62 4.8 [3.6–6.1]
Cigarettes + e-cigarettes	13 1.5 [0.7–2.5]	15 1.7 [0.9–2.8]	11 0.8 [0.4–1.6]
IQOS + e-cigarettes	5.0 0.6 [0.1–1.4]	4 0.4 [0.1–1.2]	15 1.2 [0.6–1.9]
IQOS + other product	4 0.5 [0.1–1.2]	2 0.2 [0.0–0.9]	11 0.8 [0.4–1.6]
E–cigarettes + other product	1 0.1 [0.0–0.7]	-	8 0.6 [0.2–1.3]
Two other products	–	–	1 0.1 [0.0–0.5]
Poly use	19 2.1 [1.2–3.4]	55 6.1 [4.6–7.9]	131 10.0 [8.4–11.9]
Cigarettes + *IQOS* + e-cigarettes	10 1.1 [0.5–2.1]	16 1.8 [1.0–2.9]	36 2.8 [1.9–3.9]
Cigarettes + *IQOS* + other product(s)	4 0.5 [0.1–1.2]	7 0.8 [0.3–1.6]	18 1.4 [0.8–2.2]
Cigarettes + e-cigarettes + other product(s)	3 0.3 [0.0–1.0]	18 2.0 [1.1–3.2]	45 3.5 [2.5– 4.6]
Cigarettes + other products	2 0.2 [0.0–0.9]	1 0.1 [0.0–0.7]	8 0.6 [0.2–1.3]
Cigarettes + *IQOS* + e-cigarettes + other product(s)	–	9 1.0 [0.4–1.9]	18 1.4 [0.8–2.2]
IQOS + e-cigarettes + other product(s)	–	4 0.4 [0.1–1.2]	5 0.4 [0.1–0.9]
IQOS + other products	–	–	1 0.1 [0.0–0.5]
E-cigarettes + other products	–	–	–
Three or more other products	–	–	–
Undefined	11 1.2 [0.6–2.3]	15 1.7 [0.9–2.8]	37 2.8 [2.0–3.9]

Abbreviations: CI, confidence interval; JGAP, representative sample of the Japanese general adult population.

*Cigarettes include hand-rolled cigarettes

Table 5. Frequency and intensity of cigarette consumption among current cigarette smokers in the JGAP samples and of *HEETS*™/*HeatSticks*™ consumption among current *IQOS* users in the JA*IQOS* samples across the three study years.

	Mean [95% CI]		
	Year 1*	**Year 2**	**Year 3**
Current cigarette smokers — JGAP	(n=852)	(n=825)	(n=1,150)
Cigarettes smoked per day			
Number of days of cigarette smoking in the last 30 days	29.4 [29.1–29.7]	29.2 [28.9–29.5]	29.3 [29.0–29.5]
Average number of cigarettes smoked per day (based on smoking days only)	16.2 [15.5–16.8]	15.9 [15.3–16.6]	15.8 [15.3–16.3]
Average number of cigarettes smoked per day in terms of the last 30-day period	16.0 [15.3–16.6]	15.7 [15.1–16.4]	15.5 [14.9–16.0]
Current *IQOS*™ users — JA*IQOS*	(n=2,000)	(n=2,044)	(n=2,013)
HEETS™/*HeatSticks*™ used per day			
Number of days of *IQOS*™ use in the last 30 days	29.1 [28.9–29.3]	28.9 [28.7–29.1]	28.8 [28.5–29.0]
Average number of *HEETS/HeatSticks* used per day (based on usage days only)	16.2 [15.8–16.6]	16.5 [16.1–16.9]	15.9 [15.5–16.3]
Average number of *HEETS/HeatSticks* used per day in terms of the last 30-day period	15.9 [15.5–16.3]	16.1 [15.7–16.5]	15.5 [15.1–15.9]

Abbreviations: CI, confidence interval; JA*IQOS*, sample of adult Japanese *IQOS*™ users from PMI's *IQOS* owner database in Japan; JGAP, representative sample of the Japanese general adult population; PMI, Philip Morris International

* Year 1 (2016/2017), Year 2 (2017/2018), Year 3 (2018/2019)

Table 6. TNP initiation in JGAP samples among never TNP users.

	Never TNP Users Number (n) and percentage (% [95% CI])		
	Year 1* (n=3,066)	**Year 2 (n=3,109)**	**Year 3 (n=4,685)**
Initiation with			
Cigarettes**	7 0.2 [0.0–0.5]	9 0.3 [0.1–0.6]	10 0.2 [0.1–0.4]
IQOS™ with *HEETS*™/*HeatSticks*™	1 0.03 [0.0–0.2]	4 0.1 [0.0–0.4]	5 0.1 [0.0–0.3]

Abbreviations: CI, confidence interval, JA*IQOS*, sample of adult Japanese *IQOS*™ users from PMI's *IQOS* owner database in Japan; JGAP, representative sample of the Japanese general adult population; NA, not applicable; PMI, Philip Morris International; TNP, tobacco or nicotine-containing product.

*Year 1 (2016/2017), Year 2 (2017/2018), and Year 3 (2018/2019)

** Cigarettes include hand-rolled cigarettes

Note: Initiation with e-cigarettes was not measured as part of the study.

Table 7. Relapse and reinitiation of TNP use with *IQOS*™ among current TNP users in the JGAP samples.

	Current TNP users Number (n) and percentage (% [95% CI])		
	Year 1* (n=894)	**Year 2 (n=900)**	**Year 3 (n=1,304)**
Relapse to *IQOS*™	0 0.0 [0.0–0.5]	0 0.0 [0.0–0.5]	0 0.0 [0.0–0.3]
Reinitiation with *IQOS*	1 0.1 [0.0–0.7]	1 0.1 [0.0–0.7]	1 0.07 [0.0–0.5]

Abbreviations: CI, confidence interval; JGAP, representative sample of the Japanese general adult population; TNP, tobacco or nicotine-containing product.

*Year 1 (2016/2017), Year 2 (2017/2018), and Year 3 (2018/2019)

Table 8. Distribution of TNP use patterns in the JA*IQOS* sample.

	Number (n) and percentage (% [95% CI])		
	Year 1* (n=1,946)	**Year 2 (n=1,972)**	**Year 3 (n=1,977)**
IQOS™ only	1,234 63.4 [61.2–65.6]	1,032 52.3 [50.1–54.6]	976 49.4 [47.1–51.6]
IQOS + combustible TNP	552 28.4 [26.3–30.5]	501 25.4 [23.4–27.4]	467 23.6 [21.7–25.6]
IQOS + smoke-free TNP	148 7.6 [6.4–8.9]	350 17.7 [16.0–19.6]	534 27.0 [25.0–29.1]
Undefined	12 0.6 [0.3-1.1]	89 4.5 [3.6-5.6]	0

Abbreviations: CI, confidence interval; JA*IQOS*, sample of adult Japanese *IQOS* users from PMI's *IQOS*™ owner database in Japan; JGAP, representative sample of the Japanese general adult population; PMI, Philip Morris International; TNP, tobacco or nicotine-containing product.

*Year 1 (2016/2017), Year 2 (2017/2018), and Year 3 (2018/2019)

smoke-free TNPs does not lead to an unintended increase in overall TNP use in the general adult population, but rather drives a shift in TNP use patterns from cigarettes to smoke-free TNPs. When considered alongside the low TNP use initiation rates with *IQOS*™, the present findings further imply that the introduction of smoke-free TNPs has not led to an unintended increase in TNP use among adult non-users. This assumption is partially supported by the findings of other studies[32,33] and is consistent with the findings of Cummings *et al.*[4], who reported an accelerated reduction in cigarette sales in Japan concurrent with the introduction and increase in HTP sales.

In agreement with Cummings *et al.*[4] and others[30,31], the total HTP use prevalence in year 3 of the present study was over 5%. A previous study had reported a total HTP use prevalence of 11%[34]. The prevalence of cigarette smoking observed in each year of the present study was in agreement with the prevalence data from the Japan National Health and Nutrition Survey for 2017 (18.8%)[27], 2018 (18.9%)[28], and 2019 (17.7%)[29]. Additionally, the present cigarette and overall TNP use data were well in line with those from other contemporaneous surveys[30,31,35,36]. Tabuchi *et al.*[32] reported an *IQOS*™ use prevalence of 3.6% in 2017, which is higher than that observed in the present study (1.8%) for the same year. For 2018, Sutanto *et al.*[37] reported an any-brand HTP use prevalence (i.e., *IQOS*™, glo, and Ploom/Ploom Tech) of 2.7%, which is less than that observed in our study (3.2%) for *IQOS* use alone. These discrepancies are likely due to methodological differences (i.e., cross-sectional vs. longitudinal design or in-person vs. online interview) as described previously[23].

The above mentioned rather large difference in total HTP use prevalence between our study (5%) and the study of Hori *et al.* (11%)[34], respectively, may have resulted from multiple conceptual and methodological differences including i.a., (i) cross-sectional vs. longitudinal design, (ii) in-person vs. online interview (iii) age ≥20 years vs. age range 15–69 years, (iv) no weighting methods vs. inverse probability weighting, (v) no adjustments vs. adjustment of the data, (vi) definition of current use [at the time of the survey vs. past 30 days], and (vii) lifetime use criterion [100 tobacco sticks] vs. no lifetime use criterion to qualify as a HTP user. Of all these aspects, however, we believe that the difference in the age groups included in both studies (i.e., age ≥20 year in our study vs. 15–69 years in the Hori *et al.* study[34]) with very low HTP use prevalence in 60+ age groups, had the largest impact on the difference in the total HTP prevalence observed between our study and the study of Hori *et al.*[34]

In the JGAP samples, the age and sex distribution observed among current tobacco product users in each of the study year as well as the current HTP use patterns are similar to the corresponding data of the Japan National Health and Nutrition Survey for the same years[27–29]. Similarly, in agreement with the Japanese national survey[27–29], the results presented here indicate that the majority of HTP users are using HTP exclusively. The average number of *HEETS*™*/HeatSticks*™ used per day (Y1-Y3: 15.9, 16.1, and 15.5, respectively) in the JA*IQOS* samples was relatively stable across the study years and comparable with the 14.3 *HEETS/HeatSticks* used per day reported for Japan by Jones *et al.*[31] in 2019. Moreover, the *HEETS/HeatSticks* consumption per day in the JA*IQOS* samples was very close to the average number of cigarettes consumed per day (Y1-Y3: 16.0, 15.7, and 15.5, respectively) among cigarette smokers in the JGAP samples, suggesting that *IQOS* users are not increasing their daily consumption upon switching from cigarettes to *IQOS*™.

TNP initiation, relapse, and reinitiation rates observed with *IQOS*™ in the present study were in all three years and in

both samples relatively low, suggesting that *IQOS* uptake was limited to existing smokers who had switched to *IQOS*. Similarly, Sutanto *et al.*[37] concluded that "*virtually all HTP users were current cigarette smokers (67.8%) or former smokers (25.0%); and that only 1.0% of HTP users were never smokers*." Jones *et al.*[31] observed that HTP uptake in 2019 occurred "*almost exclusively among current tobacco users in Japan, with negligible uptake among never tobacco users*." In both samples in the present study, nearly all current *IQOS* users had started TNP use with cigarette smoking. These findings suggest that *IQOS* uptake is occurring among current adult smokers, which is in alignment with both the principles of harm reduction and the United States Food and Drug Administration's (FDA) conclusion that *IQOS* has "*potential benefit to population health*"[20].

Our study is based on Japanese adult participants only, but with regard to tobacco harm reduction, also unintended uptake of *IQOS*™/HTPs among youth and young adults may be of concern. In the literature, tobacco initiation with *IQOS*/HTPs and prevalence of *IQOS*/HTP use among youth has been reported to be low in Japan. Based on data from the representative longitudinal internet-based JASTIS study in Japan, the 2015, 2016, and 2017 prevalence of ever use of *IQOS* with *HEETS*™/*HeatSticks*™ among youth (15–19 years) in the past 30 days was estimated to be 0.6%, 2.3%, and 2.0%, respectively[32]. Similarly, in a nationwide survey in Japan among middle-school and high-school students, respectively, the estimated 2017/2018 prevalence for ever-HTP use (even one puff) in lifetime (1.1% and 2.2%), ever HTP use in the past 30 days (0.5% and 0.9%), and daily HTP use (0.1% and 0.1%) was very low[38].

Lastly, regarding the decline in response rates observed for the JA*IQOS* samples across the three study years, this decline can be explained by the fact that over time the *IQOS* users increasingly received email invitations to various PMI surveys which probably has generated a lower willingness to participate in our scientific surveys.

Strengths and limitations

Major strengths of this study, among those previously described[23], include the annual repeated data collection using the same sampling framework and methods, face-to-face interviews, and nationally representative samples.

The limitations of the current study include foremost the cross-sectional and observational design that does not allow for cause-effect inference or investigation of switching/transition behaviors over time. Moreover, the study may have suffered from all biases typically associated with self-reported measures, such as response bias including i.a., recall, social desirability, or order effect bias, as well as sampling and selection bias. To overcome possible sampling and selection bias, particularly in the JA*IQOS* samples, the response rates were monitored and compared against pre-established quotas on the basis of age and sex. Furthermore, the JA*IQOS* samples, which we used to obtain reliable estimates for investigating the patterns of *IQOS*™ use, were not representative of the *IQOS* users in the Japanese general adult population, but only of the *IQOS* users registered in the large database of PMI's affiliate in Japan. Similarly, because *IQOS* was the first HTP and had the highest use prevalence in Japan, *IQOS* use behavior may not have represented the use behavior of other HTPs available in Japan. Finally, the present study neither addresses quitting behavior, e.g., investigation of whether *IQOS*™/HTP use prevents those TNP users who are willing to quit all TNPs to do so, nor does the study cover *IQOS*/HTP underage use, which are critical aspects for assessing the impact of *IQOS*/HTP use on tobacco harm reduction.

Conclusions

While cigarette smoking remains the most prevalent way of consuming TNPs in Japan, a significant and growing number of adult Japanese smokers have switched to smoke-free alternatives such as *IQOS*™, with the majority using these products exclusively. Additionally, there has been low initiation with *IQOS* among TNP never and former users. Taken together, the findings of the present study on the prevalence and patterns of *IQOS* use indicate that the trends in *IQOS* use behavior suggest that *IQOS* has the potential to switch adult smokers from cigarettes to smoke-free tobacco products, which presents a harm reduction opportunity, and that HTPs are effective tools for complementing current tobacco control efforts[14].

Data availability

Underlying data

INTERVALS: YEAR 1–3 DATA (SAS DATASETS, CC-BY 4.0), https://doi.org/10.26126/intervals.r35iml.1[39]

This project contains the following underlying data:

- SAS datafiles in the Clinical Data Interchange Standards Consortium (CDISC) Analysis Data Model (ADaM) structure (www.cdisc.org/standards) for each of the study years 1–3.
  - The ADSL (adsl_y1_jp.sas7bdat, adsl_y2_jp.sas7bdat, and adsl_y3_jp.sas7bdat,) datasets are the Subject Level Analysis Datasets and contain the main information on participants identifier, demographics, and tobacco and/or nicotine product use groups and patterns to facilitate analysis and interpretation of analysis.
  - The ADQS (adqs_y1_jp.sas7bdat, adqs_y2_jp.sas7bdat, and adqs_y3_jp.sas7bdat) datasets are the Questionnaire Analysis Datasets and contain specific information on the study survey, i.e., all questions and items answered by participants in the survey.
  - The ADEX (adex_y1_jp.sas7bdat, adex_y2_jp.sas7bdat, and adex_y3_jp.sas7bdat) datasets are the Exposure Analysis Datasets and contain specific

information on the TNP use exposure, i.e., all questions and items answered by participants in the survey related to their product use.

- The ADAM Metadata Files (ADaM_PMX01JP_AnY1_Metadata, ADaM_PMX01JP_AnY2_Metadata, and ADaM_PMX01JP_AnY3_Metadata) contain the datasets and variable labels and definitions, code lists to decode the variables names, terms and values, and the methods and computational algorithms to derive the analytical datasets.

- Study Year 1 Data and Metadata: https://doi.org/10.26126/intervals.8ybcxu
- Study Year 2 Data and Metadata: https://doi.org/10.26126/intervals.hxaf2v
- Study Year 3 Data and Metadata: https://doi.org/10.26126/intervals.6jbifs

Extended data

INTERVALS: Tobacco Use Prevalence Questionnaire. https://doi.org/10.26126/intervals.rxhx4a.1[39]

This project contains the following extended data:

- Tobacco Use Prevalence questionnaire (Tobacco Use Prevalence Questionnaire_engl_jap.pdf) is the questionnaire administered in the general population and *IQOS* user surveys (English and Japanese version).

Reporting guideline

This study followed the STROBE reporting guideline.

INTERVALS: STROBE checklist and flow chart for "Trends in Prevalence and Patterns of Use of a Heated Tobacco Product (*IQOS*™) in Japan: A 3-Year Repeated Cross-Sectional Study", are available: https://doi.org/10.26126/intervals.dluspw

Acknowledgements

The authors would like to thank all those who participated in this study. The authors also would like to thank Antonio Ramazzotti for reviewing and providing insightful comments on this publication.

References

1. West R: **Tobacco smoking: Health impact, prevalence, correlates and interventions.** *Psychol Health.* 2017; **32**(8): 1018–1036.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
2. Institute of Medicine Committee to Assess the Science Base for Tobacco Harm R: **Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction.** Washington (DC): National Academies Press (US); 2001.
Reference Source
3. General OotS: **Smoking cessation: a report of the Surgeon General.** In: Services USDoHaH, ed. Rockville, MD: Public Heath Service; 2020.
Reference Source
4. Cummings KM, Nahhas GJ, Sweanor DT: **What Is Accounting for the Rapid Decline in Cigarette Sales in Japan?** *Int J Environ Res Public Health.* 2020; **17**(10): 3570.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
5. Le Houezec J, McNeill A, Britton J: **Tobacco, nicotine and harm reduction.** *Drug Alcohol Rev.* 2011; **30**(2): 119–123.
PubMed Abstract | **Publisher Full Text**
6. Ng M, Freeman MK, Fleming TD, *et al.*: **Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012.** *JAMA.* 2014; **311**(2): 183–192.
PubMed Abstract | **Publisher Full Text**
7. **Tobacco.** Paris: OECD Publishing; 2020.
Reference Source
8. Gowing LR, Ali RL, Allsop S, *et al.*: **Global statistics on addictive behaviours: 2014 status report.** *Addiction.* 2015; **110**(6): 904–919.
PubMed Abstract | **Publisher Full Text**
9. Warner KE: **How to Think-Not Feel-about Tobacco Harm Reduction.** *Nicotine Tob Res.* 2019; **21**(10): 1299–1309.
PubMed Abstract | **Publisher Full Text**
10. Centers for Disease Control and Prevention: **Best Practices for Comprehensive Tobacco Control Programs.** In: Department of Health and Human Services CDC, Prevention National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, eds. Atlanta, GA, USA, 2014.
Reference Source
11. Gottlieb S, Zeller M: **A Nicotine-Focused Framework for Public Health.** *N Engl J Med.* 2017; **377**(12): 1111–1114.
PubMed Abstract | **Publisher Full Text**
12. Abrams DB, Glasser AM, Pearson JL, *et al.*: **Harm Minimization and Tobacco Control: Reframing Societal Views of Nicotine Use to Rapidly Save Lives.** *Annu Rev Public Health.* 2018; **39**: 193–213.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
13. Peitsch MC, Polosa R, Proctor C, *et al.*: **Next-generation tobacco and nicotine products: Substantiating harm reduction and supporting tobacco regulatory science.** *Toxicol Res Appl.* 2018; **2**.
Publisher Full Text
14. Hatsukami DK, Carroll DM: **Tobacco harm reduction: Past history, current controversies and a proposed approach for the future.** *Prev Med.* 2020; **140**: 106099.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
15. Smith MR, Clark B, Lüdicke F, *et al.*: **Evaluation of the Tobacco Heating System 2.2. Part 1: Description of the system and the scientific assessment program.** *Regul Toxicol Pharmacol.* 2016; **81 Suppl 2**: S17–S26.
PubMed Abstract | **Publisher Full Text**
16. Lüdicke F, Picavet P, Baker G, *et al.*: **Effects of Switching to the Tobacco Heating System 2.2 Menthol, Smoking Abstinence, or Continued Cigarette Smoking on Biomarkers of Exposure: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confinement and Ambulatory Settings (Part 1).** *Nicotine Tob Res.* 2018; **20**(2): 161–172.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
17. Lüdicke F, Picavet P, Baker G, *et al.*: **Effects of Switching to the Menthol Tobacco Heating System 2.2, Smoking Abstinence, or Continued Cigarette Smoking on Clinically Relevant Risk Markers: A Randomized, Controlled, Open-Label, Multicenter Study in Sequential Confinement and Ambulatory Settings (Part 2).** *Nicotine Tob Res.* 2018; **20**(2): 173–182.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
18. Haziza C, de La Bourdonnaye G, Donelli A, *et al.*: **Reduction in Exposure to Selected Harmful and Potentially Harmful Constituents Approaching Those Observed Upon Smoking Abstinence in Smokers Switching to the Menthol Tobacco Heating System 2.2 for 3 Months (Part 1).** *Nicotine Tob Res.* 2020; **22**(4): 539–548.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
19. Haziza C, de La Bourdonnaye G, Donelli A, *et al.*: **Favorable Changes in Biomarkers of Potential Harm to Reduce the Adverse Health Effects of Smoking in Smokers Switching to the Menthol Tobacco Heating System 2.2 for 3 Months (Part 2).** *Nicotine Tob Res.* 2020; **22**(4): 549–559.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**
20. FDA: **FDA Authorizes Marketing of IQOS Tobacco Heating System with 'Reduced Exposure' Information.** FDA, 2020.
Reference Source

21. Costanzo R, Baker G: **Are heated tobacco products (HTPs) a public health opportunity?** *Medical Word.* 2020; **1**: 95–100.
Reference Source

22. Administration FDA: **Guidance for industry - Modified risk tobacco product applications - Draft guidance.** In: Services United States Department of Health and Human Services, eds. Center for Tobacco Products; Silver Spring, MD, USA, 2012.
Reference Source

23. Afolalu EF, Langer P, Fischer K, *et al.*: **Prevalence and patterns of tobacco and/or nicotine product use in Japan (2017) after the launch of a heated tobacco product (*IQOS*®): a cross-sectional study [version 2; peer review: 2 approved].** *F1000Res.* 2021; **10**: 504.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

24. NHIS: **Adult Tobacco Use - Glossary**. 2019.
Reference Source

25. Statistics Bureau of Japan: **Japan 2015 Population Census**. 2015.
Reference Source

26. Hoffmann W, Latza U, Baumeister SE, *et al.*: **Guidelines and recommendations for ensuring Good Epidemiological Practice (GEP): a guideline developed by the German Society for Epidemiology (DGEpi).** *Eur J Epidemiol.* 2019; **34**(3): 301–17.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

27. Welfare MoHLa: **Summary: The Japan National Health and Nutrition Survey.** In: Innovation NIoB, Nutrition NIoHa, eds. Japan, 2017.
Reference Source

28. Welfare MoHLa: **Summary: The Japan National Health and Nutrition Survey.** In: Innovation NIoB, Nutrition NIoHa, eds. Japan, 2018.
Reference Source

29. Welfare MoHLa: **Summary: The Japan National Health and Nutrition Survey.** In: Innovation NIoB, Nutrition NIoHa, eds. Japan, 2019.
Reference Source

30. Adamson J, Kanitscheider C, Prasad K, *et al.*: **Results from a 2018 cross-sectional survey in Tokyo, Osaka and Sendai to assess tobacco and nicotine product usage after the introduction of heated tobacco products (HTPs) in Japan.** *Harm Reduct J.* 2020; **17**(1): 32.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

31. Jones JD, Adamson J, Kanitscheider C, *et al.*: **Cross-sectional Survey to Assess Tobacco and Nicotine Product Use since the Introduction of Tobacco Heating Products in Japan: Wave 1.** *Tob Regul Sci.* 2021; **7**(3): 210–220.
Publisher Full Text

32. Tabuchi T, Gallus S, Shinozaki T, *et al.*: **Heat-not-burn tobacco product use in Japan: its prevalence, predictors and perceived symptoms from exposure to secondhand heat-not-burn tobacco aerosol.** *Tob Control.* 2018; **27**(e1): e25–e33.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

33. Matsuyama Y, Tabuchi T: **Heated tobacco product use and combustible cigarette smoking relapse/initiation among former/never smokers in Japan: the JASTIS 2019 study with 1-year follow-up.** *Tob Control.* 2022; **31**(4): 520–526.
PubMed Abstract | **Publisher Full Text**

34. Hori A, Tabuchi T, Kunugita N: **Rapid increase in heated tobacco product (HTP) use from 2015 to 2019: from the Japan 'Society and New Tobacco' Internet Survey (JASTIS).** *Tob Control.* 2020; **30**(4): 474–475.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

35. Japan Tobacco Inc: **Japan Tobacco Annual Survey**. 2017.
Reference Source

36. Japan Tobacco Inc: **Japan Tobacco Annual Survey**. 2018.
Reference Source

37. Sutanto E, Miller C, Smith DM, *et al.*: **Prevalence, Use Behaviors, and Preferences among Users of Heated Tobacco Products: Findings from the 2018 ITC Japan Survey.** *Int J Environ Res Public Health.* 2019; **16**(23): 4630.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

38. Kuwabara Y, Kinjo A, Fujii M, *et al.*: **Heat-not-burn tobacco, electronic cigarettes, and combustible cigarette use among Japanese adolescents: a nationwide population survey 2017.** *BMC Public Health.* 2020; **20**(1): 741.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

39. Fischer K, Bajec M, Mainy N, *et al.*: **Trends in Prevalence and Patterns of Use of a Heated Tobacco Product (*IQOS*™) in Japan: A 3-Year Repeated Cross-Sectional Study.** YEAR 1-3 DATA. (Year1: **https://doi.org/10.26126/intervals.8ybcxu**, Year 2: **https://doi.org/10.26126/intervals.hxaf2v**, Year 3: **https://doi.org/10.26126/intervals.6jbifs**). 2022.
http://www.doi.org/10.26126/intervals.r35iml.1

Open Peer Review

Current Peer Review Status: ✔ ?

Version 2

Reviewer Report 11 May 2023

https://doi.org/10.5256/f1000research.140767.r156232

✔ **Mohamadi Sarkar**
Center for Research and Technology, Altria Client Services LLC, Richmond, VA, USA
Brendan Noggle
Center for Research and Technology, Altria Client Services LLC, Richmond, VA, USA

The authors have adequately addressed the comments and I approve this manuscript.

Competing Interests: The reviewers are employees of Altria Client Services LLC (ALCS). Philip Morris USA Inc., which is an affiliate of ALCS, has distributed and sold iQOS® heated tobacco products in the U.S. This research was funded by Philip Morris International Inc., which is an independent entity not affiliated with ALCS or Philip Morris USA Inc.. This potential conflict of interest did not impact the impartiality of our review, which was conducted to assess the scientific merit of the research regardless of the source of funding or author affiliations.

Reviewer Expertise: Tobacco regulatory science.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 21 September 2022

https://doi.org/10.5256/f1000research.134482.r144380

David T. Levy
Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA

This study provides interesting results on trends in IQOS use as related to smoking and vaping. The methodology and results are well presented. With regards to data underlying the results, I don't recall that the authors provided for data transferred to others. While desired, there may be issues of confidentiality. Using cross-sectional data, their results show increasing use of IQOS with and without e-cigarettes and a decline in smoking. Their results, however, in the Discussion section, I had problems with the failure to adequately discuss the limitations of the study and the author's generalization of the results.

The limitations of the study merit further attention in the Discussion section. The authors fail to recognize the limited nature of their sample. In particular, the sample is limited to IQOS users and the sample is based on IQOS users who chose to register on the PMI website, thus presenting the potential problem of selection bias. Indeed, IQOS was the first and has a dominant share in Japan and may not represent other HTP use and its relationship to smoking. These limitations should be clearly recognized and discussed. It wasn't clear to me whether there was a switching between IQOS and other HTPs. The use of cross-sectional rather than longitudinal data also merits discussion.

In addition, the authors attempt to generalize the results for IQOS and e-cigarette use in their sample to the rest of the Japanese population by comparing to NHNS and other samples. As currently presented, I did not feel that the conclusions, ie. Upward exclusive use of IQOS as cigarette use decline, are well supported. The authors do compare some trends, but the comparisons are not rigorous. It would be useful to compare relative changes over time in their sample to relative changes other more representative samples (e.g., NHNS, JASTIS), and provide direct comparisons by age and gender in a table. The authors may then be able to compare whether the trends related to IQOS and cigarette use are the same or different. Given the potential for selection bias, which should be made explicit, these comparisons are important.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
No

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Modelling and empirical analyses

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 04 Nov 2022

Karina Fischer

Author Responses to Comments of Reviewers

We thank Reviewer 1 and Reviewers 2 for their critical and comprehensive review as well as their constructive suggestions to improve the manuscript. We addressed all comments by point-to-point responses and referred to the related updates in the manuscript by page and line numbers (Note: *page and line numbers reflect the tracked changes version 2 of the manuscript, not the edited version that reviewers will receive. Reviewers may have to additionally request the tracked changes version*).

Reviewer 1: *David T. Levy Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA.*

Reviewer 1 comments

Reviewer 1 Comment 1. This study provides interesting results on trends in IQOS use as related to smoking and vaping. The methodology and results are well presented. With regards to data underlying the results, I don't recall that the authors provided for data transferred to others. While desired, there may be issues of confidentiality.

Authors' Response 1. We thank Reviewer 1 for this comment. All data and extended data underlying the results and conclusions of this study as well as the questionnaire and reporting guideline related information (Strobe Checklist) have already been made publicly available on the INTERVALS platform as part of the manuscript submission to F1000Reserach (see **Data Availability section [pages 25-26] of the manuscript**). Therefore, all data and information underlying the manuscript, are publicly available on the INTERVALS platform and have a Digital Object Identifier (DOI) that directs to the related data/information on INTERVALS.

Reviewer 1 Comment 2. Using cross-sectional data, their results show increasing use of IQOS with and without e-cigarettes and a decline in smoking. Their results, however, in the Discussion section, I had problems with the failure to adequately discuss the limitations of the study and the author's generalization of the results.

Authors' Response 2. We agree with Reviewer 1 to highlight the limitations of the study in more detail. We amended the discussion (page 22, lines 305-308) and limitation (page 24, lines 382-384) section with regard to the limitations of the cross-sectional design, as well as the limitation section in view of the limited generalizability of the results from the *IQOS* user

(JA*IQOS*) samples (page 24, lines 389-392).

Reviewer 1 Comment 3. The limitations of the study merit further attention in the Discussion section. The authors fail to recognize the limited nature of their sample. In particular, the sample is limited to IQOS users and the sample is based on IQOS users who chose to register on the PMI website, thus presenting the potential problem of selection bias. Indeed, IQOS was the first and has a dominant share in Japan and may not represent other HTP use and its relationship to smoking. These limitations should be clearly recognized and discussed. It wasn't clear to me whether there was a switching between IQOS and other HTPs. The use of cross-sectional rather than longitudinal data also merits discussion.

Authors' Response 3. We would like to clarify that In each of the three study years, the study included both (i) ***representative*** samples of the ***Japanese General Adult Population*** (**JGAP** samples based on **three-stage stratified proportional random sampling** covering the whole of Japan) as well as (ii) "**convenience"** samples of Japanese adult *IQOS* users registered in the *IQOS* owner database of Philip Morris International's affiliate in Japan (**JA *IQOS*** samples ***randomly selected*** from about 350,000 *IQOS* users in 2017 and 6 million *IQOS* users in 2019 ***registered in the Japanese adult IQOS owner database***). As stated at the end of the introduction, we used the *IQOS* user samples (JA*IQOS* samples) alongside the representative JGAP samples because in the first and second year of the study *IQOS* was relatively new on the Japanese tobacco market, and thus, the *IQOS* use prevalence in the general population (representative JGAP samples) was expected to be low. Therefore, to obtain reliable estimates of the use patterns of *IQOS* (i.e., exclusive *IQOS* use, *IQOS* use with combustible tobacco products, and *IQOS* use with non-combustible tobacco products, the differentiation of which is important regarding the impact on tobacco harm reduction), we conducted additional surveys among *IQOS* users.

Because we are aware of the limitations of the JA*IQOS* samples, most of the results presented in our study are based on the representative JGAP samples (Tables 1-7 and the related text in the results section), whereas only the results presented in Table 1 (demographics), Table 5 (frequency and intensity of use) and Table 8 (*IQOS* use patterns) are also presented for the *IQOS* user samples.

Both (i) the representative samples of the Japanese General Adult Population (JGAP samples) as well as (ii) the samples of Japanese adult *IQOS* users registered in Japanese the *IQOS* owner database (JA*IQOS* samples) were random samples. Therefore, we believe that the likelihood of selection bias was rather low.

Because the present study provides cross-sectional but not longitudinal data of the same participants over time, investigating switching behaviors was not intended for this manuscript.
As already stated in our response to comment 2, we amended the discussion (page 22, lines 305-308) and limitation section (page 24, lines 382-384) with regard to the limitations of the cross-sectional design, as well as the limitation section in view of the limited generalizability of the results from the *IQOS* user (JA*IQOS*) samples (page 24, lines 389-392). Moreover, in the limitation section we added the fact even though *IQOS*™ was the first HTP and had the

highest use prevalence in Japan, *IQOS* use behavior may not represent the use behavior of other HTPs available in Japan (page 24, lines 392-394).

Reviewer 1 Comment 4. In addition, the authors attempt to generalize the results for IQOS and e-cigarette use in their sample to the rest of the Japanese population by comparing to NHNS and other samples. As currently presented, I did not feel that the conclusions, i.e. Upward exclusive use of IQOS as cigarette use decline, are well supported. The authors do compare some trends, but the comparisons are not rigorous. It would be useful to compare relative changes over time in their sample to relative changes other more representative samples (e.g., NHNS, JASTIS), and provide direct comparisons by age and gender in a table. The authors may then be able to compare whether the trends related to IQOS and cigarette use are the same or different. Given the potential for selection bias, which should be made explicit, these comparisons are important.

Authors' Response 4. We thank Reviewer 1 for raising this point. Regarding the prevalence data of overall tobacco product as well as *IQOS* and other individual tobacco product use, in the discussion, we compared the study results from the representative JGAP samples with the corresponding data from one of the most comprehensive surveys measuring tobacco use, the representative Japan National Health and Nutrition Survey (Japan NHNS) from the Japanese Ministry of Health, Labour and Welfare.

While we indeed present data on exclusive *IQOS* use, we did not state that with increasing exclusive *IQOS* use the use of cigarettes declined as Reviewer 1 remarked. Rather, in the manuscript (page 22, lines 302-304) we stated "there was a trend towards a declining prevalence of cigarette smoking concurrent with an increase in smoke-free TNP and total HTP use, especially in case of *IQOS* use. So, with regard to the decline in overall cigarette smoking prevalence, we are not referring to exclusive *IQOS* use but to overall smoke-free TNP, total HTP, and *IQOS* use.

Regarding the point that our survey may have suffered from selection bias (see also our response on selection bias to Reviewer 1's comment 3), we mentioned this aspect in the limitation section (page 24, line 386-389). However, because both (i) the ***representative*** samples of the ***Japanese General Adult Population*** (**JGAP** samples, ***three-stage stratified proportional sampling***) as well as (ii) the samples of Japanese adult *IQOS* users registered in Japanese adult *IQOS* owner database (**JA*IQOS*** samples ***randomly selected*** from about 350,000 *IQOS* users in 2017 and 6 million *IQOS* users in 2019 registered in the Japanese adult *IQOS* owner database) were random samples from the respective reference populations, we believe that the likelihood of selection bias was rather low.
As opposed to our *cross-sectional* study that includes adult participants ≥20 years and presents unadjusted data, the Japan Society and New Tobacco Internet Survey (JASTIS) is a *longitudinal* (cohort) study following both youth and adults aged 15-73 years over time and presents adjusted data. Therefore, given the different study design and age groups included, we cannot directly compare our results from the cross-sectional JGAP and JA*IQOS* samples with the longitudinal JASTIS study as Reviewer 1 suggested (*see also Authors' Response to Reviewers 2 Minor Comment 2*). However, we compared our prevalence data from the representative JGAP samples with the sales data of cigarettes and heated tobacco product (HTP) use (**Chart 1 below)** as well as with the prevalence data from the

representative Japan National Health and Nutrition Survey (Japan NHNS) conducted yearly by the Japan Ministry of Health, Labour and Welfare (**Chart 2 below**) over time.

In 2021, HTP units represented almost 1/3 of the total cigarette and HTP market. The increase in HTP sales was accompanied by a decline in cigarette sales (**Chart 1 below)**.

Chart 1 Cummings K. F. et al.(2020) What Is Accounting for the Rapid Decline in Cigarette Sales in Japan? Int J Environ Res Public Health; 17(10): 3570. Doi: 10.3390/ijerph17103570. The sales data for 2020 and 2021 was added to the data published for 2011-2019 by Cummings et al.

The prevalence data from the Japan NHNS (**Chart 2 below**) suggests that the decline in cigarette sales shown in **Chart 1** was accompanied by a decrease in smoking prevalence. Until 2017, the Japan NHNS measured only the prevalence of smoking. However, because between 2015 and 2017 HTP sales had already rapidly increased as shown in **Chart 1**, it can be assumed that between 2015 and 2017 also the HTP use prevalence increased.

In 2018 the Japan NHNS was updated to capture the prevalence of both cigarettes and HTPs separately. In 2019, 12% of the adult population were smoking only combustible cigarettes, shown in dark grey, 3.4% were using only HTPs, shown in light blue, 1.1% were using both cigarettes and HTPs, and 0.2% used other or undefined tobacco products (**Chart 2 below**). Because the Japan NHNS was discontinued in 2020 and 2021 due to the Covid pandemic, there is unfortunately no data for more recent trends.

Chart 2. Prevalence data on cigarette and HTP use from the Japan National Health and Nutrition Survey (Japan NHNS) conducted by the Japan Ministry of Health, Labour and Welfare

The data presented in Table 4 of our manuscript for cigarette and *IQOS* use prevalence in the representative GAP samples from 2016-2019 (**shown as Chart 3 below**; the chart includes also the most recent 2020/2021 GAP data) are similar to the 2016 -2019 data from the Japan NHNS, which shows a decline in cigarette smoking prevalence accompanied with a marked uptake of HTP use as of 2018 when both cigarettes and HTPs were separately measured in the Japan NHNS.

Chart 3. Data presented in Table 4 of the manuscript for cigarette and IQOS use prevalence in the representative GAP samples from 2016 -2019 (**on the left side of the green dashed line**) as well as most recent 2020/2021 prevalence data for cigarette and IQOS use (**on the right side of the green dashed line**) that are not shown in the manuscript.

Given all the information presented above, we believe that our observation of a decline in cigarette smoking prevalence accompanied with an increase in *IQOS*/HTP use prevalence over the three study years in Japan is supported by independent data.

Competing Interests: No competing interests were disclosed.

Reviewer Report 28 July 2022

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17/10/22: The reviewers' COI statement, "The reviewers are employees of Altria Client Services LLC.", was updated to include more detail on the potential link between the funders of this research and the reviewers, which was not fully declared at the time of publishing of this report.

We read the manuscript submitted by Fischer *et al* in F1000Research with great interest. The authors report results from cross-sectional surveys conducted over a period of three in representative samples of the Japanese general adult population and samples of Japanese adult IQOS users registered in the IQOS owner database. The authors conclude that the trend towards declining prevalence of cigarette smoking concurrent with an increase in smoke-free TNP and total HTP use, especially in the case of IQOS^{TM} use are in line with the principles of tobacco harm reduction and that HTPs are effective tools for complementing current tobacco control measures. We have the following major and minor comments as listed below. We recommend that the authors address each comment and accordingly modify the manuscript.

Major comments

1. The authors report results from the general population survey among Japanese adults, which given the representativeness is appropriate to compare over time. However, the IQOS user survey was based on a convenience sample, and comparing trends over time is less robust. Therefore, comparing the results across the two surveys is not ideal. The authors should discuss this as a limitation of their approach. Instead of a direct comparison of the survey results between the general population and IQOS sample the authors should have considered characterizing IQOS sample tobacco use behaviors and benchmark that to the current adult tobacco users from the general population survey.

2. We were confused by the individual TNP use prevalence values among the general population reported in Table 3. The overall prevalence for cigarettes ranges from 17.6, 17.3, and 16 % each year. If add the prevalence values for IQOS and e-cigarettes, results in total TNP prevalence of 20.1, 22.1, and 21.3% for each year. These values differ from the overall TNP prevalence of 18.5, 18.9, and 18.2 reported for each year in Table 2. Perhaps the authors can offer an explanation for this discrepancy

3. While we agree that this evidence supports or does not contradict that switching to a smoke-free product like IQOS supports harm reduction, we suggest that the authors should be careful in drawing broader conclusions like “IQOS use behavior trends are in line with the

principles of tobacco harm reduction". Tobacco harm reduction cannot be viewed only in the narrow perspective of switching. An important consideration of unintended consequence is not only initiation among adults but also among youth. Additionally, as pointed in our comment above, the total TNP prevalence as calculated by us does not indicate a reduction in total tobacco product use, on the contrary, appears to increase over time. The authors should provide some context regarding these observations. Therefore, the authors should consider modifying the conclusions as "The use behavior trends suggest that IQOS has the potential to switch adult smokers from cigarettes to smoke-free products, which presents a harm reduction opportunity."

4. We caution the authors to avoid making causality inferences based on association. The authors should consider revising the conclusion - "The introduction of smoke-free TNPs does not lead to an unintended increase in overall TNP use in the general population, but rather drives a shift in TNP use patterns from cigarettes to smoke-free TNPs." to reflect association rather than causation.

5. The survey lacks an appropriate characterization of quitting behavior among IQOS users. The survey does not present evidence regarding the likely interception of smokers who may have otherwise quit using TNP. If the survey did not assess this domain, the authors should cite this as a limitation. This further warrants a revision of the conclusions from not being so definitive but reflect the limitations of the survey results.

6. The authors should include an explanation of the drop in response rates for JA*IQOS* samples from 19.4% in Y1 to 4.7% and 2.0% in Y2 and Y3. Given that the IQOS users changed significantly, from 350,000 to 6 million, the IQOS population likely changed over the course of the 3 surveys. The authors should consider accounting for the change in IQOS population by adjusting either during recruitment or during the data analysis.

7. The authors only present descriptive analyses of survey findings, however, they may want to consider including some trend analysis or other statistical testing to determine whether the changes over time are significant. Perhaps such an analysis may not yield robust findings from a three-year survey and authors may consider providing more statistical rigor in future reports.

8. We understand that the focus of this manuscript was among adults age ≥20 years. However, an important consideration is the impact of IQOS and other smoke-free products among youth, which is an important public health concern. The authors should mention that this manuscript only addresses adult use behavior and either briefly describe data for youth use based on published literature or national surveys. Some indication of initiation among different age groups of youth and young adults would have provided useful insights in the overall harm reduction potential of IQOS and other smoke-free products.

Minor comments

1. The authors should consider including the supporting literature citations in the statement – "The existing standard TNP use questions are available in the literature.".

2. The authors should provide a possible explanation of the discrepancy in the reported total HTP use prevalence of 11% by Hori *et al* (ref 34) which is almost twice of that reported in the

current manuscript. This discrepancy cannot be solely explained by methodological differences.

3. In this manuscript, the IQOS sample could have been better characterized. Given that the authors had access to the IQOS user database, they could have followed transition behavior over time rather than indirectly comparing changes in average smoking prevalence against increase in IQOS user prevalence. Moreover, they may also report transitions between dual use to exclusive switching behavior. Perhaps in future reports, the authors can include more detailed analyses of transition behaviors.

4. We believe that the title for Table 6 should include JGAP not JPAG. Please correct the typo.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: The reviewers are employees of Altria Client Services LLC (ALCS). Philip Morris USA Inc., which is an affiliate of ALCS, has distributed and sold iQOS® heated tobacco products in the U.S. This research was funded by Philip Morris International Inc., which is an independent entity not affiliated with ALCS or Philip Morris USA Inc.. This potential conflict of interest did not impact the impartiality of our review, which was conducted to assess the scientific merit of the research regardless of the source of funding or author affiliations.

Reviewer Expertise: Tobacco regulatory science.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 04 Nov 2022

Karina Fischer

Author Responses to Comments of Reviewers
We thank Reviewer 1 and Reviewers 2 for their critical and comprehensive review as well as their constructive suggestions to improve the manuscript. We addressed all comments by point-to-point responses and referred to the related updates in the manuscript by page and line numbers (Note: *page and line numbers reflect the tracked changes version 2 of the manuscript, not the edited version that reviewers will receive. Reviewers may have to additionally request the tracked changes version*).

Reviewers 2:
Mohamadi Sarkar, Center for Research and Technology, Altria Client Services LLC, Richmond, VA, USA
Brendan Noggle, Center for Research and Technology, Altria Client Services LLC, Richmond, VA, USA

Reviewers 2 comments
We read the manuscript submitted by Fischer et al in F1000Research with great interest. The authors report results from cross-sectional surveys conducted over a period of three years in representative samples of the Japanese general adult population and samples of Japanese adult IQOS users registered in the IQOS owner database. The authors conclude that the trend towards declining prevalence of cigarette smoking concurrent with an increase in smoke-free TNP and total HTP use, especially in the case of *IQOS*™ use are in line with the principles of tobacco harm reduction and that HTPs are effective tools for complementing current tobacco control measures. We have the following major and minor comments as listed below. We recommend that the authors address each comment and accordingly modify the manuscript.

Major comments

Reviewers 2 Major Comment 1. The authors report results from the general population survey among Japanese adults, which given the representativeness is appropriate to compare over time. However, the IQOS user survey was based on a convenience sample and comparing trends over time is less robust. Therefore, comparing the results across the two surveys is not ideal. The authors should discuss this as a limitation of their approach. Instead of a direct comparison of the survey results between the general population and IQOS sample the authors should have considered characterizing IQOS sample tobacco use behaviors and benchmark that to the current adult tobacco users from the general population survey.

Authors' Response Major Comment 1. As stated at the end of the introduction, we used the "convenience" JA*IQOS* samples (random samples from about 350,000 *IQOS* users in 2017 and 6 million *IQOS* users in 2019 registered in the adult *IQOS* owner database of PMI's affiliate in Japan) alongside the representative JGAP samples because in the first and second year *IQOS* was relatively new on the Japanese tobacco market, and thus, the *IQOS* use prevalence in the representative JGAP samples was expected to be low. Therefore, to obtain reliable estimates of the use patterns of *IQOS* (e.g., exclusive *IQOS* use, *IQOS* use with combustible tobacco products, and *IQOS* use with non-combustible tobacco products, the differentiation of which is important regarding the impact on tobacco harm reduction), additional surveys

among *IQOS* users were conducted.

Although we presented the results of both samples in the results section, we only directly compared the study results on age and sex distribution, intensity of use, initiation, relapse, and reinitiation between the two samples because we believe it was important to show the study results of the two independent samples.

Because we are well aware of the limitations of the *IQOS* user (JA*IQOS*) samples, most of the results presented are based on the representative JGAP samples (Tables 1 [demographics] and Tables 2-7) and the related text in the results section. Only the results presented in Table 1 [demographics], Table 5 [frequency and intensity of use] and Table 8 [*IQOS* use patterns] are also presented for the *IQOS* user samples. We amended the discussion to highlight the limited generalizability of the *IQOS* user (JA*IQOS*) samples (page 24, lines 389-392).

Reviewers 2 Major Comment 2. We were confused by the individual TNP use prevalence values among the general population reported in Table 3. The overall prevalence for cigarettes ranges from 17.6, 17.3, and 16 % each year. If add the prevalence values for IQOS and e-cigarettes, results in total TNP prevalence of 20.1, 22.1, and 21.3% for each year. These values differ from the overall TNP prevalence of 18.5, 18.9, and 18.2 reported for each year in Table 2. Perhaps the authors can offer an explanation for this discrepancy.

Authors' Response Major Comment 2. We thank Reviewers 2 for this question on prevalence that often creates confusion when individual TNP prevalence values are shown that do not sum up to the overall TNP prevalence reported. Prevalence data for different tobacco product categories (e.g., cigarettes, HTPs, and e-cigarettes) can only be directly summed up to a higher-level use prevalence group (e.g., total prevalence of cigarette, HTP, and e-cigarette use) if each person only uses one category of tobacco product (e.g., only cigarettes, only HTPs, or only e-cigarettes). As soon as the same person uses more than one category (i.e., dual or poly use of different tobacco product categories), the person would be counted twice (dual use) or even more (poly use) in the higher-level prevalence group if the individual prevalence values would just be summed up, while correctly the person should only count once in the higher-level prevalence group (total prevalence of cigarette, HTP, and e-cigarette use).

Reviewers 2 Major Comment 3. While we agree that this evidence supports or does not contradict that switching to a smoke-free product like IQOS supports harm reduction, we suggest that the authors should be careful in drawing broader conclusions like "IQOS use behavior trends are in line with the principles of tobacco harm reduction". Tobacco harm reduction cannot be viewed only in the narrow perspective of switching. An important consideration of unintended consequence is not only initiation among adults but also among youth. Additionally, as pointed in our comment above, the total TNP prevalence as calculated by us does not indicate a reduction in total tobacco product use, on the contrary, appears to increase over time. The authors should provide some context regarding these observations. Therefore, the authors should consider modifying the conclusions as "The use behavior trends suggest that IQOS has the potential to switch adult smokers from cigarettes to smoke-free products, which presents a harm reduction opportunity."

Authors' Response Major Comment 3. We thank Reviewers 2 for this comment. As suggested by Reviewers 2, we rephrased the conclusion section in the abstract (page 3) and discussion (page 24, lines 405-409) to make this point clearer. Regarding the overall TNP prevalence we reported, please see our response and explanations to Reviewers 2 Major Comment 2.

Reviewers 2 Major Comment 4. We caution the authors to avoid making causality inferences based on association. The authors should consider revising the conclusion - "The introduction of smoke-free TNPs does not lead to an unintended increase in overall TNP use in the general population, but rather drives a shift in TNP use patterns from cigarettes to smoke-free TNPs." to reflect association rather than causation.

Authors' Response Major Comment 4. We agree with Reviewers 2 that because our study results are based on cross-sectional and descriptive data only, cause-effect inference cannot be drawn. We consider this limitation as a well-known fact inherent to cross-sectional studies. However, to make this point clearer, we amended the discussion (page 22, lines 305-308) and limitation section (page 24, lines 382-384) with regard to the limitations of the cross-sectional design.

Reviewers 2 Major Comment 5. The survey lacks an appropriate characterization of quitting behavior among IQOS users. The survey does not present evidence regarding the likely interception of smokers who may have otherwise quit using TNP. If the survey did not assess this domain, the authors should cite this as a limitation. This further warrants a revision of the conclusions from not being so definitive but reflect the limitations of the survey results.

Authors' Response Major Comment 5. We agree with Reviewers 2 that without addressing quitting behavior in our manuscript, we do not cover the information whether switching from cigarettes to *IQOS* may have prevented cigarette smokers from quitting all TNP. However, assessing quitting behavior was not in the scope of our manuscript. We still added the information that quitting behavior was not investigated to the limitation section of the discussion (page 24, lines 394-396).

Reviewers 2 Major Comment 6. The authors should include an explanation of the drop in response rates for JAIQOS samples from 19.4% in Y1 to 4.7% and 2.0% in Y2 and Y3. Given that the IQOS users changed significantly, from 350,000 to 6 million, the IQOS population likely changed over the course of the 3 surveys. The authors should consider accounting for the change in IQOS population by adjusting either during recruitment or during the data analysis.

Authors' Response Major Comment 6. The decline in response rates across the three study years observed for the JA*IQOS* samples can be explained by the fact that over time, the *IQOS* users increasingly received email invitations to various PMI surveys which might have generated a lower willingness to participate in our surveys.

We included the explanation for the decreasing response rates related to the JA*IQOS*

surveys in the discussion section (page 24, lines 374-377).

As stated in the limitations section of the discussion (page 24, lines 386-389), because during the study years, we continuously monitored the response rates and compared them against pre-established quotas on the basis of age and sex, there was no need for further adjustment during recruitment or the data analysis because we still had sufficient samples (500 completed surveys) in each survey wave available.

Reviewers 2 Major Comment 7. The authors only present descriptive analyses of survey findings, however, they may want to consider including some trend analysis or other statistical testing to determine whether the changes over time are significant. Perhaps such an analysis may not yield robust findings from a three-year survey and authors may consider providing more statistical rigor in future reports.

Authors' Response Major Comment 7. We thank Reviewers 2 for this valid comment. Our statistical analysis plan for this 3-year study did only foresee descriptive analysis. For future studies, we are considering using more sophisticated trend analysis based on statistical methods.

Reviewers 2 Major Comment 8. We understand that the focus of this manuscript was among adults age >20 years. However, an important consideration is the impact of IQOS and other smoke-free products among youth, which is an important public health concern. The authors should mention that this manuscript only addresses adult use behavior and either briefly describe data for youth use based on published literature or national surveys. Some indication of initiation among different age groups of youth and young adults would have provided useful insights in the overall harm reduction potential of IQOS and other smoke-free products.

Authors' Response Major Comment 8. We agree with Reviewers 2 and amended the discussion (page 23, lines 363-365) and limitation section (page 24, lines 396-398), mentioning that our manuscript is based on Japanese adult participants only and that with regard to tobacco harm reduction, tobacco use prevalence among youth should be taken into consideration. The available literature suggests that tobacco initiation with I*QOS*/HTPs and prevalence of *IQOS*/HTPs among youth in Japan is low (pages 23-24, lines 365-373).

Minor comments

Reviewers 2 Minor Comment 1. The authors should consider including the supporting literature citations in the statement – "The existing standard TNP use questions are available in the literature.".

Authors' Response Minor Comment 1. We thank the Reviewers 2 for this valuable comment. In the methods section, we included the links to the (i) CDC Adult Tobacco Use Questions of the National Health Interview Survey (NHIS), (ii) WHO/CDC/CPHA Questions of the Global Adult Tobacco Survey (GATS), (iii) NIH/FDA PATH Study questionnaires, and (iv) MHLW Tobacco Questions of the Japan National Health and Nutrition Survey (page 6, lines 107-112).

Reviewers 2 Minor Comment 2. The authors should provide a possible explanation of the discrepancy in the reported total HTP use prevalence of 11% by Hori et al (ref 34) which is almost twice of that reported in the current manuscript. This discrepancy cannot be solely explained by methodological differences.

Authors' Response Minor Comment 2. We believe that there are multiple conceptual and methodological differences that may have contributed to the lower overall HTP use prevalence (>5%) in our study than that observed by Hori et al. (11%). These differences between our study and the Hori et al. study, respectively, include i.a., (i) cross-sectional vs. longitudinal design, (ii) age ≥20 years vs. age range 15-69 years, (iii) no weighting methods vs. inverse probability weighting, (iv) no adjustments vs. multiple adjustment of the data, (v) definition of current use [at the time of the survey vs. past 30 days], and (vi) lifetime use criterion [100 tobacco sticks] vs. no lifetime use criterion to qualify as a HTP user.

Of all these aspects, we believe that the difference in the age groups included in both studies (i.e., age ≥20 year in our study vs. 15-69 years in the Hori et al. study) had the largest impact on the difference in the observed overall HTP prevalence between our study and the study of Hori et al. In our study, we included also older age groups above 69 years, so the age distribution was skewed towards older age groups among whom, however, the *IQOS* use prevalence was very low with only about 1 %. We added this information to the discussion section (page 23, lines 327-337).

Reviewers 2 Minor Comment 3. In this manuscript, the IQOS sample could have been better characterized. Given that the authors had access to the IQOS user database, they could have followed transition behavior over time rather than indirectly comparing changes in average smoking prevalence against increase in IQOS user prevalence. Moreover, they may also report transitions between dual use to exclusive switching behavior. Perhaps in future reports, the authors can include more detailed analyses of transition behaviors.

Authors' Response Minor Comment 3. We thank reviewers 2 for this important comment. Because the present study provides only cross-sectional but not longitudinal data of the same participants follow-ed up over time, investigating transition behaviors was not intended in this study. However, in future studies, we will consider analyzing transition behaviors based on prospective/longitudinal data.

Reviewers 2 Minor Comment 4. We believe that the title for Table 6 should include JGAP not JPAG. Please correct the typo.

Authors' Response Minor Comment 4. We thank Reviewers 2 for spotting this typo. We have corrected it.

Competing Interests: No competing interests were disclosed.