# SCIENTIFIC UPDATE

PMI SCIENCE – PHILIP MORRIS INTERNATIONAL

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# WHY PERCEPTION AND BEHAVIOR MATTER

HOW CONSUMERS' ATTITUDES INFLUENCE THEIR USE OF SMOKE-FREE PRODUCTS


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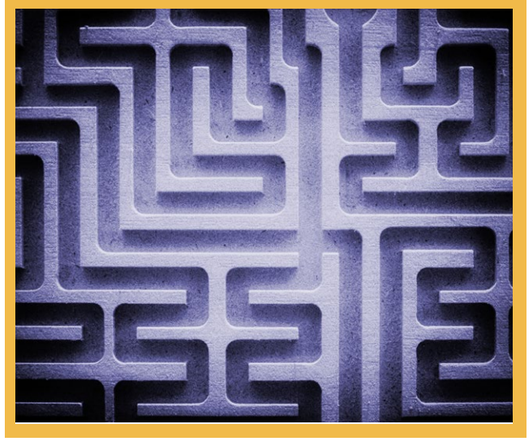

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# INTRODUCTION

For smoke-free products to have a positive impact on public health, it is not enough to know whether these products have a reduced-risk profile compared with cigarettes. It is also important to know what motivates adult smokers to transition from cigarettes to smoke-free products, as well as to measure who are using these products, and how they are used. Our perception and behavior studies provide us with this information.

Individual decisions on whether to switch from smoking to smoke-free product use are based partly on the perception of the relative risks of the products. So, understanding how and why these decisions are made is vitally important in convincing adult smokers who would otherwise continue to smoke to switch from smoking cigarettes, to using scientifically substantiated, less harmful alternatives.

Our perception and behavior team at Philip Morris International (PMI) is leading the charge in this effort. They are developing unique measurement and analysis tools to determine whether the risks and claims for our products, which are based on our aerosol chemistry and physics, toxicology, and clinical assessments are understood by both tobacco users and nonusers.

These tools can then be used to assess behaviors and outcomes related to the use of tobacco and nicotine products (TNPs), including health and functioning, risk perception, perceived dependence, and product experiences, as well as the rate at which adult smokers are transitioning to smoke-free products.

Read on to learn more about the exciting work done by our perception and behavior researchers.


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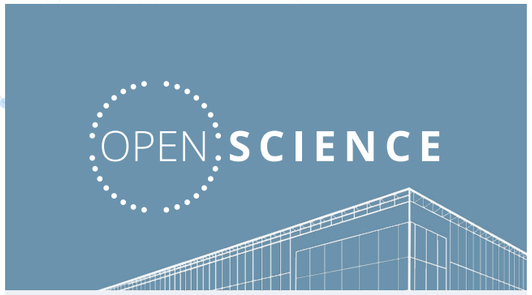
# EVENTS




## PMI Transformed: The Past, Present, and Future of Smoke-free Products

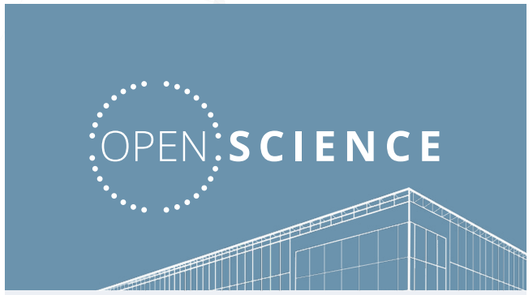
Neuchâtel, Switzerland
November 14, 2024

At our fifteenth Open Science event, a panel of experts reflected on PMI's remarkable transformation and the milestones achieved since the 2014 pilot launch of PMI's leading heated tobacco product (HTP), the Tobacco Heating System (THS). The discussion was lively, focusing on the challenges faced and the perseverance PMI has shown in overcoming mistrust and misconceptions. The success story of THS in Japan and its impact on the country's smoking prevalence was highlighted.

The panelists also delved into PMI's scientific research, which supports the potential of THS to present a lower risk of harm for adult smokers who switch to it, compared with continued smoking. They emphasized the importance of science-based regulation that differentiates between smoke-free products and cigarettes. Such regulation can encourage adult smokers who would otherwise continue to smoke to switch to smoke-free products while discouraging unintended audiences from using them.

Additionally, the experts underscored the importance of product innovation in achieving a smoke-free future. By enhancing existing products and developing new ones, PMI aims to provide adult smokers who don't quit with more options, making it easier for them to transition away from cigarettes.

Watch the replay here.




## Science-Driven Policies: The Key to Better Outcomes

Online event
April 10, 2025

At our sixteenth Open Science event, our expert panelists explored the importance of tobacco regulatory policies that are underpinned by science. Despite significant efforts through public awareness campaigns, regulatory measures, and fiscal strategies, around 1 billion people worldwide still smoke. This number hasn't meaningfully changed in decades and, based on current trends, is unlikely to change in the near future. The experts discussed how science-driven policies can complement existing tobacco control measures to help accelerate the decline in smoking rates.

A key focus was on addressing misconceptions about nicotine being the major cause of smoking-related diseases and emphasizing the importance of tobacco harm reduction strategies. By distinguishing between the risks of nicotine and those of tobacco combustion, policies can better support adult smokers who don't quit in transitioning to less harmful alternatives, thereby lowering smoking rates. The panelists highlighted examples from countries like New Zealand and Sweden, where science-based approaches have led to notable declines in smoking rates. These examples were contrasted with countries that have taken a more restrictive regulatory path for smoke-free products where the decline in smoking rates has slowed.

Watch the replay here.


## Nicotine and Tobacco Science Conference 2024

Medical University of South Carolina
October 28-29, 2024

PMI participated in the twenty-seventh Nicotine and Tobacco Science Conference (NTSC), which focused on *"Risks and Benefits of Consumer Nicotine Delivery Systems: Emerging Evidence and Open Questions."* The NTSC brings leading academic and industry researchers together for "across the aisle" discussions on smoking cessation, tobacco harm reduction, and understanding the underlying mechanisms contributing to cigarette addiction.

During this 2-day conference, PMI scientists presented a poster entitled *"Differences in biomarkers of potential harm after 2+ years of tobacco heating system use compared to cigarette smoking"*. This poster showcased new clinical data that highlights the potential benefits of switching from cigarette smoking to using THS. Results of the cross-sectional study, conducted by Ansari et al., showed significant reductions in key biomarkers of potential harm (BoPH) in people who completely switched to THS for at least 2 years compared with those who continued smoking, suggesting that switching to THS could favorably affect key pathophysiological pathways involved in smoking-related diseases.

The data in this poster have since been published in a peer-reviewed journal.



# SCIENTIST **PROFILE**

## Dr. Christelle Chrea

Christelle Chrea is Principal Scientist, Consumer Sciences, at PMI, where she leads consumer-centric research programs. Having joined PMI in 2013, one of Christelle's key responsibilities has been advancing the development of reliable, valid, and fit-for-purpose Consumer Reported Outcome Measures (CROM) through the ABOUT™ (Assessment of Behavioral OUtcomes related to Tobacco and nicotine products) Toolbox initiative, to support the assessment of smoke-free products and strategies for message substantiation.

Christelle has participated in CORESTA (Cooperation Center for Scientific Research Relative to Tobacco) activities since 2017, attending and presenting at numerous CORESTA meetings, events, and external conferences. Within CORESTA, she joined the Product Use Behavior Sub-Group in 2017, and since 2018 she has been the Coordinator of the CROM Task Force, which serves as an interindustry consortium to establish best practices and guidelines for the integration of CROM in research on TNPs. Christelle has been extremely committed to cooperation within the international scientific community, as reflected by the unique setting of the task force she leads. As a result, she has coauthored two CROM guidelines and organized seven symposia and workshops on CROM-related science and methodologies where researchers from industry, academia, and regulatory agencies present their research. This work earned her a CORESTA Bronze Medal in 2024 for contributions to scientific cooperation.

Christelle holds a PhD in Food Sciences from the University of Burgundy, France and completed two postdoctoral fellowships before choosing to focus her career on applied research within industry. She has also published extensively in the fields of perception and behavior and CROM in peer-reviewed scientific journals.

# THE ROLE OF PERCEPTION AND BEHAVIOR RESEARCH:

## AN INTERVIEW WITH STEVE ROULET

Perception and behavior studies provide in-depth insights into the use patterns of tobacco and nicotine products (TNPs) in areas such as risk perception, product experiences, and use behaviors among adult smokers transitioning to smoke-free products. These insights, in turn, help ensure these products reach the right audience: current smokers who would otherwise continue to smoke. In this interview, Steve Roulet, Global Head of Regulatory Insights, discusses Philip Morris International's (PMI's) perception and behavior studies program and its role in advancing tobacco harm reduction.

Steve holds a degree in Science in Economics from the University of Lausanne and a degree in Business Administration from the University of Southern Indiana. In his current role, Steve leads the development and execution of PMI's regulatory consumer research on smoke-free products. He was instrumental in the implementation of PMI's perception and behavior assessment program to support the commercialization of our Tobacco Heating System (THS), commercialized as *IQOS*, as a Modified Risk Tobacco Product (MRTP) in the U.S.

He is also one of the architects of PMI's postmarket consumer research program internationally, and the program that is designed to address PMI's postmarket monitoring obligations under the U.S. Food and Drug Administration's (FDA's) exposure modification order granted to *IQOS*.



### How are perception and behavior studies conducted?

Perception and behavior studies involve both current tobacco users and nonusers. Most of these studies are based on self-reported outcomes and therefore involve the administration of survey questionnaires. For example, studies among current tobacco users include questions to measure perception and actual use behavior of smoke-free products, while studies among nonusers primarily focus on product perception and likelihood of future use.

Our perception and behavior studies are conducted in a way that is scientifically robust, complies with all applicable laws and regulations, and meets international guidelines or guidance, such as those set by the FDA. In all our perception and behavior studies, measures to protect the rights and welfare of the study subjects are put in place.

To ensure standardization and harmonization of measurements across different studies and products, PMI has developed the ABOUT™ (Assessment of Behavioral OUtcomes related to Tobacco and nicotine products) Toolbox, a suite of Consumer Reported Outcome Measures (CROM).

Read more about the ABOUT™ Toolbox on our website here.

### What can we learn from perception and behavior studies?

Overall, the study data suggest that the observed shift from combustible to smoke-free product use over time is in line with the principles of tobacco harm reduction and suggests that the marketing of THS and other smoke-free products is likely to have a positive impact on public health. This shift also suggests that smoke-free products are acceptable alternatives to cigarette smoking.

An important goal of our perception and behavior research is to examine the factors that affect switching, so the results can be applied to future product development.

These factors include, but are not limited to:

- Perceived impact on health and physical factors, such as perceptions of reduced harm from switching from cigarette to smoke-free products.
- Sensorial aspects (e.g., taste, satisfaction, and enjoyment).
- Practical aspects of smoke-free product use compared with cigarette use (e.g., issues of accessibility/availability and maintenance).
- Financial implications of switching (e.g., if it is cheaper in the long run than cigarette smoking).

*Our studies show that PMI smoke-free products are perceived to have a lower risk of harm compared with cigarettes and can support tobacco harm reduction efforts.*

### What can these studies tell us about the impact of smoke-free products on public health?

**Perception and behavior studies measure several key aspects that are important from a public health perspective. For example, our studies measure consumers' perceptions of health risks associated with the use of cigarettes and smoke-free products. This is important because, as mentioned above, risk perception influences whether smokers decide to switch to these better alternatives or not.**

**Risk perception also impacts use patterns of smoke-free products—for example, whether a smoker decides to completely switch to these products or continue using cigarettes (dual use). Moreover, these studies also provide evidence in terms of frequency and intensity of products use. This type of behavior data provides valuable evidence to measure the extent to which adult smokers find smoke-free products acceptable and satisfying, supporting their switch from cigarettes. At the same time, we also measure whether individuals understand that our smoke-free products are not risk free. Finally, and importantly, postmarket perception and behavior research provides data on whether nontobacco users initiate tobacco use with smoke-free products and whether former tobacco users relapse or reinitiate tobacco use through these products.**

**All of this data can be used to help regulators evaluate the potential role of smoke-free products in moving adult smokers away from smoking.**

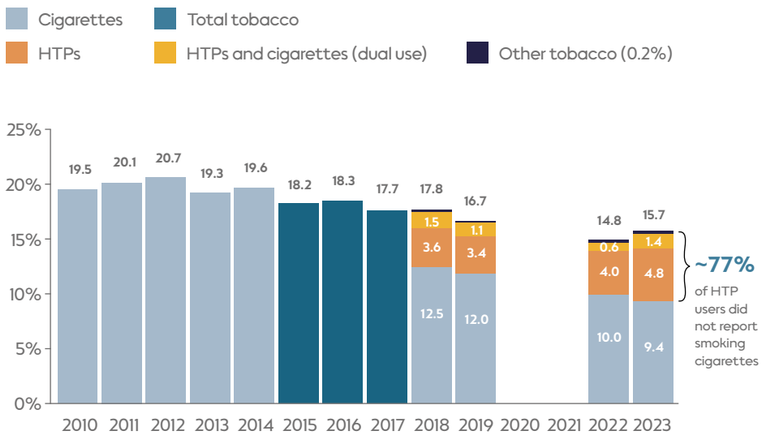
## What can we learn from postmarket studies on prevalence, uptake, and the use patterns of TNPs?

At PMI, we are conducting postmarket studies to better understand the real-world use of our smoke-free products. Following the commercialization of THS, we have been conducting repeated cross-sectional studies in Japan, Italy, and Germany, including the General Adult Population Survey and the Adult THS User Survey.

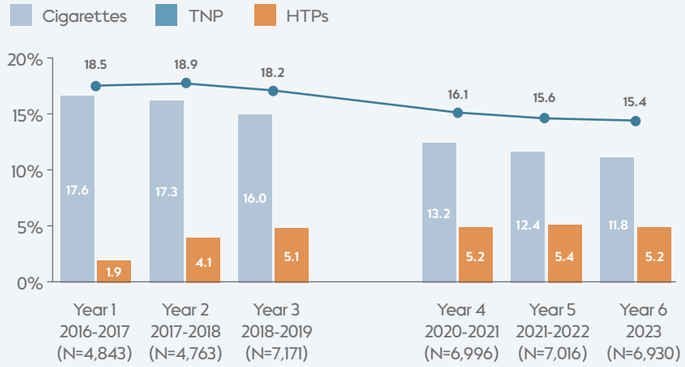
We now have a number of years of data on the evolution of TNP use prevalence in Japan, and our repeated cross-sectional studies results are aligned with the Japanese Ministry of Health, Labour and Welfare's yearly National Health and Nutritional Survey (NHNS).

Those studies show that smoking prevalence in Japan is rapidly declining, with the percentage of Japanese adults who smoke dropping from 19.6% in 2014 to 10.8% in 2023.

**CURRENT TOBACCO USE PREVALENCE**
NHNS



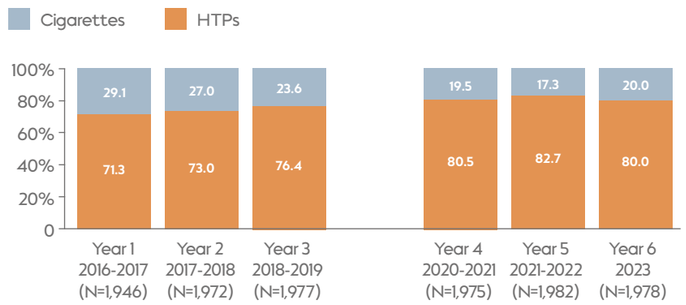

**CURRENT TOBACCO AND NICOTINE USE PREVALENCE IN JAPAN**
PMI General Adult Population Survey




The NHNS data also demonstrates that overall tobacco product use has not increased, indicating that many existing tobacco users in Japan are switching completely to heated tobacco products (HTPs), rather than using HTPs in addition to cigarettes. At the same time, data from PMI's General Adult Population Survey show that uptake of HTPs (which includes THS) among tobacco users in Japan has been increasing over the years of the study.

By year 6 (2023) of the PMI General Adult Population Survey, the proportion of HTP users who do not smoke had reached 65%. This was a similar trend to that seen in the NHNS, where the data showed that approximately 77% of HTP users were not smoking cigarettes in 2023. These results were further corroborated by the PMI Adult THS User Survey (data shown in the graph opposite), which found that in the last 3 years of the survey around 80% of THS users had not smoked tobacco products.

**COMBUSTIBLE TOBACCO USE AMONG THS USERS**
PMI Adult THS User Survey






In Italy, data from our studies is aligned with data from the Italian National Institute of Statistics (ISTAT) and Italian National Institute of Health (ISS) surveys. According to the 2022 ISS survey, consumption of HTPs (which includes THS) tripled, from 1.1% in 2019 to 3.3% in 2022. This equates to approximately 1,700,000 more Italian smokers now using HTPs.

In Germany, our studies show that the prevalence of HTP use, including THS use, has increased over time, yet it remains at a comparatively lower level than in Japan and Italy.

## What have we learned about THS use among never smokers and former smokers?

Finally, and very importantly, our cross-sectional studies also show that THS use by adults who had never smoked or had already quit using TNPs is very low and that more than 96% percent of THS users were already using tobacco products when they switched to THS.

Overall, this shift from combustible product use to smoke-free product use is in line with the principles of tobacco harm reduction. The availability of THS is likely to have a positive impact on public health across countries, given that the majority of adult smokers managed to move away from smoking completely and that their use among unintended audiences is low.

## What does the risk perception data tell us about the potential public health impact of THS?

Risk perception is an important factor that influences adult smokers to switch to smoke-free products as well as impacting smoke-free product use patterns. In other words, it is important to truthfully and accurately communicate the health risks associated with using smoke-free products, in particular, in comparison with smoking cigarettes.

Our repeated cross-sectional studies in Japan, Italy, and Germany show that THS users understand that there is a health risk associated with using THS, but also that the health risk is lower than the risk associated with smoking cigarettes.

## What have we learned about users' perception of health with THS use?

**Using the ABOUT™ – Health and Functioning instrument, we have conducted yearly surveys in Japan, Italy, and Germany, asking users whether they feel that switching from cigarettes to THS has led to perceived improvements in their health.**

**Overall, THS users report improvements in coughing, breathing, oral health, physical health (e.g., fitness), hygiene, beauty, and overall health since switching from cigarettes. These improvements were more pronounced among THS users who switched completely (i.e., stopped smoking cigarettes) than among THS users who remained dual users, showing the importance of using smoke-free products exclusively.**

# SOLVING THE PERCEPTION AND BEHAVIOR PUZZLE:

## STANDARDIZED TOOLS IN SMOKE-FREE PRODUCT RESEARCH

Picture yourself standing in front of a complex jigsaw puzzle—each piece representing a fragment of human perception, decision-making, and behavior. It's intricate, and there are many missing pieces or pieces that don't seem to fit properly. Perhaps those pieces came from a different box. This is the challenge that perception and behavior scientists face when trying to work out why adult smokers might switch from cigarettes to smoke-free products, how they use them, and how they perceive them. But what if there was a map or instruction manual to guide them?

Smoke-free products are changing the landscape for tobacco research and regulation. Designed to provide adult smokers who don't quit with less harmful alternatives to combustible products, such as cigarettes, these products have the potential to reduce the global burden of smoking-related diseases. Indeed, many countries have adopted them as part of a tobacco harm reduction strategy to improve public health. However, their role in tobacco harm reduction is only possible if adult smokers who don't quit make the switch to using these alternatives instead.



In addition to its role in guiding product development, one way that perception and behavior research can help tobacco harm reduction is by assessing consumers' perception of the relative risk of a smoke-free product before it is marketed.

This can ensure that any communications about its risks are accurate, nonmisleading, and scientifically substantiated, allowing adult smokers to gain a clear understanding of the risks and benefits of a smoke-free alternative, without encouraging nonsmokers, youth, and former smokers to initiate or reinitiate their use. Ongoing evaluation of risk perception also occurs in a postmarket setting to monitor trends that may affect product usage patterns over time.

## The problem of inconsistent data: Why standardized tools matter

For years, studying consumer behaviors and risk perceptions relating to smoke-free products was like solving a jigsaw puzzle with mismatched pieces. Researchers used various tools depending on the product that was assessed, geographical location, and consumer demographics. Although individual studies provided glimpses of insights, the resulting data have often been inconsistent and incomparable, making it difficult to understand the global picture.

Standardized tools and frameworks allow scientists to measure different parameters and outcomes accurately and consistently. Without standardized tools, it is difficult to compare findings across studies, products, regions, or consumer demographics. Additionally, policymakers and regulators rely on consistent and scientifically sound data to assess the risk reduction potential of smoke-free products. Such reliable data can only be achieved with validated methodologies. By employing standardized and validated methodologies, the data are no longer isolated pieces of the jigsaw puzzle, making it easier to build the final picture.

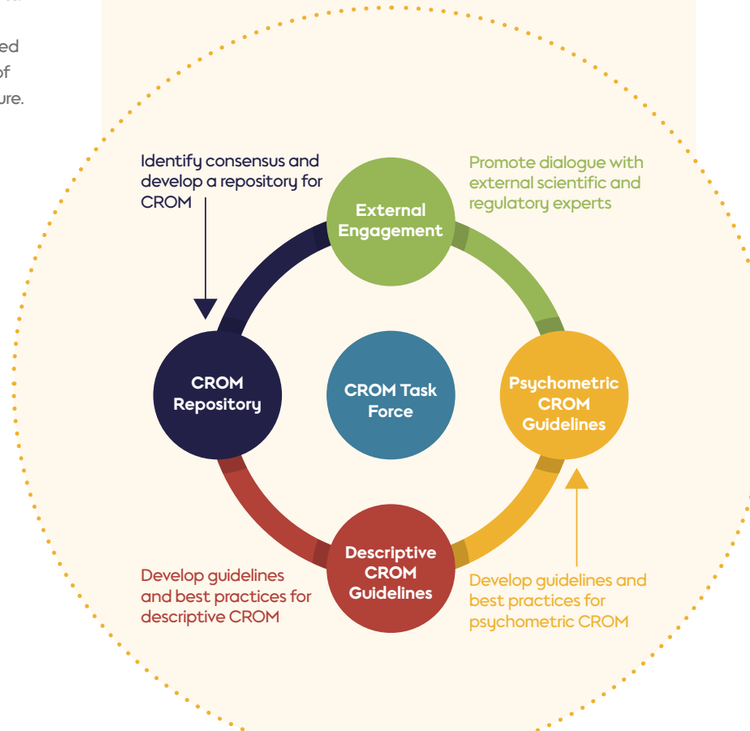
## How Philip Morris International (PMI) is shaping perception and behavior research for smoke-free products

PMI has invested heavily in research into consumer perception and behavior related to smoke-free products, with 76 studies completed to date. However, our researchers have also recognized the need for standardized methodologies and set out to create solutions, such as the CORESTA (Cooperation Center for Scientific Research Relative to Tobacco) CROM (Consumer Reported Outcome Measures) Consortium and the ABOUT™ (Assessment of Behavioral OUtcomes related to Tobacco and nicotine products) Toolbox.

## Creating consensus: The CORESTA CROM Consortium

Designing perception and behavior puzzle pieces so that they interlock properly requires collaboration among various stakeholders. Without this alignment, different stakeholders might contribute data pieces that don't quite match, leading to gaps or inconsistencies in the overall picture.

Until recently, there has been limited consensus on the CROM—self-reported observations intrinsic to the consumer—used in tobacco regulatory science. To harmonize CROM in smoke-free product research, PMI is driving an initiative within CORESTA, an international organization promoting global scientific cooperation in tobacco research. In particular, PMI coordinates the CORESTA CROM Consortium, a collaborative effort involving stakeholders from the tobacco industry, academia, and regulatory agencies, which aims to guide the development, validation, access, and use of CROM for evaluating tobacco and nicotine products (TNPs). To achieve these goals, the initiative focuses on reviewing existing standards and establishing recommendations for developing and validating new CROM. It is also working towards creating a CROM knowledge repository that will help scientists identify the appropriate CROM for their research.



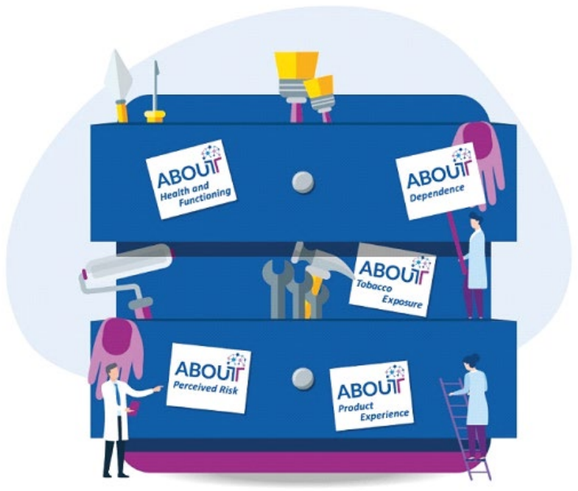
In 2024, the CORESTA CROM Task Force achieved a significant milestone by publishing two guidelines for identifying, developing, validating, and implementing both psychometric (unobservable) and descriptive (observable) CROM. Implementation of these guidelines could create a paradigm shift in the way CROM are conceptualized and implemented and help improve data consistency and comparability in TNP research.

To support dialogue and knowledge sharing, the CROM Task Force also organizes workshops and symposia, mostly as virtual events open to everyone, where researchers from industry, academia, and regulatory agencies present their work. By fostering collaboration and consensus, the CORESTA CROM Consortium is building a robust scientific framework to help provide a clearer picture of how smoke-free products may contribute to public health. This can support better, informed decisions for the regulation of TNPs, ultimately improving public health.

## The ABOUT™ Toolbox: PMI's game changer in standardizing perception and behavior research

The ABOUT™ Toolbox is a set of validated, structured research tools, comprising fit-for-purpose CROM (questionnaires). These tools help researchers piece together their understanding of the perceptions and behaviors of adult users of TNPs. This ongoing, collaborative initiative aims to establish easy-to-use, scientifically sound tools and frameworks that can be used to measure perception and behavior in a consistent way to facilitate accurate comparisons.

The ABOUT™ Toolbox consists of five separate CROM, each focusing on different priority areas of perceptions and behaviors related to the use of TNPs.




The ABOUT™ Toolbox CROM are developed using best practices in accordance with the U.S. Food and Drug Administration's (FDA's) guidelines on Patient-reported Outcome Measures and modified risk tobacco product (MRTP) applications as well as the CORESTA CROM guidelines. The iterative process involves different studies and research activities to ensure the development of scientifically validated instruments that are adaptable across various smoke-free product categories, user groups, and cultural contexts. The extensive validation performed during the development process ensures the reliability and effectiveness of the toolbox across different research and regulatory settings. Additionally, global accessibility of the toolbox is enabled through Mapi Research Trust's ePROVIDE™ platform.

By sharing the toolbox with tobacco research and public health communities, PMI can help ensure that everyone is working with data pieces that can fit together seamlessly. This approach allows researchers to build a more accurate and complete picture of consumer perception and behavior regarding smoke-free products.



## Driving collaboration: The Delphi study example

**Collaboration and the use of standardized methodologies are key to ensuring consistency and reliability of results and generating comparable and compatible data. A recent example is the global Delphi Panel study, sponsored by PMI, which brought together international experts to align on metrics for evaluating consumer reported outcomes of using smoke-free products. This study formed part of the research phase during the development of one of the five instruments of the ABOUT™ Toolbox: the ABOUT™ – Health and Functioning instrument. The aim was to identify concepts that are important to measure when assessing the health and functioning status of adult smokers switching to smoke-free products, ensuring clinical and cross-cultural relevance.**

**Experts from diverse fields, including psychology, public health, dentistry, oncology, and internal medicine, refined and ranked health and functioning concepts through three rounds of surveys until a consensus was reached. They identified several core areas to focus on, including physical health, mental well-being, and social functioning, highlighting the importance of capturing both objective and subjective aspects of health and functioning to assess the impact of smoke-free products comprehensively. The consensus-building approach helped address cultural and professional differences, ensuring the concepts were relevant across various populations.**

**By achieving expert consensus, the Delphi study strengthens the validity and reliability of the ABOUT™ – Health and Functioning instrument, showcasing the value of collaboration in developing scientifically sound and globally accepted instruments for examining consumer perception and behavior in smoke-free product research.**

## Conclusion: A unified path forward

Evidence-based research on the perceptions and behaviors of smoke-free product users is a key steppingstone in the journey toward minimizing tobacco harm. The development of standardized tools and frameworks, like the ABOUT™ Toolbox and the CORESTA CROM Consortium, is paving the way for a more collaborative, data-driven future. With alignment of methodologies, researchers and policymakers ensure each piece of the puzzle fits perfectly with the others, creating a comprehensive picture of consumer perception and behavior. As more researchers adopt these tools, tobacco regulation will move toward a unified approach that allows for reliable, large-scale comparisons across products, populations, and geographies. Stronger evidence collected using validated tools can enable policymakers to create effective regulations while addressing concerns about misuse. By fostering global partnerships, aligning methodologies, and generating reliable and comparable data, these tools provide a much-needed foundation for understanding and meeting the needs of adult smokers who don't quit, aiding their transition away from cigarettes and—the big piece of the puzzle—ultimately promoting public health.

# WHAT PERCEPTION AND BEHAVIOR STUDIES REVEAL: TOBACCO AND NICOTINE USE IN A CHANGING WORLD

For many adult smokers who don't quit, the development of less harmful, smoke-free alternatives has opened a new chapter in the way they consume nicotine. As the landscape of tobacco and nicotine products (TNPs) evolves, perception and behavior studies can provide a critical lens for understanding which products people use, what drives their choices, how they perceive these alternatives, what are their tobacco use patterns, and what this could imply for public health.

Two studies conducted by scientists at Philip Morris International (PMI), alone or in collaboration with other research groups, provide a closer look at users of smoke-free products in the U.S.—their sociodemographic characteristics, TNP use patterns, and preferences. These findings offer a window into how these products fit into users' lives and contribute to the growing body of evidence on the role of smoke-free products in tobacco harm reduction.



**Study 1**

## HOW LIKELY ARE U.S. ADULT SMOKERS TO SWITCH TO A NOVEL E-VAPOR PRODUCT?

PMI has conducted an actual use study to better understand whether an e-vapor product can have an impact on adult smokers' use patterns in settings close to real world, and to what extent these patterns would shift in favor of smoke-free product use. The results were presented at the 77th Tobacco Science Research Conference, held in September 2024, in Atlanta, Georgia, U.S. and at the CORESTA (Cooperation Center for Scientific Research Relative to Tobacco) Congress 2024, in Edinburgh, Scotland.

### What were the goals of the study?

Conducted under actual use conditions over an 8-week observational period in 2022, our study investigated the ability of a novel e-vapor product (an electronic nicotine delivery system [ENDS], specifically, the P4M3 Generation 2.0 System, featuring nonrefillable, replaceable cartridges filled with nicotine-containing e-liquid) in helping adult smokers either reduce their cigarette consumption or completely transition away from cigarettes.

The study was designed to assess how likely adult smokers are to switch to the e-vapor product (including the proportion of participants who become exclusive users of the study product), and to assess the impact of product availability on cigarettes consumption.

Previous studies have indicated that adult smokers who switch completely from cigarettes to e-vapor products, or reduce their cigarette consumption by 50% or more, may reduce their exposure to the harmful and potentially harmful constituents (HPHCs) present in tobacco smoke. In addition, findings from cohort studies and randomized controlled trials, summarized in the recent Cochrane Review, demonstrate that adult smokers who use e-vapor products exhibit higher rates of smoking reduction and higher rates of stopping or abandoning smoking than those who use cessation methods.

## How was the study conducted?

This multi-site prospective study was conducted among existing daily adult smokers in the U.S., where research has indicated that switching to e-vapor products is the most common method used when attempting to stop smoking. Both exclusive cigarette smokers and dual users of cigarettes and e-vapor products were recruited.

A total of 821 U.S. daily adult smokers were enrolled in the 10-week study, with 720 included in the final analytical sample (353 exclusive cigarette smokers and 367 dual users). Participants were randomly selected from consumer databases and sampled to obtain a study population that represents the U.S. adult smoking population in terms of sex, age, and race.

The study product was available *ad libitum* in two variants (tobacco and menthol), with a single nicotine concentration (3.5%). The study design was based on previously conducted actual use studies and took place in three phases:

1. A 1-week baseline phase to assess cigarette and other TNP use prior to the introduction of the study product.
2. An 8-week observational phase where participants were provided the study product and were followed to assess study product use and changes in cigarette and other TNP use.
3. A 1-week closeout phase for continued surveillance of potential adverse events. No new safety concerns related to the study product emerged during this study.

Participants self-reported their daily use of cigarettes and other TNP use (during the baseline and observational phases) and the study product (during the observational phase) in an app-based e-diary. Participants were also interviewed following weeks 2, 5, and 8 of the observational phase, to evaluate sensory attributes of the study product.

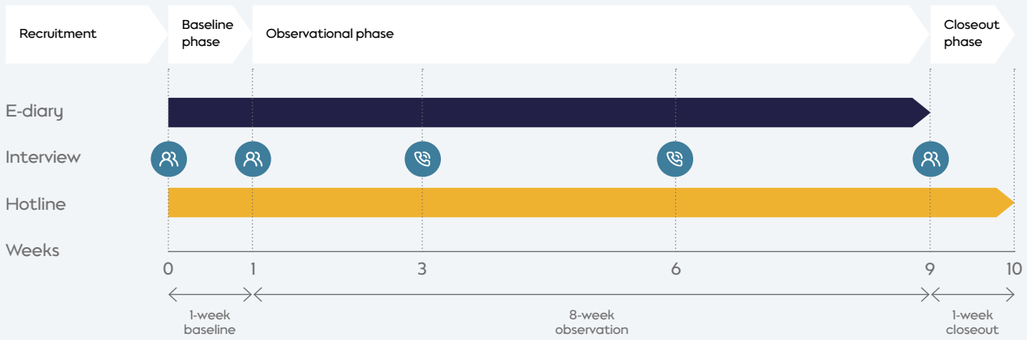
Outcomes for actual product use were assessed by comparing results between the end of the observational phase and baseline.

This included:

- The proportion of participants who exclusively used (i.e., switched completely to) the study product.
- The absolute change in cigarettes smoked per day.
- The proportion of participants who reduced cigarettes smoked per day by 50% or more.
- The proportion of participants who transitioned from daily to nondaily cigarette smoking.

Each of the outcomes was assessed separately for exclusive cigarette smokers and dual users and was stratified by the variant of the study product (tobacco, menthol, or both) used in week 8.

**STUDY DESIGN**






## What were the results of the study?

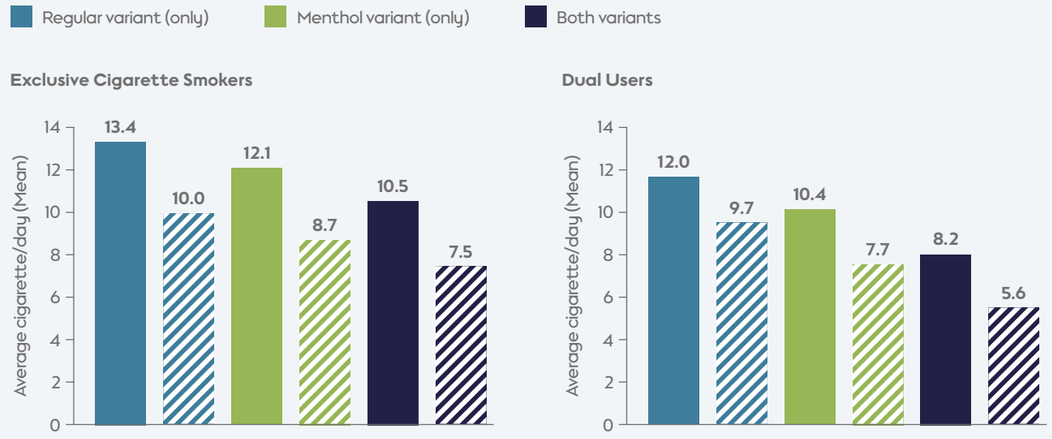
During the baseline phase, exclusive cigarette smokers and dual users smoked, on average, 13 and 12 cigarettes per day, respectively. At the end of the observational period (week 8), 86.2% of exclusive cigarette smokers and 92.1% of dual users used the study product, with 4.0% of exclusive cigarette smokers and 4.1% of dual users having switched completely. Dual users used the study product more often (mean: 7.3 times per day) than exclusive cigarette smokers (5.0 times per day).

Overall, participants in both study groups reduced their daily cigarette consumption from baseline to week 8, with 25.8% of exclusive cigarette smokers and 28.1% of dual users reducing their cigarettes smoked per day by 50% or more.

At week 8, more exclusive cigarette smokers (54.6%) and dual users (49.4%) used only the menthol variant than used only the regular variant (33.2% and 33.1%, respectively). At the same time, 12.2% of exclusive cigarette smokers and 17.5% dual users used both variants.

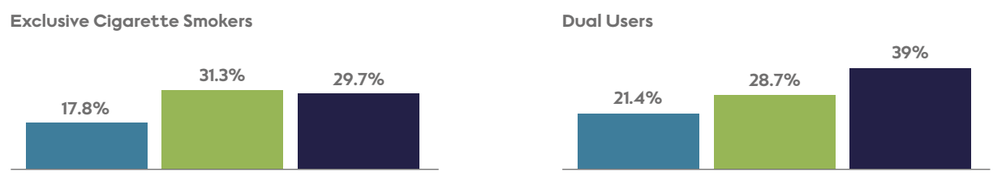
There was also a reduction in the proportion of participants who smoked daily at week 8 compared with baseline. At week 8, 87.1% of exclusive smokers smoked daily, compared with 98.3% at baseline. For dual users, there was a reduction from 91.8% smoking cigarettes daily at the start to 79% smoking daily at week 8.

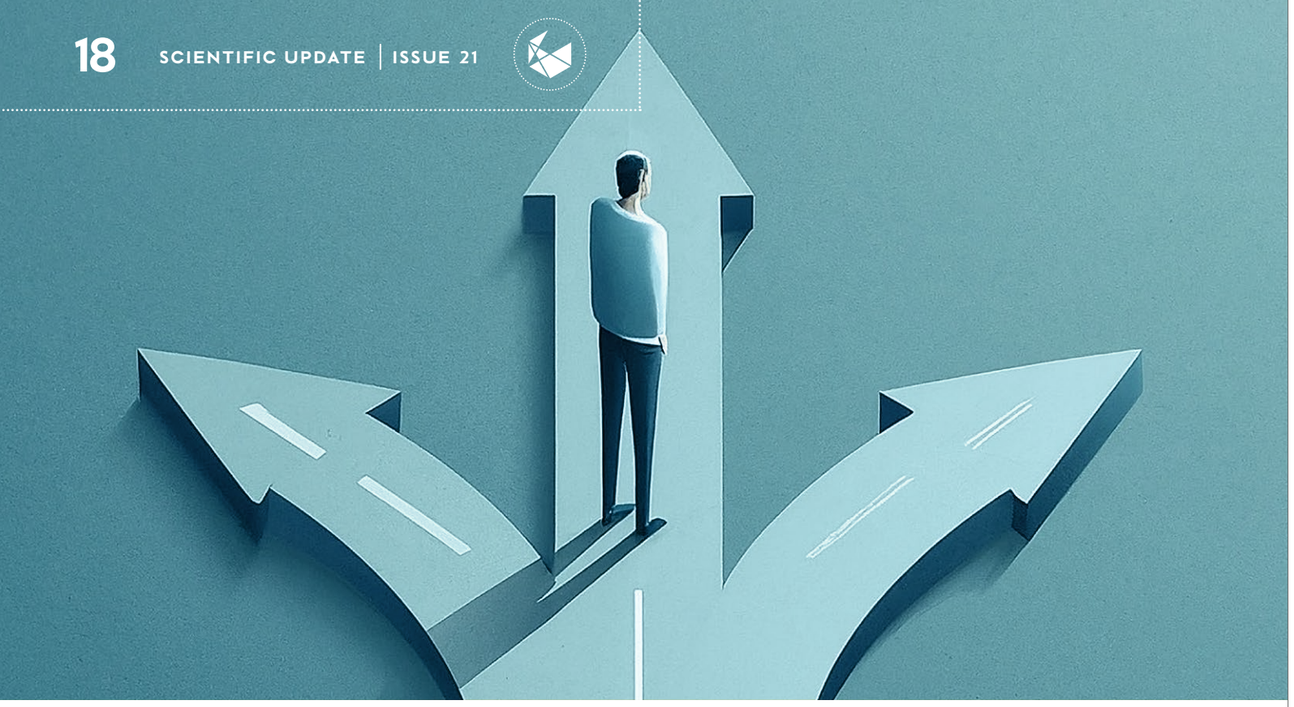
**AVERAGE DAILY CIGARETTE CONSUMPTION AT BASELINE (SOLID-FILLED BARS) AND AT WEEK 8 (STRIPED BARS) BY PRODUCT VARIANT**



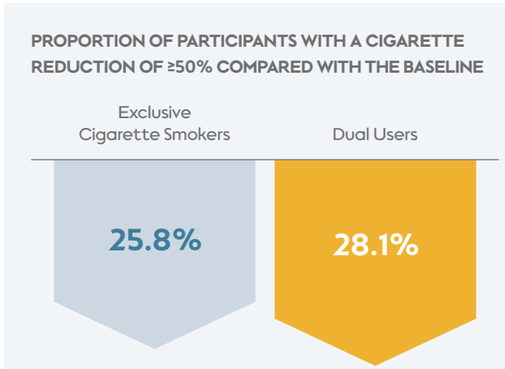

In both study groups, the proportion of participants who reduced their cigarette consumption by ≥50 was higher among participants who used menthol or both variants of the study product, compared with those who used only the regular variant.

**PROPORTION OF PARTICIPANTS WHO REDUCED CIGARETTE CONSUMPTION BY ≥50%, COMPARED WITH THE BASELINE, BY PRODUCT VARIANT USED AT WEEK 8**





## Do the study results indicate that smoke-free products are an acceptable alternative for cigarette smokers who don't quit?




This study focused on use patterns of an e-vapor product among adult cigarette smokers who have little or no prior experience of using smoke-free products, or who are dual users of cigarettes and smoke-free products. These groups are the intended users of the study product.

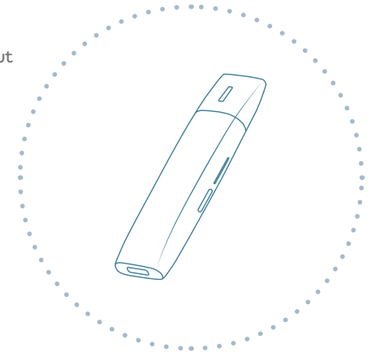
The results indicated that the study product was an acceptable alternative to both current adult cigarette smokers and dual users, dual users, with a large proportion of subjects using the study product after 8 weeks (some of whom switched completely).

Over a quarter of subjects in each group had reduced their cigarette consumption by ≥50%.

The study also showed that participants had a greater average liking (in terms of smell, taste, and aftertaste) for the menthol variant than the regular variant. A high proportion of participants (in both subject groups) who used the menthol or both variants exclusively had reduced cigarette consumption by >50% at week 8 than the regular variant alone. These results suggest that the availability of menthol e-vapor product variants may be a factor in the number of cigarette smokers or dual users who reduce their consumption or switch completely to e-vapor products.

The study did have limitations, including: participants did not have to pay for the e-vapor product but did have to pay for any other existing tobacco product they used; use of all products was based on self-reported measures; and the e-vapor product was only available in two variants, which may have affected existing users of smoke-free products who were accustomed to a wider range of flavors.

Overall, the results support existing evidence that e-vapor products, including the one used in this study, are an acceptable alternative to cigarettes for existing adult smokers who don't quit and so may aid in reducing the harm from cigarette use.





**Study 2**

# SPOTLIGHT ON USERS OF THE TOBACCO HEATING SYSTEM (THS) IN THE U.S.

Investigators from Altria and PMI explored the profiles of users of THS in the U.S., shedding light on their tobacco use behaviors and perceptions of health risks compared with cigarettes. This research contributes to the growing body of evidence on the role of heated tobacco products (HTPs) in tobacco harm reduction.

## Why was this study conducted?

THS produces aerosol with on average 95% lower levels of harmful and potentially harmful constituents (HPHCs) compared with cigarettes, based on the World Health Organization (WHO) list of nine priority HPHCs mandated for lowering in cigarette smoke. In clinical studies, subjects who switched from cigarettes to THS had favorable differences in biomarkers of potential harm (BoPH) linked to smoking-related diseases compared with those who continued to smoke. For adult smokers who don't quit, THS may reduce the risk of harm to their health compared with continued smoking.

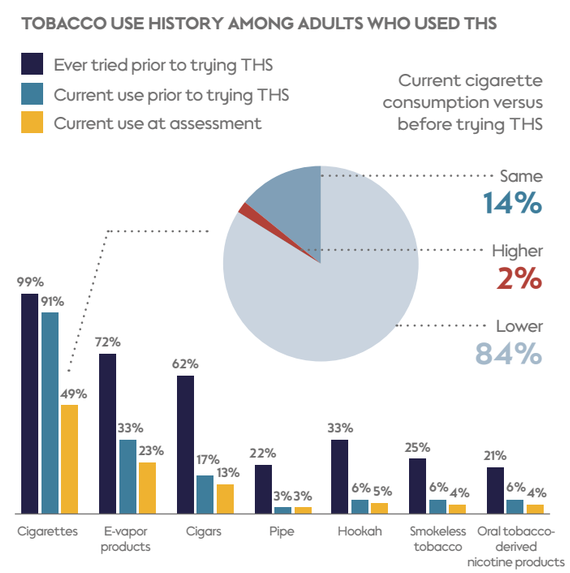
A recent cross-sectional study delves into the tobacco use behaviors and perceptions of the relative health risks among U.S. consumers of THS. This survey-based study involved 688 adult THS users (aged 21 years or older) who had used at least 100 heated tobacco units (HTUs) with THS. Participants were recruited through PMI's THS consumer database and completed a detailed online questionnaire between September 15 and November 14, 2021, to assess their sociodemographic characteristics, tobacco use history, current smoking behaviors, and perceptions of health risks associated with THS compared with cigarettes. The survey included both closed and open-ended questions to capture a comprehensive picture of users' experiences and attitudes.

## Sociodemographic characteristics of THS users in the study

Most of the participants were middle-aged (mean age 45 years), non-Hispanic White (73%) males (62%). Almost all had a history of smoking cigarettes—20 years on average before trying THS. Most (82%) had never tried a smoking cessation treatment or had not used one in the past year. This demographic supports the notion that THS may be used predominantly by established long-term adult smokers who don't quit rather than unintended audiences.

## Tobacco use patterns: A shift in behavior

On average, participants had used THS for just over 1 year, with many showing notable changes in their tobacco use habits. Just over half of participants (51%) were not smoking cigarettes at all at the time of the survey. Even among those who still smoked both cigarettes and THS, 84% reported smoking fewer cigarettes than before. This shift in behavior highlights the potential of THS to help adult smokers switch away from cigarettes completely or reduce their cigarette consumption.



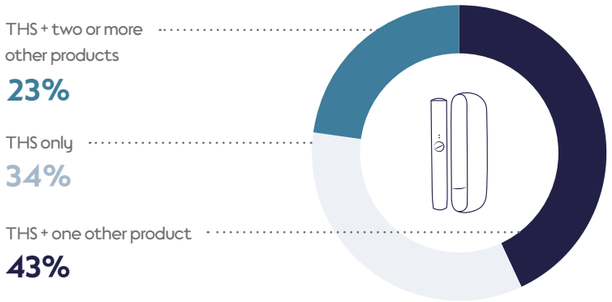

Tobacco use among study participants (N=688) before first trying THS and at time of assessment. Current use was defined as using a product 'every day' or 'some days' in response to the question "Do you now use/smoke... every day, some days, or not at all?"

## Understanding THS daily use patterns

A substantial portion (69%) of participants who were using THS at the time of assessment reported using it daily in the month before the assessment. Those who had used THS for over 1 year were more likely to use it daily compared with those who had used it for 1 year or less (73% versus 65%; *P*=0.04).

On the days they used THS, participants typically used 15 HTUs. THS users who previously smoked menthol cigarettes tended to prefer menthol HTUs (93%), while those who smoked nonmenthol cigarettes leaned towards nonmenthol HTUs (74%). However, a sizable percentage of participants who currently smoked nonmenthol cigarettes preferred menthol HTUs when using THS. This highlights the potential role menthol varieties can play in encouraging adult smokers to switch to THS use and away from cigarettes.

**THS USE PATTERNS**




Number of days used:

- Median = 30 days (interquartile range [IQR]=25 to 30)
- 69% used daily

Number of HTUs used per day (on days used)

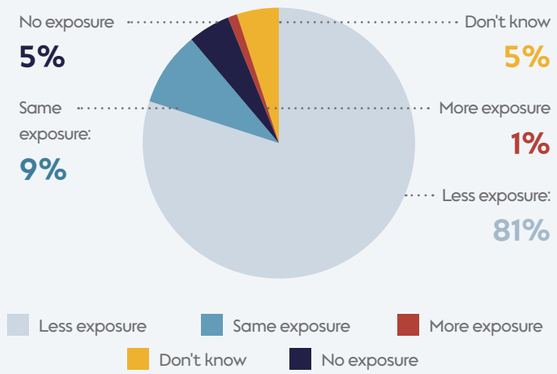
- Median 15 (IQR = 10 to 20)

## Perceptions of the relative risks of THS

One of the most compelling findings was how participants perceived the health risks associated with THS compared with cigarettes. A vast majority (81%) of participants understood the MRTP information authorized for THS by the FDA. In addition, 85% of this 81% understood that smokers must stop smoking completely and only use THS to reduce their exposure to HPHCs. Participants also indicated that they perceived THS as less harmful than smoking cigarettes. This perception of relative health risk is crucial in encouraging adult smokers who don't quit to make the switch to THS or other smoke-free alternatives that are scientifically substantiated to be less harmful than cigarettes.

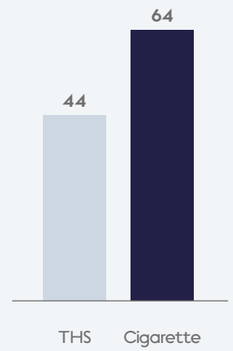
**STUDY PARTICIPANTS' RISK PERCEPTIONS OF SWITCHING FROM CIGARETTES TO THS**

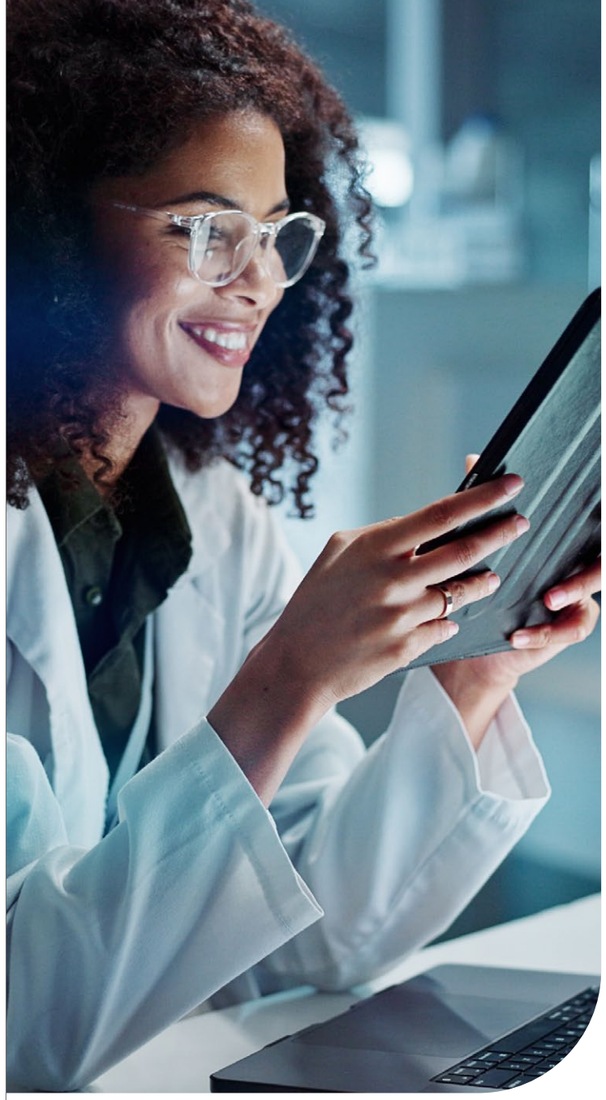
**THS USERS' PERCEPTIONS OF THEIR EXPOSURE TO HPHCS WHEN SWITCHING TO THS VERSUS CIGARETTES**




**MEAN RISK PERCEPTION COMPOSITE SCORE**

Theoretical range: 18-90
Higher score means higher perceived risk





## What are the limitations of this study?

Limitations of the study include its cross-sectional design, which limits causal interpretations of switching patterns or long-term health outcomes. It is also based on self-reported data, which may be subject to recall bias. In addition, the study primarily focuses on THS users in specific U.S. regions and may, therefore, not represent broader national or international patterns.

## What are the implications of these findings for THS?

This study underscores the potential of THS as a harm reduction tool for adult smokers who don't quit. The results provide supportive evidence for the potential of THS to help users switch from smoking by comprehensively assessing use behaviors and risk perceptions of THS users in a real-world setting in the U.S. The study also highlights the importance of accurate communication and education efforts to ensure that smokers are well informed about the benefits and risks of switching to smoke-free alternatives.

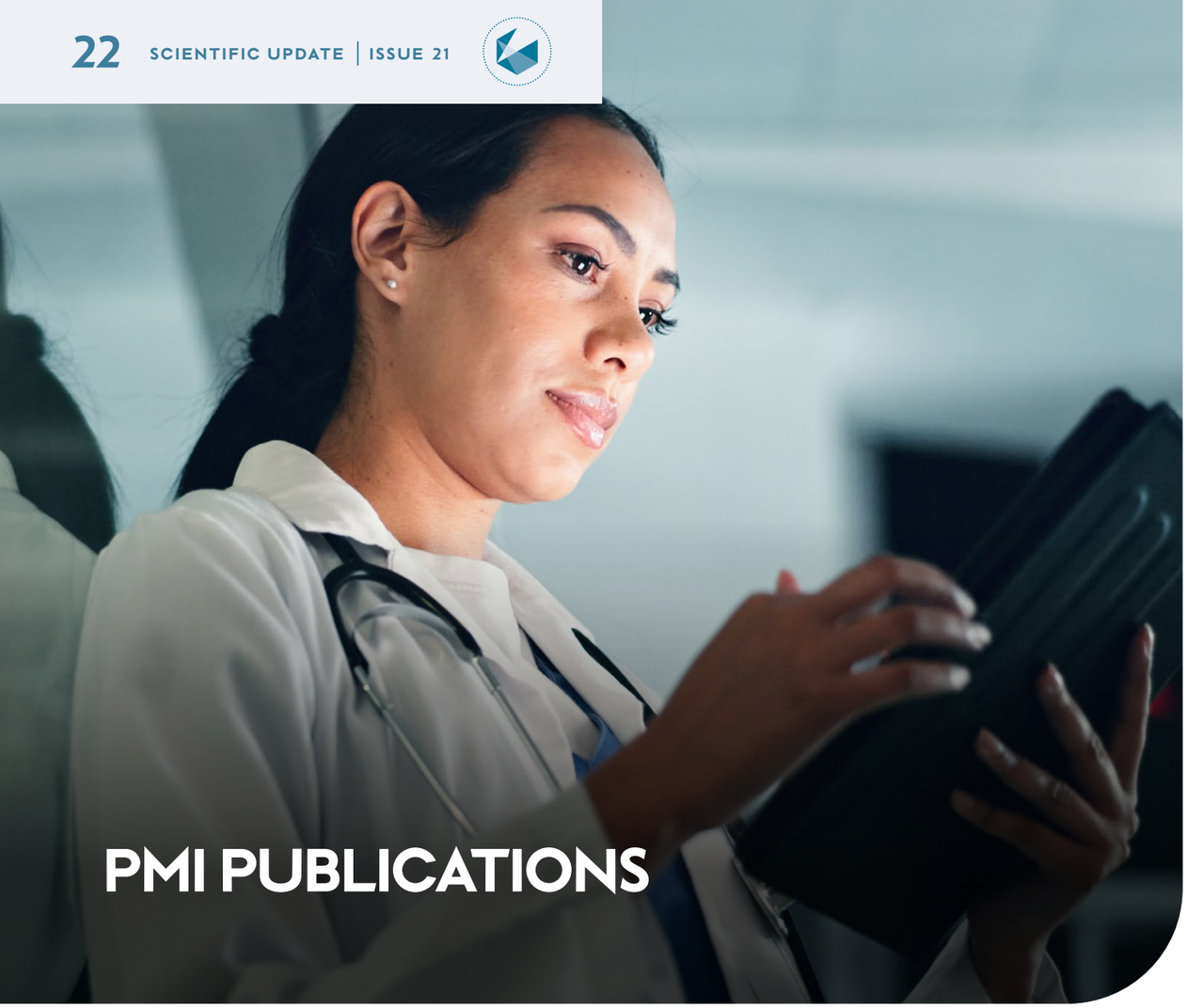
In the future, population-based research will be crucial to fully understand the potential public health implications of THS use across countries, including the U.S.

*"Overall, this research underlines the role of in helping adult smokers transition away from cigarettes and potentially improving public health."*

## THE BIGGER PICTURE

Perception and behavior studies are more than just data; they offer a glimpse into the lives of users of smoke-free products—who uses them, how they use them, how/whether they use other TNPs in conjunction, and how they perceive the relative health risks of these alternatives.

Studies like these show that people who use scientifically substantiated smoke-free alternatives tend to reduce their cigarette consumption or even stop their cigarette consumption altogether. They also underscore the importance of providing accurate information and education about smoke-free alternatives for adult smokers. By understanding the experiences and risk perceptions of users of smoke-free products, we can better support adult smokers who don't quit in their transition to less harmful alternatives to cigarettes.



# PMI PUBLICATIONS

## Differences in biomarkers of potential harm after 2+ years of Tobacco Heating System (THS) use compared to cigarette smoking: a cross-sectional study

Growing evidence indicates smoke-free products, such as THS could be a harm reduction tool for smokers who don't quit. In this real-world, cross-sectional study, researchers investigated the effects of switching from cigarette smoking to THS use on nine biomarkers of potential harm (BoPH) linked to smoking-related diseases. The co-primary BoPH endpoints were: carboxyhemoglobin (oxygen delivery), total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (tobacco-specific genotoxicity), white blood cells (inflammation), and 8-epi-prostaglandin-$F_{2\alpha}$ (oxidative stress). Key secondary endpoints were: high-density lipoprotein cholesterol (lipid metabolism), soluble intercellular adhesion molecule-1 (endothelial function),11-dehydrothromboxane B2 (blood clotting), central vascular augmentation index (arterial stiffness), and forced expiratory volume in 1 second %predicted, post-bronchodilator (lung function). Conducted across 37 healthcare institutions in Asia and Europe, this study involved 974 participants divided into three groups: current smokers, voluntary THS users (for ≥2 years), and former smokers (complete cessation for ≥2 years). Compared with current smokers, THS users had significantly favorable differences in nine BoPH. These differences in BoPH were similar to those observed in former smokers. Nicotine exposure remained similar between THS users and current smokers. The results add to the existing body of evidence indicating that completely switching from cigarette smoking to THS can lead to improvements in biological pathways negatively impacted by smoking. Further longitudinal studies are required to comprehensively understand the long-term health effects of THS usage.



## Development and initial validation of a new self-report measure to assess perceived dependence on tobacco and nicotine products

With the advent of novel smoke-free products, understanding perceived dependence on tobacco and nicotine products (TNPs) across the various available products has become increasingly important for both research and public health. Existing self-report measures to assess this were geared primarily towards cigarette use and do not recognize that dependence can vary across different TNPs. The ABOUT™ (Assessment of Behavioral OUtcomes related to Tobacco and nicotine products) Toolbox initiative uses best practice guidelines to develop fit-for-purpose self-report measures to assess perceptions and behaviors associated with the use of a wide range of TNPs. This article describes the multiphase development and validation of ABOUT™- Dependence, a new self-report measure within the ABOUT™ Toolbox, to assess perceived dependence on TNPs among exclusive and poly-TNP users. The measure was constructed based on literature review, qualitative research, and expert opinion. Data for scale formation and psychometric assessment was obtained through a U.S.-based web survey with 2,334 participants. Psychometric analyses confirmed the measure's reliability, validity, and test-retest reliability. The final measure consists of a 12-item questionnaire across three domains: behavioral impact, signs and symptoms, and extent/timing of use. ABOUT™- Dependence provides a psychometrically reliable, validated, standardized tool for research on perceived dependence across various TNPs, supporting tobacco harm reduction efforts and informing public health policy.

## Monoamine Oxidase Inhibitors Present in Tobacco Modulate Dopamine Balance Via the Dopamine Transporter

The effects of nicotine on dopamine release and activation of the brain's reward system has been extensively documented. However, other compounds in cigarette smoke may also influence dopamine regulation. This *in vitro* study investigates the effects of monoamine oxidase inhibitors (MAOIs) found in tobacco smoke on dopamine regulation. Using an *in silico* approach, researchers selected 12 putative novel MAOIs from data sets of candidate compounds in tobacco smoke. These compounds were tested for their ability to inhibit human MAO-A and MAO-B enzymes and their impact on dopamine transporter (DAT) activity in overexpressing cell lines and dopamine release and uptake in rat striatal synaptosomes. Four tobacco-derived MAOIs were identified: harman, norharman, harmaline, and 1-ethyl-β-carboline. Notably, harmaline and 1-ethyl-β-carboline had not been previously associated with MAOI activity in the context of tobacco. Results showed that these MAOIs reduced MAO activity and influenced dopamine homeostasis by significantly attenuating DAT activity and consequent dopamine uptake and eliciting pronounced dopamine release in crude synaptosomal preparations. This is the first evidence of 1-ethyl-β-carboline as a modulator of dopamine balance by stimulating dopamine release and reducing reuptake. These insights enhance our understanding of how tobacco constituents beyond nicotine contribute to dopamine dysregulation. Further *in vivo* studies are required to understand the underlying mechanisms behind the impact of tobacco smoke on dopamine regulation and homeostasis.

# PMI SCIENCE

PHILIP MORRIS INTERNATIONAL

## Important information

This Scientific Update provides an overview of the most recent scientific developments behind PMI's approach to achieving a smoke-free future through a range of alternatives to cigarettes that do not burn tobacco. The text in these pages include our product development and assessment efforts, our initiatives to share our methodologies and results, as well as our publications.

More detailed information can be found at www.pmiscience.com.