v1: 16 October 2024

Research Article

Tobacco- and Nicotine-Containing Product Use in Italy: Results from Two Cross-Sectional Studies

Peer-approved: 16 October 2024

Qeios, Vol. 6 (2024)
ISSN: 2632-3834

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Background: Heated tobacco products (HTPs) are alternatives to cigarettes that heat rather than burn tobacco. The first HTP sold in Italy was *IQOS*® (I-HTP), and while it has been available for nearly a decade, limited data are available on the use of these products.
Objective: To characterize how Italian adults (users of legal age) use tobacco- and nicotine-containing products (TNPs), including smoke-free products (SFPs), we surveyed this population about their current and past use of TNPs from 2018 to 2020.
Methods: Two consecutive cross-sectional surveys were conducted in representative samples of the general adult population (6,095 subjects from 2018 to 2019 and 6,118 from 2019 to 2020) and among adult I-HTP users (1,371 subjects from 2018 to 2019 and 1,401 from 2019 to 2020) in Italy. We assessed the prevalence of current TNP use in the general population sample and use patterns in the I-HTP users sample.
Results: In the first cross-sectional study (2018-2019), cigarettes were the most used TNP (24.3%), while only a small proportion of the surveyed general population sample used e-cigarettes or I-HTPs (1.4% and 0.7%, respectively). Nearly all current I-HTP users were current adult cigarette smokers when they started using I-HTPs (98.0%). Both surveys showed low initiation, re-initiation, and relapse with I-HTPs, with the majority of current I-HTP users belonging to the intended audience of adults who already used TNPs. Some participants used both I-HTPs and combustible TNPs (38.6%); however, most (59.2%) used I-HTPs exclusively. I-HTP users perceived the health risk (score 0 = no risk; score 100 = very high risk) associated with cigarette smoking higher (63.7) than that for I-HTP use (42.6). Exclusive I-HTP users reported improved respiratory symptoms (reduced cough and phlegm) and exercise capacity compared to a year before they started using I-HTPs. Most current I-HTP users also reported improved smell and taste, better breath smell, and reduced stains or yellowing of teeth. Overall, these results were more pronounced among exclusive I-HTP users. The results of the second cross-sectional study (2019-2020) were similar, except for an increase in I-HTP use (1.1% vs. 0.7% in 2018 to 2019).
Conclusions: These studies show that most TNP users in Italy smoke cigarettes. The uptake of I-HTPs suggests that they are a viable alternative to

 doi.org/10.32388/F3LAEC.2

cigarettes. Nearly all I-HTP users switched from cigarettes to I-HTPs. Furthermore, most I-HTP users exclusively use the product. I-HTP users considered the health risk associated with I-HTP use to be lower compared to cigarette smoking, but they did not perceive I-HTPs as risk-free. Study participants reported improvements in some health, hygiene, and appearance aspects after switching from cigarettes to I-HTPs. Our results suggest that SFPs can play a role in a harm reduction approach. Further studies are needed to continually monitor the prevalence of SFP use to provide long-term evidence of their impact.

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Introduction

Epidemiological data collected over several decades show that cigarette smoking causes a range of serious diseases (e.g., cardiovascular and obstructive pulmonary diseases, lung cancers) [1]. Annually, about 8 million deaths are attributed to cigarette smoking [2]. The harmful health effects of cigarette smoking are primarily caused by toxic substances produced during the combustion of tobacco, [3][4] which the U.S. Food and Drug Administration refers to as Harmful or Potentially Harmful Constituents (HPHCs) [5].

Cessation is the most effective way to reduce the risk of diseases in smokers, and the primary strategy to reduce smoking-related diseases has focused on preventing smoking initiation and promoting smoking cessation [3][4]. Unfortunately, ~1 billion people continue to smoke cigarettes despite these efforts [6]. In Italy, among those who attempted to quit smoking over 4 years (2017-2020), just 9.6% remained abstinent for more than 6 months [7]. Moreover, the success of smoking cessation therapy tends to decrease 1 year after treatment [8].

The number of adult smokers who stop cigarette smoking may increase by encouraging those who don't quit to switch completely to lower-risk smoke-free products (SFPs). For harm reduction strategies to be successful, such alternatives must have the potential to be less harmful than cigarette smoking, and adults who would otherwise continue smoking must switch completely [9]. At the same time, SFPs should not be attractive to youth, non-smokers, or former smokers.

In recent years, various tobacco- and/or nicotine-containing products (TNPs) that can be used to support harm reduction strategies have emerged, including electronic cigarettes (e-cigs) and heated tobacco products (HTPs). Both products eliminate tobacco combustion, which is the primary source of high levels of HPHCs to which smokers are exposed. To generate a nicotine-containing aerosol, HTPs heat tobacco without burning it, while e-cigs heat a liquid.

In 2014, Philip Morris International (PMI) launched the HTP *IQOS*® (I-HTP) in test markets in Nagoya (Japan) and Milan (Italy), which became nationally available in both countries in 2016. It is a heating system used with tobacco sticks that are inserted into the device, which heats them to generate an aerosol that contains reduced toxicant emissions [10][11] and lowers exposure to HPHCs [12][13] in clinical studies. However, there are limited data on I-HTP use in Italy [14][15][16], and there is concern that these products may be used by individuals who did not previously use TNPs. In response to this gap in the literature, two cross-sectional studies were conducted from 2018 to 2019 ("Year One") and from 2019 to 2020 ("Year Two") to investigate the current and past use of TNPs. The aim was to understand how Italian adults (users of legal age) are using I-HTPs, through surveys similar to those conducted in other countries [17][18].

Overall aim and study objectives

The goal of this work was to investigate current and past TNP use in the general adult population in Italy, and in I-HTP users registered in PMI's Italy *IQOS* user database.

More specifically, the studies' objectives were:

1. To estimate the prevalence of current status of TNP use in the study populations categorized as (a) never user, former user, and current user; (b) daily and occasional user; and (c) exclusive user, dual user, and poly-user.
2. To describe past TNP user status to estimate (a) TNP initiation (based on the first product regularly used); (b) relapse and re-initiation (based on the most recent attempt to quit TNPs); and (c)

intention to quit, quit attempts, and successful quitting of TNPs.
3. To estimate the perception of the health risk associated with cigarette smoking and I-HTP use.
4. To estimate self-reported perceived changes in respiratory symptoms (i.e., cough and phlegm), hygiene, beauty, and fitness, and exercise capacity among current I-HTP users.

Methods

Study design and setting

We conducted observational cross-sectional surveys in two population samples: a general adult population sample and an I-HTP user sample. We completed two surveys for each sample. The first one from 2018 to 2019 (the general adult sample from March 20, 2018, to January 27, 2019, and the I-HTP user sample from April 12, 2018, to February 15, 2019). The second one from 2019 to 2020 (the general adult sample from March 18, 2019, to January 31, 2020, and the I-HTP user sample from April 12, 2019, to January 31, 2020). Each annual sampling (i.e., data collected within a 12-month period) included the general adult population sample and the I-HTP user sample. The general adult population sample consisted of six waves per 12-month period, and the I-HTP user sample consisted of four waves. Both annual surveys were conducted according to protocols described elsewhere [19].

General adult population sample

In each wave, the surveys were conducted through face-to-face interviews as part of a multi-purpose survey (Omnibus). Although most of the data collected in the Omnibus used a face-to-face interview approach, participants completed the main study questionnaire on TNP use through computer-assisted self-interviewing (CASI). This approach was used to avoid social desirability bias, reasoning that participants may feel uncomfortable answering specific questions on tobacco use in the presence of an interviewer.

I-HTP user sample

In each wave, the surveys were conducted online. A sample of I-HTP users registered in PMI Italy's database of registered adult purchasers was randomly selected and invited to participate in the survey.

Selection of study population and sample size: Year One (2018-2019) and Year Two (2019-2020)

The study population for the general adult sample comprised adults (≥18 years of age) living in registered households in Italy (50,396,628 based on the 2011 Italian Census [22]). Participants were randomly selected from the electoral lists of about 140 municipalities in Italy. The sampling frame was subdivided into strata through two characteristics: region and municipality size. The number of interviews carried out in each stratum (e.g., municipalities in Piedmont with less than 5,000 inhabitants) was set in proportion to the population of the strata in the area (proportional stratified sample). Within each stratum, the sampling units (municipalities, electoral wards within municipalities, individuals) were chosen using multi-stage selection. Individuals meeting the following criteria were included in the study: legally permitted to buy TNP in Italy (≥18 years of age); residing in Italy; able to read, write, and understand Italian; and consented to participate in the survey. The sample size was based on an expected prevalence of I-HTP use among the surveyed population of 1.0%. A sample size of 6,085 participants per year is sufficient to estimate the prevalence with 95% confidence and a precision of +/- 0.25 percent units.

The study population for the I-HTP user sample comprised adults (≥18 years of age) registered in PMI's Italy user database who agreed to be contacted for research purposes at the time of registration. In addition to the inclusion criteria applied for the general adult sample, the inclusion criteria for the I-HTP user sample were as follows: has used more than 100 tobacco sticks in their lifetime; currently using I-HTPs; has access to the Internet; and is not currently employed by PMI or any of its affiliates. The sample size was calculated based on an expected percentage of I-HTP users exclusively using I-HTPs of 63.4% (based on cross-sectional study results among I-HTP users in Japan [17]). A sample size of 1,384 participants per year is sufficient to estimate the proportion of users who switched completely from cigarette smoking to using I-HTP with 95% confidence and a precision of +/- 2.5 percent units.

Study questionnaires

TNP use assessment: The study questionnaire was developed on the basis of several existing standard TNP use questions available in the literature to capture information about TNP use, such as the Adult Tobacco Use Questions of the National Health Interview

Survey [20], Questions of the Global Adult Tobacco Survey [21], and Population Assessment of Tobacco and Health Study questionnaires [22].

Risk perception assessment: Participants were asked to separately rate the general perceived risk of getting 18 different diseases or adverse health conditions due to cigarette smoking or using I-HTPs on a five-point Likert-like scale (ranging from 0 [no risk] to 4 [very high risk]) using the general version of ABOUT-Perceived Risk, a psychometrically validated instrument (18-item) for measuring participants' perceptions of their health risk. Based on the 18 rated items, an overall score ranging from 0 [no risk] to 100 [very high risk] was derived from the total raw score by Rasch model analysis. The general version of ABOUT–Perceived Risk was formerly called the Perceived Risk Instrument General (PRI-G) [23].

Respiratory symptoms assessment:

Participants were asked to evaluate the presence of cough (3 items) and phlegm symptoms (3 items) using two subscales of the Medical Research Council Questionnaire (MRCQ) [24]. Additionally, participants were asked if their respiratory symptoms changed as compared to 12 months ago based on a seven-point rating scale ranging from "very much worse" to "very much improved."

Hygiene, beauty, and fitness:

Participants were asked to rate their level of agreement with six hygiene, beauty, and fitness-related perceived benefits (i.e., my breath smells better, my teeth appear less stained or yellowish, it is easier to exercise, my sense of smell has improved, my sense of taste has improved, and my face skin appears smoother and firmer) since they switched from cigarettes to I-HTPs. This self-reported change questionnaire is based on a seven-point rating scale ranging from "strongly disagree" to "strongly agree."

Exercise capacity:

Participants were asked to rate their maximal perceived exercise capacity using the rating of perceived capacity scale, which is based on Metabolic Equivalents of Tasks (METs) [25]. MET values range from 1 to 20 in males and 1 to 18 in females and are listed on a progressive scale linked to specific physical activities by choosing the most strenuous activity that they could sustain for at least 30 min.

The risk perception, respiratory symptoms, hygiene, beauty, and fitness, and exercise capacity assessments were only administered to the I-HTP user sample because they were familiar with and had used the product.

Data analysis

All analyses undertaken were descriptive. Categorical outcome measures were described by presenting the overall number of participants in each group and the number and proportion of participants endorsing each category. Table 1 shows the adopted terms and definitions that were metrics in both surveys.

Continuous outcome measures were described by presenting the number of participants in each group with non-missing values, as well as the mean, standard deviation, median, and minimum and maximum. In addition, unadjusted 95% confidence intervals were calculated for the point estimates. The number of missing data points was reported. All analyses were performed with SAS® software (version 9.2 or higher, Statistical Analysis System; Cary, NC, USA).

Term	Definition
Lifetime criteria	Defined for each TNP category. For cigarettes: smoked ≥100 cigarettes; for heated tobacco products: used ≥100 sticks; for other innovative products such as e-cigarettes or similar products: used ≥100 times; for other TNPs: used 50 times or sticks for cigars, 50 times or sticks for cigarillos, 50 times or bowls for tobacco pipe, and 50 times or sessions/sittings or "consistent use" for water pipe; for smokeless tobacco: 20 times or pouches (snus), pieces (dissolvable tobacco)
Cigarettes	Include manufactured and roll/make-your-own cigarettes
TNP(s)	Include tobacco or nicotine-containing product(s)
Other Products(s)	Include (a) smokeless tobacco; (b) other combustible products (such as cigars, cigarillos, pipes, water pipes); (c) nicotine replacement therapy (NRT)) products (e.g., patch, gum, tablet, inhaler, lozenge, pill). They are only displayed as a sum category
Other Innovative Product(s)	Include products such as *Ploom*^{TM} and *Glo*^{TM}
Current use	Defined as having used any TNP more than the respective lifetime criteria and using the TNP either daily or occasionally at the time of the survey
Former use	Defined as having used any TNP more than the respective lifetime criterion and not using any TNP at the time of the survey
Never used	Defined as not having used any TNP up to the respective lifetime criterion
Regular use	Defined as using a TNP either daily or occasionally
Daily use	Defined as those who report currently using at least one TNP daily and have used more than the respective lifetime criterion
Occasional use	Defined as those who report currently using at least one TNP occasionally (i.e., less than once per day) and have used more than the respective lifetime criterion
Exclusive use	Defined as currently using only one TNP
Dual use	Defined as currently using two TNPs (e.g., cigarettes & e-cig or cigarettes & I-HTPs, etc.)
Poly use	Defined as currently using more than two TNPs (e.g., cigarettes & I-HTPs & e-cig, etc.)
Initiation of TNP use	Defined as the first time in life a TNP is used regularly. This implies using the product daily or occasionally and having used more than the respective lifetime criterion
Initiation rate of TNP use	Defined as the proportion of the surveyed population that initiated the use of a particular TNP in the last 12 months
Quitting/Stop using	Defined as having used a particular TNP according to the lifetime criterion (e.g., >100 cigarettes in lifetime) and at the time of the survey not using the TNP anymore, regardless of the consumption of other TNPs
Quit/Attempt to stop using	Defined as having used a particular TNP according to the lifetime criterion (e.g., >100 cigarettes in lifetime) and at the time of the survey having at least once tried to stop using the TNP, regardless of the consumption of other TNPs
Relapse to a TNP	Defined as using a particular TNP again after stopping/quitting TNPs for ≤12 months during the most recent attempt to quit TNPs
Re-initiation with a TNP	Defined as using a particular TNP again after stopping/quitting TNPs for >12 months during the most recent attempt to quit TNPs

Table 1. Terms and definitions. TNP, tobacco- or nicotine-containing product.

Ethical considerations

Each participant was informed about the survey's aim, the duration of their participation, the voluntary nature of their participation, confidentiality, and data use and privacy. Participants provided informed consent through the completion and return of the questionnaire. To ensure data confidentiality and anonymity, data were anonymized and irreversibly de-identified to protect participants. A waiver for the study was provided by the Istituto Superiore di Sanità on December 23, 2017.

Results

Year One: General adult population survey

The survey included 6,095 subjects aged between 18 and 97 (mean age, 51.7); 51.4% of participants were female, and 48.6% were male. Most (59.2%) had a relatively high level of education (attended university with/without a degree or graduated from senior high school).

Prevalence: Current TNP use prevalence was 25.7%; 12.8% of participants used TNPs in the past, and 61.5% had never used them. Cigarettes were the most frequently used TNPs (24.3%) with very few participants using e-cigs (1.4%) and even fewer using I-HTPs (0.7%). The prevalence of other TNP use (e.g., smokeless tobacco products, cigars, cigarillos, pipes, and hookahs) was 1.3%.

The prevalence of cigarette smoking was higher in males (27.5%) than in females (21.3%) and decreased with age (36.6% in the group 18-29 years vs. 19.4% in the group >50 years). The prevalence of e-cig use was slightly higher in males (1.7%) than in females (1.1%) and also decreased with age (4.0% for 18-29 years vs. 0.9% for >50 years). The prevalence of I-HTP use was slightly higher in males (0.9%) than in females (0.5%) and stable with increasing age (0.6% for 18-29 years vs. 0.4% >50 years).

Frequency of use: Among cigarette smokers, 92.8% were daily smokers and 5.7% occasional smokers (<1 cigarette/day). Average cigarette consumption was 12.7 cigarettes/day. Among e-cig users, 82.1% were daily users and 13.1% occasional users. E-cigs were used 18.4 times/day on average. Among I-HTP users, 71.4% were daily users and 23.8% occasional users. The average consumption of I-HTPs was 7.9 tobacco sticks/day.

Patterns of use: Among TNP users, 92.7% were exclusive users (one TNP), 6.1% were dual users (two TNPs), and 1.2% were poly-users (more than two TNPs). The highest percentages of dual users and poly-users were observed among cigarette smokers.

Initiation/relapse/re-initiation: In the last 12 months, of all never TNP users, 0.5% of participants initiated with cigarette smoking, 0.08% initiated with e-cigs, and 0.03% initiated with I-HTPs. Among current TNP users, 17 participants relapsed with cigarettes while no participants relapsed with I-HTPs or e-cigs. Among current TNP users, two participants re-initiated TNP use with cigarettes, one participant (0.06%) re-initiated TNP use with I-HTPs, and no participants re-initiated TNP use with e-cigs.

Quitting: Among current cigarette smokers, 65.7% did not plan to quit smoking, 12.5% planned to quit smoking within the next 6 months, and 21.9% stated they "don't know/couldn't say" in response to being asked about their plans for quitting. Meanwhile, 19.1% of I-HTP users and 14.3% of e-cig users planned to stop using I-HTPs and e-cigs, respectively, in the next 6 months. Among current cigarette smokers, 9.6% had tried to quit in the last 12 months, with an average of 2.2 attempts to quit and an average duration of 2.6 months. Furthermore, 16.7% of current I-HTP users and 8.3% of current e-cig users had tried to quit I-HTPs and e-cigs, respectively, in the last 12 months (Figure 1). Among all participants who were cigarette smokers more than a year prior to the survey, 2.9% had stopped cigarette smoking in the last 12 months, and 2.0% had stopped all types of TNPs.

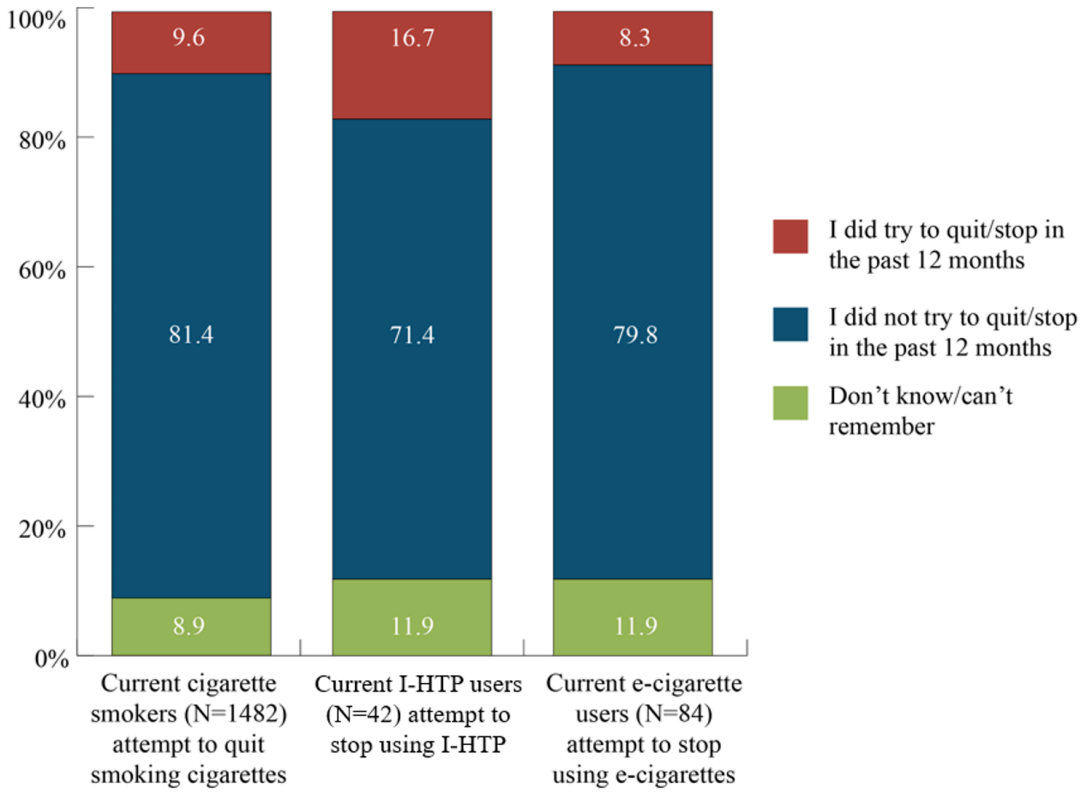

Figure 1. Attempt to quit smoking/stop using TNP in the last 12 months in the Year One general Italian adult population sample (data collected 2018-2019). Note: "Cigarettes" include manufactured and roll/make-your own cigarettes.

Year One: I-HTP user survey

The survey included 1,371 I-HTP users between 18 and 72 years old (mean age, 39.5); 55.7% of participants were female, and 44.3% were male. Most I-HTP users (87%) had a relatively high level of education (attended university with/without a degree or graduated senior high school).

Frequency and intensity of use: Among I-HTP users, 96.8% were daily users (average daily number of tobacco sticks: 13.7), 2.9% were occasional users, and 0.3% did not provide information. These results were similar when stratified by age or sex.

Patterns of use: Most (59.2%) current I-HTP users used I-HTPs exclusively, 38.6% also used combustible TNPs, and 2.2% used I-HTPs in combination with non-combustible TNPs. The distribution of product use patterns was similar across age and sex.

History of TNP use: Among current I-HTP users, 98.0% were cigarette smokers when they started using I-HTPs, 1.6% were former cigarette smokers, and 0.3% had never smoked.

Quitting: Among cigarette-smoking I-HTP users, 34.6% intended to quit cigarettes within the next 30 days or 6 months. This was considerably higher than in the general population of smokers (12.4%). Moreover, 13.6% intended to stop using I-HTPs, 18.1% of I-HTP users who also used combustible TNPs planned to stop using I-HTPs, and 10.7% of exclusive I-HTP users planned to stop using I-HTPs.

A quarter of current I-HTP users had attempted to quit cigarettes in the 12 months prior to the survey, with an average of 2.2 attempts to quit and an average duration of 1.8 months. Additionally, 5.0% of current I-HTP users attempted to stop using I-HTPs in the 12 months prior to the survey, with an average of 3.6 attempts to quit and an average duration of 1.4 months.

doi.org/10.32388/F3LAEC.2

Risk perception: I-HTP users scored the health risk (score 0 = no risk; score 100 = very high risk) associated with cigarettes higher (63.7) than the health risk associated with I-HTPs (42.6). At the same time, I-HTP users did not perceive I-HTPs as risk-free. The perceived health risk of cigarette smoking compared to using I-HTPs was slightly higher among exclusive I-HTP users (difference: 23.2) due to [1] (a) a higher perceived risk of cigarette smoking, and (b) a lower perceived risk of using I-HTPs.

Respiratory symptoms: Among exclusive I-HTP users, 10.1% reported respiratory symptoms (i.e., cough or phlegm) compared with 13.9% of I-HTP users who also used combustible TNPs. It should be noted that the majority of exclusive I-HTP users indicated an overall improvement in terms of cough (58.0%) and phlegm (56.5%) compared to the 12 months prior to the survey. The number of exclusive I-HTP users who reported improvements in respiratory symptoms was greater than in I-HTP users who also used combustible TNP (cough: 41.0%, phlegm: 35.2%).

Hygiene, beauty, and fitness: When asked to list any perceived benefits of switching from cigarettes to I-HTPs (using a seven-point scale ranging from "strongly disagree" to "strongly agree"), most exclusive I-HTP users agreed with the following statements: "my breath smells better" (73.8%), "my teeth appear less stained or yellow" (71.4%), "exercise is easier" (70.2%), and "my sense of smell and taste has improved" (62.6% and 61.2%, respectively).

Exercise capacity: The number of exclusive I-HTP users who reported improvements in exercise capacity was greater than in I-HTP users who also used combustible TNPs; 56.5% of exclusive users reported improved exercise capacity from the 12 months prior to the survey compared to 46.6% of users of I-HTPs plus combustible TNPs.

Year Two: General adult population survey

TNP use prevalence by age and sex is summarized in Table 2. In total, 6,118 subjects participated in the survey. 51.2% of participants were female, and 48.8% were male. Participants were aged between 18 and 98 years, with an average age of 51.0 years. The level of education of the participants in study Year Two was similar to that of those in Year One (2018-2019).

	Age (years)	TNP, n (%) [95% CI]		Cigarettes, n (%) [95% CI]		I-HTP, n (%) [95% CI]		E-cig, n (%) [95% CI]	
		Year 1 2018-2019	Year 2 2019-2020	Year 1 2018-2019	Year 2 2019-2020	Year 1 2018-2019	Year 2 2019-2020	Year 1 2018-2019	Year 2 2019-2020
Total Population	Total	1,568 (25.7) [24.6; 26.9]	1,636 (26.7) [25.6; 27.9]	1,482 (24.3) [23.2; 25.5]	1,535 (25.1) [24.0; 26.2]	42 (0.7) [0.4; 1.0]	67 (1.1) [0.8; 1.4]	84 (1.4) [1.1; 1.8]	88 (1.4) [1.1; 1.8]
	18-29	283 (37.8) [34.3; 41.5]	246 (31.5) [28.2; 34.9]	274 (36.6) [33.1; 40.2]	231 (29.6) [26.3; 33.0]	5 (0.7) [0.2; 1.6]	17 (2.2) [1.2; 3.5]	30 (4.0) [2.7; 5.7]	22 (2.8) [1.7; 4.3]
	30-39	242 (32.2) [28.8; 35.7]	253 (32.3) [29.0; 35.7]	225 (29.9) [26.6; 33.4]	234 (29.8) [26.6; 33.2]	13 (1.7) [0.9; 3.0]	16 (2.0) [1.6; 3.3]	7 (0.9) [0.3; 2.0]	10 (1.3) [0.6; 2.4]
	40-49	336 (28.3) [25.7; 31.0]	416 (32.4) [29.8; 35.1]	319 (26.9) [24.3; 29.5]	403 (31.4) [28.8; 34.0]	10 (0.8) [0.4; 1.6]	12 (0.9) [0.4; 1.7]	18 (1.5) [0.9; 2.4]	13 (1.0) [0.5; 1.8]
	>50	707 (20.7) [19.3; 22.2]	721 (22.1) [20.6; 23.6]	664 (19.5) [18.1; 20.9]	667 (20.4) [19.0; 22.9]	14 (0.4) [0.2; 0.7]	22 (0.7) [0.4; 1.1]	29 (0.9) [0.5; 1.3]	43 (1.3) [0.9; 1.8]
Males	Total	868 (29.3) [27.6; 31.0]	927 (31.1) [29.3; 32.8]	814 (27.5) [25.8; 29.2]	866 (29.0) [27.3; 30.7]	27 (0.9) [0.6; 1.4]	38 (1.3) [0.9; 1.8]	50 (1.7) [1.2; 2.3]	61 (2.0) [1.5; 2.7]
	18-29	154 (40.6) [35.6; 45.8]	145 (34.7) [30.1; 39.5]	148 (39.1) [34.1; 44.2]	139 (33.3) [28.7; 38.0]	5 (1.3) [0.4; 3.1]	9 (2.2) [0.9; 4.1]	20 (5.3) [3.2; 8.1]	17 (4.1) [2.3; 6.5]
	30-39	133 (36.5) [31.5; 41.8]	150 (40.7) [35.5; 45.9]	124 (34.1) [29.2; 39.2]	143 (38.8) [33.7; 44.0]	9 (2.5) [1.1; 4.7]	8 (2.2) [0.9; 4.3]	5 (1.4) [0.4; 3.2]	8 (2.2) [0.9; 4.3]
	40-49	178 (33.0) [29; 37.2]	215 (36.4) [32.4; 40.5]	170 (31.5) [27.5; 35.6]	207 (35.0) [31.1; 39.1]	4 (0.7) [0.2; 1.9]	8 (1.4) [0.5; 2.7]	8 (1.5) [0.6; 2.9]	8 (1.4) [0.5; 2.7]
	>50	403 (24.0) [21.9; 26.2]	417 (25.9) [23.8; 28.2]	372 (22.2) [20.1; 24.3]	377 (23.5) [21.4; 25.7]	9 (0.5) [0.2; 1.1]	13 (0.8) [0.4; 1.4]	17 (1.0) [0.5; 1.7]	28 (1.7) [1.1; 2.6]
Females	Total	700 (22.3) [20.8; 23.9]	709 (22.6) [21.1; 24.2]	668 (21.3) [19.8; 22.8]	669 (21.4) [19.9; 22.9]	15 (0.5) [0.2; 0.8]	29 (0.9) [0.6; 1.4]	34 (1.1) [0.7; 1.6]	27 (0.9) [0.5; 1.3]
	18-29	129 (35.0) [30; 40.1]	101 (27.8) [23.2; 32.8]	126 (34.1) [29.3; 39.3]	92 (25.3) [20.9; 30.2]	0 (0.0) [0.0; 1.0]	8 (2.2) [0.9; 4.3]	10 (2.7) [1.3; 5.0]	5 (1.4) [0.4; 3.2]
	30-39	109 (28.1) [23.6; 32.9]	103 (24.8) [20.7; 29.3]	101 (26.0) [21.7; 30.7]	91 (21.9) [18.0; 26.3]	4 (1.0) [0.2; 2.7]	8 (1.9) [0.8; 3.8]	2 (0.5) [0.0; 1.9]	2 (0.5) [0.0; 1.8]
	40-49	158 (24.4) [21.1; 28.0]	201 (29.0) [25.6; 32.5]	149 (23.0) [19.8; 26.5]	196 (28.2) [24.9; 31.8]	6 (0.9) [0.3; 2.1]	4 (0.6) [0.1; 1.5]	10 (1.5) [0.7; 2.9]	5 (0.7) [0.2; 1.7]
	>50	304 (17.6) [15.8; 19.5]	304 (18.3) [16.4; 20.3]	292 (16.9) [15.1; 18.8]	290 (17.5) [15.6; 19.4]	5 (0.3) [0.0; 0.7]	9 (0.5) [0.2; 1.1]	12 (0.7) [0.3; 1.3]	15 (0.9) [0.5; 1.5]

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Table 2. Prevalence of Use of Different Products by Age and Sex for Year One (2018-2019) and Year Two (2019-2020) General Italian Adult Population Sample.

CI=Confidence Interval

Prevalence: TNP use prevalence was 26.7% (vs. 25.7% in Year One). Cigarettes were still the most frequently used product (25.1% vs. 24.3%); e-cigarette use prevalence (1.4% vs. 1.4%) and I-HTP use prevalence (1.1% vs. 0.7%) remained limited. The prevalence of other TNPs was 1.1% (Figure 2).

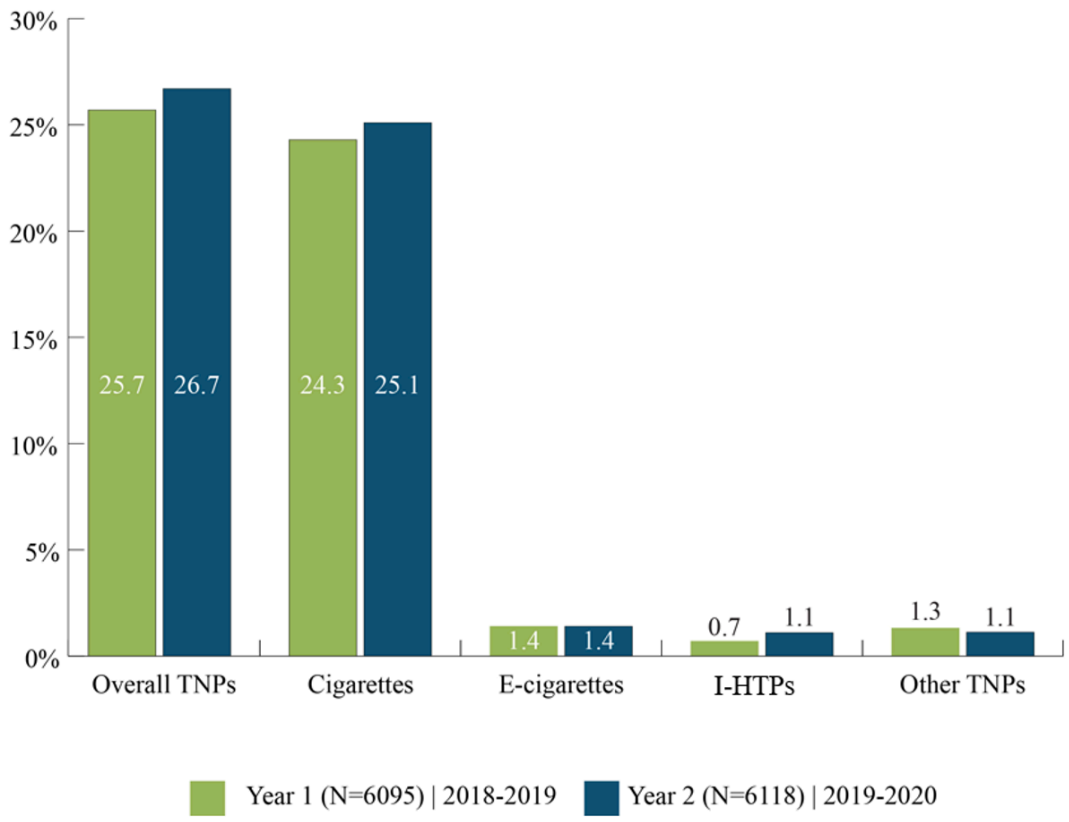

Figure 2. Prevalence of current TNP use in the Year One (2018-2019) and Two (2019-2020) general Italian adult population samples (trend). Note: "Cigarettes" include manufactured and roll/make-your-own cigarettes. Other TNPs include (a) smokeless tobacco (e.g., chewing tobacco, snus, snuff, dissolvable), (b) other combustible products (e.g., cigars, cigarillos, pipes, water pipes), and (c) nicotine replacement therapy products (NRTs; e.g., patch, gum, tablet, inhaler, lozenge, pill). HTP, heated tobacco product; TNP, tobacco- or nicotine-containing product.

TNP use prevalence in males (31.1%) was higher than in females (22.6%). The prevalence of cigarette smoking, e-cigarette use, and I-HTP use was higher in males than in females, with respectively 29.0% and 21.4% for cigarette smoking, 2.0% and 0.9% for e-cigarette use, and 1.3% and 0.9% for I-HTP use. Year Two use prevalence across sex was similar to Year One.

Across age groups, the prevalence of cigarette smoking was highest among 40-49 years (31.4%), followed by 18-29 years (29.6%), and lowest among 50+ years (20.4%). The prevalence of e-cigarette use was highest among 18-29 years (2.8%) and lowest among 40-49 years (1.0%), while the prevalence of I-HTP use decreased with age, from 2.2% among 18-29 years, 2.0% among 30-39 years, 0.9% among 40-49 years, and 0.7% among 50+ years.

Frequency and intensity of TNP use: Among cigarette smokers, 95.2% were daily smokers, with an average consumption of 12.9 cigarettes/day, and 3.5% were occasional smokers. Compared to Year One, the prevalence of daily cigarette smoking was slightly higher (95.2% vs. 92.8%). Among e-cigarette users, 81.8% were daily users, with an average of 19.2 uses/day, and 15.9% were occasional users. Compared to Year One, these rates were relatively stable; however, occasional consumption slightly increased (19.2% vs. 18.4% and 15.9% vs. 13.1%, respectively). Among I-HTP users, 76.1% were daily users, with an average of 8 tobacco sticks/day, and 20.9% were occasional users. Compared to Year One, the prevalence of daily I-HTP use was higher (71.4% vs. 76.1%) and the prevalence of occasional use was slightly lower (23.8% vs. 20.9%);

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meanwhile, average daily consumption remained stable (7.9 vs. 8.0 tobacco sticks/day).

Patterns of TNP use: Table 3 details the patterns of TNP use. Among all current TNP users, 93.8% were exclusive users (one TNP), while 4.5% were dual users (two TNPs), and 1.7% were poly-users (more than two TNPs). Cigarettes were the most commonly used TNP among dual and poly users. Compared to Year One, the prevalence of exclusive TNP users was higher (93.8% vs. 92.7%), dual use was lower (4.5% vs. 6.1%), and the prevalence of poly-use was slightly higher (1.7% vs. 1.2%).

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	Year 1 (2018-2019)			Year 2 (2019-2020)		
	N	%	95% CI	N	%	95% CI
Exclusive product use	**1,453**	**92.7**	**91.2; 94.0**	**1,534**	**93.8**	**92.5; 94.9**
Cigarettes	1,373	87.6	85.8; 89.2	1,442	88.1	86.4; 89.7
I-HTP	24	1.5	0.9; 2.3	28	1.7	1.1; 2.5
E-cig	35	2.2	1.5; 3.1	39	2.4	1.7; 3.3
One other product	21	1.3	0.8; 2.1	25	1.5	0.9; 2.3
Dual product use	**96**	**6.1**	**4.9; 7.5**	**74**	**4.5**	**3.6; 5.7**
Cigarettes & I-HTP	11	0.7	0.3; 1.3	19	1.2	0.7; 1.9
Cigarettes & e-cig	46	2.9	2.1; 3.9	31	1.9	1.2; 2.7
Cigarettes & other product	37	2.4	1.6; 3.3	18	1.1	0.6; 1.8
Other innovative product & other product	1	0.1	0.0; 0.4	-	-	-; -
Two other products	1	0.1	0.0; 0.4	3	0.2	0.0; 0.6
I-HTP & e-cig	-	-	-; -	2	0.1	0.0; 0.5
I-HTP & other product	-	-	-; -	1	0.1	0.0; 0.4
Poly product use	**19**	**1.2**	**0.7; 1.9**	**28**	**1.7**	**1.1; 2.5**
Cigarettes & I-HTP & e-cig & other product(s)	2	0.1	0.0; 0.5	9	0.6	0.2; 1.1
Cigarettes & other products	7	0.4	0.1; 1.0	5	0.3	0.0; 0.8
Cigarettes & I-HTP & e-cig	-	-	-; -	4	0.2	0.0; 0.7
Cigarettes & I-HTP & other product(s)	5	0.3	0.1; 0.8	4	0.2	0.0; 0.7
Three other products	4	0.3	0.0; 0.7	3	0.2	0.0; 0.6
Cigarettes & e-cig & other product(s)	1	0.1	0.0; 0.4	2	0.1	0.0; 0.5
Cigarettes & e-cig & other innovative product(s)	-	-	-; -	1	0.1	0.0; 0.4

Table 3. TNP Use Patterns for Year One (2018-2019) and Year Two (2019-2020) General Italian Adult Population Sample.

CI=Confidence Interval

Initiation/relapse/re-initiation: Among participants who had not used a TNP for over a year prior to the study, 0.41%, 0.05%, and 0.03% started using cigarettes, I-HTPs, and e-cigs, respectively, in the year prior to the Year Two survey. Among current TNP users, 0.92%, 0.06%, and 0.00% relapsed with cigarettes, I-HTPs, and e-cigs, respectively, after ≤ 12 months of abstinence; only 0.06% re-initiated with I-HTPs after a period >12 months of smoking abstinence, and none re-initiated TNP use with cigarettes or e-cigs.

Quitting: In Year Two, 69.1% of current cigarette smokers did not plan to quit smoking, 10.7% planned to quit smoking within the next 6 months, and 20.2% stated they "don't know/couldn't say" in response to being asked about their plans for quitting smoking. Among I-HTP users, 16.4% planned to stop using I-HTPs within the next 30 days or 6 months, 65.7% did not plan to, and 17.9% did not know. Among e-cig users, 20.5% planned to stop using e-cigarettes in the next 30 days or 6 months, 54.5% were not interested, and 25.0% did not know.

Moreover, 7.7% of cigarette users tried to quit smoking in the 12 months preceding the Year Two survey, with

an average of 2.5 attempts and an average duration of 3 months. Among participants who were cigarette smokers over a year before the survey, 1.9% had quit smoking in the last 12 months, and 1.0% had quit TNP use altogether (Figure 3). Compared to Year One, the rates of smokers who intended to quit cigarette smoking (12.5% Year One vs. 10.7% Year Two), had already tried to quit in the previous 12 months (9.6% Year One vs. 7.7% Year Two), or had successfully stopped using cigarettes (2.9% Year One vs. 1.9% Year Two) or all TNPs (2.0% Year One vs. 1.0% Year Two) in the past 12 months were somewhat lower in Year Two; however, the number (2.2 Year One vs. 2.5 Year Two) and duration (2.6 months Year One vs. 3 months Year Two) of attempts were slightly higher.

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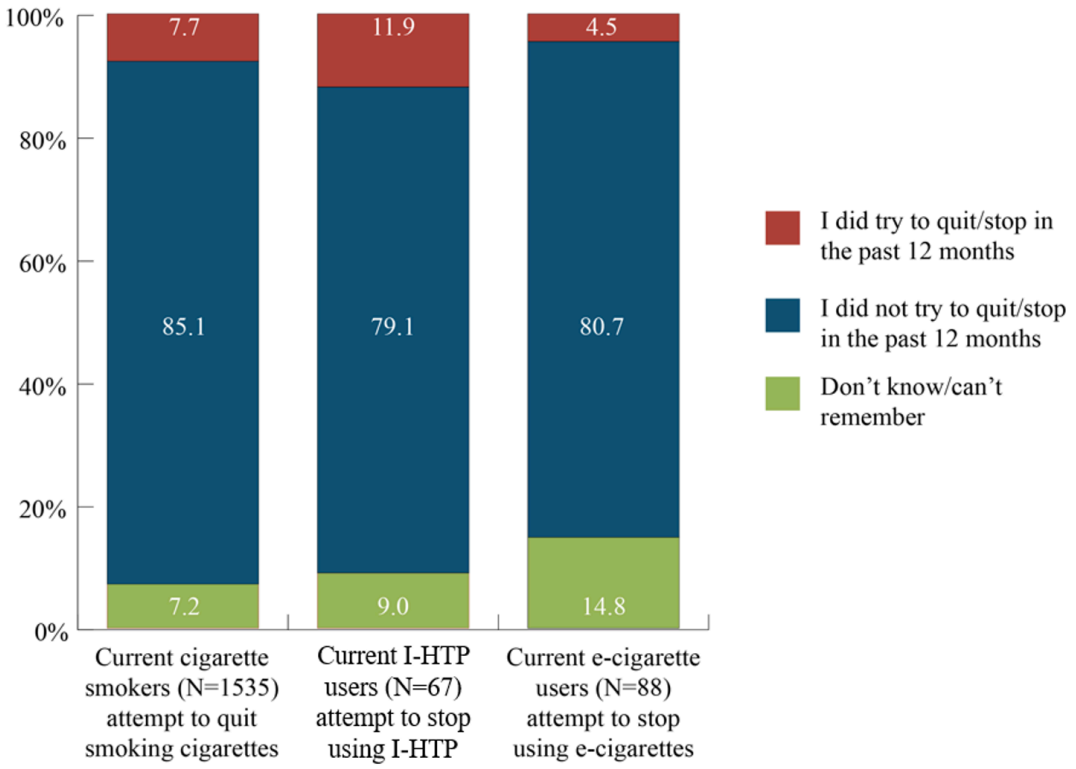

Figure 3. Attempt to quit smoking/stop using TNPs in the last 12 months in the Year Two (2019-2020) general Italian adult population sample. Note: "Cigarettes" include manufactured and roll/make-your-own cigarettes.

Year Two: I-HTP user survey

In total, 1,401 I-HTP users completed the survey. 57.4% of the participants were male, and 42.6% were female. Participants were aged between 18 and 72 years, with an average age of 36.7 years. Most I-HTP users (86%) had relatively high levels of education (attended university with/without a degree or graduated from senior high school).

Frequency and intensity of use: Among I-HTP users, 96.1% were daily users, with an average of 13.3 tobacco sticks/day; 3.2% were occasional users; and 0.6% did not provide information. Overall, these results were similar to those in Year One. While the rate of daily use was similar across sexes, the average daily number of tobacco sticks was higher in males than in females (14.3 vs. 12.0/day).

Patterns of use: In line with the Year One results, 61.7% of all I-HTP users were exclusive users, while 36.0% and 2.3% used I-HTPs in combination with combustible TNPs and non-combustible TNPs, respectively. The prevalence of exclusive users was lower in males (57.8%) than in females (66.8%), but similar across age groups (58.4% for ages 18-29 and 64.8% for ages 30-39).

History of use: In Year Two, 97.0% of current I-HTP users were adult cigarette smokers when they started using I-HTPs, while 2.5% were former cigarette smokers, and 0.5% were never smokers. This indicates that a total of 99.5% of all I-HTP users had a smoking history before they started using I-HTPs, and only 0.5% started TNP use with I-HTPs.

Quitting: Among I-HTP users who smoked cigarettes, 33.3% intended to quit cigarettes within 30 days or 6 months. In comparison, just 10.7% of cigarette smokers in the general population planned to quit smoking. Furthermore, 15.2% of users intended to stop using I-HTPs in the next 30 days or 6 months. A total of 53.1% of all I-HTP users who smoked more than a year before the Year Two survey had quit cigarette smoking in the last 12 months. Among this group, 92.1% had switched to I-HTPs.

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Risk perception: I-HTP users did not perceive the product to be risk-free (Figure 4), but they scored the health risk (score 0 = no risk; score 100 = very high risk) associated with cigarettes higher (64.3) than the health risk associated with I-HTPs (44.4).

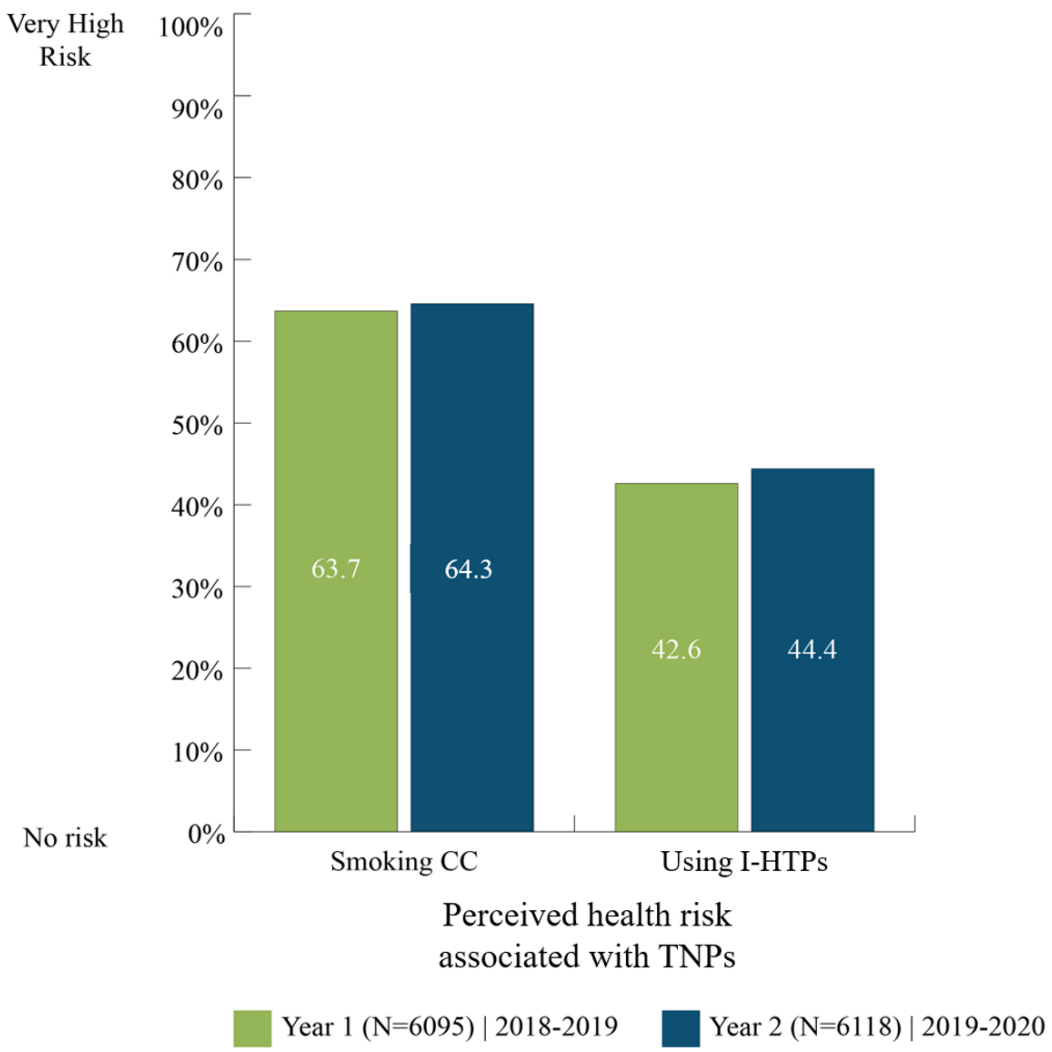

Figure 4. Perceived health risks associated with smoking cigarettes/using I-HTPsin the Year One (2018-2019) and Two (2019-2020) Italian I-HTP user samples (trend). Note: CC, cigarettes, including manufactured and roll/make-your own cigarettes.

Respiratory symptoms: The Year Two results for respiratory symptoms; exercise capacity (Table 4); and hygiene, beauty, and fitness were similar to those observed in Year One.

doi.org/10.32388/F3LAEC.2

Change in exercise capacity	Exclusive I-HTP users		I-HTP + combustible TNP	
[n (%)]	Year 1 (n = 812) 2018-2019	Year 2 (n = 864) 2019-2020	Year 1 (n = 529) 2018-2019	Year 2 (n = 505) 2019-2020
Has improved	117 (55.5%)	438 (50.7%)	52 (42.6%)	202 (40.0%)
No change	82 (39.6%)	364 (42.1%)	58 (47.5%)	242 (47.9%)
Has worsened	8 (3.9%)	62 (7.2%)	12 (9.8%)	61 (12.1%)

Table 4. Perceived Change in Exercise Capacity by I-HTP Use Patterns for Year One (2018-2019) and Year Two (2019-2020)

Discussion

The prevalence of cigarette smoking in Italy has been stable over the last decade but increased with the COVID-19 lockdowns from 23.3% in January 2020 to 26.2% in May 2021 [26]. Cessation is and must remain the primary goal in the fight against smoking. However, for adult smokers who continue to smoke cigarettes, a harm reduction approach is an alternative. Smoke-free products can offer smokers who would otherwise continue to smoke a better alternative than cigarettes by reducing exposure to HPHCs. There is some evidence that smoke-free TNPs are beginning to compete with cigarettes [27] and may be contributing to declining cigarette sales [28], but it is important to assess population use patterns.

Cigarettes were the most used TNP in the general Italian adult population surveys in 2018-2019 and 2019-2020. The prevalence rates of cigarette smoking in Year One (24.3%) and Year Two (25.1%) are in line with the Italian ISS PASSI Surveillance System's report of a 25.2% prevalence of cigarette smoking from 2017-2020 [29].

Current I-HTP use prevalence reached 1.1% in the general Italian adult population Year Two survey, just a few years after the 2016 national launch in Italy. This aligns with the results of a study of a representative sample (n = 9,428) of the Italian population surveyed between 2017 and 2019, which reported a 1.1% prevalence rate of HTP users (including all HTP brands) [15]. Meanwhile, in both Years One and Two, I-HTP use prevalence was higher in males (1.3%) than in females (0.9%); this also aligns with previous findings [15]. Notably, the rate of I-HTP use in Italy is lower than the rates observed in two Japanese surveys conducted in 2019 and 2020 (5.3% and 10.9%, respectively) [30][31].

In terms of age, I-HTP use was most common among middle-aged adults, corresponding to previous findings in Japan [17]. While cigarette smoking was most prevalent among individuals with lower levels of education [32], I-HTP use was most prevalent among individuals with higher levels of education. These characteristics are typical of early adopters of a new product or technology, and product use may evolve as more adult smokers switch.

These two cross-sectional surveys consistently show that nearly all current I-HTP users were adult cigarette smokers when they started using the product, which confirms the findings of other independent studies [14][15][33][34].

Less than 1% of TNP users initiated TNP use with I-HTPs, and >99% had used other TNPs prior to using I-HTPs. The low initiation, re-initiation, and relapse observed with I-HTPs align with previous studies [17][35][36][37][38][39][40][41][42]. The present findings demonstrate that the majority of current Italian I-HTP users are the intended users for such smoke-free products, which aligns with the overall principle of tobacco harm reduction [43].

Moreover, the rate of quitting smoking remained stable across the study years and aligns with the recent findings of another European survey [44] that suggested that the commercialization of I-HTPs did not prevent adult smokers from quitting cigarettes.

While the survey data show that there is some degree of I-HTP use in combination with combustible TNPs, most

I-HTP users switched from cigarettes and use I-HTPs exclusively, as in other surveys [45][46] (even if a period of dual use may be expected prior to exclusive I-HTP use [47][48]). Furthermore, we found that I-HTP use with combustible TNPs decreased between Year One and Year Two; the same trend was observed in other large and independent surveys [49][50]. Taken together, these findings suggest that HTPs are an acceptable alternative to cigarettes for adult smokers [51].

While users did not perceive I-HTPs as risk-free, they perceived I-HTP use as associated with a lower health risk than smoking cigarettes. This aligns with what is acknowledged and shown elsewhere [52][53][54][55][56].

Across the survey years, the majority of exclusive I-HTP users indicated an overall improvement in their respiratory symptoms (cough and phlegm) and their exercise capacity compared to a year before they started using I-HTPs. These results generally showed higher proportions of exclusive I-HTP users who perceived an improvement in terms of respiratory symptoms and exercise capacity than dual users with combustible TNPs. Moreover, most current I-HTP users also reported an improved sense of smell and taste, better breath smell, and reduced stains or yellowing of teeth.

These surveys have some limitations. First, they relied on self-reported measures, which could introduce reporting bias. Previous studies have shown that the reliability of self-reported smoking in adults has generally been high, suggesting that self-reported data provide reasonably valid estimates of cigarette smoking in the population [57][58]. However, the reliability of self-report assessments for smoke-free products has not yet been investigated and confirmed to the same extent. Second, some survey questions were about the participant's history of TNP use (e.g., the age at which the participant started regularly using a TNP); participants with long histories of TNP use may have had difficulty accurately remembering such information, and thus such responses may have been subject to recall bias. Third, the sample of I-HTP users comprised those who had registered their devices as part of PMI's Italy I-HTP user database and agreed to be contacted for research purposes; therefore, the findings collected from this particular sample may not be generalizable to all Italian I-HTP users. Related to this, the general adult sample was not asked about their risk perception of I-HTPs. Finally, the study design's cross-sectional nature prevented us from drawing cause–effect conclusions.

These surveys also have several strengths. They were annually repeated collections of data using the same sampling framework and methods, namely: 1) face-to-face interviews with a nationally representative sample of participants gathered using a multi-stage random selection of the electoral lists of about 140 Italian municipalities, and 2) a web survey with a large I-HTP user sample to gain insights from a sizeable number of early adopters of the product. Meanwhile, the study applied widely accepted definitions of TNP use in accordance with the guidelines for controlling and monitoring the tobacco epidemic of the World Health Organization [59]. Additionally, the general adult population and I-HTP user sample sizes were large and provided a sufficiently high level of precision for the main study outcomes. Lastly, conducting numerous surveys throughout the year ensured the representation of a full year.

Smoke-free TNPs have the potential to improve public health if they help adults who smoke switch away from cigarettes, and there is evidence that this is happening in countries where such products are available [27][60]. At the same time, these smoke-free alternatives should not be attractive to youth, nonsmokers, or former smokers. The present results show that the vast majority of current I-HTP users switched from cigarettes rather than continuing to smoke, and there was low TNP initiation and low TNP relapse or re-initiation with I-HTPs, which is in line with the principles of tobacco harm reduction [43]. Future studies should continue to monitor the prevalence of TNP use to provide long-term evidence on the impact of SFPs on population health in Italy.

Statements and Declarations

Acknowledgments

Steve Roulet: Conceptualization, Formal Analysis, Methodology, Funding Acquisition, Writing - Review & Editing; Tommaso Pellegatti: Writing – Original Draft Preparation, Writing - Review & Editing, Visualization; Karina Fischer: Data Analysis/Interpretation, Writing - Review & Editing; Pierpaolo Magnani: Conceptualization, Formal Analysis, Methodology, Funding Acquisition, Writing - Review & Editing; Umberto Di Luzio Paparatti: Visualization, Writing - Original Draft Preparation, Writing - Review & Editing. Philip Morris International is the sole source of funding and sponsor of this research. The funder was involved in study design, the collection, analysis, and interpretation of data, and the writing of the report, and in the decision to submit the article for publication. The authors thank Lindsay Reese for editorial review.

Conflicts of interest

S.R., K.F., and P.M. are employees of Philip Morris International; T.P. is an employee of Philip Morris Italia S.r.l.; U.D.L.P. is an Independent Researcher, Sr. Medical Advisor for Philip Morris Italia S.r.l. *IQOS*® is manufactured by Philip Morris Products S.A.

Ethical considerations

The present survey was carried out in compliance with the principles set forth in the Declaration of Helsinki and with Good Epidemiological Practice and International Ethical Guidelines for Epidemiological Studies and Market Research Society Code of Conduct.

Data availability

The datasets generated during this study are available from the corresponding author on reasonable request.

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Declarations

Funding: Philip Morris International is the sole source of funding and sponsor of this research.

Potential competing interests: S.R., K.F., and P.M. are employees of Philip Morris International; T.P. is an employee of Philip Morris Italia S.r.l.; U.D.L.P. is an Independent Researcher, Sr. Medical Advisor for Philip Morris Italia S.r.l. IQOS® is manufactured by Philip Morris Products S.A.