

Philip Morris Products S.A.	Confidential
2022 Annual Report for PM0000424-PM0000426, PM0000479 and PM0000634	
Annex 2: List of Scientific Publications	Version 1.0

Annex 2:

List of Scientific Publications

In this Annex the significant findings in publications is provided for the following products:

Product Name	FDA STN number
<i>IQOS</i> System Holder and Charger	PM0000479
<i>IQOS</i> 3 System Holder and Charger	PM0000634
<i>Marlboro Heatsticks</i>	PM0000424
<i>Marlboro</i> Smooth Menthol <i>Heatsticks</i>	PM0000425
<i>Marlboro</i> Fresh Menthol <i>Heatsticks</i>	PM0000426

The publications are grouped by the study sponsor as following:

1. Scientific Publications performed by PMI
2. Scientific Publications sponsored by PMI or other Tobacco Product Manufacturers
3. Independent Scientific Publications

Confidentiality Statement

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Scientific Publications performed by PMI

Summary of scientific publications performed by PMI

Reporting Period	March 1, 2021 – February 28, 2022
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Category	Publication	Abstract
Chemistry & Physics	Mitova MI, Cluse C, Correia D, et al. Comprehensive Air Quality Assessment of the Tobacco Heating System 2.2 under Simulated Indoor Environments, Atmosphere, 2021, 12(8):989	Despite the growing popularity of heated tobacco products, there are few comprehensive studies on their environmental aerosols. Therefore, the impact of the Tobacco Heating System 2.2 (THS 2.2) on indoor air quality was evaluated on the basis of a comprehensive list of 31 airborne constituents along with targeted screening of the gas-vapor and particulate phases of the environmental aerosol. The assessments were conducted at three ventilation rates. Indoor use of THS 2.2 increased the levels of nicotine, acetaldehyde, glycerin, and (if mentholated products were used) menthol relative to background levels, with a corresponding increase in total volatile organic compounds (TVOC) values. Moreover, a temporary increase in ultrafine particles was observed when two or more tobacco sticks were used simultaneously or with a short time lapse between usages, but the concentrations returned to close to background levels almost immediately. This is because THS 2.2 generates an aerosol of liquid droplets, which evaporate quickly. Nicotine, acetaldehyde, glycerin, and TVOC levels were measured in the low µg/m3 range and were below the existing guideline limits. A comparison of airborne constituent levels during indoor THS 2.2 use with emissions from combustion products and common everyday activities revealed a substantially lower impact of THS 2.2 on the indoor environment.
Chemistry & Physics	Poget L, Goujon CG, Kleinhans S, et al. Robustness of HPHC Reduction in THS 2.2 Aerosol Relative to 3R4F Reference Cigarette Smoke under Extreme Climatic Conditions, Contributions to Tobacco & Nicotine Research, 2021, 30(3):111-126	In order to assess robustness for the reduction of harmful and potentially harmful constituent (HPHC) levels generated by the Tobacco Heating System 2.2 (THS 2.2), a heated tobacco product, we compared the aerosol of this product with mainstream smoke from the 3R4F reference cigarette under different conditions of temperature and humidity. The desired climatic conditions were achieved by using an air-conditioning system coupled with the smoking-machine housing. Two extreme climatic conditions were selected, representing a “Hot and Dry” climate (30 °C and 35% relative humidity RH) and a “Hot and Very Humid” climate (30 °C and 75% RH). In addition, aerosol and smoke were generated using the standard conditions recognized for smoking-machine analyses of tobacco products (22 °C and 60% RH), which were close to the climatic conditions defined for “Subtropical and Mediterranean” environments (25 °C and 60% RH). The experimental conditions were chosen to simulate the use of THS 2.2 and cigarettes under extreme conditions of temperature and humidity. HeatSticks and cigarettes taken from freshly opened packs were subjected to short-term conditioning from two to a few more days under the same experimental conditions. We analyzed 54 HPHCs in THS 2.2 aerosol and 3R4F cigarette smoke, generated in accordance with the Health Canada Intense (HCI) standard, using modified temperature and humidity conditions for sample conditioning and machine-smoking experiments. We used a volume-adjusted approach for comparing HPHC reductions across the different climatic conditions investigated. Although a single puffing regimen was used, the total puff volume recorded for the 3R4F cigarette smoke varied due to the influence of temperature and humidity on combustion rate, which justified the use of a volume-adjusted approach. Volume-adjusted yields were derived from HPHC yields expressed in mass-per-tobacco stick normalized per total puff volume.
Preclinical Toxicology	Batthey JND, Szostak J, Phillips B, et al. Impact of 6-Month Exposure to Aerosols From Potential Modified Risk Tobacco Products Relative to Cigarette Smoke on the Rodent Gastrointestinal Tract, Frontiers in Microbiology, 2021, 12:587745.	Cigarette smoking causes adverse health effects that might occur shortly after smoking initiation and lead to the development of inflammation and cardiorespiratory disease. Emerging studies have demonstrated the role of the intestinal microbiome in disease pathogenesis. The intestinal microbiome is susceptible to the influence of environmental factors such as smoking, and recent studies have indicated microbiome changes in smokers. Candidate modified risk tobacco products (CMRTP) are being developed to provide substitute products to lower smoking-related health risks in smokers who are unable or unwilling to quit. In this study, the ApoE-/- mouse model was used to investigate the impact of cigarette smoke (CS) from the reference cigarette 3R4F and aerosols from two CMRTPs based on the heat-not-burn principle [carbon-heated tobacco product 1.2 (CHTP 1.2) and tobacco heating system 2.2 (THS 2.2)] on the intestinal microbiome over a 6-month period. The effect of cessation or switching to CHTP 1.2 after 3 months of CS exposure was also assessed. Next-generation sequencing was used to evaluate the impact of CMRTP aerosols in comparison to CS on microbiome composition and gene expression in the digestive tract of mice. Our analyses highlighted significant gene dysregulation in response to 3R4F exposure at 4 and 6 months. The findings showed an increase in the abundance of Akkermansia spp. upon CS exposure, which was reversed upon cessation. Cessation resulted in a significant decrease in Akkermansia spp. abundance, whereas switching to CHTP 1.2 resulted in an increase in Lactobacillus spp. abundance. These microbial changes could be important for understanding the effect of CS on gut function and its relevance to disease pathogenesis via the microbiome.
Standards & Systems Toxicology	Bovard D, Renggli K, Marescotti D, et al. Impact of aerosols on liver xenobiotic metabolism: A comparison of two methods of exposure, Toxicology In Vitro, 2022,79:105277	Assessment of aerosols effects on liver CYP function generally involves aqueous fractions (AF). Although easy and efficient, this method has not been optimized recently or comparatively assessed against other aerosol exposure methods. Here, we comparatively evaluated the effects of the AFs of cigarette smoke (CS) and Tobacco Heating System (THS) aerosols on CYP activity in liver spheroids. We then used these data to develop a physiological aerosol exposure system combining a multi-organs-on-a-chip, 3D lung tissues, liver spheroids, and a direct aerosol exposure system. Liver spheroids incubated with CS AF showed a dose-dependent increase in CYP1A1/1B1, CYP1A2, and CYP2B6 activity and a dose-dependent decrease in CYP2C9, CYP2D6, and CYP3A4 activity relative to untreated tissues. In our physiological exposure system, repeated CS exposure of the bronchial tissues also caused CYP1A1/1B1 and CYP1A2 induction in the bronchial tissues and liver spheroids; but the spheroids showed an increase in CYP3A4 activity and no effect on CYP2C9 or CYP2D6 activity relative to air-exposed tissues, which resembles the results reported in smokers. THS aerosol did not affect CYP activity in bronchial or liver tissues, even at 4 times higher concentrations than CS. In conclusion, our system allows us to physiologically test the effects of CS or other aerosols on lung and liver tissues cultured in the same chip circuit, thus delivering more <i>in vivo</i> like data.
Standards & Systems Toxicology	Zanetti F, Iskandar A. Effects of aerosol from the Tobacco Heating System (THS) on human organotypic cultures of the aerodigestive tract, Medicinska reč, 2021, 2(1):42-46.	Cigarette smoking is responsible for a multitude of health risks and is one of the major modifiable risk factors for many smoking-related diseases. Tobacco Heating System (THS) is an electronic device, which heats tobacco instead of burning it. The THS aerosol has a different chemical composition to cigarette smoke, with its levels of harmful and potentially harmful constituents reduced on average by 90-95%. Advances in tissue engineering have enabled the development of sophisticated, three-dimensional organotypic culture systems that closely resemble human physiology. In several recent studies, buccal, gingival, nasal, bronchial, and small airway human epithelial organotypic cultures were exposed to aerosol from the THS and cigarette smoke. Standard toxicological assays were combined with network-based systems toxicology analyses to identify otherwise undetectable cellular-level effects. The results showed that the THS aerosol has a minimal biological impact on cells in comparison to cigarette smoke.

	Standards & Systems Toxicology	<p>Poussin C, Van der Toorn M, Scheuner S, et al. Systems toxicology study reveals reduced impact of heated tobacco product aerosol extract relative to cigarette smoke on premature aging and exacerbation effects in aged aortic cells in vitro, Archives of Toxicology, 2021, 95(10):3341-3359</p>	<p>Aging and smoking are major risk factors for cardiovascular diseases (CVD). Our <i>in vitro</i> study compared, in the context of aging, the effects of the aerosol of Tobacco Heating System 2.2 (THS; an electrically heated tobacco product) and 3R4F reference cigarette smoke (CS) on processes that contribute to vascular pathomechanisms leading to CVD. Young and old human aortic smooth muscle cells (HAoSMC) were exposed to various concentrations of aqueous extracts (AE) from 3R4F CS [0.014-0.22 puffs/mL] or THS aerosol [0.11-1.76 puffs/mL] for 24 h. Key markers were measured by high-content imaging, transcriptomics profiling and multianalyte profiling. In our study, <i>in vitro</i> aging increased senescence, DNA damage, and inflammation and decreased proliferation in the HAoSMCs. At higher concentrations of 3R4F AE, young HAoSMCs behaved similarly to aged cells, while old HAoSMCs showed additional DNA damage and apoptosis effects. At 3R4F AE concentrations with the maximum effect, the THS AE showed no significant effect in young or old HAoSMCs. It required an approximately ten-fold higher concentration of THS AE to induce effects similar to those observed with 3R4F. These effects were independent of nicotine, which did not show a significant effect on HAoSMCs at any tested concentration. Our results show that 3R4F AE accelerates aging in young HAoSMCs and exacerbates the aging effect in old HAoSMCs <i>in vitro</i>, consistent with CS-related contributions to the risk of CVD. Relative to 3R4F AE, the THS AE showed a significantly reduced impact on HAoSMCs, suggesting its lower risk for vascular SMC-associated pathomechanisms leading to CVD.</p>
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**Scientific Publications sponsored by PMI or other Tobacco
Product Manufacturers**

Reporting Period	March 1, 2021 – February 28, 2022
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Category	Title	Authors	Journal	Date of first Publication	Abstract
Aerosol Chemistry & Physics	Interconversion of nicotine enantiomers during heating and implications for smoke from combustible cigarettes, heated tobacco products, and electronic cigarettes	Moldoveanu, S. C.	Chirality	2022-01-27	Physiological properties of (R)-nicotine have differences compared with (S)-nicotine, and the subject of (S)- and (R)-nicotine ratio in smoking or vaping related items is of considerable interest. A Liquid Chromatography-Mass Spectrometry/Mass Spectrometry (LC-MS/MS) method for the analysis of (S)- and (R)-nicotine has been developed and applied to samples of nicotine from different sources, nicotine pyrolyzates, several types of tobacco, smoke from combustible cigarettes, smoke from heated tobacco products, e-liquids, and particulate matter obtained from e-cigarettes aerosol. The separation was achieved on a ChiraCel OJ-3 column, 250 × 4.6 mm with 3-µm particles using a nonaqueous mobile phase. The detection was performed using atmospheric pressure chemical ionization (APCI) in positive mode. The only transition measured for the analysis of nicotine was 163.1 → 84.0. The method has been summarily validated. For the analysis, the samples of tobacco and smoke from combustible cigarettes were subject to a cleanup procedure using solid phase extraction (SPE). It was demonstrated that nicotine upon heating above 450°C for several minutes starts decomposing, and some formation of (R)-enantiomer from a sample of 99% (S)-nicotine is observed. An analogous process takes place when a 99% (R)-nicotine is heated and forms low levels of (S)-nicotine. This interconversion has the effect of slightly increasing the content of (R)-nicotine in smoke compared with the level in tobacco for combustible cigarettes and for heated tobacco products. The (S)/(R) ratio of nicotine enantiomers in e-liquids was identical with the ratio for the particulate phase of aerosols generated by e-cigarette vaping.
Aerosol Chemistry & Physics	Solid matter and soluble compounds collected from cigarette smoke and heated tobacco product aerosol using a laboratory designed puffing setup	Amorós-Pérez, A.; Casanova, L.; Román-Martínez, M. D. C.; Lillo-Róderas, M.	Environ Res	2021-12-28	A laboratory setup recently designed has been used to perform puffing experiments in conditions similar to those of Health Canada Intense regime with the purpose of collecting and studying any particulate and/or soluble matter generated as a result of cigarette smoking or Heets use in an IQOS device. Smoke or aerosol can leave deposited matter in several parts of the setup, roughly resembling the interaction with the human body. Samples have been collected from different parts of the setup. For cigarettes, the extracted solutions were yellowish, whereas they remained colourless for Heets. This indicates that the content of both the deposited particulate matter and the amount soluble compounds were much higher in cigarettes smoke than in Heets aerosol. Not only quantitative differences have been found. Thus, the solid matter collected from cigarettes smoke contains some insoluble fractions mainly composed by C and O, but also by traces of S, K, Ca, Fe, As, Na, Al, Si, and Ba, while the analogous samples from Heets are mainly composed of C and O and are soluble in isopropanol. In addition, in Heets aerosol a relatively low fraction of the detected compounds corresponds to polycyclic aromatic hydrocarbons (PAHs), compared to the percentage of PAHs present in the cigarette smoke. When cigarettes were smoked under a continuous smoking regime (continuous air flow) solid matter was found to be deposited on a part of the setup. This collected solid matter was composed mainly of C and O (being mostly insoluble in water and partially soluble in isopropanol) and contained traces of heavy metals (As, Cd, Cr, Ni, Cu, and Pb).
Aerosol Chemistry & Physics	Comparison of 3R4F cigarette smoke and IQOS heated tobacco product aerosol emissions	Kärkela, T.; Tapper, U.; Kajolinn, T.	Environ Sci Pollut Res Int	2021-12-22	In this study, the smoke from a 3R4F research cigarette and the aerosol generated by the Heated Tobacco Product IQOS, also referred to as the Tobacco Heating System (THS) 2.2 in the literature, were compared. The objective was to characterize the gas and suspended particulate matter compositions in the mainstream smoke from a combusted 3R4F cigarette and in the aerosol generated by IQOS during use. The results indicated that the determined aerosol emissions from IQOS were notably lower than in the cigarette smoke under a Health Canada Intense puffing regimen. As an interesting detail in this study, the maximum nicotine concentrations within a puff were practically the same in both the 3R4F smoke and the IQOS aerosol, but the average concentration was lower for the IQOS aerosol. For both products, water constituted a significant proportion of the particulate matter, although it was substantially higher in the IQOS aerosol. Furthermore, combustion-related solid particles observed in the 3R4F smoke contained elements such as carbon, oxygen, potassium, calcium, and silicon. In contrast, IQOS aerosol particulate matter was composed of semi-volatile organic constituents with some minor traces of oxygen and silicon. The particulate matter found in the IQOS aerosol was volatile, which was especially noticeable when exposed to the electron beam of the scanning electron microscope (SEM) and Transmission Electron Microscope (TEM).

Aerosol Chemistry & Physics	The applicability of different tobacco types to heated tobacco products	Chen, Jie; He, Xian; Zhang, Xuyan; Chen, Yi; Zhao, Lu; Su, Jie; Qu, Shengbin; Ji, Xinwei; Wang, Tao; Li, Zhenjie; He, Chenggang; Zeng, Erqing; Jin, Yan; Lin, Zhonglong; Zou, Congming	Industrial Crops and Products	2021-05-01	<p>Heated tobacco (<i>Nicotiana tabacum</i> L.) products develop rapidly because of its low toxicity. In order to evaluate the industrial applicability of the existing types of characteristic tobacco as raw materials for heated tobaccos, this research ascertained differences in the main chemical compositions in tobacco leaves from different types to establish a relationship between chemical composition and sensory evaluation to select types suitable for producing heated tobaccos. Nine tobacco types (K326, Yunyan 97, Cherry-red tobacco, Han tobacco, Dao tobacco, Tiandeng tobacco, Sun-cured yellow tobacco, fresh-cut tobacco, and aromatic tobacco) planted in Yunnan Province, China were selected. Their sensory quality was evaluated by the method for sensory evaluation of heated tobaccos and chemical composition and content of aroma substances in tobacco leaves were determined. In the evaluation of sensory quality of heated tobaccos, the total score of Tiandeng tobacco was significantly higher than those of the other types, followed by Cherry-red tobacco and K326; There were significant differences in chemical composition in the nine tobacco types and the total alkaloid content in Cherry-red tobacco was notably higher than in the other tobacco types. The amounts of total sugar, reducing sugar, and starch in Han tobacco were significantly lower than other types, while the amounts of total nitrogen, potassium oxide, chloride ions, and protein were much higher than in the other tobacco types. The total amounts of polyphenols and aroma compounds in fresh-cut tobacco were significantly higher than in the other tobacco types. The contents of nicotine, neonicotine, anatabine, and total alkaloid showed a significant positive correlation with the total sensory evaluation score. The contents of neotyrine and 2,3-bipyridine were significantly and negatively correlated with the total sensory evaluation score. A remarkable negative correlation was found between starch content and score on irritation. Furthermore, the amounts of neochlorogenic acid, chlorogenic acid, caffeic acid, and total polyphenols were significantly and positively correlated with the total sensory evaluation score. The amounts of aldehydes and phenolic compounds had a significant negative correlation, while the amount of olefin compounds had a significant positive correlation, with the total sensory evaluation score. These chemicals in tobacco leaves can be used as in analyses screening of other suitable tobacco types, and as reference standards for selecting tobacco raw materials suitable for high-quality heated tobaccos. © 2021 The Authors</p>
Aerosol Chemistry and Physics	Targeted Characterization of the Chemical Composition of JUUL Systems Aerosol and Comparison with 3R4F Reference Cigarettes and IQOS Heat Sticks	Chen, X.; Bailey, P. C.; Yang, C.; Hrakci, B.; Oldham, M. J.; Gillman, I. G.	Separations	2021-10-03	<p>Aerosol constituent yields have been reported from a wide range of electronic nicotine delivery systems. No comprehensive study has been published on the aerosol constituents generated from the JUUL system. Targeted analyses of 53 aerosol constituents from the four JUUL products currently on the US market (Virginia Tobacco and Menthol flavored e-liquids in both 5.0% and 3.0% nicotine concentration by weight) was performed using non-intense and intense puffing regimens. All measurements were conducted by an ISO 17025 accredited contract research organization. JUUL product aerosol constituents were compared to published values for the 3R4F research cigarette and IQOS Regular and Menthol heated tobacco products. Across the four JUUL products and two puffing regimens, only 10/53 analytes were quantifiable, including only two carbonyls (known propylene glycol or glycerol degradants). The remaining analytes were primary ingredients, nicotine degradants and water. Average analyte reductions (excluding primary ingredients and water) for all four JUUL system aerosols tested were greater than 98% lower than 3R4F mainstream smoke, and greater than 88% lower than IQOS aerosol. In summary, chemical characterization and evaluation of JUUL product aerosols demonstrates a significant reduction in toxicants when compared to mainstream cigarette smoke from 3R4F reference cigarettes or aerosols from IQOS-heated tobacco products.</p>
Aerosol Chemistry and Physics	Comparison of particulate matter emission and soluble matter collected from combustion cigarettes and heated tobacco products using a setup designed to simulate puffing regimes	Amorós-Pérez, Ana; Cano-Casanova, Laura; Román-Martínez, María del Carmen; Lillo-Ródenas, María Angeles	Chemical Engineering Journal Advances	2021-07-05	<p>An experimental setup was designed and optimized to collect particulate matter suspended in cigarettes smoke or in the aerosol generated during the use of heated tobacco products (HTPs). The setup is mainly based on a gas washing flask containing water where particulate matter and soluble compounds can be trapped, resembling interaction in the body. This system allows to perform puffing experiments in conditions similar to those of the Health Canada Intense puffing regime. In the study, cigarettes and Heets (in IQOS heater) from Philip Morris Products were used. Complementary characterization of this particulate matter has been extracted from experiments on a gas washing flask containing isopropanol. Total organic carbon analysis, laser diffraction, UV-vis spectrophotometry and transmission electron microscopy measurements have shown that cigarette smoke contains a large number and content of compounds soluble in water and isopropanol, together with solid particles generated during combustion. In contrast, negligible presence of non-combustion related particles was detected in Heets aerosol samples. These facts, together with the higher amount of water soluble compounds and higher number of polyaromatic hydrocarbons detected in the cigarettes smoke, allow to conclude that HTPs are less harmful than combusted cigarettes.</p>
Aerosol Chemistry and Physics	Investigation into the Presence or Absence of Solid Particles Generated from Thermal Processes in the Aerosol from an Electrically Heated Tobacco Product with and without Filter Elements	Kirkkela, Teemu; Ebinger, Jean-Christophe; Tapper, Unto; Robyr, Olivier; Jalanti, Tauno	Aerosol and Air Quality Research	2021-05-31	<p>Heated Tobacco Products (HTP) were developed as better alternatives to cigarettes to avoid the release of thousands of chemicals formed when the tobacco is being burnt. One such HTP is the Electrically Heated Tobacco System (EHTS) (from Philip Morris International), in which the tobacco material in the Electrically Heated Tobacco Product (EHTP) is heated instead of being burnt. The significant reduction in emissions from EHTPs compared to combusted cigarettes have been extensively substantiated by independent research groups. The absence of solid particle emissions from the EHTP has also been confirmed in published research. As EHTPs have filter elements between the tobacco portion and the mouth-end, their role associated to the conclusion that no solid particles are formed during use has never been investigated to our knowledge. In this work, aerosol collected from the EHTP with and without filter elements during heating as well as without heating was studied to investigate whether solid particles were formed in any part of the product during use. Two different analytical methods were used and the results from both methods showed that no solid particles originating from thermal processes was present in the EHTP aerosol.</p>

Aerosol Chemistry and Physics	Effects of Glycerol and Propylene Glycol on Smoke Release of Heat-not-burn Tobacco Products	Tong, Yuxing; Xiong, Yimin; Yan, Qunshan; Gao, Song; Le, Xi; Wei, Pei; Shu, Hao; Wang, Zhiwei; Tang, Xiangbin; Li, Pengfei; Xiong, Zhe; Wang, Yi	Journal of Physics: Conference Series	2021-04-22	Glycerin and propylene glycol are the main components of the atomizing agent in heat-not-burn tobacco products (HnB), which affect the smoke release of HnB significantly. In this study, the roles of the glycerin and propylene glycol as the atomizing agent on smoke release of HnB were studied by using a fixed-bed reactor system. The effects of glycerin to propylene glycol ratio in the atomizing agent, and the content of atomizing agent in the HnB were investigated. Gas chromatography-mass spectrometer (GC-MS) was used to analyze the condensable components in the released smoke, and gas chromatography (GC) was used to analyze the gaseous products. The results showed that glycerol could promote the thermal cracking of tobacco and smoke release during pyrolysis. The amount of smoke was the largest when the glycerol ratio was 60%, meanwhile the nicotine content in the smoke was also the highest. When using the glycerin and propylene glycol mixture as the atomizing agent, the amount of smoke and concentration of nicotine and CO in the smoke were increased when the content of atomizing agent decreased in the HnB. The results indicated that the interactions between glycerin and propylene glycol, and the interactions between the atomizing agent and the tobacco were both existed during smoking, which could change the characteristics of the atomizing agent and the smoke release property of HnB.
Aerosol Chemistry and Physics	Structural Characteristics and Properties of Poly(lactic Acid) (PLA) and Cellulose Triacetate (CTA) Fibers for Heat-Not-Burn (HNB) Cigarettes	Ke, Weichang; Mao, Mengyu; Liu, Bing; Wu, Qiao; Liu, Tong	IOP Conference Series: Earth and Environmental Science	2021-04-12	In this work, two commonly used filter fibers for heat-not-burn (HNB) cigarettes, poly(lactic acid) (PLA) and cellulose triacetate (CTA) fibers, have been extensively investigated by characterizing their morphologies, thermal and wetting properties. It is found that plenty of small pores can be observed in PLA fibers, which can provide more effective surface areas for the adsorption of mainstream smoke than CTA fibers with smooth surface. At the same time, thermal properties results including differential scanning calorimetry data, thermogravimetry data, and thermal conductivities of PLA and CTA fibers indicate that CTA fibers have an amorphous phase, while PLA fibers present a mixture of amorphous phase and crystalline phase with better thermal properties. Additionally, wetting properties demonstrate that PLA fibers have better adsorption properties than CTA fibers.
Aerosol Chemistry and Physics	The Dynamics of Exhaled Aerosol Following the Usage of Heated Tobacco Product, Electronic Cigarette, and Conventional Cigarette	Meštrović-Akhtarčeva, Marija; Prasauskas, Tadas; Čižas, Darius; Kaunelienė, Violeta; Martuzevičius, Dainius	Aerosol and Air Quality Research	2021-04-04	Heated tobacco products (HTPs) and electronic cigarettes (ECs) represent a potentially less harmful alternative to traditional tobacco products, such as conventional cigarettes (CCs), with growing popularity amongst adult smokers worldwide. Their users exhale a very dynamic aerosol to indoor air which undergoes rapid transformations. In the present study, we assessed the dynamics of the generated exhaled aerosols following use of a new HTP (branded as "Pulse", operating in eco and standard modes) and an e-cigarette ("myblu") in a chamber environment by three volunteers, controlling for the distance to bystander, ventilation intensity and microclimate. The HTP and EC data was compared against conventional cigarette data. HTP generally resulted in lower aerosol number concentration during puffs reaching 1.66E+06 # cm-3 at 0.5 m from bystander, compared to EC (averaging 4.3E+06 # cm-3), and CC (1.47E+08 # cm-3). No significant difference was observed between "eco" and "standard" modes of HTP. At the same time, EC concentration decrease after puffs was also faster, indicating higher volatility of particles. EC also featured higher mode during puff (120 nm) compared to HTP (90 nm), which was significantly different from conventional cigarette (165-200 nm). The evaporation/shrinkage of particles has been observed within 10 sec after puff with the HTP and EC. Distance to a bystander was shown to be as a significant factor affecting aerosol dynamics, however ventilation intensity and relative humidity did not have statistically significant effect.
Aerosol Chemistry and Physics Product Design	Influence of natural deep eutectic solvents on the release of volatile compounds from heated tobacco	Tan, J.; Li, N.; Wang, X.; Yan, J.; Wentao, Z.; Dou, Y.	Industrial Crops and Products	2021-10-19	Inspired by the emergence of natural deep eutectic solvents (DESs), we herein used thermogravimetry and pyrolysis-gas chromatography/mass spectrometry to probe the influence of six DESs (hydrogen bond acceptor=choline chloride, betaine, or l-proline; hydrogen bond donor=glycerol, 1,4-butanediol, or propylene glycol) on the release of volatiles from tobacco at 300 °C. DES treatment induced a 3.5–4.6% increase in second-stage weight loss and promoted the release of 28 aroma constituents (furans, aldehydes, ketones, and organic acids). Treatment with choline chloride-glycerol-propylene glycol increased the relative contents of the released 5-hydroxymethylfurfural and megastigmatienone by factors of 1.2 and 3.6, respectively, whereas treatment with l-proline-glycerol promoted the release of 2,3-dihydro-3,5-dihydroxy-6-methyl-(4H)-pyran-4-one. Therefore, DES treatment facilitated the release of volatiles from tobacco powder and was inferred to be promising for the development of novel cigarette constituents.
Awareness & Perceptions Prevalence & Use Patterns	Influence of HNB Product Packaging Health Warning Design on Risk Perception Based on Eye Tracking	Sun, Lili; Hu, Lizhong; Zheng, Feng; Sun, Yue; Cao, Hui;	Lecture Notes in Computer Science	2021-07-03	This paper reports on an experimental psychology study in the field of HNB packaging design, which used to measure the influence of health warning design on consumer's risk perception. Based on eye tracking method, we conducted an experimental design. The independent variables were the presentation form of the health warning design (text warning, picture warning). The dependent variable included the eye movement data and subjective scores. A total of 68 subjects participated in the experiment. The main finding of this study were as follows: (1) the presentation form of the health warning design significant affects the consumer's visual attention; (2) picture warning has stronger visual impact than text warning which easier to stimulate the user's pupil diameter; (3) the presentation form of the health warning design significant affects the consumer's risk perception. Furthermore, the research results provide an approach of using eye-tracking evaluation method in the relevant consumer products packaging design field.

Clinical	A novel clinical method to measure skin staining reveals activation of skin damage pathways by cigarette smoke	Dalrymple, A.; McEwan, M.; Brandt, M.; Bieffeldt, S.; Bean, E. J.; Moga, A.; Coburn, S.; Hardie, G.	Skin Res Technol	2021-11-10	<p>BACKGROUND: Long-term use of cigarettes can result in localised staining and aging of smokers' skin. The use of tobacco heating products (THPs) and electronic cigarettes (ECs) has grown on a global scale; however, the long-term effect of these products' aerosols on consumers' skin is unknown. This pilot clinical study aimed to determine whether THP or EC aerosol exposure results in skin staining or activation of biomarkers associated with oxidative stress. MATERIALS AND METHODS: Eight areas were identified on the backs of 10 subjects. Two areas were used for air control, and two areas exposed to 32-puffs of cigarette smoke (CS), THP or EC aerosols, which were delivered to the skin using a 3-cm diameter exposure chamber and smoke engine. Skin colour was measured using a Chromameter. Squalene (SQ), SQ and monohydroperoxide (SQOOH) and malondialdehyde (MDA) levels were measured in sebum samples by mass spectrometry and catalase colorimetry. RESULTS: CS exposure significantly increased skin staining, SQOOH and MDA levels and SQOOH/SQ ratio. THP and EC values were significantly lower than CS; EC values being comparable to air control. THP values were comparable to EC and air control at all endpoints, apart from skin staining. SQ and catalase levels did not change with exposure. CONCLUSIONS: CS stained skin and activated pathways known to be associated with skin damage. THPs and ECs produced significantly lower values, suggesting they could offer hygiene and cosmetic benefits for consumers who switch exclusively from smoking cigarettes. Further studies are required to assess longer-term effects of ECs and THPs on skin function.</p>
Clinical	Changes in biomarkers after 180 days of tobacco heating product use: a randomised trial	Gale, N.; McEwan, M.; Camacho, O. M.; Hardie, G.; Proctor, C. J.; Murphy, J.	Intern Emerg Med	2021-07-01	<p>The aim of this study was to investigate whether biomarkers of exposure (BoE) and potential harm (BoPH) are modified when smokers switch from smoking cigarettes to exclusive use of a tobacco heating product (THP) in an ambulatory setting. Participants in this randomised, controlled study were healthy volunteer smokers assigned either to continue smoking or switch to a THP, and a control group of smokers who abstained from cigarette smoking. Various BoE and BoPH related to oxidative stress, cardiovascular and respiratory diseases, and cancer were assessed at baseline and up to 180 days. In continuing smokers, BoE and BoPH remained stable between baseline and day 180, while THP users' levels of most BoE reduced significantly, becoming similar to those in controls abstaining from cigarette smoking. Also at 180 days, significant changes in numerous BoPH, including total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, 8-epi-prostaglandin F2α type III, fractional concentration of exhaled nitric oxide and white blood cell count, were directionally consistent with lessened health impact. Our findings support the notion that the deleterious health impacts of cigarette smoking may be reduced in smokers who completely switch to using THPs.</p>
Clinical	A randomized controlled study in healthy participants to explore the exposure continuum when smokers switch to a tobacco heating product or an E-cigarette relative to cessation	McEwan, M.; Gale, N.; Ebjenito, J. K.; Camacho, O. M.; Hardie, G.; Proctor, C. J.; Murphy, J.	Toxicol Rep	2021-05-08	<p>Background: Cigarette smoking is associated with a number of diseases, such as cancer and cardiovascular diseases. Recently, there has been an increase in the use of electronic cigarettes (ECs) and tobacco-heating products (THPs) as an alternative to cigarettes, which may reduce the health burden associated with smoking. However, an exposure continuum when smokers switch to ECs or THPs compared to complete smoking cessation is not well established. Methods: 148 healthy smokers were randomized to either continue smoking cigarettes, switch to using the glo THP or a prototype EC, or completely quit any nicotine or tobacco product use for 5 days, after a 2-day baseline period. During this study breath and 24-h urine samples were collected for Biomarker of Exposure (BoE) analysis. Results: After a 5-day switching period BoE levels showed a substantial significant decrease in levels from baseline in the groups using the glo THP, the prototype EC, and having quit all nicotine and tobacco use. On an exposure continuum, smokers who completely quit nicotine had the lowest levels of assessed BoEs, followed by those who switched to the EC and then those who switched to glo THP use. Participants who continued to smoke had the highest levels of BoEs. Conclusions: THP or EC use over a 5-day period resulted in significant reductions in exposure to smoke toxicants, in some cases to levels similar to those for nicotine cessation. These results show that on an exposure continuum, nicotine cessation gives the greatest reduction in exposure to tobacco smoke toxicants, closely followed by the EC and the glo THP. These significant reductions in exposure to toxicants suggest that the glo THP and EC have the potential to be Reduced Risk Products. Study Registration: ISRCTN80651909.</p>
Clinical Health Outcomes	Respiratory Function and Physical Capacity in Combustible Cigarettes and Heated Tobacco Products Users: a Two-Year Follow-Up Cohort Study	Sharmun, A.; Yermakova, I.; Erenchina, E.; Tyulebekova, G.; Bakzhanova, A.	Global Journal of Respiratory Care	2021-11-12	<p>Background: Cigarette smoking is the most common risk factor for chronic obstructive pulmonary disease (COPD), which is the fourth leading cause of death in Kazakhstan. Prior literature suggests that heated tobacco products (HTP) might be a better option for people who cannot quit smoking. The aim of this paper was to analyze the long-term effects of shifting to HTP use compared to continued combustible cigarettes (CC) use in long-term smokers. Methods: A cohort of 1200 participants (400 HTP and 800 CC) aged 40-59 years with a minimum of 10 pack-year smoking history were recruited. The functional outcomes compared between HTP and CC users included: (1) COPD Assessment Test (CAT); (2) post-bronchodilator lung function; (3) 6-minute walking distance (6MWD) test; and (4) metabolic syndrome components. Multivariable linear mixed models were used to test associations between health outcomes and smoking type (HTP vs. CC) over time. Results: After 24-month 188 (117 CC users and 71 HTP users) participants were lost to follow-up, while 107 (9%) participants quit smoking. The loss to follow-up was similar in both groups with 15% for CC users and 18% for HTP users. Linear mixed models showed HTP use was associated with lesser decrease in functional outcomes over time compared to CC users. Lung function decrease was significantly less in HTP users, while CAT scores, waist circumference, and systolic blood pressure were significantly better compared to CC users. Conclusion: This study demonstrated that while both CC and HTP users experienced decrease in lung function, HTP users experienced it to a significantly lesser degree, while demonstrating better CAT score and physical characteristics compared to CC users. The results of this study suggest that HTP might be a less deleterious alternative compared to CC in people with long history of CC use and who cannot quit smoking.</p>

Indoor Air Quality	Comparison of the effects of three types of heating tobacco system and conventional cigarettes on indoor air quality	Enomoto, Y.; Imai, R.; Nanjo, K.; Fukui, Y.; Ishikawa, K.; Kotaki, M.	SN Applied Sciences	2021-12-07	Environmental tobacco smoke (ETS) from conventional cigarettes is reported to affect indoor air quality (IAQ) in various real indoor environments. Recently, Japan Tobacco Inc. introduced three types of tobacco product that are heated rather than combusted. These comprise one direct heating tobacco system and two in-direct heating tobacco systems. In this study, the impact of using these products on IAQ was evaluated in an environmentally controlled chamber. Two environmental conditions, simulating restaurant and residential spaces, were examined. Under the same conditions, cigarette smoking and the presence of people only were used as positive and negative controls, respectively. The indoor air concentrations of 48 constituents (tobacco-specific nitrosamines, carbonyls, volatile organic compounds, total volatile organic compounds, polycyclic aromatic hydrocarbon, polycyclic aromatic amines, mercury, metals, ETS markers, propylene glycol, glycerol, carbon monoxide, carbon dioxide, suspended particle matter, ammonia, and nitrogen oxides) were measured. Compared with the presence of people, the concentrations of some constituents were actually increased when using heated tobacco products under both environmental conditions, simulating restaurant and residential spaces. However, the constituent concentrations were lower than those obtained by cigarette smoking, except for propylene glycol and glycerol, and below the exposure limits for constituents in air, as defined by air quality guidelines or regulations. Based on these data, the use of heated tobacco systems in appropriate indoor environments has less impacts compared to conventional cigarettes.
Population Modeling	Investigating the Health Effects of 3 Coexisting Tobacco-Related Products Using System Dynamics Population Modeling: An Italian Population Case Study	Camacho, O. M.; Hill, A.; Fiebelkorn, S.; Williams, A.; Murphy, J.	Front Public Health	2021-11-16	With the proliferation of tobacco products, there might be a need for more complex models than current two-product models. We have developed a three-product model able to represent interactions between three products in the marketplace. We also investigate if using several implementations of two-product models could provide sufficient information to assess 3 coexisting products. Italy is used as case-study with THPs and e-cigarettes as the products under investigation. We use transitions rates estimated for THPs in Japan and e-cigarettes in the USA to project what could happen if the Italian population were to behave as the Japanese for THP or USA for e-cigarettes. Results suggest that three-product models may be hindered by data availability while two product models could miss potential synergies between products. Both, THP and E-Cigarette scenarios, led to reduction in life-years lost although the Japanese THP scenario reductions were 3 times larger than the USA e-cigarette projections.
Population Modeling	Modeling the Population Health Impacts of Heated Tobacco Products in Japan	Camacho, Oscar M.; Hill, Andrew; Fiebelkorn, Stacy; Jones, Joshua D.; Prasad, Krishna; Proctor, Christopher; Murphy, James	Tobacco Regulatory Science	2021-05-01	Objective: We evaluated the potential population health impact of launching heated tobacco products (HTP) in Japan. Method: We use a modeling approach to project the effects of HTP use in overall mortality up to 2100 and compare those projections against a baseline scenario based on smoking rates pre-HTP launch, ie, smoking only. The model was informed using data from publicly available sources and the literature, including population size, yearly deaths, and smoking prevalence with the initial year of 2004, and births and migration from 2004 to 2065. Transitions between products were estimated from cross-sectional population surveys in Japan. Result: In a worst-case scenario, population health gains would be seen with HTPs risk about 50% lower risk than smoking. Assuming equal risk for dual use and smoking, HTP risk would need to be at least 10% lower than smoking to achieve a population health benefit by 2100. Potential reduction in life-years lost with the introduction of HTPs was 13 million by 2100 compared with smoking only. Conclusions: In credible scenarios, substantial population harm reduction will follow the introduction of HTPs in Japan.
Pre Clinical Toxicology	Application of ToxTracker for the toxicological assessment of tobacco and nicotine delivery products	Smart, D. E.; Bozhilova, S.; Miazzi, F.; Haswell, L. E.; Gaea, M. D.; Thorne, D.; Breheny, D.	Toxicology Letters	2022-01-19	Consumer demands and innovation have led to an increasingly diverse range of nicotine delivery systems, driven by a desire to reduce risk associated with traditional combustible cigarettes. This speed of change provides a mandate for rapid new product assessment. We have used the validated technology ToxTracker®, to assess biomarkers of DNA damage, protein misfolding, oxidative and cellular stress, across the categories of cigarette (1R6F), tobacco heating product (THP1-4) and electronic cigarette (ePen 3). In addition, we compared the commonly used test matrices for tobacco and nicotine products: whole aerosol aqueous extracts (AqE) and gas vapour phase (GVP), determining their suitability across the product categories. We demonstrated a significant reduction in oxidative stress and cytotoxicity for THP1-4 over cigarette, further reduced for ePen 3, when assessed by both dilution and nicotine dosimetry. We also identified that while the extraction matrices AqE and GVP from combustible products were equivalent in the induced responses, this was not true of the other category examples, moreover THP GVP demonstrates a >50 % reduction in both toxicity and cytotoxicity endpoints over AqE. This indicates that unlike cigarette, the active components or toxicants for THP and electronic cigarette (eCig) are associated with the aerosol fraction of these categories.

Pre Clinical Toxicology	Comparative study of the effects of cigarette smoke versus next generation tobacco and nicotine product extracts on endothelial function	Giebe, S.; Hofmann, A.; Bruix, M.; Lowe, F.; Breheny, D.; Morawietz, H.; Brunssen, C.	Redox Biol	2021-09-26	<p>Tobacco smoking and hemodynamic forces are key stimuli for the development of endothelial dysfunction. As an alternative to smoking, next generation tobacco and nicotine products (NGP) are now widely used. However, little is known about their potential pro-inflammatory and atherogenic effects on the endothelium. In this study, we analyzed key parameters of endothelial function after exposure to aqueous smoke extracts (AqE) of a heated tobacco product (HTP), an electronic cigarette (e-cig), a conventional cigarette (3R4F) and pure nicotine. All experiments were performed under atheroprotective high laminar or atherogenic low flow with primary human endothelial cells. Treatment with 3R4F, but not alternative smoking products, reduced endothelial cell viability and wound healing capability via the PI3K/AKT/eNOS(NOS) pathway. Laminar flow delayed detrimental effects on cell viability by 3R4F treatment. 3R4F stimulation led to activation of Nrf2 antioxidant defense system at nicotine concentrations $\geq 0.56 \mu\text{g/ml}$ and increased expression of its target genes HMOX1 and NQO1. Treatment with HTP revealed an induction of HMOX1 and NQO1 at dosages with $\geq 1.68 \mu\text{g/ml}$ nicotine, whereas e-cig and nicotine exposure had no impact. Analyses of pro-inflammatory genes revealed an increased ICAM1 expression under 3R4F treatment. 3R4F reduced VCAM1 expression in a dose-dependent manner; HTP treatment had similar but milder effects; e-cig and nicotine treatment had no impact. SELF expression was induced by 3R4F under static conditions. High laminar flow prevented this upregulation. Stimulation with laminar flow led to downregulation of CCL2 (MCP-1). From this downregulated level, only 3R4F increased CCL2 expression at higher concentrations. Finally, under static conditions, all components increased adhesion of monocytes to endothelial cells. Interestingly, only stimulation with 3R4F revealed increased monocyte adhesion under atherosclerosis-prone low flow. In conclusion, all product categories activated anti-oxidative or pro-inflammatory patterns. NGP responses were typically lower than in 3R4F exposed cells. Also, 3R4F stimulation led to an impaired endothelial wound healing and induced a pro-inflammatory phenotype compared to NGP treatment.</p>
Pre Clinical Toxicology	Use of a rapid human primary cell-based disease screening model, to compare next generation products to combustible cigarettes	L. Simms; E. Mason; E. L. Berg; F. Yu; K. Rudd; L. Czekala; E. Trellis; Sicken; O. Brinster; R. Wiczorek; M. Stevenson; T. Walele	Curr Res Toxicol	2021-08-17	<p>A growing number of public health bodies, regulators and governments around the world consider electronic vapor products a lower risk alternative to conventional cigarettes. Of critical importance are rapid new approach methodologies to enable the screening of next generation products (NGPs) also known as next generation tobacco and nicotine products. In this study, the activity of conventional cigarette (3R4F) smoke and a range of NGP aerosols (heated tobacco product, hybrid product and electronic vapor product) captured in phosphate buffered saline, were screened by exposing a panel of human cell-based model systems using Biologically Multiplexed Activity Profiling (BioMAP® Diversity PLUS® Panel, Eurofins Discovery). Following exposure, the biological activity for a wide range of biomarkers in the BioMAP panel were compared to determine the presence of toxicity signatures that are associated with specific clinical findings. NGP aerosols were found to be weakly active in the BioMAP Diversity PLUS Panel ($\leq 3/148$ biomarkers) whereas significant activity was observed for 3R4F (22/148 biomarkers). Toxicity associated biomarker signatures for 3R4F included immunosuppression, skin irritation and thrombosis, with no toxicity signatures seen for the NGPs. BioMAP profiling could effectively be used to differentiate between complex mixtures of cigarette smoke or NGP aerosol extracts in a panel of human primary cell-based assays. Clinical validation of these results will be critical for confirming the utility of BioMAP for screening NGPs for potential adverse human effects.</p>
Pre Clinical Toxicology	The development of an in vitro 3D model of goblet cell hyperplasia using MUC5AC expression and repeated whole aerosol exposures	Haswell, L. E.; Smart, D.; Jamky, T.; Baxter, A.; Santopietro, S.; Meredith, S.; Carracho, O. M.; Breheny, D.; Thome, D.; Gaca, M. D.	Toxicology Letters	2021-04-20	<p>Goblet cell hyperplasia and overproduction of airway mucin are characteristic features of the lung epithelium of smokers and COPD patients. Tobacco heating products (THPs) are a potentially less risky alternative to combustible cigarettes, and through continued use <i>solus</i> THPs may reduce smoking-related disease risk. Using the MucilAir in vitro lung model, a 6-week feasibility study was conducted investigating the effect of repeated cigarette smoke (1R6F), THP aerosol and air exposure. Tissues were exposed to nicotine-matched whole aerosol doses 3 times/week. Endpoints assessed were dosimetry, tight-junction integrity, cilia beat frequency (CBF) and active area (AA), cytokine secretion and airway mucin MUC5AC expression. Comparison of incubator and air exposed controls indicated exposures did not have a significant effect on the transepithelial electrical resistance (TEER), CBF and AA of the tissues. Cytokine secretion indicated clear differences in secretion patterns in response to 1R6F and THP exposure. 1R6F exposure resulted in a significant decrease in the TEER and AA ($p=0.000$ and $p=0.000$, respectively), and an increase in MUC5AC positive cells ($p=0.002$). Repeated THP exposure did not result in a significant change in MUC5AC positive cells. This study demonstrates repeated cigarette smoke whole aerosol exposure can induce these morphological changes in vitro.</p>
Pre Clinical Toxicology	Evaluation of the Biological Effects of Novel Tobacco Product Vapor Using Two- or Three-Dimensional Culture Systems of Human Bronchial Epithelia	Mori, Sakura; Ishimori, Kanae; Tanabe, Ikuya; Ishikawa, Shinkichi	Applied In Vitro Toxicology	2021-03-17	<p>Introduction: Because of the rising popularity of novel tobacco products, there has been an increasing interest in the biological effects of these products. This study was performed to investigate the biological effects of vapor from a novel tobacco vapor product (NTV) in comparison with cigarette smoke (CS) from a 3R4F reference cigarette by using two types of in vitro model. Materials and Methods: A two-dimensional (2D) culture system composed of a submerged monolayer of BEAS-2B cells was used to detect cellular oxidative stress responses. A three-dimensional (3D) culture system composed of a pseudostratified air-liquid interface culture of normal human bronchial epithelial cells was used to detect tissue inflammation. In both culture systems, exposures were conducted with an aqueous extract (AqE) of NTV vapor or CS. Results: In the 2D culture system, exposure to CS AqE induced glutathione oxidation and antioxidant response element reporter gene activation. NTV vapor AqE also induced reporter gene activity, but the concentration required for activation was higher than that of CS AqE. In the 3D culture system, exposure to CS AqE increased the secretion of various inflammatory mediators. In contrast, the effect of NTV vapor AqE on tissue inflammation was limited, and only interferon-γ showed a slight increase in expression. Conclusions: Overall, these results demonstrate that NTV vapor has fewer effects on cellular oxidative stress and tissue inflammatory responses as compared with CS in vitro models using human cells.</p>

Prevalence & Use Patterns	Cross-sectional Survey to Assess Tobacco and Nicotine Product Use since the Introduction of Tobacco Heating Products in Japan: Wave 1	Jones, Joshua D.; Adamson, Jason; Kaitscheider, Claudia; Prasad, Krishna; Camacho, Oscar M.; Bellaeva, Ekaterina; Bauer, Hans; Keralapura, Yoga; Murphy, James	Tobacco Regulatory Science	2021-03-05	<p>Objective: In this study, we obtained key population-level data on use patterns and behavior relating to tobacco and nicotine products in Japan. Methods: We performed a nationwide cross-sectional survey of the general population in Japan in 2019 to assess use patterns after the introduction of tobacco heating products (THPs). Eligible participants were Japanese residents, aged 20 years or older who consented to complete the survey. Individuals living in institutions were excluded. A 3-stage probability sampling method was applied that was geographically stratified by street blocks proportionate to population density. Respondents self-reported patterns of product use and reasons for THP use. Results: Complete responses were available from 5306 individuals, of whom 933.5 (17.6%) were current users, 984.2 (18.5%) were former users, and 3388.4 (63.9%) were never users of tobacco products (weighted respondent totals). Cigarettes were used by 14.6% of current tobacco product users and THPs by 5.3%. Cigarettes and THPs were used exclusively by 64.5% and 12.2%, respectively, and both were used by 12.7%. The most common reasons reported for THP use were perceived reduction in harm to self and others compared to cigarettes. Conclusions: Whereas the prevalence of cigarette use in Japan is decreasing, THPs seem to be increasingly used as long-term alternatives to cigarette smoking.</p>
Clinical	Pharmacokinetic and subjective assessment of prototype JUUL2 electronic nicotine delivery system in two nicotine concentrations, JUUL system, IQOS, and combustible cigarette	Goldenson, N. L.; Augustson, E. M.; Chen, J.; Shiffman, S.	Psychopharmacology (Berl)	2022-02-20	<p>RATIONALE: Electronic nicotine delivery systems and heated tobacco products are noncombustible alternatives for adult smokers. Evidence suggests sufficient nicotine delivery and satisfying effects are necessary to facilitate switching away from smoking; nicotine delivery varies across electronic nicotine delivery systems within limited nicotine concentrations. OBJECTIVES: To assess the nicotine delivery and subjective effects of prototype JUUL2 System in two nicotine concentrations, currently-marketed US JUUL System ("JUUL"), IQOS-brand heated tobacco product, and combustible cigarettes. METHODS: Adult smokers (N = 40) completed a 5-arm cross-over product-use laboratory confinement study. Nicotine pharmacokinetics and subjective effects were assessed following use of: (1) JUUL2 prototype 18 mg/mL nicotine; (2) JUUL2 prototype 40 mg/mL; (3) JUUL 59 mg/mL; (4) IQOS 18 mg/g; and (5) usual brand combustible cigarette, each evaluated during ad libitum (10 min) and controlled (5 min, 10 standardized puffs) use. RESULTS: Nicotine delivery was greatest for combustible cigarettes, followed by JUUL2 prototype 40 mg/mL, IQOS, JUUL2 prototype 18 mg/mL, and JUUL 59 mg/mL. Nicotine delivery from JUUL2 prototype 18 mg/mL was significantly greater than JUUL 59 mg/mL after ad libitum use. JUUL products were significantly more satisfying and effective at reducing craving than IQOS. JUUL2 prototype 40 mg/mL was significantly more aversive than other JUUL products. CONCLUSIONS: Prototype JUUL2 and JUUL 59 mg/mL products were rated higher than IQOS on subjective measures associated with switching away from smoking. The JUUL2 prototype 40 mg/mL produced aversive responses and would require modifications to be a viable product for adult smokers. Nicotine delivery and subjective responses to JUUL2 prototype 18 mg/mL suggest a product based on this prototype may facilitate increased switching among adult smokers.</p>
Pre Clinical Toxicology Aerosol Chemistry & Physics	Bridging: Accelerating Regulatory Acceptance of Reduced-Risk Tobacco and Nicotine Products	Gaca, M.; Williamson, J.; Digard, H.; Adams, L.; Hawbridge, L.; Proctor, C.	Nicotine Tob Res	2022-02-16	<p>INTRODUCTION: The number and variety of alternative tobacco and nicotine products that can potentially provide reduced-risk choices for cigarette smokers who switch completely to such products instead of continued smoking have grown substantially in the past decade. Innovation and choice are likely to improve the prospects of smokers making the switch, but this provides challenges to regulators and manufacturers to ensure that changes to regulations and products promote and not hinder contributions to tobacco harm reduction. METHODS: This paper looks at where bridging of data sets for tobacco heating products, closed system vaping products and oral nicotine products might enable innovation while protecting interests of consumers. RESULTS: We review product data from chemical studies and a toxicological study showing how bridging can be applied and consider what product development changes might allow bridging from existing datasets or trigger the need for new. CONCLUSIONS: Bridging across specific product ranges can increase the speed of innovation, foster competition and limit the burden of assessment for regulators while maintaining product safety and quality. IMPLICATIONS: Bridging of partial data sets is an established practice within other industries, that aims to improve efficiency with regulatory approvals, accepts natural product variation and supports product innovation. We review product data from chemical studies and a toxicological study showing how bridging can be applied and consider what product development changes might allow bridging from existing datasets or trigger the need for new. This in turn can increase the speed of innovation, foster competition and limit the burden of assessment for regulators while maintaining product safety and quality.</p>

Independent Scientific Publications

March 1, 2021 – February 28, 2022

Reporting Period	March 1, 2021 – February 28, 2022				
Category	Title	Authors	Journal	Date of first Publication	Abstract
Aerosol Chemistry & Physics	Acrylamide levels in smoke from conventional cigarettes and heated tobacco products and exposure assessment in habitual smokers	Esposito, F.; Squillante, J.; Nolasco, A.; Montuori, P.; Macri, P. G.; Cirillo, T.	Environ Res	2022-01-03	Acrylamide (AA) is a neurotoxic, genotoxic, and carcinogenic compound developed during heating at high temperatures. Foods such as potatoes, biscuits, bread and coffee are the main foodstuffs containing AA. Cigarette smoke may be a significant additional source of exposure. However, AA content may vary among different types of cigarettes. The study aimed to evaluate the AA content in conventional cigarettes (CC) and heated tobacco products (HTP) and its resulting exposure through their use. AA levels from the two types of cigarettes were determined by GC-MS and the daily exposure to AA was also ascertained. The margin of exposure approach (MOE) was calculated for neurotoxic and carcinogenic risk based on benchmark dose lower confidence limit for a 10% response (BMDL(10)) of 0.43 and 0.17, 0.30, and 1.13 mg/kg body weight/day. AA level in CC ranged from 235 ng to 897 ng/cigarette, whereas HTP reported AA levels in the range of 99-187 ng/cigarette. The data showed a low neurotoxic risk for either in CC or HTP, whereas a carcinogenic risk emerged through the smoking of CC based on different Benchmark doses. The carcinogenic risk for CC based on the highest Benchmark dose that was considered showed unsafe levels, as little as 10 CC cigarettes/day, whereas it was almost always of low concern for HTP. Another approach based upon the incremental lifetime cancer risk (ILCR) analysis led to similar results, exceeding, in some cases, the safety value of 10 ⁻⁴), as far as CC are concerned. Overall, the results confirmed that CC is a significant source of AA, and its levels were five times higher than in HTP.
Aerosol Chemistry & Physics	Acid-Catalyzed Isomerization of Carbonyls-2,4-dinitrophenylhydrazine in Mainstream Smoke of Heat-Not-Burn Tobacco Product for HPLC Analysis	Zhang, H.; Zhu, F.; Chen, C.; Li, X.; Luo, Y.; Jiang, X.; Pang, Y.; Zhang, W.; Hou, H.; Hu, Q.	LCGC North America	2022-01-01	Carbonyls (such as acrolein, acetaldehyde, and formaldehyde) are the critical type of carcinogens and toxicants contained within the heat-not-burn (HNB) tobacco products. Using HNB products can have negative effects on human health; therefore, it is important to measure carbonyl contents within the HNB mainstream smoke. Typically, the 2,4-dinitrophenylhydrazine (DNPH) approach involves forming the 2,4-dinitrophenylhydrazone derivatives, which is the most extensively adopted approach to qualitatively and quantitatively analyze carbonyl compounds. However, the approach can result in analytical error because 2,4-dinitrophenylhydrazones contains the E-stereoisomer as well as the Z-stereoisomer. Only an E-isomer exists in the purified carbonyls-2,4-dinitrophenylhydrazones, but when acid is added, the E-isomer and Z-isomer can be observed. For propionaldehyde, acetaldehyde, crotonaldehyde, acrolein-, and 2-butanone-2,4-dinitrophenylhydrazones, their equilibrium Z/E isomer ratios are 0.143, 0.309, 0.093, 0.028, and 0.154. In the case of adding trace water into hydrazone derivatives dissolved within the acetonitrile solution, the derivative contents decrease, whereas the free DNPH content increases. Therefore, catalytic acid should be added in the low content. To determine carbonyls-2,4-dinitrophenylhydrazones through HPLC, the optimal approach is adding phosphoric acid into the samples and the standard reference solution to form the 0.02–1.0% acid solution.
Aerosol Chemistry & Physics	The Emission of VOCs and CO from Heated Tobacco Products, Electronic Cigarettes, and Conventional Cigarettes, and Their Health Risk	Lu, F.; Yu, M.; Chen, C.; Liu, L.; Zhao, P.; Shen, B.; Sun, R.	Toxics	2021-12-28	The differences in aerosol composition between new tobacco types (heated tobacco products and electronic cigarettes) and conventional cigarettes have not been systematically studied. In this study, the emissions of volatile organic compounds (VOCs), carbon monoxide (CO), nicotine, and tar from heated tobacco products (HTPs), electronic cigarettes (e-cigarettes) and conventional cigarettes were compared, and their health risks were evaluated by applying the same smoking regime and a loss mechanism of smoking. Twenty VOCs were identified in aerosols from HTPs, 18 VOCs were identified in aerosols from e-cigarettes, and 97 VOCs were identified in aerosols from cigarettes by GC-MS and HPLC analysis. The concentrations of total VOCs (TVOCs) emitted by the three types of tobacco products decreased as follows: e-cigarettes (795.4 mg/100 puffs) > cigarettes (83.29 mg/100 puffs) > HTPs (15.65 mg/100 puffs). The nicotine content was 24.63 ± 2.25 mg/100 puffs for e-cigarettes, 22.94 ± 0.03 mg/100 puffs for cigarettes, and 8.817 ± 0.500 mg/100 puffs for HTPs. When using cigarettes of the same brand, the mass concentrations of VOCs, tar, and CO emitted by HTPs were approximately 81.2%, 95.9%, and 97.5%, respectively, lower than the amounts emitted by cigarettes. The health risk results demonstrated that the noncarcinogenic risk of the three types of tobacco products decreased as follows: cigarettes (3609.05) > HTPs (2449.70) > acceptable level (1) > e-cigarettes (0.91). The lifetime cancer risk (LCR) decreased as follows: cigarettes (2.99 × 10 ⁻⁴) > HTPs (9.92 × 10 ⁻⁵) > e-cigarettes (4.80 × 10 ⁻⁵) > acceptable level (10 ⁻⁶). In general, HTPs and e-cigarettes were less harmful than cigarettes when the emission of VOCs and CO was considered.

Aerosol Chemistry & Physics	Chemical Feedstock Recovery via the Pyrolysis of Electronically Heated Tobacco Wastes	Choi, Y.; Jeong, S.; Park, Y.; Kim, H.; Lim, S.; Woo, G.; Pyo, S.; Siddiqui, M. Z.; Kim, Y.	Sustainability	2021-11-20	<p>The pyrolysis of waste electronically heated tobacco (EHT), consisting of tobacco leaves (TL), a poly-lactic acid (PLA) filter, and a cellulose acetate (CA) filter, was investigated using thermogravimetric (TG) and pyrolyzer-gas chromatography/mass spectrometry (Py-GC/MS) analysis. The pyrolytic properties of waste EHT obtained after smoking were comparable to those of fresh EHT. Although the maximum decomposition temperatures (TmaxS) of waste TL and CA were similar to those of fresh EHT components, the Tmax of waste PLA was slightly higher than that of fresh PLA due to smoldering. The Tmax of PLA and CA were lowered when they were co-pyrolyzed with TL due to interactions between pyrolysis intermediates. The apparent activation energies for the non-isothermal pyrolysis of waste EHT components were higher than those of fresh EHT components. Py-GC/MS analysis results indicated that considerable amounts of chemical feedstocks, such as nicotine and limonene from TL, caprolactone and lactide from PLA, and acetic acid and triacetin from CA, can be recovered by simple pyrolysis of EHT. Co-pyrolysis of TL, PLA, and CA revealed that the experimental amount of lactide was much larger than the calculated value, suggesting its synergistic formation.</p>
Aerosol Chemistry & Physics	Time-resolved online analysis of the gas- and particulate-phase of cigarette smoke generated by a heated tobacco product using vacuum ultraviolet photoionization mass spectrometry	Wen, Z.; Gu, X.; Tang, X.; Li, X.; Pang, Y.; Hu, Q.; Wang, J.; Zhang, L.; Liu, Y.; Zhang, W.	Talanta	2021-11-12	<p>We present a vacuum ultraviolet (VUV) lamp-based photoionization time-of-flight (TOF) mass spectrometer coupled with a capillary inlet and an aerodynamic lens to online analyze the chemical compositions of the gas- and particulate-phase of cigarette smoke of a heated tobacco product (HTP). Both phase compositions of the fresh cigarette smoke, without dilution and pretreatment, are softly photoionized and their mass spectra are measured with a time resolution of 1 s. It is shown that the gas-phase compositions with low mass are volatile organic compounds (VOCs), and the particulate-phase compositions are also clearly identified and cover the full mass range of the mass spectrometer. The time- or puff-by-puff resolved dynamic data are obtained for each species and provide abundant information to unravel the chemistry of the HTP smoke. In addition, the present results show that besides thermal vaporization, a couple of chemical reactions including pyrolysis and degradation have also occurred in the HTP smoking process, although its operation temperature is less than 350 °C. Even if not done here, this study paves the way to analyze the gas- and particulate-phase chemical compositions of a complex system in real time, like the cigarette smoke presented here, by using advanced soft ionization mass spectrometry.</p>
Aerosol Chemistry & Physics	Assessing acute inhalation health risk caused by exposure to products created by nicotine-containing stuff consumption in enclosed spaces	Zaritskaya, E. V.; Fedorov, V. N.; Iakubova, I. S.	Health Risk Analysis	2021-09-30	<p>Contemporary research reveals that electronic devices for nicotine consumption produce not so negative effects on health due to adverse chemicals being emitted in substantially lower quantities. Nevertheless, such consumption still results in emission of various organic and non-organic substances with their effects on health being rather unpredictable. It is necessary to conduct additional studies, including those focusing on passive smoking of electronic cigarettes and assessing health risks caused by exposure to them. Our research goal was to assess acute health risks caused by passive consumption of tobacco and nicotine-containing products. We built a model for tobacco or nicotine consumption by actual consumers (volunteers) and the process was evoked as per a number of consumption sessions. We examined three products: tobacco cigarettes (cigarettes), electronic nicotine delivery system (ENDS), and a tobacco heating system (IQOS). Background air quality parameters were measured in a specifically organized enclosed space prior to each study session. We also conducted experiments in so called «reference groups» when research participants didn't consume the examined products but were in the same conditions. Health risks were assessed as per the Guide R 2.1.10.1920-04 «The Guide on assessing health risks caused by exposure to chemicals that pollute the environment». Use of ENDS and IQOS does not result in significant changes in air composition and does not cause unacceptable acute health risk. Combined effects produced by contaminants on organs and systems resulted in health risks for respiratory organs, eyes, and body as a whole being insignificantly higher than permissible levels; these risks were practically the same as those detected for a reference group. Tobacco smoking resulted in unacceptable acute risks 1.5 hours after an experiment started; these risks were caused by elevated concentrations of such contaminants as acetaldehyde, formaldehyde, PM2.5, PM10, and carbon monoxide. © Zaritskaya E. V., Fedorov V. N., Iakubova I. S., 2021</p>
Aerosol Chemistry and Physics	Qualitative and quantitative comparison of flavor chemicals in tobacco heating products, traditional tobacco products and flavoring capsules	Lim, H. H.; Choi, K. Y.; Shin, H. S.	J Pharm Biomed Anal	2021-10-01	<p>A gas chromatography-mass spectrometric (GC-MS) method was developed for the qualitative and quantitative analysis of flavor chemicals in tobacco heating products (THPs), traditional tobacco products (TTPs) and their flavoring capsules. A total of 283 compounds were identified through non-target analysis, and the final 302 compounds were selected to develop an analytical method. The lower limits of detection (LOD) of analytes were 0.00074–12 mg/kg and their LOD range was wide depending on the presence or absence in the reference cigarette. The precision of the 302 compounds was less than 24.5%, and the accuracy ranged from 80.0% to 120%. A total of 190 flavors and 5 contaminants were determined in 21 THP, 10 TTP, 8 THP capsules and 11 TTP capsules. When comparing the total flavor content of flavors per cigarette, it was in the order of THP capsule > TTP capsule > THP > TTP. The correlations between the 53 cigarette products and 190 flavor chemicals were analyzed using PCA. It has been demonstrated that PCA results can be a useful tool in differentiating brands and manufacturers of tobacco products.</p>
Aerosol Chemistry and Physics	Analysis of furans and pyridines from new generation heated tobacco product in Japan	K. Bekki; S. Uchiyama; Y. Inaba; A. Uchiyama	Environ Health Prev Med	2021-09-13	<p>Analysis of furans and pyridines from new generation heated tobacco product in Japan</p>

Aerosol Chemistry and Physics	Investigation of Volatile Organic Compounds and Benzo[a]pyrene Contents in the Aerosols of Cigarettes and IQOS Tobacco Heating System Using High-Performance Gas Chromatography/Mass Spectrometry	T. A. Perezhogina; E. V. Gnuchikh; R. I. Faizullin; S. N. Medvedeva; T. A. Zaytseva; N. A. Durunchai; L. V. Kokorina; D. K. Glukhov; T. I. Pokrovskaya; N. V. Popova; I. M. Eremina; I. I. Galich; S. G. Anushyan; S. R. Abdulkhakov; I. M. Ostapchenko	BioNanoScience	2021-09-06	Investigation of Volatile Organic Compounds and Benzo[a]pyrene Contents in the Aerosols of Cigarettes and IQOS Tobacco Heating System Using High-Performance Gas Chromatography/Mass Spectrometry
Aerosol Chemistry and Physics	Effect of a mesoporous catalyst on the flash pyrolysis of tobacco	E. Calabuig; A. Marcella	Thermochemica Acta	2021-09-01	Effect of a mesoporous catalyst on the flash pyrolysis of tobacco
Aerosol Chemistry and Physics	Puff-resolved analysis and selected quantification of chemicals in the gas phase of E-Cigarettes, Heat-not-Burn devices and conventional cigarettes using single photon ionization time-of-flight mass spectrometry (SPI-TOFMS): A comparative study	Heide, J.; Adam, T. W.; Jacobs, E.; Wolter, J. M.; Ehlert, S.; Walte, A.; Zimmermann, R.	Nicotine & Tobacco Research	2021-05-16	INTRODUCTION: A wide array of alternative nicotine delivery devices (ANDD) has been developed and they are often described as less harmful than combustible cigarettes. This work compares the chemical emissions of three ANDD in comparison to cigarette smoke. All the tested ANDD are characterized by not involving combustion of tobacco. METHOD: Single photon ionization time-of-flight mass spectrometry (SPI-TOFMS) is coupled to a linear smoking machine, which allows a comprehensive, online analysis of the gaseous phase of the ANDD aerosol and the conventional cigarette smoke (CC). The following devices were investigated in this study: a tobacco cigarette with a glowing piece of coal as a heating source, an electric device for heating tobacco and a first-generation electronic cigarette. Data obtained from a standard 2R4F research cigarette are taken as a reference. RESULTS: The puff-by-puff profile of all products was recorded. The ANDD show a substantial reduction or complete absence of known harmful and potentially harmful substances compared to the CC. In addition, tar substances (i.e. semivolatile and low volatile aromatic and phenolic compounds) are formed to a much lower extent. Nicotine, however, is supplied in comparable amounts except for the investigated electronic cigarette. CONCLUSIONS: The data shows that consumers switching from CC to ANDD are exposed to lower concentrations of harmful and potentially harmful substances. However, toxicological and epidemiological studies must deliver conclusive results if these reduced exposures are beneficial for users. IMPLICATION: The comparison of puff-resolved profiles of emissions from different tobacco products, traditional and alternative, may help users switch to lower emission products. Puff-resolved comparison overcomes technical changes, use modes between products and may help in their regulation.
Aerosol Chemistry and Physics	Early Chemistry of Nicotine Degradation in Heat-Not-Burn Smoking Devices and Conventional Cigarettes: Implications for Users and Second- and Third-Hand Smokers	Chavarrio Cañas, Javier E.; Monge-Palacios, M.; Grajales-González, E.; Mani Sarathy, S.	Journal of Physical Chemistry A	2021-04-09	Nicotine exposure results in health risks not only for smokers but also for second- and third-hand smokers. Unraveling nicotine's degradation mechanism and the harmful chemicals that are produced under different conditions is vital to assess exposure risks. We performed a theoretical study to describe the early chemistry of nicotine degradation by investigating two important reactions that nicotine can undergo: hydrogen abstraction by hydroxyl radicals and unimolecular dissociation. The former contributes to the control of the degradation mechanism below 800 K due to a non-Arrhenius kinetics, which implies an enhancement of reactivity as temperature decreases. The latter becomes important at higher temperatures due to its larger activation energy. This change in the degradation mechanism is expected to affect the composition of vapors inhaled by smokers and room occupants. Conventional cigarettes, which operate at temperatures higher than 1000 K, are more prone to yield harmful pyridinyl radicals via nicotine dissociation, while nicotine in electronic cigarettes and vaporizers, with operating temperatures below 600 K, will be more likely degraded by hydroxyl radicals, resulting in a vapor with a different composition. Although low-temperature nicotine delivery devices have been claimed to be less harmful due to their nonburning operating conditions, the non-Arrhenius kinetics that we observed for the degradation mechanism below 873 K suggests that nicotine degradation may be more rapidly initiated as temperature is reduced, indicating that these devices may be more harmful than it is commonly assumed.

Aerosol Chemistry and Physics Pre Clinical Toxicology	Novel Solvent-Free Extraction Method for Analyzing Tobacco Heating Product Aerosols: An Analytical and In Vitro Toxicological Five-Way Product Comparison	Wang, H.; Chen, H.; Huang, L.; Han, S.; Wang, L.; Li, S.; Liu, M.; Zhang, M.; Fu, Y.; Tian, Y.; Liu, T.; Shi, Z.; Hou, H.; Hu, Q.	Chem Res Toxicol	2021-11-08	Harmful and potentially harmful constituents (HPHCs) in tobacco smoke are thought to be responsible for the increased health risks. Tobacco heating products (THPs) heat tobacco instead of burning it to achieve significantly fewer toxicants than conventional cigarettes. To assess the toxicity of THP aerosols, it is often desirable to extract the main constituents using a solvent method. In this study, we developed a high-speed centrifugal method for extracting the total particulate matter (TPM) from THPs to quantitatively compare the toxicity of different THPs and conventional cigarettes. Its TPM extraction efficiency exceeded 85%, and the primary aerosol components and typical HPHCs were comparable to those of the solvent method. The TPMs extracted from five THPs were subjected to 14 in vitro toxicology assessments, and the results were compared with those of a 3R4F reference cigarette. Physical separation can improve biases from solvent selectivity and potential interactions between solvent and aerosol constituents. By eliminating solvent influence, the extraction method could achieve high-dose exposures, enabling the toxicity comparison of different THPs. The relative toxicity of the THPs differed under different dosage units, including the TPM concentration, nicotine equivalent, and puff number.
Aerosol Chemistry and Physics Product Design	A Simple Method to Simultaneously Determine the Level of Nicotine, Glycerol, Propylene Glycol, and Triacetin in Heated Tobacco Products by Gas Chromatography Flame Ionization Detection	Chen, A. X.; Akmam Morsed, F.; Cheah, N. P.	J AOAC Int	2021-10-14	<p>BACKGROUND: Currently, there is no validated and available method internationally to determine the contents of nicotine and the aerosolizing agents, namely glycerol and propylene glycol, added onto the heatsticks for use in heated smoking devices.</p> <p>OBJECTIVE: To determine the concentrations of nicotine, propylene glycol, glycerol and triacetin in HTPs which is essential to understanding their health effects on smokers as well as secondhand smokers. METHOD: A simple methodology was developed and validated to simultaneously determine nicotine, propylene glycol, glycerol and triacetin concentration present in heatsticks. The tobacco material was extracted with a mixture of 70% methanol/30% acetonitrile with 1,3-butanediol and n-heptadecane as internal standards and analyzed with gas chromatography with flame-ionization detection (GC-FID).</p> <p>RESULTS: Good linearity was achieved over the concentration range of 0.1-1.0 mg/mL for nicotine, 0.03-2.0 mg/mL for propylene glycol, 0.5-10.0 mg/mL for glycerol and 0.1-4.0 mg/mL triacetin with correlation of determination ≥ 0.995. The limits of detection and quantification were 0.0009 and 0.003 mg/mL for nicotine, 0.02 and 0.02 mg/mL for propylene glycol, 0.03 and 0.09 mg/mL for glycerol, and 0.005 and 0.02 mg/mL for triacetin, respectively. Good recoveries were obtained for nicotine at 89.8-102.0%, propylene glycol at 95.5-102.5%, glycerol at 95.2-102.6%, and triacetin at 90.6-103.1%.</p> <p>CONCLUSION: This method provides an affordable and reliable technique for routine analysis of nicotine and aerosolizing chemicals present in HTPs which is necessary to assess their impact to public health. HIGHLIGHTS: Many gaps remain in research on heated tobacco products, in particular, country levels information on the content of the products are limited. This paper contains information on a newly developed method to simultaneously determine nicotine, propylene glycol, glycerol and triacetin present in the tobacco material and butts of heatsticks for HTPs.</p>
Awareness & Perceptions	Validation of a questionnaire to assess smoking habits, attitudes, knowledge, and needs among university students: A pilot study among obstetrics students	Campo, L.; Vecera, F.; Fustinoni, S.	International Journal of Environmental Research and Public Health	2021-11-12	In Italy, smoking is still widespread among a relatively high percentage of young people. This study aimed to develop and validate a questionnaire to assess smoking habits, passive smoke exposure, electronic cigarette (e-cig) and heated tobacco product (HTP) use, attitudes, knowledge, and needs among undergraduates. A questionnaire consisting of 84 items was developed starting from a literature review and existing questionnaires. A two-round validation was performed by a team of 10 experts. The item-level content validity index (I-CVI), the scale-level content validity index (S-CVI), and the kappa statistics k, taking into account chance agreement, were calculated from the experts' rating. The questionnaire was emailed to 114 students from the Obstetrics Degree of the University of Milan (Italy) to be pilot tested. After the second round of validation, all indexes were above the respective acceptability criteria: the I-CVI was 1.00 for all but three items, k was >0.74 ("excellent") for all items, and the S-CVI was 0.964. Eighty-nine students participated in the survey: 17 classified themselves as smokers, eight as new product users, and four as former smokers, 72% students declared to routinely spend free time with smokers, while almost all students believed that healthcare professionals play a pivotal role in preventing smoking towards their patients and society. This questionnaire will be used in a survey among students from the University of Milan as a first step for future campaigns targeting health promotion.

Awareness & Perceptions	Effects of IQOS health warnings and modified risk claims among young adult cigarette smokers and non-smokers	Mayes, D., Johnson, A. C., Glasser, A., Mercincavage, M., Strasser, A. A.	Tobacco Control	2021-10-29	<p>INTRODUCTION: Heated tobacco products, including Marlboro IQOS, are available globally. In the USA, IQOS was authorised to be advertised with claims about reduced toxicant exposure relative to cigarettes. The effects of such modified risk claims and health warnings have not been studied among young adult cigarette smokers and non-smokers. METHODS: In 2020, US young adult (18-30 years, n=1328) cigarette smokers and non-smokers viewed an IQOS ad in a 4 (modified risk claim variations or none) by 3 (warning variations or none) between-subjects experiment. Outcome measures assessed perceived credibility and effectiveness of the health or risk message for discouraging IQOS use, perceived harms, efficacy beliefs, and IQOS use intentions. RESULTS: Smokers reported significantly higher ($p<0.05$) perceived credibility, lower perceived effectiveness, higher efficacy beliefs about switching to IQOS and higher intentions to use IQOS than non-smokers. Among smokers, health warnings increased perceived credibility ($p<0.001$) and effectiveness ($p<0.05$), but claims did not affect outcomes examined. Among non-smokers, warnings and claims increased perceived credibility, and warnings increased perceived effectiveness ($p<0.003$). The reduced exposure claim increased non-smokers' intentions to use IQOS ($b=0.40$, 95% CI 0.07 to 0.73). CONCLUSIONS: Among young adult smokers, health warnings increased perceived effectiveness at discouraging IQOS use and perceived credibility. Among non-smokers, warnings and claims increased perceived credibility and warnings increased perceived effectiveness, but the Food and Drug Administration-authorised reduced exposure claim increased intentions to use IQOS. Research is warranted to understand how the content of modified risk claims and health warnings for IQOS affects IQOS use in this population.</p>
Awareness & Perceptions	Effective package warning label systems for communicating relative risks of cigarettes, heated tobacco products, and e-cigarettes: An experimental study with Korean adults	Cho, Y. J.; Thrasher, J. F.; Davis, R.; Kim, S. H.; Hardin, J.; Popova, L.	Int J Drug Policy	2021-10-06	<p>BACKGROUND: Warning labels are a fundamental public health strategy for communicating about tobacco product risks, but effective warning labels for heated tobacco products (HTPs) and e-cigarettes (ECs) are yet to be determined. We examined the effect of two warning label systems for communicating the relative risks of using cigarettes, HTPs, and ECs. METHODS: 1,280 Korean adults were recruited from an online commercial panel, including susceptible non-users of cigarettes, HTPs, or ECs aged 19 to 29 ($n = 444$) and current users of these tobacco products aged 19 or older ($n = 836$). Participants viewed packages for cigarettes, HTPs, and ECs in a 2×2 between-subject experiment: "dashboard" icons integrated into warnings vs. no dashboard; different-sized warnings (70% of cigarette packages, 50% of HTP packs, 30% of EC packages) vs. current equal-sized warnings (50% of cigarette/HTP/EC packages). RESULTS: Participants exposed to the dashboard warning system were more likely than those who were not to report higher perceived harm of cigarettes than ECs, cigarettes than HTPs, and HTPs than ECs, as well as perceived benefit of switching from cigarettes to HTPs, cigarettes to ECs, and HTPs to ECs. Participants exposed to the different-sized warning system did not report differences in perceived relative harm or benefit compared to those who were not, and no interaction of dashboard warnings with warning sizes was found. CONCLUSION: The use of dashboard icons with texts and colors representing different levels of risk may promote public understanding about the continuum of risk across tobacco products.</p>
Awareness & Perceptions	E-learning course improves knowledge in tobacco dependence, electronic nicotine delivery systems and heat-not-burn products in Medical School students	Milella, M. S.; Sansone, A.; Basili, S.; Battaglia, G.; La Torre, G.; Ferketich, A. K.; Grassi, M. C.	Clin Ter	2021-10-01	<p>BACKGROUND: Adequate training in tobacco, nicotine dependence and treatment is lacking in Medical School education. With the rise in popularity of electronic alternatives to cigarettes, future physicians should also be provided with the more recent scientific evidence on these products during their undergraduate studies. We introduced an e-learning course for Medical School students and assessed its effectiveness of increasing knowledge on these topics. METHODS: We developed 16 didactic modules divided in 3 courses: tobacco dependence (TDI), treating tobacco dependence (TDII) and electronic products and tobacco control (TDIII). The course was offered to 4th, 5th, and 6th year Medical School students in Italy. To assess learning outcomes, we examined the pre- to post- changes in knowledge scores associated with each course. Paired and independent samples t-tests were performed overall, and among smokers and non-smokers separately. RESULTS: A total of 1318 students completed at least one of the courses; 21% were self-reported smokers. A significant increase in knowledge was observed at the end of TDI (pre-course: 52.1 ± 15.9, post-course: 79.9 ± 13.5, $p<0.001$), TDII (pre-course: 52.5 ± 13.0, post-course: 66.5 ± 12.0, $p<0.001$) and TDIII (pre-course: 52.2 ± 15.3, post-course: 76.1 ± 17.7, $p<0.001$). Smokers showed significantly lower improvements compared to non-smokers. CONCLUSIONS: The e-learning course was effective in increasing knowledge about tobacco dependence, treatments, and electronic nicotine products in advanced medical students. Given the fundamental role for healthcare practitioners in encouraging and assisting people in quitting smoking, e-learning may be a useful tool in providing up-to-date and standardized training in the area during Medical School.</p>

Awareness & Perceptions	Harm perceptions of nicotine-containing products, and associated sources of information, in UK adults with and without mental ill-health: a cross-sectional survey	<p>Perman-Howe, P. R.; Horton, M.; Robson, D.; McDermott, M. S.; McNeill, A.; Brose, L. S.</p>	Addiction	2021-08-02	<p>BACKGROUND AND AIMS: People with mental ill-health are more likely to smoke and experience smoking-related harm than those without. Switching from combustible tobacco to lower risk nicotine-containing products may be of benefit; however, misperceptions of harm may prevent their use. We aimed to assess, among adults with and without mental ill-health, (1) perceptions of harm from nicotine and relative harm and addictiveness of different nicotine-containing products and (2) sources of information associated with harm perceptions. DESIGN: Cross-sectional study. SETTING AND PARTICIPANTS: Online survey of adults (n=3400) who smoke cigarettes and/or use e-cigarettes, or recently stopped, in the United Kingdom. MEASUREMENTS: Outcomes: harm perceptions of nicotine; relative perceived harm and addictiveness of different nicotine-containing products; sources of information for harm perceptions of nicotine, cigarette smoking, e-cigarettes. Demographics: sex, age, education, ethnic group, region. Other measures: self-reported smoking, vaping, and mental health status. ANALYSES: frequencies and logistic regressions adjusting for demographic/other measures. FINDINGS: Among those with serious mental distress (versus no/low mental distress): 9.6% (13.9%, adjusted odds ratio (AOR) 0.69 (0.50-0.97)) correctly identified that none/very small amount of the health risks of smoking cigarettes come from nicotine; 41.7% (53.5%, AOR 0.67 (0.54-0.84)) perceived e-cigarettes; and 53.2% (70.3%, AOR 0.62 (0.50-0.77)) perceived nicotine replacement therapy, to be less harmful than cigarettes; 42.1% (51.3%, AOR 0.77 (0.62-0.95)) perceived e-cigarettes as being less likely than cigarettes to cause cancer, 35.4% (45.5%, AOR 0.71 (0.57-0.88)) heart attacks and 34.9% (42.3%, AOR 0.80 (0.64-0.99)) lung problems. The most popular sources of information for cigarette smoking, e-cigarettes and nicotine were scientific experts' opinions and media reports, with little variation by mental distress. CONCLUSIONS: Among adults with a history of tobacco and/or e-cigarette use, those with serious mental distress appear to have less accurate harm perceptions of nicotine and nicotine-containing products than those with no/low distress, despite reporting similar sources of information.</p>
Awareness & Perceptions	Effect of a hypothetical modified risk tobacco product claim on heated tobacco product use intention and perceptions in young adults	<p>Chen-Sankey, J. C.; Kechter, A.; Barrington-Trimis, J.; McConnell, R.; Krueger, E. A.; Cruz, T. B.; Unger, J. B.; Chaffee, B. W.; Leventhal, A.</p>	Tobacco Control	2021-05-31	<p>INTRODUCTION: Modified risk tobacco product (MRTP) claims for heated tobacco products (HTPs) that convey reduced exposure compared with conventional cigarettes may promote product initiation and transition among young people. We assessed the effects of a hypothetical MRTP claim for HTPs on young adults' intention and perceptions of using HTPs and whether these effects differed by their current cigarette and e-cigarette use. METHODS: We embedded a randomised between-subjects experiment into a web-based survey administered among a cohort of 2354 Southern California young adults (aged 20-23) in 2020. Participants viewed depictions of HTPs with an MRTP claim (n=1190) or no claim (n=1164). HTP use intention and HTP-related harm and use perceptions relative to cigarettes and e-cigarettes were assessed. RESULTS: Overall, participants who viewed versus did not view the claim did not differ in HTP use intention (28.5% vs 28.7%) but were more likely to perceive HTPs as less harmful than cigarettes (11.4% vs 7.0%, p<0.001). The experimental effect on HTP use intention did not differ among past 30-day cigarette smokers versus non-smokers (interaction adjusted OR (AOR)=0.78, 95% CI 0.36 to 1.76) but differed among past 30-day e-cigarette users versus non-users (interaction AOR=1.67, 95% CI 1.02 to 2.68). DISCUSSION: The hypothetical MRTP claim may lower young adults' HTP harm perceptions compared with cigarettes but may not change HTP use intention overall or differentially for cigarette smokers. The larger effect on HTP use intention among e-cigarette users than non-users raises the question of whether MRTP claims may promote HTP use or HTP and e-cigarette dual use among young e-cigarette users.</p>
Awareness & Perceptions	Risk Perceptions of Low Nicotine Cigarettes and Alternative Nicotine Products across Priority Smoking Populations	<p>Denlinger-Apte, R. L.; Paack, L. R.; Ross, J. C.; Bansal-Travers, M.; Donny, E. C.; Hatsukami, D. K.; Carroll, D. M.</p>	Int J Environ Res Public Health	2021-05-02	<p>BACKGROUND: As the U.S. Food and Drug Administration considers a low nicotine product standard for cigarettes, it is important to examine how people who smoke, especially individuals from priority populations disproportionately affected by smoking, perceive low nicotine content (LNC) cigarettes and their relative risk perceptions of alternative nicotine delivery system (ANDS) products, including e-cigarettes and snus, and medicinal nicotine. METHODS: Data are from Wave 4 (2016-2017) of the adult Population Assessment of Tobacco Use and Health (PATH) Study. We examined respondents' absolute risk perceptions about nicotine, LNC cigarettes, ANDS products and medicinal nicotine; their relative risk perceptions of LNC cigarettes and ANDS products compared to conventional cigarettes; and their relative risk perceptions of medicinal nicotine compared to ANDS products. RESULTS: The majority of respondents across priority smoking populations indicated snus, e-cigarettes, and LNC cigarettes were 'about the same' level of harmfulness or addictiveness as conventional cigarettes. The majority of respondents indicated e-cigarettes to be 'about the same' harmfulness as medicinal nicotine. CONCLUSIONS: Our study indicates that adults who smoke cigarettes generally have misperceptions about the harms of nicotine and the relative risks of ANDS products and such misperceptions exist regardless of their racial/ethnic identity, sexual orientation, and gender identity.</p>

Awareness & Perceptions	Effects of tobacco product type and characteristics on appeal and perceived harm: Results from a discrete choice experiment among Guatemalan adolescents	Monzon, J.; Islam, F.; Mus, S.; Thrasher, J. F.; Barroja, J.	Prev Med	2021-04-27	<p>Guatemala is one of the few countries where both heated tobacco products (HTPs) and electronic cigarettes (e-cigarettes) remain unregulated. We used a discrete choice experiment (DCE) administered to 2038 high school students to assess how tobacco product attributes influence their appeal among Guatemalan adolescents. Participants were randomly assigned to evaluate 4 of 32 contrasting sets, each containing 3 packs (1 of each product type). Experimental manipulations included: product type, brand, nicotine content and flavor. Participants then indicated which product they were most and least interested in trying and would be most and least harmful to their health. Conditional logistic regression models were used to assess the impact of product characteristics on choice. Product type accounted for almost 90% of variation in choices. Respondents were less interested in trying HTPs ($B = -0.93$; $p < 0.001$) and viewed them as more harmful ($B = 2.77$; $p < 0.001$) compared to e-cigarettes. They were more interested in trying e-cigarettes ($B = 1.22$; $p < 0.001$), which were also perceived as less harmful ($B = -1.47$; $p < 0.001$) compared to e-cigarettes. Products without nicotine were of more interest for trying ($B = 0.14$; $p < 0.001$) and perceived as more harmful ($B = 0.20$; $p < 0.001$) than those with. Students were more interested in trying a flavor compared to regular tobacco and among the flavors, berry was the highest rated one ($B = 0.28$; $p < 0.001$). Finally, in this country with weak tobacco control, e-cigarettes appear to be more appealing and perceived as less harmful than HTPs and cigarettes. Packaging and flavoring regulations are urgently needed on these products as they are a marketing strategy targeting adolescents.</p>
Awareness & Perceptions	I perceive it to be less harmful, I have no idea if it is or not: a qualitative exploration of the harm perceptions of IQOS among adult users	East, K. A.; Tompkins, C. N. E.; McNeill, A.; Hitchman, S. C.	Harm Reduct J	2021-04-13	<p>BACKGROUND: Harm perceptions of tobacco and nicotine products can influence their use and could be targeted by policies to change behaviour. IQOS was introduced to the UK in 2016, and there is little independent qualitative research on IQOS harm perceptions. This study explored the perceived health harms of IQOS to users and those exposed to the emissions, what shapes these perceptions, and what participants wanted to know about the harms of IQOS. METHODS: Qualitative interviews in London, UK, with 30 adult current and former IQOS users who currently smoked or quit smoking in the last 2 years. RESULTS: IQOS was perceived as less harmful than smoking but not risk-free, although there was great uncertainty. Influences on harm perceptions were consolidated into six themes: (1) dominance of manufacturer claims influenced perceptions that IQOS is less harmful than smoking to users and those around them, although mistrust of the tobacco industry heightened scepticism about harms; (2) limited independent and long-term research led to uncertainty about harms, although some participants trusted IQOS would not be marketed if it were very harmful. Participants wanted more independent and long-term studies into harm; (3) appearance of HEETS (tobacco sticks) packaging conveyed reduced harm because packets were 'pretty', without graphic/specific warnings, although written warnings conveyed some harm. Participants wanted more information on HEETS packets about harms; (4) process of heating and HEETS contents-heating, compared with burning, tobacco was perceived to produce fewer harmful chemicals, while tobacco, nicotine, and chemicals in HEETS were perceived to cause some harm. Participants wanted clarification about the harms of heating tobacco and HEETS ingredients; (5) improvements in physical health and personal appearance reduced perceptions of harm; (6) differences in sensory experiences (taste, sight, smell) when using IQOS over smoking reduced perceptions of harm, while 'black' deposits inside IQOS led to perceptions of some harm. Reduced volume and smell of IQOS emissions also reduced perceptions of harm to non-users exposed to the emissions. CONCLUSIONS: IQOS was perceived as less harmful than smoking but not risk-free, although there was great uncertainty. Participants wanted clarification about IQOS harms from independent sources in accessible forms, specifically related to HEETS ingredients, heating tobacco, and emissions to others.</p>
Awareness & Perceptions	Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS	Yang, B.; Massey, Z. B.; Popova, L.	Tobacco Control	2021-03-09	<p>INTRODUCTION: Tobacco industry studies on consumers' perceptions of modified risk claims (MRCs) often had important omissions (eg, no control group, not investigating whether consumers understand what 'switching completely' means). This study examined the effects of IQOS MRCs on risk perceptions and behavioural intentions. METHOD: Based on tobacco companies' MRCs, we manipulated three MRC language features: explanation about 'switching completely' (absent vs present), number of diseases (single vs multiple) and language certainty (hypothetical vs certain). In an online experiment, we randomised 1523 US adult current smokers and 1391 young adult non-smokers to 1 of 9 conditions following a 2x2x2+1 control design. People reported their comprehension of 'switching completely', IQOS risk perceptions and behavioural intentions after message exposure. RESULTS: More smokers exposed to MRCs that included an explanation about 'switching completely' (22.2%) (vs explanation absent (11.2%) and control (10.7%)) mentioned that 'switching completely' meant smoking 0 cigarettes. Compared with the control, several MRCs (eg, certain language) produced lower perceived risk of IQOS, including for diseases not mentioned in the MRCs. MRCs using certain and hypothetical language did not differ on any outcomes. MRCs highlighting reduced risk for a single disease and multiple diseases did not differ on any outcomes. MRCs did not influence behavioural intentions. CONCLUSION: The Food and Drug Administration should ensure that consumers understand what 'switching completely' means in an MRC and recognize that some language features may mislead consumers into believing that a product reduces the risk of diseases not mentioned in an MRC.</p>

Awareness & Perceptions	Perceived relative harm of heated tobacco products and electronic cigarettes and its association with use in smoke-free places: A cross-sectional analysis of Korean adults	Kim, C. Y.; Lee, K.; Lee, C. M.; Kim, S.; Cho, H. J.	Tobacco Induced Diseases	2022-02-22	<p>Introduction Electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs) are often considered to be less harmful and safer than combustible cigarettes (CCs). As a result, numerous tobacco product users opt to use e-cigarettes or HTPs as a safer alternative, though the safety of these products is not fully warranted. The present study aimed to assess the various attitudes towards e-cigarettes and/or HTPs among Korean tobacco product users and their associations with the practical use of e-cigarettes and/or HTPs in private or smoke-free public places. Methods A cross-sectional study using self-administered questionnaires was conducted from March 2019 to July 2019 on 2971 adult tobacco product users. Attitude towards e-cigarettes and/or HTPs, as well as the relative harm perceptions, in association with their practical use in private or smoke-free areas, were also analyzed. Results Among those surveyed, 46.8% were exclusive users (CC-only smokers 23.5%, e-cigarette-only users 10.7%, HTP-only users 12.7%), and 47.6% were poly-users. Compared with non-e-cigarette or non-HTP users, current e-cigarette or HTP users perceived e-cigarettes or HTPs as less harmful than CCs and they were more acceptable to e-cigarettes or HTPs being used indoors. Their positive attitudes were associated with their more frequent use at home or in their car. Less number of participants supported that the government should regulate e-cigarettes or HTPs in the same way as CCs, their attitude being associated with more frequent use in smoke-free public places. Conclusions E-cigarettes or HTPs users have more positive attitudes toward their tobacco products than non-e-cigarette or non-HTP users. Those with more positive attitudes toward e-cigarettes or HTPs are closely related to their use in smoke-free places.</p>
Awareness & Perceptions Health Outcomes	Perception of Harmfulness of Various Tobacco Products and E-Cigarettes in Poland: A Nationwide Cross-Sectional Survey	Jankowski, Mateusz; Wrześniewska-Wal, Iwona; Ostrowska, Aurelia; Lusawa, Aleksandra; Wierzbna, Waldemar; Pinkas, Jarosław	International Journal of Environmental Research and Public Health	2021-08-20	<p>Perceptions of the harmfulness of tobacco products may be a determinant of smoking behaviors. This study aimed to: (1) assess the perception of harmfulness of various tobacco products and e-cigarettes in Poland as well as (2) to assess the awareness of the health effects of using tobacco and e-cigarettes. A cross-sectional survey was conducted in 2019 with a nationally representative sample of 1011 individuals aged 15 and over. In the studied group, 22.3% were smokers. Smokeless tobacco was most likely to be perceived as less harmful than cigarettes (25%), followed by water pipe (24.5%), heated tobacco products (22%), e-cigarettes (21.6%), slim cigarettes (17.1%), flavored cigarettes (except menthol ones) (16.1%), menthol cigarettes (15.6%) and cigarillos (12.6%). In this study, 10% of respondents denied that smoking causes serious diseases. Most of the respondents (88.9%) were aware that smoking causes lung cancer (88.9%), but only 70.4% were aware that smoking causes stroke. Smokers compared to non-smokers were less likely to declare that smoking causes a stroke (OR: 0.43, 95%CI: 0.31-0.59; p < 0.001) or myocardial infarction (OR: 0.41, 95%CI: 0.29-0.60; p < 0.001). There were no significant differences (p > 0.05) in the perception of harmfulness of various tobacco products and e-cigarettes by gender, age, or occupational status.</p>
Awareness & Perceptions	International expert consensus on electronic nicotine delivery systems and heated tobacco products: a Delphi survey	Berlin, Ivan; Jacot-Sadowski, Isabelle; Humair, Jean-Paul; Cornuz, Jacques	BMJ Open	2021-09-07	<p>Objectives: To provide a consensus from a panel of international experts about electronic nicotine delivery systems (ENDS) and heated tobacco products (HTP). Design: Cross-sectional survey. Methods: A Delphi survey was conducted among international experts in tobacco control and smoking cessation. The first part addressed statements or recommendations about ENDS, the second about HTP, both divided into four categories: regulation, sale, use and general issues. Setting: Experts from 15 countries. Participants: Individuals with clinical, public health or research expertise in tobacco control and/or smoking cessation. Results: 268 experts were contacted, 92 (34%) completed the first, 55/92 (60%) the second round. Consensus for ENDS: components of e-liquids, an upper limit of nicotine concentration should be defined; a warning on the lack of evidence in long-term safety and addiction potential should be stated; ENDS should not be regulated as consumer products but either as a new category of nicotine delivery or tobacco products; ENDS should not be sold in general stores but in specialised shops, shops selling tobacco or in pharmacies with restriction on sale to minors; administration of illegal drugs is likely with ENDS. Consensus for HTP: HTP have the same addictive potential as cigarettes; they should be regulated as a tobacco product with similar warning messages as cigarettes; their advertisement should not be allowed. ENDS and HTP use should not be allowed in indoor public places; a specific tax should be implemented for ENDS, taxes on HTP should not be lower than those for cigarettes; use of cigarettes is more likely with both ENDS and HTP (dual use) than quitting smoking. Conclusions: Experts in tobacco control and/or smoking cessation recommend differential regulation for ENDS and HTP. The results of this survey may be useful for health authorities, decision makers and researchers of the tobacco use and cessation field.</p>

Awareness & Perceptions	Perceptions of the IQOS Heated Tobacco Product on Twitter in the United States	Zou, C.; Wang, X.; Xie, Z.; Li, D.	Frontiers in Communication	2021-08-20	After the approval of the sales of IQOS in the United States market, discussions about IQOS have become active on social media. Twitter is a popular social media platform to understand public opinions toward IQOS. This study aims to explore public perceptions toward IQOS on Twitter in the United States. IQOS-related tweets from the United States between November 19, 2019, and August 24, 2020, were collected using a Twitter streaming application programming interface (API). Sentiment analysis was performed to determine whether the public perceptions toward IQOS were positive, neutral, or negative. In addition, topics discussed in these tweets were manually coded. From November 2019 to August 2020, the number of tweets discussing IQOS was relatively constant except for a peak starting from July 7, 2020, which lasted for 4 days. Among IQOS tweets with positive sentiments, the most popular topic is "IQOS is safer than cigarettes," followed by "IQOS helps quit smoking." Among tweets with negative sentiments, the most popular topic is "illegal marketing/selling to youth," followed by "health risks/fire hazards." "FDA approval/regulation" is the most popular topic for tweets with neutral sentiments. After the announcement of the United States Food and Drug Administration (FDA) enforcement policy on unauthorized flavored e-cigarette products on January 2, 2020, the proportion of tweets with positive attitudes toward IQOS significantly increased, while the proportion of negative tweets significantly decreased. Our study showed that the public perception of IQOS in the United States became more positive after the FDA enforcement policy on flavored e-cigarettes. While many Twitter users thought IQOS is safer than cigarettes and helps quit smoking, some Twitter users complained about the illegal marketing and health risks of IQOS. These findings provide useful information on future tobacco regulations.
Awareness & Perceptions Prevalence & Use Patterns	Awareness, use and perceptions of cigarillos, heated tobacco products and nicotine pouches: a survey among Dutch adolescents and adults	Havermans, A.; Pennings, J. L. A.; Hegger, I.; Elling, J. M.; de Vries, H.; Pauwels, C. G. G. M.; Talhout, R.	Drug Alcohol Depend	2021-10-28	ABSTRACT Objectives Many tobacco and related products (TRPs) are less strictly regulated and marketed as less harmful than cigarettes. Little is known about their awareness, use, user profile, use behavior, reasons for use and risk perception, especially for the newest products. In an exploratory survey study among Dutch adolescents and adults, we have investigated three examples of non-cigarette TRPs available on the worldwide market. Methods In a two-step web-based design, data on cigarillos, heated tobacco products (HTPs) and nicotine pouches were collected. In the first step (N=5805), a representative sample (≥13 years) was studied to quantify their awareness, ever and current use in the Dutch population. In the second step (N=526), in-depth data regarding use behavior, reasons for use and risk perception were collected among users and non-users. Results Awareness (<50%) and use (<15% ever use and <2% current use) is relatively low for all three products, but overall higher among men, (e-)cigarette users and respondents with higher education and social economic status. Most participants became aware of the products through people they knew. Reasons for use were mainly curiosity, pleasant taste, flavour variety, and lower harmfulness. All products were perceived as (slightly) less harmful and addictive than cigarettes. Conclusions This study is one of the first to investigate awareness and use of cigarillos, HTPs and nicotine pouches. To prevent increased use, we recommend regulators to extend flavour and smoking bans to these products. In addition, public information may discourage use by increasing awareness of health risks.
Awareness & Perceptions Prevalence & Use Patterns	Alternative Tobacco Product Use and Smoking Quit Attempts Among Teenagers in the United States: A Cross-Sectional Study	Brown, Colvette; Nkemijika, Stanley; Yankey, Barbara; Okosun, Ike	Cureus	2021-07-29	Background Public health interventions have heightened awareness of risk factors and ill effects of tobacco use. Though sales of conventional tobacco products have been steadily declining, there is the advent of a new generation of alternative tobacco products marketed with claims of reduced harms and smoking cessation aids. These products are increasing in prevalence and popularity among adolescents. Aim The aim of this study is to assess the prevalence of tobacco quit attempts in adolescents in the United States and examine its relationship to the use and self-reported awareness of two alternative tobacco products: e-cigarettes and heated tobacco products (HTPs). Methods This is a cross-sectional analysis of data (2,271) from the 2019 National Youth Tobacco Survey (NYTS) of middle and high school students in the United States. Logistic regression analysis was employed to determine the odds of tobacco quit attempts adjusting for age, race, gender, school type, and household tobacco exposure. Results The overall prevalence of tobacco quit attempts among e-cigarette users and HTP users was 52.50% and 5.20%, respectively. Results of multivariate regression analyses identified age (OR=0.74, 95% CI:0.57-0.96), race (OR=1.41, 95% CI:1.14-1.75), and household tobacco smoke exposure (OR=1.19, 95% CI:1.01-1.39) as the main factors that are significantly associated with tobacco quit attempts adjusting for all other covariates. Conclusion This study did not show a statistically significant association between the awareness and use of e-cigarettes, and heated tobacco products and tobacco smoking quit attempts. Race, age, and exposure to household tobacco smoking were positively associated with quit attempts. Further studies are needed to clarify whether the use and awareness of e-cigarettes and HTPs are associated with tobacco smoking quit attempts within the US adolescent population.

Awareness & Perceptions Prevalence & Use Patterns	Adolescent Use of and Susceptibility to Heated Tobacco Products	Li, S.; Braden, K.; Zhuang, Y. L.; Zhu, S. H.	Pediatrics	2021-06-26	<p>BACKGROUND AND OBJECTIVES: A leading brand of heated tobacco products (HTPs), IQOS, was authorized to be sold in the United States in 2019. Researchers have examined the awareness and use of HTPs among US adults. In this study, we examined high school students' awareness, use, and susceptibility pertaining to HTPs. METHODS: A large, cross-sectional population survey of randomly sampled 10th- and 12th-graders in California (N = 150 516) was conducted online during school hours from September 2019 to March 2020. RESULTS: Overall, 8.9% (95% confidence interval [CI], 8.7%-9.1%) of California high school students had heard of HTPs. Approximately 0.67% (95% CI, 0.61%-0.73%) had ever tried HTPs, and 0.20% (95% CI, 0.17%-0.23%) were current users (ie, ~30% of ever users continued to use HTPs at the time of survey). Among those who never tried HTPs, 18.3% (95% CI, 17.9%-18.8%) were susceptible to future use. The susceptibility to HTP use was greater among users of cigarettes or e-cigarettes than among nonusers. CONCLUSIONS: The awareness of HTPs among adolescents was remarkable given the low availability of products at the time of survey. Only a small percentage of adolescents experimented with HTPs. However, almost a third of those who had experimented with HTPs continued to use them. This high ratio and the fact that almost 1 out of 5 never users were susceptible to future HTP use should put the public health community on high alert as more HTP products are coming into the market, with promotion of these products likely to increase.</p>
Awareness & Perceptions Prevalence & Use Patterns	The Frequency of Use and Harm Perception of Heated Tobacco Products (HTPs): The 2019 Cross-Sectional Survey among Medical Students from Poland	Majek, P.; Jankowski, M.; Nowak, B.; Macherski, M.; Nowak, M.; Gil, A.; Nakielna, P.; Lewicka, B.; Lawson, J. A.; Zejda, J. E.; Brozek, G. M.	Int J Environ Res Public Health	2021-03-24	<p>Heated tobacco products (HTPs) are devices for generating a nicotine aerosol by heating the tobacco sticks. This study aimed to assess (1) the prevalence of HTP and tobacco cigarette usage among medical students, (2) to characterize smoking habits and (3) to assess students' awareness and opinions about HTPs. A cross-sectional survey on the frequency and attitudes toward cigarettes, e-cigarettes and HTP use was performed between 2019-2020 at the Medical University of Silesia in Katowice (Poland). The data were obtained from 1344 students aged 21.8 ± 1.9 years (response rate: 66.9%). Current traditional tobacco use was 13.2%, e-cigarettes use 3.5%, and HTP use 2.8% of students. Duration of use was shorter among HTPs users comparing to cigarette smokers (p < 0.001) although the number of tobacco sticks used daily was similar (p = 0.1). Almost 30% of respondents have ever tried HTPs. HTPs were considered safe by 5.3% of respondents (43.2% of HTP users vs. 3.9% of non-HTP users, p < 0.001). HTP users were more likely to report that heating tobacco is not addictive (odds ratio (OR) = 8.9, 95% confidence interval (CI): 1.8-45.8) and disagreed with a public ban on HTP use (OR = 4.9, 95%CI: 2.5-9.8). Among students, HTP use was less popular than cigarette smoking, but awareness of their presence is widespread.</p>
Awareness & Perceptions Prevalence & Use Patterns Clinical Health Outcomes	Changes in smoking habits and behaviors following the introduction and spread of heated tobacco products in Japan and its effect on FEV(1) decline: a longitudinal cohort study	Harada, S.; Sata, M.; Matsumoto, M.; Iida, M.; Takeuchi, A.; Kato, S.; Hirata, A.; Kuwabara, K.; Shibuki, T.; Ishibashi, Y.; Sugiyama, D.; Okamura, T.; Takebayashi, T.	J Epidemiol	2021-10-16	<p>BACKGROUND: Heated tobacco product (HTP) use in Japan has rapidly increased. Despite this rapid spread, little is known about the health effects of HTP use. We conducted a longitudinal cohort study to investigate the change in smoking habits following the spread of HTP use and its effect on forced expiratory volume in one second (FEV(1)) decline. METHODS: Participants consisted of a resident population (n=2,612, aged 67.7) with FEV(1) measurement in 2012-2014 and 2018-2019, and a worksite population (n=722, aged 49.3) without FEV(1) data. Participants were categorized as never, past and combustible cigarette-only smokers, and HTP-only and dual users. The association between smoking group and the change in smoking consumption for 5.6 years was examined. Differences in annual FEV(1) change between smoking groups were examined in the resident population. RESULTS: Prevalence of HTP-only and dual users in 2018-2019 was 0.8% and 0.6% in the resident population, and 5.0% and 1.9% in the worksite population, respectively. The overall number of tobacco products smoked/used increased in dual users compared to baseline, but not in others. Annual FEV(1) decline in dual users tended to be greater than that in cigarette-only smokers (16 mL/yr [95% CI: -34, 2] after full adjustment). Participants switching to HTP-only use 1.7 years before had a similar FEV(1) decline as cigarette-only smokers. CONCLUSIONS: HTP use, including dual use, is prevalent even in a rural region of Japan. Dual users appear to smoke/use tobacco products more and have a greater FEV(1) decline. Tobacco policy should consider dual use as high-risk.</p>
Clinical	Influence of Nicotine from Diverse Delivery Tools on the Autonomic Nervous and Hormonal Systems	Menshov, V. A.; Trofimov, A. V.; Zagurskaya, A. V.; Berdnikova, N. G.; Yablonskaya, O. I.; Platonova, A. G.	Biomedicines	2022-01-06	<p>BACKGROUND: Through measurements of the heart rate variability (HRV) accompanied by the pertinent biomarker assays, the effects of nicotine and byproducts derived from alternative nicotine delivery systems (ANDS) on the autonomic nervous system (ANS) and hormonal system have been investigated. METHODS: HRV was studied in a group of volunteers (17 people), involving non-smokers, i.e., who never smoked before (11), ex-smokers (4) and active smokers (2). ANDS and smoking simulators, including regular, nicotine-free and electronic cigarettes; tobacco heating systems; chewing gums and nicotine packs of oral fixation (nic-packs), were used. Blood pressure, levels of stress hormones in saliva and catecholamines in the blood were also monitored. RESULTS: HRV analysis showed relatively small changes in HRV and in the other studied parameters with the systemic use of nic-packs with low and moderate nicotine contents (up to 6 mg) compared to other ANDS. CONCLUSIONS: The HRV method is proven to be a promising technique for evaluation of the risks associated with smoking, dual use of various ANDS and studying the biomedical aspects of smoking cessation. Nic-packs are shown to be leaders in biological safety among the studied ANDS. A sharp surge in the activity of the sympathetic division of the ANS within the first minutes of the use of nicotine packs implies that nicotine begins to act already at very low doses (before entering the blood physically in any significant amount) through fast signal transmission to the brain from the nicotine and taste buds located in the mouth area.</p>

Clinical	Knowledge and self-efficacy among healthcare providers towards novel tobacco products in Japan	Mittal, S.; Uchida, T.; Nishikawa, Y.; Okada, H.; Schnoll, R.A.; Takahashi, Y.; Nakayama, T.; Takahashi, Y.	Preventive Medicine Reports	2021-11-24	<p>Several new tobacco products, including e-cigarettes and heated tobacco products (HTPs), have become highly prevalent in Japan. As safety data continues to evolve, healthcare providers are considered important sources for product use, yet little is known about provider knowledge or self-efficacy to counsel patient about novel tobacco product use. This cross-sectional study used data from a Japanese Association of Smoking Control Science (JASCS) online survey of physicians, pharmacists, nurses, and public health practitioners (N = 277) to assess provider knowledge of novel tobacco products and self-efficacy to counsel patients about product use. Correlates of knowledge and self-efficacy were also assessed. More than half the sample had received previous training in treating tobacco use, but 62% of respondents had no knowledge of HTPs; 80% of respondents indicated that they occasionally or always provide smoking cessation support. Overall knowledge of HTPs was low (41.4% correct) with higher knowledge for HTPs containing nicotine (89% correct) vs. HTPs emitting no carbon monoxide (25%). Self-efficacy to counsel patients about novel tobacco products was low on a scale ranging from 10 to 70 (Mean = 31.2; Standard Deviation = 16.7). Greater knowledge of HTPs was associated with male gender, higher rates of training at JASCS and previous learning about HTPs at JASCS. (p < 0.05). The results suggested that healthcare providers' knowledge and self-efficacy regarding novel tobacco products remains low in Japan, but additional training may improve it.</p>
Clinical	Impact of exclusive e-cigarettes and heated tobacco products use on mucociliary clearance	R. Polosa; R. Emma; F. Cibella; M. Caruso; G. Conte; F. Benfano; S. Ferlito; A. Gulino; M. Malerba; P. Capomnetto	Ther Adv Chronic Dis	2021-08-12	<p>Background: Tobacco smoking impairs mucociliary clearance (MCC) efficiency as shown by prolonged saccharin test transit time (STTT). Avoiding exposure to tobacco smoke from combustible cigarettes may restore MCC function and former smokers have been shown to exhibit similar STTT as never smokers. The impact on STTT of switching from smoking to combustion-free tobacco products such as e-cigarettes (ECs) and heated tobacco products (HTPs) is not known.</p> <p>Methods: We report STTT of exclusive EC and HTP users. Test results were compared with those obtained in current, former, and never smokers.</p> <p>Results: STTT were obtained from 39 current, 40 former, 40 never smokers, and from 20 EC and 20 HTP users. Comparison of STTT values showed significant difference among the five study groups (p < 0.00001) with current smokers having a median [interquartile range (IQR)] STTT of 13.15 min, which was significantly longer compared with that of all other study groups. In particular, compared with former (7.26 min) and never smokers (7.24 min), exclusive EC users and exclusive HTP users had similar STTT at 7.00 and 8.00 min, respectively.</p> <p>Conclusion: Former smokers who have switched to exclusive regular use of combustion-free nicotine delivery systems (i.e., ECs and HTPs) exhibit similar saccharin transit time as never and former smokers. This suggests that combustion-free nicotine delivery technologies are unlikely to have detrimental effects on MCC function.</p>
Clinical	Identification of biomarkers specific to five different nicotine product user groups: Study protocol of a controlled clinical trial	Sibul, F.; Burkhardt, T.; Kachhadia, A.; Pitz, F.; Scherer, G.; Seherer, M.; Pluym, N.	Contemp Clin Trials Commun	2021-06-02	<p>BACKGROUND: Assessing biomarker profiles in various body fluids is of large value to discern between the sole use of nicotine products. In particular, the assessment of the product compliance is required for long-term clinical studies. The objective of this study was the identification of biomarkers and biomarker patterns in body fluids, to distinguish between combustibles, heated tobacco products, electronic cigarettes, oral tobacco and oral/dermal nicotine products used for nicotine replacement therapy (NRT), as well as a control group of non-users. METHODS: A controlled, single-center study was conducted with 60 healthy subjects, divided into 6 groups (5 nicotine product user groups and one non-user group) based on their sole use of the products of choice. The subjects were confined for 76 h, during which, free and uncontrolled use of the products was provided. Sample collections were performed according to the study time schedule provided in Table 2. The primary outcome will be validated through analysis of the collected biospecimens (urine, blood, saliva, exhaled breath and exhaled breath condensate) by means of untargeted omics approaches (i.e. exposomics, breathomics and adductomics). Secondary outcome will include established biomarker quantification methods to allow for the identification of typical biomarker patterns. Statistical analysis tools will be used to specifically discriminate different product use categories. RESULTS/CONCLUSIONS: The clinical trial was successfully completed in May 2020, resulting in sample management and preparations for the quantitative and qualitative analyses. This work will serve as a solid basis to discern between biomarker profiles of different nicotine product user groups. The knowledge collected during this research will be required to develop prototype diagnostic tools that can reliably assess the differences and evaluate possible health risks of various nicotine products.</p>

Clinical	Comparison of IQOS (heated tobacco) and cigarette smoking on cardiac functions by two-dimensional speckle tracking echocardiography	Yaman, B.; Akpınar, O.; Kemal, H. S.; Cerit, L.; Yüksel, Ü.; Söylemez, N.; Durgu, H.	Toxicol Appl Pharmacol	2021-05-14	<p>AIMS: IQOS is a novel tobacco product claimed to be safer than conventional cigarette smoking due to the heat-not-burn system. This study aimed to evaluate the acute effects of IQOS smoking on myocardial systolic and diastolic functions and also compare the acute impacts of IQOS with cigarette smoking. METHODS: In this prospective study, twenty-seven healthy participants who were using IQOS were included. Transthoracic echocardiography was performed three times for each participant; before smoking any tobacco product (group1), after IQOS smoking (group 2), after cigarette smoking (group3). In addition to conventional echocardiographic measurements, left ventricle (LV) and right ventricle (RV) strain analyses were performed by speckle tracking echocardiography. RESULTS: In comparison with non-smoking status, LV global longitudinal strain (GLS) decreased after IQOS and cigarette smoking ($-18.9 \pm 2.4\%$ in baseline vs. $-17.9 \pm 2.4\%$ in IQOS vs. $-17.9 \pm 2.8\%$ in cigarette smoking; $p = 0.003$; $p = 0.001$; respectively). LV global circumferential strain (GCS) reduced after IQOS and cigarette smoking ($-19.8 \pm 4.4\%$ in baseline vs. $-18.3 \pm 3.9\%$ in IQOS vs. $-17.5 \pm 3.9\%$ in cigarette smoking; $p = 0.005$, $p < 0.001$; respectively). RV GLS was significantly lower in groups smoking IQOS and cigarette ($-23.2 \pm 4.6\%$ in baseline vs. $-21.4 \pm 4.1\%$ in IQOS vs. $-19.4 \pm 4.1\%$ in cigarette smoking; $p < 0.001$, $p = 0.001$; respectively). CONCLUSION: IQOS (heat-not-burn) tobacco smoking impairs myocardial systolic and diastolic functions in the acute phase like conventional cigarette smoking. The use of IQOS is rising among young adults in recent years, so further studies should be designed to evaluate the chronic effects of IQOS on myocardial function.</p>
Clinical	Comparison of Nicotine Dependence and Biomarker Levels among Traditional Cigarette, Heat-Not-Burn Cigarette, and Liquid E-Cigarette Users: Results from the Think Study	Rudasingwa, G.; Kim, Y.; Lee, C.; Lee, J.; Kim, S.; Kim, S.	Int J Environ Res Public Health	2021-04-29	<p>This study aimed to compare Korean smokers' smoking-related biomarker levels by tobacco product type, including heat-not-burn cigarettes (HNBC), liquid e-cigarettes (EC), and traditional cigarettes (TC). Nicotine dependence levels were evaluated in Korean adult study participants including TC-, EC-, HNBC-only users and nonsmokers ($n = 1586$) from March 2019 to July 2019 in Seoul and Cheonan/Asan South Korea using the Fagerstrom Test Score. Additionally, urine samples ($n = 832$) were collected for the measurement of urinary nicotine, cotinine, OH-cotinine, NNAL(4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol), CYMA(N-acetyl-S-(2-cyanoethyl)-L-cysteine), or CEMA (2-cyanoethylmercapturic acid) using LC-MS/MS. The median(interquartile range) nicotine dependence level was not different among the three types of smokers, being 3.0 (2.0-5.0) for TC- ($n = 726$), 3.0 (1.0-4.0) for EC- ($n = 316$), and 3.0 (2.0-4.0) for HNBC- ($n = 377$) only users. HNBC-only users presented similar biomarker levels compared to TC-only users, except for NNAL (HNBC: 14.5 (4.0-58.8) pg/mL, TC: 32.0 (4.0-69.6) pg/mL; $p = 0.0106$) and CEMA (HNBC: 60.4 (10.0-232.0) ng/mL, TC: 166.1 (25.3-532.1) ng/mL; $p = 0.0007$). TC and HNBC users showed increased urinary cotinine levels as early as the time after the first smoke of the day. EC users' biomarker levels were possibly lower than TC or HNBC users' but higher than those of non-smokers.</p>
Clinical	International randomised controlled trial evaluating metabolic syndrome in type 2 diabetic cigarette smokers following switching to combustion-free nicotine delivery systems: the DIASMOKE protocol	Kryszinski, A.; Russo, C.; John, S.; Belsky, J. D.; Campagna, D.; Caponnetto, P.; Vudu, L.; Lin, C. W.; Purrello, F.; Di Mauro, M.; Iqbal, F.; Fluck, D.; Franek, E.; Polosa, R.; Sharma, P.; Diasmoke collaborators	BMI Open	2021-04-27	<p>INTRODUCTION: Reducing exposure to cigarette smoke is an imperative for public health and for patients with diabetes. Increasingly, combustion-free nicotine delivery systems (C-F NDS) such as e-cigarettes and heated tobacco products are substituting conventional cigarettes and accelerating the downward trends in smoking prevalence. However, there is limited information about the long-term health impact in patients with diabetes who use C-F NDS. This randomised trial of type 2 diabetic cigarette smokers will test the hypothesis that following a switch from conventional cigarettes to C-F NDS a measurable improvement in metabolic syndrome (MetS) factors will be shown over the course of 2 years. METHODS AND ANALYSIS: The study is multicentre and thus will take place in five locations in four countries in an ambulatory setting. A total of 576 patients with diabetes will be randomised (1:2 ratio) to either a control arm (Study Arm A), in which they will be offered referral to smoking cessation programmes or to an intervention arm (Study Arm B) assigned to C-F NDS use. Participants will be at least 23 years old and of any gender. Patient recruitment will start in February 2021 and is expected to be completed by December 2021. Primary outcome measures include fasting plasma glucose, blood pressure, triglycerides, high-density lipoprotein and waist circumference, while secondary feature absolute change in the sum of the individual factors of MetS and change in each individual factor of MetS measured at each study time point. ETHICS AND DISSEMINATION: The approval of research ethics committees (REC) regarding the trial protocol, informed consent forms and other relevant documents is required to commence the study. Substantial amendments to the study protocol cannot be implemented until the REC grants a favourable opinion. The results of the study are intended to be published as articles in high quality peer-reviewed journals and disseminated through conference papers. TRIAL REGISTRATION NUMBER: NCT04231838. Pre-results stage.</p>

Clinical	Impact of chronic use of heat-not-burn cigarettes on oxidative stress, endothelial dysfunction and platelet activation: the SUR-VAPES Chronic Study	Loffredo, L.; Carnevale, R.; Battaglia, S.; Marti, R.; Pizzolo, S.; Bartimoccia, S.; Nocella, C.; Cammisotto, V.; Sciarretta, S.; Chimenti, I.; De Falco, E.; Cavarretta, E.; Peruzzi, M.; Marullo, A.; Miraldi, F.; Violi, F.; Morelli, A.; Biondi-Zoccai, G.; Frati, G.	Thorax	2021-04-19	Tobacco habit still represents the leading preventable cause of morbidity and mortality worldwide. Heat-not-burn cigarettes (HNBCs) are considered as an alternative to traditional combustion cigarettes (TCCs) due to the lack of combustion and the absence of combustion-related specific toxicants. The aim of this observational study was to assess the effect of HNBC on endothelial function, oxidative stress and platelet activation in chronic adult TCC smokers and HNBC users. The results showed that both HNBC and TCC display an adverse phenotype in terms of endothelial function, oxidative stress and platelet activation. Future randomised studies are strongly warranted to confirm these data.
Clinical Health Outcomes	Differential effects of heat-not-burn and conventional cigarettes on coronary flow, myocardial and vascular function	Ikonomidou, I.; Vlastos, D.; Kostelli, G.; Kourca, K.; Katogiannis, K.; Tsoumani, M.; Parissis, J.; Andreadou, I.; Alexopoulos, D.	Scientific Reports	2021-06-03	We compared the effects of Heat-not-Burn cigarette (HNBC) to those of tobacco cigarette (Tcig), on myocardial, coronary and arterial function as well as on oxidative stress and platelet activation in 75 smokers. In the acute study, 50 smokers were randomised into smoking a single Tcig or a HNBC and after 60 min were crossed-over to the alternate smoking. For chronic phase, 50 smokers were switched to HNBC and were compared with an external group of 25 Tcig smokers before and after 1 month. Exhaled carbon monoxide (CO), pulse wave velocity (PWV), malondialdehyde (MDA) and thromboxane B2 (TxB2) were assessed in the acute and chronic study. Global longitudinal strain (GLS), myocardial work index (GWI), wasted myocardial work (GWW), coronary flow reserve (CFR), total arterial compliance (TAC) and flow-mediated dilation (FMD) were assessed in the chronic study. Acute HNBC smoking caused a smaller increase of PWV than Tcig (change 1.1 vs 0.54 m/s, $p < 0.05$) without change in CO and biomarkers in contrast to Tcig. Compared to Tcig, switching to HNBC for 1-month improved CO, FMD, CFR, TAC, GLS, GWW, MDA, TxB2 (differences: 10.42 ppm, 4.3%, 0.98, 1.8 mL/mmHg, 2.35%, 19.72 mmHg%, 0.38 mmol/L and 45 pg/mL respectively, $p < 0.05$). HNBCs exert a less detrimental effect on vascular and cardiac function than tobacco cigarettes. Trial registration Registered on https://clinicaltrials.gov/ (NCT03452124, 02/03/2018).
Clinical Health Outcomes	Combustible cigarettes, heated tobacco products, combined product use, and periodontal disease: A cross-sectional JASTIS study	Yoshioka, Takashi; Tabuchi, Takahiro	PLOS one	2021-03-30	Abstract; Background: Combustible cigarettes have detrimental effects on periodontal disease. However, little evidence is available regarding new heated tobacco product (HTP) use and combined product use (both combustible cigarettes and HTPs). This study aimed to examine the association of combustible cigarettes, HTPs, and combined product use with periodontal disease simultaneously.; ; Materials and methods: This cross-sectional study was conducted using data from the 2019 arm of the longitudinal Japan Society and New Tobacco Internet Survey. Combustible cigarette users, HTP users, combined product users, never-users, and former users' data were separately obtained. In the present study, the primary outcome was self-reported periodontal disease. We estimated adjusted prevalence ratios (PRs) and confidence intervals (CIs) using multivariable modified Poisson regression analysis after adjusting for 12 confounders.; ; Results: Of the 10,439 JASTIS respondents, the numbers of users of combustible cigarettes only, HTPs only, and both products were 1,304, 437, and 1,049, respectively. Compared with never-users, HTP use was significantly associated with the prevalence of self-reported periodontal diseases (PR 1.43, 95% CI 1.03-1.62). Moreover, former users, combustible cigarette users, and combined product users also showed significant associations (PR 1.56, 95% CI 1.35-1.80; PR 1.29, 95% CI 1.03-1.62; and PR 1.55, 95% CI 1.20-1.99, respectively).; ; Conclusions: Users of HTPs, combustible cigarettes, and combined products as well as former users were all significantly associated with a higher prevalence of periodontal diseases compared to never-users.

Health Outcomes	Smoking Cessation and Mental Health According to Use of E-cigarettes and Heated Tobacco Products by Korean Adults	Han, M. A.	International Journal of Mental Health and Addiction	2021-11-10	<p>The health burden due to smoking, including mental health, is well documented. Previous studies reported the beneficial effect of smoking cessation on mental health. This study investigates depression and the effect of smoking cessation according to use of e-cigarettes or heated tobacco products among Korean adults. Data were obtained from the Korea Community Health Study (2019). Use of cigarettes, e-cigarettes, and heated tobacco products was assessed, and former cigarette smokers were categorized according to use of e-cigarettes and heated tobacco products. Depression, as defined by depressed mood or depressive symptoms, was assessed with the Patients Health Questionnaire-9 (PHQ-9). Study participants consisted of lifetime smokers of cigarettes (36.9%), e-cigarettes (6.0%), and heated tobacco products (7.6%). Among former smokers, complete smoking cessation was associated with decreased prevalence of depression. However, former cigarette smokers who had ever used e-cigarettes were more likely to experience a depressed mood (aOR = 1.36, 95% CI = 1.10-1.68) and depressive symptoms (aOR = 1.90, 95% CI = 1.47-2.46), compared to former smokers who had not used them. Former cigarette smokers who had ever used heated tobacco products were more likely to experience depressed mood, compared to former smokers who had not used them. Similarly, current use of e-cigarettes and current use of heated tobacco products by former smokers were both associated with higher prevalence of depressed mood and depressive symptoms. Smoking cessation altogether was associated with decreased depression in Korean adults. However, the use of e-cigarettes or heated tobacco products at any time may reduce the beneficial effect of smoking cessation.</p>
Health Outcomes	Subacute Lung Injury Associated with Heated Tobacco Products	Sayın Gülsensoy E.; Yitkisel A.; Ogan N.; Unudum H.; Akpinar E. Subacute	Duzce Medical Journal	2021-08-30	<p>Heated tobacco products release nicotine without burning tobacco with an electronically controlled heating system. 56-year-old male patient admitted with sudden onset of chest pain and shortness of breath. He had been using a heated tobacco product (I quit ordinary smoking. IQOS) for 2.5 years. Thoracic computed tomography scan revealed pleural-based atelectasis and fibroatelectatic changes in the lower lobe of the right lung, pleural fluid in the right upper lobe, fibroatelectatic changes and pleural thickening in the left lung. Biopsy taken with video-assisted thoracic surgery (VATS) showed lymphoid aggregation in nodular form and widespread anthracosis around the lung, fibrillar material that double-refracting the light in the alveoli, hyaline membrane-like material in the alveoli, type 2 pneumocyte hyperplasia, an interstitial organization, and a subacute lung injury picture with exogenous lipid material. These findings were evaluated in accordance with toxic substance-induced chemical pneumonia. It was thought that it might be related to 2.5 years of using heated tobacco product.</p>
Health Outcomes	Characterization of Respiratory Symptoms Among Youth Using Heated Tobacco Products in Hong Kong	Wang, L.; Chen, J.; Leung, L. T.; Mai, Z. M.; Ho, S. Y.; Lam, T. H.; Wang, M. P.	JAMA Netw Open	2021-07-01	<p>IMPORTANCE: Heated tobacco products (HTPs) are promoted as less harmful than combustible cigarettes but epidemiological evidence is scarce, especially in youth. OBJECTIVE: To investigate the associations of persistent respiratory symptoms with HTP use, cigarette use, and dual use among Hong Kong youth. DESIGN, SETTING, AND PARTICIPANTS: This was a territorywide cross-sectional school-based survey conducted from October 2018 to July 2019 using an anonymous questionnaire. Schools were randomly invited from a proportionate stratified sample in all 18 districts of Hong Kong. Poisson regression models using generalized estimating equations yielded adjusted prevalence ratios (APRs) of respiratory symptoms in (1) former and current HTP (vs never) users in the whole sample and stratified by cigarette use status and (2) exclusive HTP and dual users vs exclusive cigarette users. Statistical analysis was performed from October 2020 to March 2021. EXPOSURES: Former and current use of cigarettes, HTPs, e-cigarettes, and other tobacco products. MAIN OUTCOMES AND MEASURES: Respiratory symptoms for 3 consecutive months in the past 12 months. RESULTS: The study included 33 627 students with a mean (SD) age of 14.8 (1.9) years; 51.3% (18 171) were boys. Respiratory symptoms were reported by 16.3% (n = 5549) of all students, 29.3% (n = 226) of current users of e-cigarettes, 31.2% (n = 314) of current users of cigarettes, and 33.5% (n = 179) of current users of HTPs. Respiratory symptoms were associated with former (APR, 1.30; 95% CI, 1.06-1.59) and current (APR, 1.59; 95% CI, 1.23-2.06) vs never HTP use and current vs never cigarette use (APR, 1.50; 95% CI, 1.30-1.74) after adjusting for various tobacco use. Associations between respiratory symptoms and current vs never HTP use were observed in never (APR, 1.88; 95% CI, 1.36-2.59) and former (APR, 2.15; 95% CI, 1.12-4.12) cigarette users, but not in current cigarette users (APR, 1.24; 95% CI, 0.97-1.59). Respiratory symptoms were associated with exclusive ever HTP use (APR, 1.46, 95% CI, 1.15-1.86) and ever dual use (APR, 1.29; 95% CI, 1.08-1.54) vs exclusive ever cigarette use. There was no association between exclusive current HTP (vs cigarette) use and respiratory symptoms (1.40; 95% CI, 0.93-2.11). CONCLUSIONS AND RELEVANCE: This cross-sectional study found that former and current HTP use were associated with persistent respiratory symptoms among youth, especially among never and former cigarette users. Respiratory symptoms were more prevalent in ever exclusive HTP users and ever dual users than ever exclusive cigarette users. These findings suggest that using HTPs instead of cigarettes may not reduce health risks.</p>

Health Outcomes Clinical	Combined Associations of Changes in Noncombustible Nicotine or Tobacco Product and Combustible Cigarette Use Habits With Subsequent Short-Term Cardiovascular Disease Risk Among South Korean Men: A Nationwide Cohort Study	Choi, S.; Lee, K.; Park, S. M.	Circ J	2021-10-04	<p>BACKGROUND: The associations of changes in noncombustible nicotine or tobacco product (NNTP) and combustible cigarette (CC) use habits with subsequent cardiovascular disease (CVD) risk are still unclear.</p> <p>METHODS: The study population consisted of 5 159 538 adult men who underwent health screening examinations during both the first (2014-2015) and second (2018) health screening periods from the Korean National Health Insurance Service database. All participants were divided into continual CC-only smokers, CC and NNTP users, recent (<5 years) CC quitters without NNTP use, recent CC quitters with NNTP use, long-term (>5 years) CC quitters without NNTP use, long-term CC quitters with NNTP use, and never smokers. Propensity score matching analysis was conducted to further compare CVD risk among CC quitters according to NNTP use. Starting from the second health screening date, participants were followed up until the date of CVD event, death, or December 31, 2019, whichever came earliest. Multivariable Cox proportional hazards regression was used to determine the adjusted hazard ratios (aHRs) and 95% CIs for CVD risk according to changes in NNTP and CC smoking habits.</p> <p>RESULTS: Compared with continual CC-only smokers, CC and NNTP users (aHR, 0.83 [95% CI, 0.79-0.88]) and initial CC smokers who quit CCs and switched to NNTP use only (recent CC quitters with NNTP use, aHR, 0.81 [95% CI, 0.78-0.84]) had lower risk for CVD. After propensity score matching, recent CC quitters with NNTP use (aHR, 1.31 [95% CI, 1.01-1.70]) had higher risk for CVD than recent CC quitters without NNTP use. Similarly, compared with long-term CC quitters without NNTP use, long-term CC quitters with NNTP use (aHR, 1.70 [95% CI, 1.07-2.72]) had higher CVD risk.</p> <p>CONCLUSIONS: Switching to NNTP use among initial CC smokers was associated with lower CVD risk than continued CC smoking. On CC cessation, NNTP use was associated with higher CVD risk than CC quitting without NNTPs. Compared with CC smokers who quit without NNTP use, CC quitters who use NNTPs may be at higher future CVD risk.</p>
Health Outcomes Clinical	Health outcomes in COPD smokers using heated tobacco products: a 3-year follow-up	Polosa, Riccardo; Morjaria, Jaymin B.; Morjaria, Umberto; Busà, Barbara; Pennisi, Alfio; Gussone, Gualberto; Rust, Sonja; Maglia, Marilena; Capomnetto, Pasquale	Internal and Emergency Medicine	2021-03-23	<p>Given that many patients with chronic obstructive pulmonary disease (COPD) smoke despite their symptoms, it is important to understand the long-term health impact of cigarette substitution with heated tobacco products (HTPs). We monitored health parameters for 3 years in COPD patients who substantially attenuated or ceased cigarette consumption after switching to HTPs. Changes in daily cigarette smoking, annualized disease exacerbations, lung function indices, patient-reported outcomes (CAT scores) and 6-minute walk distance (6MWD) from baseline were measured in COPD patients using HTPs at 12, 24 and 36 months. These were compared to a group of age- and sex-matched COPD patients who continued smoking. Complete data sets were available for 38 patients (19 in each group). Subjects using HTPs had a substantial decrease in annualized COPD exacerbations within the group mean (\pm SD) from 2.1 (\pm 0.9) at baseline to 1.4 (\pm 0.8) and 1.3 (\pm 0.8) at 12-, 24- and 36-month follow-up ($p < 0.05$ for all visits). In addition, substantial and clinically significant improvements in CAT scores and 6MWD were identified at all three time points in the HTP cohort. No significant changes were observed in COPD patients who continued smoking. This study is the first to describe the long-term health effects of HTP use in COPD patients. Consistent improvements in respiratory symptoms, exercise tolerance, quality of life, and rate of disease exacerbations were observed in patients with COPD who abstained from smoking or substantially reduced their cigarette consumption by switching to HTP use.</p>
Health Outcomes Prevalence & Use Patterns	Heated tobacco product use and hypertensive disorders of pregnancy and low birth weight: analysis of a cross-sectional, web-based survey in Japan	Zaitse, M.; Hosokawa, Y.; Okawa, S.; Hori, A.; Kobashi, G.; Tabuchi, T.	BMJ Open	2021-09-21	<p>OBJECTIVES: Knowledge on the impact of heated tobacco product (HTP) use in pregnant women with associated maternal and neonatal risks for hypertensive disorders of pregnancy (HDP) and low birth weight (LBW) is limited. We aimed to assess the status of HTP use among pregnant women in Japan and explore the association of HTP use with HDP and LBW. DESIGN: Cross-sectional study. SETTING: Data from the Japan 'COVID-19 and Society' Internet Survey study, a web-based nationwide survey. PARTICIPANTS: We investigated 558 postdelivery and 365 currently pregnant women in October 2020. PRIMARY AND SECONDARY OUTCOME MEASURES: Information on HDP and LBW was collected from the postdelivery women's Maternal and Child Health Handbooks (maternal and newborn records). We estimated the age-adjusted ORs and 95% CIs of ever HTP smokers for HDP and LBW and compared them with those of never HTP smokers in a logistic regression analysis. RESULTS: The prevalence of ever and current HTP use were 11.7% and 2.7% in postdelivery women and 12.6% and 1.1% in currently pregnant women, respectively. Among currently pregnant women who were former combustible cigarette smokers, 4.4% (4/91) were current HTP smokers. Among postdelivery women, ever HTP smokers had a higher HDP incidence (13.8% vs 6.5%, $p=0.03$; age-adjusted OR=2.48, 95% CI 1.11 to 5.53) and higher LBW incidence (18.5% vs 8.9%, $p=0.02$; age-adjusted OR=2.36, 95% CI 1.16 to 4.87). CONCLUSIONS: In Japan, the incidence of ever HTP use exceeded 10% among pregnant women, and HTP smoking may be associated with maternal and neonatal risks.</p>

Health Outcomes Prevalence & Use Patterns	Association of heated tobacco product use and secondhand smoke exposure with suicidal ideation, suicide plans and suicide attempts among Korean adolescents: A 2019 national survey	Park, S.; Lee, K. S.	Tob Induc Dis	2021-09-20	INTRODUCTION: The consumption of heated tobacco products (HTPs) is increasing among adolescents worldwide. Although suicide and HTP use are linked, the association between suicide-related behavior, HTP use, and indirect smoking exposure are not yet properly studied. This study examined the association of HTP use and exposure to secondhand smoke (SHS) with suicidal ideation, suicide plans, and suicide attempts among South Korean adolescents. METHODS: Data from 57303 respondents (95.3% response rate) were obtained from the 2019 Korean Youth Risk Behavior Web-based Survey. Chi-squared tests and multivariable logistic regression analyses were used to examine the association of HTP use and SHS exposure with suicidal ideation, suicide plans, and suicide attempts among adolescents. Multivariable logistic regression analyses included: Model 1, which was adjusted for demographic characteristics such as sex, school type, perceived school performance, economic status, and residence type; and Model 2, which was adjusted for demographics, depression, and drug use. RESULTS: The risk of suicidal ideation was 1.37 (95% CI: 1.10-1.70) and 1.44 (95% CI: 1.18-1.75) times higher among HTP users who were exposed to SHS at home and at public places, respectively, compared to non-users. The risk of suicide attempts was 1.88 (95% CI: 1.37-2.57), 1.45 (95% CI: 1.63-2.00), and 2.21 (95% CI: 1.63-3.00) times higher among HTP users exposed to SHS at home, school, and at public places, respectively. CONCLUSIONS: HTP use, and SHS exposure are likely indicators of risk behaviors. Our findings suggest possible directions for initiating, implementing, and evaluating programs and services to monitor HTP use and SHS exposure among Korean adolescents.
Indoor Air Quality	Exposure of heat-not-burn tobacco effect on the quality of air and expiratory plume	D. Gallart-Mateu; Z. Dhauadi; M. de la Guardia	Microchemical Journal	2021-08-11	The increasing interest to avoid the consumption of regular tobacco has led in the development of several types of devices to decrease the effects of this practice on active and bystanders. In this work, the impact of the use of new heat-not-burn (HnB) devices has been evaluated and compared with that of regular cigarettes and electronic cigarettes (e-cigs). Portable monitoring devices were employed for CO, CO ₂ , particulate matter (PM) and volatile organic compounds (VOCs) to evaluate the quality of indoor air and expiratory plume of both, active and passive, users during these practices. It can be noticed that the levels of VOCs in active HnB smokers expiratory air are five times lower in particular cases than those provided by regular tobacco and three times lower than those obtained for e-cigs, while the contribution of particulate matter to air pollution decreases between 200 and 600 times regarding the values obtained for e-cig vaping and regular tobacco smoking. The level of contaminants as CO decreases significantly in both, active and passive HnB smokers, in comparison with active and passive regular tobacco smokers, due to the absence of organic material combustion. Regarding passive HnB smokers, the exposure to HnB smoke do not increases the level of VOCs in ambient air nor in expiratory plume, remaining at the basal levels, being three times lower than values obtained to an exposure to regular tobacco smoke and two times lower than exposure to e-cigs vapours. On the other hand, the use of HnB devices decreases the concentration of PM in bystanders around thirty five times in relation with values obtained for passive regular tobacco smokers. Concerning the nicotine content delivered by HnB tobacco, data shown that HnB tobacco provides values from 0.5 to 1.7 mg of nicotine to the mainstream, being these values similar to those found in conventional tobacco.
Indoor Air Quality Clinical	Protecting Children From Tobacco Smoke Exposure: A Randomized Controlled Trial of Project Zero Exposure	Rosen, Laura; Zucker, David; Guttman, Nurit; Brown, Nili; Bitan, Michal; Rule, Ana; Berkovitch, Mati; Myers, Vicki	Nicotine & Tobacco Research	2021-05-22	Young children are vulnerable to harm from tobacco smoke exposure (TSE). This study assessed the effect of Project Zero Exposure—an intervention program designed to help parents protect children from TSE—on children's exposure. Randomized controlled trial of a home-based, theory-driven intervention. Parents of young children (<8 y) in families with a smoking parent were eligible. The intervention included feedback on child TSE (hair nicotine), and home air quality (PM _{2.5}), with motivational interviewing. Families were randomized to: intervention group (IG, N = 69), regular control group (RCG, N = 70), or to a secondary enhanced control group, (ECG, N = 20). Child hair samples were taken at baseline and follow-up. We report on child TSE in the IG versus RCG at six months. Most enrolled families completed the trial (IG: 98.6% [68/69], RCG: 97.1% [68/70]). Log hair nicotine (LHN [ng/mg]) decreased in both the IG (Baseline: -1.78 ± 1.91, Follow-up: -2.82 ± 1.87, p = .003) and RCG (Baseline: -1.79 ± 1.54, Follow-up: -2.85 ± 1.73, p = .002), but did not differ between groups at study end (p = .635). Three of five parentally-reported outcomes showed improvement over time in the IG, and one in the RCG. Among IG participants, 90% found hair nicotine feedback useful. No difference between the intervention and control groups was found on the objective biomarker, LHN. Child TSE decreased during the trial in intervention and control groups. Trial participation, which included hair nicotine monitoring, may have contributed to decreasing exposure in both groups. Concurrent control group improvements may partially explain lack of proven intervention benefit. Biomarker monitoring warrants further investigation for reduction of child TSE. Project Zero Exposure is an intervention program designed to help parents protect their children from TSE. Results from the randomized controlled trial of the program showed no difference between groups at study end, but a clear and substantial reduction in child exposure to tobacco smoke from beginning to end of the trial, in both intervention and control groups. Biomarker monitoring, a key element of the trial, was used with all participants. Biomarker monitoring of child exposure to tobacco smoke may help parents become aware of their child's exposure and better protect them, and should be explored as a means to reduce child TSE. Clinical Trial Registration: NCT02867241

Pre Clinical Toxicology	Comparable Impairment of Vascular Endothelial Function by a Wide Range of Electronic Nicotine Delivery Devices	Rao, P. Han, D. D.; Tan, K.; Mohammadi, L.; Derakhshandeh, R.; Navabzadeh, M.; Goyal, N.; Springer, M. L.	Nicotine Tob Res	2022-01-31	INTRODUCTION: Electronic nicotine delivery systems (ENDS; i.e., vaping devices) such as e-cigarettes, heated tobacco products, and newer coil-less ultrasonic vaping devices are promoted as less harmful alternatives to combustible cigarettes. However, their cardiovascular effects are understudied. We investigated whether exposure to aerosol from a wide range of ENDS devices, including a new ultrasonic vaping device, impairs endothelial function. METHODS: We measured arterial flow-mediated dilation (FMD) in rats (n=8/group) exposed to single session of 10 cycles of pulsatile 5s exposure over 5 minutes to aerosol from e-liquids with and without nicotine generated from a USONICIG ultrasonic vaping device, previous generation e-cigarettes, 5% nicotine JUUL pods (Virginia Tobacco, Mango, Menthol), and an IQOS heated tobacco product; with Marlboro Red cigarette smoke and clean air as controls. We evaluated nicotine absorption and serum nitric oxide levels after exposure, and effects of different nicotine acidifiers on platelet aggregation. RESULTS: Aerosol/smoke from all conditions except air significantly impaired FMD. Serum nicotine varied widely from highest in the IQOS group to lowest in USONICIG and previous generation e-cig groups. NO levels were not affected by exposure. Exposure to JUUL and similarly acidified nicotine salt e-liquids did not affect platelet aggregation rate. Despite lack of heating coil, the USONICIG under airflow conditions heated e-liquid to ~77°C. CONCLUSIONS: A wide range of ENDS, including multiple types of e-cigarettes with and without nicotine, a heated tobacco product, and an ultrasonic vaping device devoid of heating coil, all impair FMD after a single vaping session comparably to combusted cigarettes. IMPLICATIONS: The need to understand the cardiovascular effects of various ENDS is of timely importance, as we have seen a dramatic increase in the use of these products in recent years, along with the growing assumption among its users that these devices are relatively benign. Our conclusion that a single exposure to aerosol from a wide range of ENDS impairs endothelial function comparably to cigarettes indicates that vaping can cause similar acute vascular functional impairment to smoking and is not a harmless activity.
Pre Clinical Toxicology	Diluted aqueous extract of heat-not-burn tobacco product smoke causes less oxidative damage in fibroblasts than conventional cigarette	Lyu, Q.; Jiang, L.; Zheng, H.; Hayashi, S.; Sato, K.; Toyokuni, S.	Journal of Clinical Biochemistry and Nutrition	2022-01-25	Smoke from conventional cigarettes (C-cigarettes) contains various reactive oxygen species and toxic chemicals, which potentially cause oxidative damage not only to airways but also to the whole body, leading eventually to diseases, including emphysema, advanced atherosclerosis, and cancer. Many heat-not-burn tobacco products (HTPs) have been commercialized recently in Japan to maintain the smoking population by advertising that HTPs are less toxic. However, there were few studies reported from neutral organizations whether HTPs are indeed less damaging. To evaluate the potential capacity of HTPs to induce oxidative stress, we here compared two different HTPs with two types of C-cigarettes, using human fibroblast IMR90SV cells and 5% aqueous extracts in 10-ml phosphate-buffered saline (50-ml smoke/10 s). HTPs exhibited significantly lower oxidative toxicity in comparison to C-cigarettes. Whereas C-cigarettes induced ferroptosis in fibroblasts, the effects of HTPs were significantly reduced by measuring the levels of peroxides, pro-inflammatory cytokine expression, autophagy, catalytic Fe(II) and 8-hydroxy-2'-deoxyguanosine. Notably, major portions of C-cigarettes-induced pathogenic responses were inhibited by catalase. However, HTPs still induced p62 autophagy-adaptor at 5%-dilution and caused lethal effects to fibroblasts with undiluted solution. In conclusion, HTPs smoke per se can be toxic despite less toxicity in comparison to C-cigarettes, which warrants further investigation.
Pre Clinical Toxicology	Exposure to aerosol extract from heated tobacco products causes a drastic decrease of glutathione and protein carbonylation in human lung epithelial cells	Nishimoto-Kusunose, S.; Sawa, M.; Inaba, Y.; Ushiyama, A.; Ishii, K.; Hattori, K.; Ogasawara, Y.	Biochem Biophys Res Commun	2021-12-06	Heated tobacco products (HTPs) are an emerging class of tobacco goods that claim to have lower health risks than those of smoking combustible tobacco products. In this study, we exposed human lung epithelial cell lines to extracts prepared from HTP aerosols and combustible cigarette smoke to compare cytotoxicity. We focused on the effects of aldehydes present in the aerosols of HTPs at levels close to those in combustible cigarette smoke. Significant toxicity was confirmed for the HTP extract, albeit to a lesser extent than that with the combustible cigarette extract. When redox balance was evaluated by the oxidative loss of low-molecular-weight thiols in the cells, we found that total glutathione (GSH) contents and low-molecular-weight thiol levels were significantly decreased after exposure to the aerosol extract of HTPs. These results indicated that GSH is rapidly consumed during the detoxification of xenobiotics, such as aldehydes from tobacco extracts. Accordingly, exposure to the aerosol extract of HTPs resulted in the enhanced carbonylation of many proteins. In a simple comparison, the results for HTPs were significantly different from those obtained with combustible cigarette smoke, suggesting reduced toxicity of HTPs. However, we found significant and harmful effects after exposing lung epithelial cells to the aerosol extract of HTPs. Thus, a further comprehensive study is needed to clarify the lung damage induced via the long-term inhalation of aerosols from HTPs.

Pre Clinical Toxicology	DNA methylation abnormalities and altered whole transcriptome profiles after switching from combustible tobacco smoking to heated tobacco products	Ohmomo, H.; Harada, S.; Komaki, S.; Ono, K.; Sutoh, Y.; Otomo, R.; Umekage, S.; Hachiya, T.; Katanoda, K.; Takebayashi, T.; Shimizu, A.	Cancer Epidemiol Biomarkers Prev	2021-11-02	<p>BACKGROUND: The use of heated tobacco products (HTPs) has increased exponentially in Japan since 2016; however, their effects on health remain a major concern. METHODS: Tsuruoka Metabolome Cohort Study participants (n = 11,002) were grouped based on their smoking habits as never smokers (NS), past smokers (PS), combustible tobacco smokers (CS), and HTP users for <2 years. Peripheral blood mononuclear cells were collected from 52 participants per group matched to HTP users using propensity scores, and DNA and RNA were purified from the samples. DNA methylation (DNAm) analysis of the 17 smoking-associated DNAm biomarker genes (such as AHR, F2RL3, LRRN3 and GPR15), as well as whole transcriptome analysis were performed. RESULTS: Ten of the 17 genes were significantly hypomethylated in CS and HTP users compared to NS, among which AHR, F2RL3 and RARA showed intermediate characteristics between CS and NS; nonetheless, AHR expression was significantly higher in CS than in the other three groups. Conversely, LRRN3 and GPR15 were more hypomethylated in HTP users than in NS, and GPR15 expression was markedly upregulated in all the groups when compared to that in NS. CONCLUSIONS: HTP users (switched from CS <2 years) display abnormal DNAm and transcriptome profiles, albeit to a lesser extent than the CS. However, since the molecular genetic effects of long-term HTP use are still unknown, long-term molecular epidemiological studies are needed. IMPACT: This study provides new insights into the molecular genetic effects on DNAm and transcriptome profiles in HTP users that switched from CS.</p>
Pre Clinical Toxicology	Toxic mechanisms of cigarette smoke and heat-not-burn tobacco vapor inhalation on rheumatoid arthritis	Helluany, C. S.; Scharf, P.; Schneider, A. H.; Donat, P. B.; Dos Reis Pedreira Filho, W.; de Oliveira, T. F.; Cunha, F. Q.; Farsky, S. H. P.	Sci Total Environ	2021-10-23	<p>Tobacco combustion exposure worsens rheumatoid arthritis (RA). Non-combustible tobacco devices, as heat-not-burn tobacco (HNBT), are emerging as harm reduction to smokers by releasing nicotine and lower combustible tobacco products. Nevertheless, HNBT toxicity remains unclear. Hence, here we investigated the impacts of the tobacco combustible product (cigarette smoke; CS) or HNBT vapor exposures on antigen-induced arthritis (AIA) in C57BL/6 mice. Animals were exposed to airflow, HNBT vapor, or CS during 1 h/twice a day, under the Health Canada Intense (HCI) smoking regime, between days 14 to 20 after the first immunization. At day 21, 16 h after the last exposures, mice were i.a. challenged and the AIA effects were evaluated 24 h later. CS- or HNBT-exposed mice presented equivalent blood nicotine levels. CS exposure worsened articular symptoms, pulmonary inflammation, and expression of lung metalloproteinases. Nevertheless, CS or HNBT exposures reduced lymphoid organs' cellularity, splenocyte proliferation and IL-2 secretion. Additional in vitro CS or HNBT exposures confirmed the harmful effects on splenocytes, which were partially mediated by the activation of nicotine/α7nAChR pathway. Associated, data demonstrate the toxic mechanisms of CS or HNBT inhalation at HCI regime on RA, and highlight that further investigations are fundamental to assure the toxicity of emerging tobacco products on the immune system during specific challenges.</p>
Pre Clinical Toxicology	Cigarette smoke extract and heated tobacco products promote ferritin cleavage and iron accumulation in human corneal epithelial cells	W. Otsu; K. Ishida; N. Chinen; S. Nakamura; M. Shimazawa; H. Tsusaki; H. Hara	Scientific Reports	2021-09-17	<p>The cornea is directly exposed to cigarette smoke, and smoking is a risk factor for several corneal diseases including dry eye syndrome. Currently, heated tobacco products (HTPs) are widely used as substitutes for cigarette smoking around the world. In the present study, we investigated the molecular mechanism(s) leading to cellular injury induced by cigarette smoke extract (CSE) or HTPs. Exposure to CSE perturbed the formation of tight junctions, leading to an increase in cell volume, a decrease in trans epithelial electrical resistance (TER) in the human corneal epithelial cell-transformed (HCE-T) cell line. Moreover, CSE exposure induced both lipid peroxidation and ferrous [Fe(II)] ion accumulation in autolysosomal compartments. Interestingly, a cleaved form of ferritin appeared when HCE-T cells were incubated with CSE. This aberrant ferritin processing was suppressed by treatment with autophagy inhibitors. Furthermore, the CSE-induced cell death was suppressed by either ferrostatin-1 or deferoxamine (DFO). CSE exposure also promoted the expression of cytokines whereas DFO treatment inhibited the CSE-induced expression of these cytokines. Exposure to HTPs also induced both HCE-T cell death and cleaved ferritin accumulation in a concentration- and time-dependent manner. These results indicated that CSE or HTPs activated the ferroptosis signaling pathway, which contributed to corneal epithelial cell injury.</p>

Pre Clinical Toxicology	Heated Tobacco Products Impair Cell Viability, Osteoblastic Differentiation, and Bone Fracture-Healing	K. Nishino; K. Tamai; K. Orita; Y. Hashimoto; H. Nakamura	JBS	2021-08-11	<p>BACKGROUND: The negative impact of cigarette smoking on bone union has been well documented. However, the impact of heated tobacco product (HTP) use on bone fracture-healing remains unclear. The present study investigated the effect of HTPs on preosteoblast viability, osteoblastic differentiation, and fracture-healing and compared the effects with those of conventional combustible cigarettes.</p> <p>METHODS: Cigarette smoke extracts (CSEs) were generated from combustible cigarettes (cCSE) and HTPs (hCSE). CSE concentrations were standardized by assessing optical density. Preosteoblast (MC3T3-E1) cells were incubated with normal medium, cCSE, or hCSE. The cell viability was assessed via MTT assay. After osteoblastic differentiation of CSE-exposed cells, alkaline phosphatase (ALP) activity was assessed. To assess the in vivo effects of CSEs, a femoral midshaft osteotomy was performed in a rat model; thereafter, saline solution, cCSE, or hCSE was injected intraperitoneally, and bone union was assessed on the basis of micro-computed tomography (μCT) and biomechanical analysis 4 weeks later.</p> <p>RESULTS: MC3T3-E1 cell viability was reduced in a time and concentration-dependent manner when treated with either cCSE or hCSE. ALP activity after osteoblastic differentiation of cCSE-treated cells was significantly lower than that of both untreated and hCSE-treated cells (mean and standard deviation, 452.4 ± 48.8 [untreated], 326.2 ± 26.2 [cCSE-treated], and 389.9 ± 26.6 [hCSE-treated] mol/L/min; $p = 0.002$). Moreover, the levels of osteoblastic differentiation in untreated and hCSE-treated cells differed significantly ($p < 0.05$). In vivo assessment of the femoral midshaft cortical region revealed that both cCSE and hCSE administration significantly decreased bone mineral content 4 weeks after surgery compared with levels observed in untreated animals (107.0 ± 11.9 [untreated], 94.5 ± 13.0 [cCSE-treated], and 89.0 ± 10.1 mg/cm³ [hCSE-treated]; $p = 0.049$). Additionally, cCSE and hCSE-exposed femora had significantly lower bone volumes than unexposed femora. Biomechanical analyses showed that both cCSE and hCSE administration significantly decreased femoral maximum load and elastic modulus ($p = 0.015$ and 0.019).</p> <p>CONCLUSIONS: HTP use impairs cell viability, osteoblastic differentiation, and bone fracture-healing at levels comparable with those associated with combustible cigarette use.</p> <p>CLINICAL RELEVANCE: HTP use negatively affects bone fracture-healing to a degree similar to that of combustible cigarettes. Orthopaedic surgeons should recommend HTP smoking cessation to improve bone union.</p>
Pre Clinical Toxicology	Role of diabetes in lung injury from acute exposure to electronic cigarette, heated tobacco product, and combustible cigarette aerosols in an animal model	Abi Zeid Daou, Michella; Shihadeh, Alan; Hashem, Yasmine; Bitar, Hala; Kassir, Alaa; El-Harakch, Mohammad; Karaoghlanian, Nareg; Eid, Assaad A; El-Sabban, Marwan; Zaatari, Ghazi; Husari, Ahmad	PLoS One	2021-08-10	<p>Background: Patients with diabetes are more vulnerable to the detrimental respiratory effects of combustible cigarette smoke (CS) when compared to the general population. Electronic cigarettes (ECIG) and heated tobacco products (HTP) are marketed as less harmful alternatives to CS. In this study, we compared the effects of acute ECIG, HTP and CS exposure on the lungs of type II diabetes versus non-diabetic mice in an animal model.</p> <p>Methods: Type II Diabetic (Diab) and Non-Diabetic (Non-Diab) mice were divided into Control, ECIG, HTP and CS groups. Animals were exposed for 6 hrs./day to either air, ECIG, HTP or CS for seven days. Lung injury was determined by a) histopathology, b) wet to dry ratio, c) albumin concentration in bronchoalveolar lavage fluid, d) expression of TNF-α, IL-6, and IL-1 β, e) reactive oxygen species production (ROS), and f) assessment of cellular apoptosis.</p> <p>Results: Lung histology revealed increased edema and inflammatory cells in diabetic mice exposed to ECIG, HTP and CS. The expression of inflammatory mediators was, in general, more significant in the Diabetic groups as well. TNF-α expression, for example, was upregulated in Diab + ECIG but not in Non-Diab + ECIG. ROS was significantly increased in Diab + CS, less in Non-Diab + CS and weakly noted in ECIG + Diab. Significant albumin leak was observed in Diab and Non-Diab HTP-exposed animals. CS exposure worsened lung injury in Diab when compared to Non-Diab mice.</p> <p>Conclusion: Comorbid medical conditions like diabetes may amplify ill effects of CS, ECIG or HTP exposure.</p>

Pre Clinical Toxicology	Comparison of cytotoxicity of cigarette smoke extract derived from heat-not-burn and combustion cigarettes in human vascular endothelial cells	Horinouchi, Takahiro; Miwa, Soichi	Journal of Pharmacological Sciences	2021-07-24	<p>The present study compared the properties of mainstream smoke generated from heat-not-burn (HNB) cigarettes and a combustion cigarette (hi-lite™ brand). Three types of cigarette heating devices were used to generate cigarette smoke at different heating temperatures [Ploom S™ (200 °C), glo™ (240 °C), and IQOS™ (300–350 °C)]. Mainstream smoke was generated using the following puffing regimen: volume, 55 mL; duration, 3 s; and interval, 30 s. The rank order of particulate phase (nicotine and tar) amounts trapped on a Cambridge filter was Ploom S < glo < IQOS < hi-lite. Heated cigarette-derived smoke extract (hCSE) from the devices except for Ploom S, and burned CSE (bCSE) decreased mitochondrial metabolic activity (glo < IQOS < hi-lite) in human vascular endothelial cells. Furthermore, the cytotoxicity was reduced by removing the particulate phase from the mainstream smoke. Endothelial nitric oxide synthase activity was reduced by nicotine- and tar-free CSE of IQOS and hi-lite (IQOS < hi-lite), but not Ploom S and glo. These inhibitory effects were diminished by removing the carbonyl compounds from the mainstream smoke. These results indicated that the cytotoxicity of hCSE was lower than that of bCSE in vascular endothelial cells.</p>
Pre Clinical Toxicology	Screening of different cytotoxicity methods for the assessment of ENDS toxicity relative to tobacco cigarettes	Caruso, M.; Emma, R.; Rust, S.; Distefano, A.; Carola, G.; Pulvirenti, R.; Polosa, R.; Li Volti, G.	Regul Toxicol Pharmacol	2021-07-24	<p>Electronic Nicotine Delivery Systems (ENDS), i.e., electronic-cigarettes (e-cigs) and Tobacco Heating Products (THPs), are rapidly growing in popularity. Nonetheless, comprehensive quality and safety requirements for regulatory purposes are still under development. Cytotoxicity studies are important initial steps in appraising the potential ENDS toxicity. The aim of the present study was to screen different in vitro cytotoxicity methods for the assessment of ENDS toxicity. We evaluated NRU, MTT, Annexin V apoptosis (AN-V), High-Content Screening (HCS) assays and Real-Time Cell Analysis (RTCA), to compare two e-cigs and two THPs with the IR6F reference tobacco cigarette. Human adenocarcinoma lung epithelial cells (H292) were exposed to tobacco smoke and ENDS vapor at air-liquid interface. All tests showed reduced cell viability following IR6F smoke exposure and slight or no reduction with ENDS at 24 h. AN-V and RTCA exhibited a further significant reduction in cell viability following IR6F exposure. AN-V allowed to discriminate viable cells from those in early/late apoptosis. RTCA and HCS being time-resolved analyses elucidate the kinetic dependency parameter for toxicity of smoke/vapor chemicals on cell viability. In conclusion, NRU assay may be considered a suitable test, especially when combined with a time-resolved analysis, for assessing the kinetic of cytotoxicity induced by these products.</p>
Pre Clinical Toxicology	A Newly Developed Aerosol Exposure Apparatus for Heated Tobacco Products for In Vivo Experiments Can Deliver Both Particles and Gas Phase With High Recovery and Depicts the Time-Dependent Variation in Nicotine Metabolites in Mouse Urine	Sawa, Marie; Ushiyama, Akira; Inaba, Yohei; Uchiyama, Shigehisa; Hattoni, Kenji; Ogasawara, Yuki; Ishii, Kazuyuki	Nicotine & Tobacco Research	2021-06-10	<p>There is no standardized aerosol exposure apparatus to deliver heated tobacco products (HTPs) for in vivo experiments. Therefore, we developed a novel HTPs aerosol exposure apparatus for mice and demonstrated that nicotine and other chemicals in HTPs aerosol generated by the apparatus can be delivered to mice which replicate human smoke. The amounts of nicotine, tar, and carbon monoxide (CO) in IQOS (Marlboro Regular HeatSticks) aerosol generated by two types of apparatuses were determined. C57BL/6N mice were exposed to IQOS aerosol, followed by determination of the urinary nicotine metabolites. Further, the skin surface temperature of mice was monitored to confirm the vasoconstriction action of nicotine. The amount of chemicals in IQOS aerosol by the novel air push-in inhalation apparatus for HTPs (APIA) was equivalent to that of the analytical vaping machine (LM4E) (1.60 ± 0.08 [APIA] vs. 1.46 ± 0.07 mg/stick [LM4E] in nicotine and 0.55 ± 0.04 [APIA] vs. 0.45 ± 0.01 mg/stick [LM4E] in CO). After mice were exposed to IQOS aerosol by APIA, the urinary nicotine metabolite levels were determined; peak values in cotinine and 3-hydroxycotinine (3-HC) were $6.82 \mu\text{g}/\text{mg}$ creatinine at 1 hour after exposure and $32.9 \mu\text{g}/\text{mg}$ creatinine at 2 hours after exposure, respectively. The skin surface temperature decreased and was lower ($33.5^\circ\text{C} \pm 0.5^\circ\text{C}$) at 30 minutes than before exposure ($37.6^\circ\text{C} \pm 0.8^\circ\text{C}$). The new apparatus for HTPs aerosol exposure to mice showed good performances in terms of both chemical analysis of collected aerosol and fluctuations in the urinary nicotine metabolites. The APIA reported in this study can expose small animals to HTPs aerosol, including nicotine and other chemical substances as same amounts as LM4E and replicate actual human smoking process by in vivo experiments. Therefore, the experiments using APIA can provide evidence to assess the health risks of HTPs use.</p>

Pre Clinical Toxicology	Unburned tobacco cigarette smoke alters rat ultrastructural lung airways and DNA	Vivarelli, F.; Canistro, D.; Cirillo, S.; Elias, R. J.; Granata, S.; Mussoni, M.; Burattini, S.; Falcieri, E.; Turrini, E.; Fimognari, C.; Buschini, A.; Lazzaretti, M.; Beghi, S.; Girotti, S.; Sangiorgi, S.; Bolelli, L.; Ghini, S.; Ferri, E. N.; Fagioli, L.; Franchi, P.; Lucarini, M.; Mercatante, D.; Rodriguez-Estrada, M. T.; Lorenzini, A.; Marchionni, S.; Gabriele, M.; Longo, V.; Paoletti, M.	Nicotine & Tobacco Research	2021-05-24	INTRODUCTION: Recently, the Food and Drug Administration (FDA) authorized the marketing of IQOS Tobacco Heating System as a Modified Risk Tobacco Product (MRTP) based on an electronic heat-not-burn technology that purports to reduce the risk. METHODS: Sprague-Dawley rats were exposed in a whole-body mode to IQOS aerosol for 4 weeks. We performed the chemical characterization of IQOS mainstream and we studied the ultrastructural changes in trachea and lung parenchyma of rats exposed to IQOS stick mainstream and tissue pro-inflammatory markers. We investigated the reactive oxygen species (ROS) amount along with the markers of tissue and DNA oxidative damage. Moreover, we tested the putative genotoxicity of IQOS mainstream through Ames and alkaline Comet mutagenicity assays. RESULTS: Here, we identified irritating and carcinogenic compounds including aldehydes and polycyclic aromatic hydrocarbons in the IQOS mainstream as sign of incomplete combustion and degradation of tobacco, that lead to severe remodeling of smaller and largest rat airways. We demonstrated that IQOS mainstream induces lung enzymes that activate carcinogens, increases tissue reactive radical concentration; promotes oxidative DNA breaks and gene level DNA damage; and stimulates mitogen activated protein kinase (MAPK) pathway which is involved in the conventional tobacco smoke-induced cancer progression. CONCLUSIONS: Collectively, our findings reveal that IQOS causes grave lung damage and promotes factors that increase cancer risk. IMPLICATIONS: IQOS has been proposed as a safer alternative to conventional cigarettes, due to depressed concentration of various harmful constituents typical of traditional tobacco smoke. However, its lower health risks to consumers have yet to be determined. Our findings confirm that IQOS mainstream contains pyrolysis and thermogenic degradation by-products, the same harmful constituents of traditional cigarette smoke, and, for the first time, we show that it causes grave lung damage and promotes factors that increase cancer risk in the animal model.
Pre Clinical Toxicology	Heat-not-burn tobacco (IQOS), oral fibroblasts and keratinocytes: cytotoxicity, morphological analysis, apoptosis and cellular cycle. An in vitro study	Pagano, Stefano; Negri, Paolo; Coniglio, Maddalena; Bruscoli, Stefano; Di Michele, Alessandro; Marchetti, Maria Cristina; Valenti, Chiara; Gambelunghe, Angela; Fanasca, Luca; Billi, Monica; Cianetti, Stefano; Marmucci, Lorella	J Periodontol Res.	2021-05-21	Objectives: The aim of this work is to investigate the biological effects of IQOS smoking on human gingival fibroblasts and human keratinocytes analysing cell viability, morphology, migration, apoptosis and cell cycle.; ; Background: Electronic cigarettes and tobacco heating systems have been marketed to reduce smoking damages caused by combustion.; ; Methods: Human gingival fibroblasts and human keratinocytes viability was determined by a colorimetric assay measuring mitochondrial dehydrogenase activity (MTT assay); after an in vitro exposure of 24 h, cell morphology was analysed with scanning electron microscope and cell migration was tested by Scratch assay, a method to mimic the migration of the cells during wound healing in vivo. Apoptosis and cell cycle were analysed with flow cytometry, and the expression of related genes (p53, Bcl2, p16 and p21) was indagated using real-time polymerase chain reaction.; ; Results: IQOS extracts increased both cell viability (23%-41% with fibroblasts and 30%-79% with keratinocytes) and migration. No morphological alterations were observed. IQOS extracts did not induced an increase in cell death, but rose the number of S- and G2/M-phase cells. IQOS extracts also significantly increased p53 expression by fibroblasts (undiluted and 6.25% dilution, 2- and 3.6-fold higher, respectively) and reduced Bcl2 (about two- and fivefold, respectively) and p21 expressions (about twofold with both extracts), while on keratinocytes both undiluted and 6.25% dilution extracts increased Bcl2 expression (about four- and threefold higher, respectively) and reduced p53 expression (about two- and fivefold, respectively); ; Conclusion: IQOS smoke seemed to induce proliferation as highlighted by a viability assay, and migration and cell cycle analysis. The increased cell proliferation induced by IQOS devices must be carefully investigated for its possible clinical effects on oral cell populations.
Pre Clinical Toxicology Acrosol Chemistry and Physics	In vitro toxicological evaluation of a tobacco heating product THP COO and 3R4F research reference cigarette on human lung cancer cells	Wang, H.; Chen, H.; Huang, L.; Li, X.; Wang, L.; Li, S.; Liu, M.; Zhang, M.; Han, S.; Jiang, X.; Fu, Y.; Tian, Y.; Hou, H.; Hu, Q.	Toxicol In Vitro	2021-04-15	Cigarette smoking increases health risks, such as respiratory diseases and heart diseases. Despite the decline in smoking rates in some countries, millions of adults still choose to smoke cigarettes. The use of next-generation nicotine delivery devices, such as tobacco heating products (THPs), may become a potentially safer alternative to smoking. Here, we report on the development of an electrically heated THP, coded as THP COO, with three different flavored tobacco sticks. The purpose of the study was to measure the levels of a list of harmful and potentially harmful constituents (HPHCs) in the total particulate matter (TPM) generated and to conduct a set of toxicological assessments of THP COO as compared with 3R4F reference cigarette. For all 55 HPHCs identified, the levels generated by the THP tobacco sticks were significantly lower in comparison to those in 3R4F TPM. The rate of reduction of HPHCs was between 68.6% and 99.9% under Health Canada Intense (HCI) smoking regimen. Human lung cancer cells (NCI-H292) exposed to 3R4F TPM showed dose-dependent responses for most of the 15 in vitro toxicity endpoints, whereas those exposed to comparable doses of THP COO TPMs did not. Therefore, exclusive use of the THP COO products may reduce the exposure of those tested HPHCs and thus potentially reduce health risk of smoking.

Prevalence & Use Patterns	PaLS Study: Tobacco, Alcohol and Drugs Usage among Polish University Students in the Context of Stress Caused by the COVID-19 Pandemic	Jodezyk, A. M.; Kasink, P. S.; Adamczyk, N.; Gębarowska, J.; Sikora, Z.; Gruba, G.; Mamcarz, A.; Śliż, D.	International Journal of Environmental Research and Public Health	2022-01-23	The COVID-19 pandemic and imposed restrictions were strong stress factors for young people, especially students. Increased alcohol consumption, smoking cigarettes, usage of heated tobacco products, and other stimulants are common methods of coping with anxiety. However, they can have serious negative health effects. A survey consisting of 12 questions related to mental health and psychoactive substance taking habits was distributed among Polish students between 22 February 2021 and 3 April 2021. A total of 1323 participants met all inclusion criteria (females = 1021, males = 297, no other gender = 5). The mean age was 22 years old (± 4.17); 47.62% were medical university students. A total of 71.92% reported negative impact, 8.25% did not notice changes, and 12.58% declared a positive pandemic impact on their mental health. A total of 12.58% declared an increase, 70.22% did not see any differences, and 17.20% reported a decrease in their psychoactive substance usage tendency due to the pandemic. Worse perceived psychology well-being was correlated with a higher tendency to use tobacco (<math>p < 0.001</math>) and alcohol (<math>p < 0.001</math>), and not with marijuana and products containing tetrahydrocannabinol ($p = 0.136$), and hard drugs ($p = 0.799$). The majority of participants declared a negative pandemic impact on mental health and did not report significant changes in psychoactive substance taking habits. Medical personnel should be aware of the current situation and apply for proper prevention and treatment programs.
Prevalence & Use Patterns	E-Cigarettes Use Behaviors in Japan: An Online Survey	Koyama, S.; Tabuchi, T.; Miyashiro, I.	Int J Environ Res Public Health	2022-01-14	Electronic cigarette (e-cigarette) use has become increasingly widespread throughout the world, including in Japan. However, little is known about how e-cigarettes are used in Japan, a country with heavy restrictions on nicotine-containing e-liquids and/or vaping products. This study examined e-cigarette use (e-cigarette use duration, frequency of use, device type, electrical resistance, nicotine use, favorite e-liquid flavors) among users in Japan, through an online survey using a web-based self-reported questionnaire which included questions about sex, age, combustible cigarette and heated tobacco product (HTP) use behaviors. Of 4689 e-cigarettes users analyzed, 93.5% were men and 52.9% had been using e-cigarettes for 1–3 years. Over 80% used e-cigarettes every day; 62.3% used nicotine liquid, and half of the nicotine liquid users used nicotine salt. The most popular liquid flavor was fruit (prevalence: 68.1%), followed by tobacco (prevalence: 48.4%). While 50.9% were e-cigarette single users, 35.2% were dual users (e-cigarettes and cigarettes or HTPs) and 13.8% were triple user (e-cigarettes, cigarettes and HTPs). This is the first comprehensive survey of Japanese e-cigarette users and our finding suggest more than half use nicotine liquid, although e-cigarettes containing nicotine liquid have been prohibited by the Pharmaceutical Affairs Act since 2010 in Japan. The study also showed 49.1% of participants used cigarettes and/or HTPs concurrently (dual or triple users).
Prevalence & Use Patterns	Use of electronic cigarettes and heated tobacco products during the Covid-19 pandemic	Gallus, S.; Sival, C.; Carreras, G.; Gorini, G.; Amerio, A.; McKee, M.; Odone, A.; van den Brandt, P. A.; Spizzichino, L.; Pacifici, R.; Lugo, A.	Scientific Reports	2022-01-13	Only a few studies investigated changes in electronic cigarette (e-cigarette) and heated tobacco product (HTP) use during pandemic restrictions. We conducted a web-based cross-sectional study of a representative sample of 6,003 Italian adults during the strictest phase of the Covid-19 lockdown (April–May 2020). Participants were asked to report changes in e-cigarette and HTP use compared to before the pandemic. E-cigarette users increased from 8.1% to 9.1% and HTP users from 4.0% to 4.5%. Among e-cigarette non-users before lockdown, 1.8% started using e-cigarettes during lockdown. New users were more frequently younger (p for trend 0.001), men (odds ratio, OR 1.56; 95% confidence interval, CI: 1.03–2.34), cannabis users (OR 2.35; 95% CI: 1.33–4.13), gamblers (OR 3.34; 95% CI: 2.18–5.11) and individuals with anxiety symptoms (OR 1.58; 95% CI: 1.00–2.52). 1.0% of HTP non-users started using it during lockdown. New users were less frequently current than never cigarette smokers (OR 0.19; 95% CI: 0.06–0.61) and more frequently gamblers (OR 2.23; 95% CI: 1.22–4.07). E-cigarettes and HTPs played little role as smoking cessation tools for hardcore smokers but rather provided opportunities for young never smokers to engage in socially acceptable activities, perhaps reflecting the obstacles they faced in obtaining other addictive substances during confinement.
Prevalence & Use Patterns	Poland is not replicating the HTP experience in Japan: a cautionary note	Liber, A. C.; Cadham, C.; Cummings, M.; Levy, D. T.; Pesko, M.	Tobacco Control	2021-12-07	In a 2019 article, Stoklosa et al found that the introduction of heated tobacco products (HTPs) to the Japanese market was strongly associated with a decline in cigarette sales. 1 This paper and another by Cummings et al2 provide suggestive evidence that the Japanese population replaced cigarettes sold with HTPs. Instead of delivering nicotine from tobacco leaves through combustion, HTPs heat tobacco to considerably lower temperatures and deliver nicotine to users via an aerosol containing fewer toxic substances than cigarettes and could reduce health risks for users.2 If this pattern of substitution in Japan reflects persistent individual behaviour changes, then health improvements could follow.

Prevalence & Use Patterns	Use of heated tobacco products by people with chronic diseases: The 2019 JASTIS study	Nakama, C.; Tabuchi, T.	PLOS One	2021-11-18	<p>Heated tobacco products (HTPs) have become popular recently. People with chronic disease, such as diabetes, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and cancer, should quit smoking for treatment and recurrence of tobacco-related diseases. However, they have difficulty in quitting smoking, and they may start HTPs use to quit smoking. The purpose of this study is to examine the use of HTPs in people with chronic disease. We used data from an internet study, the Japan Society and New Tobacco Internet Survey (JASTIS). We analyzed 9,008 respondents aged 15-73 years in 2019 using logistic regression. Current use of tobacco products was defined as use within the previous 30 days. Prevalence of current HTP use including dual use and dual use with cigarettes was 9.0% and 6.1% respectively in total. By disease: hypertension 10.2% and 7.4%, diabetes 15.9% and 12.3%, CVD 19.2% and 15.7%, COPD 40.5% and 33.3%, and cancer 17.5% and 11.9%. Diabetes, CVD, COPD, and cancer were positively associated with current use of HTPs (odds ratios (ORs) and 95% confidence intervals (CIs): 1.48 (1.06, 2.07), 2.29 (1.38, 3.80), 3.97 (1.73, 9.11), and 3.58 (1.99, 6.44), respectively) and dual use of cigarettes and HTPs (ORs and 95% CIs: 2.23 (1.61, 3.09), 3.58 (2.29, 5.60), 7.46 (3.76, 14.80), and 2.57 (1.46, 4.55), respectively) after adjusting for confounders. People with chronic disease were more likely to use HTPs and HTPs together with cigarettes. Further research on the smoking situation of HTPs in patients with chronic diseases is necessary.</p>
Prevalence & Use Patterns	Prevalence and characteristics of ever regular use of non-combustible nicotine for 1 year or more: a population survey in England	Cox, S.; Brown, J.; Koek, L.; Shahab, L.	Harm Reduct J	2021-11-17	<p>INTRODUCTION: Up-to-date monitoring of non-combustible nicotine products (e.g. e-cigarettes, nicotine replacement therapies (NRT), heated tobacco products (HTP); NNP) is important to assess their impact. To date, there is little evidence on the association between ever regular use (defined here as 1 year or more) of NNP and current smoking status.</p> <p>AIMS/METHODS: The purpose of this study was to examine the prevalence, and sociodemographic, alcohol and smoking status correlates, of ever regular use of NNP in England in 2020. A cross-sectional survey of adults in England was conducted between February and June 2020. RESULTS: A total of 8486 adults were surveyed; 94.9% (95% CI 5.0-6.0), of which 82% (n = 360; 95% CI 78.7-85.8) was single and 18% (n = 79; 95% CI 14.8-22) multiple product use. Amongst ever regular NNP users, the prevalence of ever regular NRT, e-cigarette and HTP use was 64.7% (95% CI 60.1-69), 43.4% (95% CI 38.8-48) and 2.5% (95% CI 1.4-4.5), respectively. In adjusted analysis, ever regular NNP use was associated with smoking status, being significantly higher among current (22.3%; adjusted OR (aOR) 34.9, 95% CI 24.0-50.8) and ex-smokers (12.7%; aOR 19.8, 95% CI 11.1-14.4) than among never-smokers (0.6%). More advantaged occupational grade (aOR, 1.27 95% CI 1.02-1.57) and at least hazardous alcohol use (aOR, 1.38 95% CI 1.06-1.78) were associated with greater prevalence of ever regular NNP use. CONCLUSIONS: Ever regularly using NNP was highest among smokers and ex-smokers and rare among never-smokers. Among people who have ever regularly used NNP, NRT is the most popular.</p>
Prevalence & Use Patterns	Characterizing heated tobacco product use among adult cigarette smokers and nicotine vaping product users in the 2018 ITC Four Country Smoking & Vaping Survey	Miller, C. R.; Sultano, E.; Smith, D. M.; Hitchman, S. C.; Gravely, S.; Yong, H. H.; Borland, R.; O'Connor, R. J.; Cummings, K. M.; Fong, G. T.; Hyland, A.; Quah, A. C. K.; Goniewicz, M. L.	Nicotine & Tobacco Research	2021-10-20	<p>INTRODUCTION: Heated tobacco products (HTP) have diversified global tobacco markets, and user characteristics remain understudied. This study evaluated sociodemographic characteristics, nicotine-related perceptions and behaviors of current HTP users within a sample of adult (18+ years) nicotine users across four countries. METHODS: Data were from current smokers or nicotine vaping product (NVP; known as "e-cigarettes") users from Canada, England, the United States and Australia (n=11,421) who participated in the 2018 ITC Four Country Smoking and Vaping Survey. Current (at-least-monthly) HTP users were characterized (n=441), and weighted multivariable logistic regressions examined correlates of HTP use. RESULTS: Compared to non-users, current HTP users were younger (mean age: 44.4 vs 31.0 years; p<0.001) and had higher socioeconomic status (p<0.001). A majority of current HTP users used HTPs non-daily (daily: 40.3% vs non-daily: 59.7%). Most HTP users concurrently used both cigarettes and NVPs (90.5%). Among concurrent cigarette-HTP-NVP users, 36.2% used all three products daily. Use of other combusted tobacco products (cigars, cigarillos, pipe, waterpipe/hookah), cannabis, and binge drinking were each associated with current HTP use. HTP use was more common among smokers intending to quit within 6 months or reporting a quit attempt in the past 18 months, and vapers who had experienced negative side effects. CONCLUSION: HTP users in this sample tended to be younger and more affluent. Most reported concurrent use of multiple nicotine products and other substances. Those cigarette smokers who used HTPs appeared more interested in smoking cessation, while some characteristics of concurrent HTP-NVP users were suggestive of dissatisfaction with NVPs. IMPLICATIONS: Few studies have scrutinized characteristics of HTP early-adopters in emerging markets. Our results indicate that in 2018, characteristics of established nicotine users who adopted HTP use in four high-income Western countries mirror those of HTP users in East Asian markets (South Korea and Japan) where HTPs are popular. HTP users reported high levels of concurrent use of non-cigarette combusted tobacco products (e.g., cigars, pipe tobacco). These findings point to the need for future longitudinal studies of HTP use given the implications of those use patterns on the harm reduction potential of HTPs. HTP user characteristics may yield important information to consider in regulation of these products.</p>

Prevalence & Use Patterns	Use patterns of cigarettes and alternative tobacco products and socioeconomic correlates in Hong Kong secondary school students	Wang, Lijun; Chen, Jianjiu; Tung Leung, Lok; Yin Ho, Sai; Lam, Tai Hing; Wang, Man Ping	Scientific Reports	2021-08-26	<p>Smoking is a major cause of health inequities. However, sociodemographic differences in adolescent tobacco use are unclear. In a territory-wide school-based anonymous survey in 2018/19, we investigated tobacco use and sociodemographic correlates in 33,991 students (mean age 14.8 ± 1.9 years) in Hong Kong. Tobacco use prevalence and current-ever use ratios by sociodemographic factors were calculated. Generalised linear mixed models were used in association analyses. Current use was highest for cigarettes (3.2%), closely followed by alternative tobacco products (3.0%). Current-ever use ratios were highest for heated tobacco products (HTPs, 0.60), followed by nicotine e-cigarettes (0.52), waterpipe (0.51), and cigarettes (0.35). Use prevalence and current-ever use ratios of all products showed curvilinear relations with perceived family affluence (P values < 0.01), being highest in the richest families. Tobacco use was also associated with more senior grades, the lowest parental education, and boys, but current-ever use ratios of HTPs and waterpipe were higher in girls (P values < 0.05). The results suggested that adolescent ever users of nicotine-containing alternative tobacco products were more likely to keep using them than cigarettes, and the richest adolescents were at the highest risks of tobacco use. Diverse tobacco control measures are needed to improve health equity, especially on alternative tobacco products.</p>
Prevalence & Use Patterns	Occupational difference in use of heated tobacco products: a cross-sectional analysis of retail workers in Japan	Myagmar-Ochir, Enkhguldur; Kaneko, Makiko; Tomiyama, Kiyomi; Zaitou, Masayoshi; Watanabe, Shuichi; Nishino, Yoshiaki; Takahashi, Kyo; Hanyama, Yasuo; Kobashi, Gen	BMI Open	2021-08-24	<p>Objective: Although heated tobacco products (HTPs) have become popular worldwide, research on occupational differences in smoking HTPs remains scarce. We aimed to examine the prevalence of smoking HTPs among a working population in Japan.</p> <p>Setting, design and participants: In 2018, we conducted a cross-sectional study comprised of 7714 retail business workers in the service industry in Japan.</p> <p>Primary and secondary outcome measures: For the definition of smoking HTPs, we identified current HTP smokers who only smoked HTPs, using five mutual categories of current smoking status (never, former, HTPs only, combustible cigarettes only and dual smokers who smoked both combustible cigarettes and HTPs). Occupational classes were classified into office workers (eg, upper non-manual workers) and other workers. ORs and 95% CIs of office workers were estimated for HTP usage, adjusted for age, sex, employment type and cigarette smoking-related health knowledge.</p> <p>Results: The overall prevalence of smoking HTPs was 3.0% (male 5.0%, female 2.2%). The prevalence of HTP smokers differed across occupational classes (5.6% in office workers vs 2.5% in others; $p < 0.05$). Compared with other workers, the adjusted odds of office workers for smoking HTPs remained elevated (OR: 1.97, 95% CI: 1.40 to 2.77). Sensitivity analyses with workers of all smoking status showed the same pattern. When stratified by sex, the occupational difference only remained significant in male workers.</p> <p>Conclusions: We found a positive occupational difference in smoking HTPs, particularly among male workers in the retail sector in Japan. National tobacco control should explicitly address this occupational gap and further encourage individuals to quit smoking.</p> <p>Keywords: epidemiology; health policy; preventive medicine; public health.</p>

Prevalence & Use Patterns	The association between heated tobacco product use and cigarette cessation outcomes among youth smokers: A prospective cohort study	Xia, Wei; Ho Li Cheung, William; Luo, Yuan Hui; Ting Na, Liang; Long Kwan Ho, Laurie; Tan Cheung, Ankie; Song, Peige	Journal of Substance Abuse Treatment	2021-08-14	<p>Introduction: The U.S. Food and Drug Administration authorized the marketing of heated tobacco products (HTPs) with modified-risk information for adults on July 7, 2020. However, the effects of HTP use on cigarette cessation among youth smokers remain unclear. This study aimed to explore the association of HTP use with cigarette abstinence and cessation outcomes among youth smokers in Hong Kong who were willing to receive telephone counseling for smoking cessation.</p> <p>Methods: This prospective cohort study included youth smokers aged ≤ 25 years who were enrolled in the Hong Kong Youth Quitline service. From December 1, 2016, to September 30, 2019, this study identified as HTP users 106 youth cigarette smokers who reported using HTPs on at least 1 of the past 30 days at enrollment, and identified as non-HTP users 473 smokers who reported smoking at least one conventional cigarette in the past 30 days and never using HTPs. The participants received follow-ups at 1 week and 1-, 3-, and 6-months postenrollment. The primary outcome was self-reported 7-day point prevalence of cigarette abstinence (PPA) at the 6-month follow-up. Secondary outcomes included reduction in cigarette smoking (excluding quitters), the number of cessation attempts, and the level of readiness to quit.</p> <p>Results: The self-reported 7-day PPA was statistically significantly lower among HTP users than among non-HTP users after 6 months (19.0% vs. 34.2%, $p = 0.009$), with an adjusted relative risk of 0.47 (95% confidence interval: 0.24-0.91; $p = 0.03$). The study identified no significant differences in secondary outcomes between the two groups.</p> <p>Conclusions: Youth HTP users were less likely to abstain from tobacco use than their non-HTP-using counterparts. These results suggest that HTPs should not be promoted as smoking cessation or reduction aids among the youth population.</p> <p>Keywords: Cohort study; Heated tobacco product; Smoking cessation; Youth.</p>
Prevalence & Use Patterns	Ability to Purchase Tobacco Products and Smoking Behavior of Cigarettes, E-cigarettes, and Heated Tobacco Products in Korean Adolescents	Han, M. A.	Am J Health Behav	2021-07-26	<p>Objectives: This study investigated the smoking behavior and its association with the availability of tobacco products purchases among Korean adolescents. Methods: The data of the 2019 Korea Youth Risk Behavior Survey were used ($N = 57,303$). This study assessed 3 tobacco products: cigarettes, e-cigarettes, and heated tobacco products. Smoking behavior including lifetime, current, daily, heavy smoking, and attempting to quit and its association with the availability of tobacco products for purchase was assessed. Results: Overall, 92.9% did not try to purchase tobacco products during the past 30 days, 2.2% found it impossible to purchase, 0.8% could buy with a lot of effort, 1.7% could buy with little effort, and 2.3% could buy easily without any effort. Lifetime smokers were 13.8% (12.7% for cigarettes, 7.4% for e-cigarettes, and 4.9% for heated tobacco products). Among lifetime smokers, the current smoking rates for cigarettes, e-cigarettes, and heated tobacco products were 48.5%, 22.9%, and 19.0%, and the rates were lower in adolescents who responded that it was impossible to buy tobacco products. Among current smokers, the daily smoking rates were lower in adolescents who were found it impossible to buy tobacco products. Conclusions: The ease of access to tobacco products was associated with higher use of cigarettes, e-cigarettes, and heated tobacco products and lower attempts to quit smoking in Korean adolescents.</p>
Prevalence & Use Patterns	Impact of flavours, device, nicotine levels and price on adult e-cigarette users' tobacco and nicotine product choices	Yang, Yong; Lindblom, Eric N.; Salloum, Ramzi G.; Ward, Kenneth D.	Tobacco Control	2021-07-22	<p>Introduction To understand the impact of e-cigarette devices, flavours, nicotine levels and prices on adult e-cigarette users' choices among closed-system and open-system e-cigarettes, cigarettes and heated tobacco products (HTPs). Methods Online discrete choice experiments were conducted among adult (≥ 18 years) e-cigarette users ($n = 2642$) in August 2020. Conditional logit regressions were used to assess the relative impact of product attributes and the interactions between product attributes and user characteristics, with stratified analyses to examine differences by smoking status and primarily used e-cigarette device and flavour. Results On average, participants preferred non-tobacco and non-menthol flavours most, preferred open-system over closed-system e-cigarettes and preferred regular nicotine level over low nicotine level. However, the preference varied by demographics, smoking status and the primarily used e-cigarette device and flavour. The differences in preference among products/devices were larger than the difference among flavours or nicotine levels. Participants who primarily used closed-system e-cigarettes exhibited similar preferences for closed-system and open-system e-cigarettes, but those who primarily used open-system e-cigarettes preferred much more open-system over closed-system e-cigarettes. HTP was the least preferred product, much lower than cigarettes in general, but participants living in states where IQOS is being sold had similar preferences to cigarettes and HTPs. Conclusions People are unlikely to switch to another product/device because of the restriction of flavour or nicotine level. If non-tobacco and non-menthol flavours were banned from open-system e-cigarettes, users may switch to menthol flavour e-cigarettes. Intervention strategies should be tailored to specific groups. Data are available upon reasonable request.</p>

Prevalence & Use Patterns	Prevalence and reasons for use of Heated Tobacco Products (HTP) in Europe: an analysis of Eurobarometer data in 28 countries	A. A. Lavery; C. I. Vardavas; F. T. Filippidis	Lancet Reg Health Eur	2021-07-14	Background: Heated Tobacco Products (HTP) are a relatively new class of tobacco products, with limited data on usage patterns. We assessed the prevalence and reasons for use among persons aged ≥ 15 years in 27 European Union member states and the United Kingdom. Methods: The 2020 Eurobarometer (93.2) survey was analysed (n=28,300, aged ≥ 15). Multi-level regression analyses assessed socio-demographic differences in use while separate analyses investigated reasons for starting to use HTP. Results are presented as adjusted Odds Ratios (aOR) and weighted percentages with 95% Confidence Intervals (95%CI). Findings: Overall, 6.5% (95% CI 6.1-7.0) of participants had ever used a HTP. 1.3% (1.1-1.5%) of participants were current users of HTP, and 0.7% (0.6% to 0.9%) daily users. Current and former tobacco smokers were more likely than never tobacco smokers to use HTP (aOR 36.3 (22.9;57.5), and 7.3 (4.3;12.3) respectively. Youth aged 15-24 years of age were substantially more likely to report use, e.g. aOR for ever use=7.77 (6.56;9.21) compared to those aged ≥ 25 years. 51.3% of ever HTP users reported at least weekly concurrent use of combustible tobacco. Among those who reported ever use of HTP, but not e-cigarettes, the most popular reason for use was the perception that HTP are less harmful than smoking tobacco (39.5%), followed by use by friends (28.4%) and stopping or reducing smoking (28.2%). Interpretation: Considerable numbers of people in the EU have ever used HTP, although current and daily use remains low. Current use is more common among younger people, and current and former smokers.
Prevalence & Use Patterns	Use of heated tobacco products where their use is prohibited	Lee, J. A.; Lee, C.; Cho, H. J.	Tobacco Control	2021-07-13	INTRODUCTION: Stealth use implies using tobacco products where their use is prohibited. This paper aimed to investigate stealth use of heated tobacco products (HTPs) in terms of its prevalence and associated factors. METHODS: An online survey was conducted to investigate the use of HTPs in 7000 randomly selected participants (2300 men and 4700 women, aged 20-69 years) from the database registered with an online-research company; we used a sex ratio of 1:2, considering a low female prevalence of tobacco use in Korea. Of total participants, 574 (8.2%) were current HTP users. Among them, we identified the participants who had practised HTPs stealth use, and evaluated associated factors using multivariable Poisson regression. RESULTS: A total of 574 participants were identified as current HTP users, and 455 (79.2%) reported stealth use of HTPs during the month before the survey. Stealth use was more frequent in dual cigarette users (HTPs and electronic cigarettes (ECs); adjusted prevalence ratio (aPR) 1.33, 95% CI 1.16 to 1.52) and triple users (HTPs, ECs and combustible cigarettes; aPR 1.18, 95% CI 1.04 to 1.33), as compared with single-HTP users. Stealth use was more prevalent among participants who agreed with allowing indoor HTP use (aPR 1.18, 95% CI 1.11 to 1.26). CONCLUSION: Stealth use was prevalent among current HTP users, especially among the poly-users of tobacco products. Considering the positive relationship between an agreement with allowing indoor use of HTPs and stealth use, a campaign to promote change in attitudes of HTP users about their indoor use may be warranted to protect non-users.
Prevalence & Use Patterns	Disparities in the frequency of tobacco products use by sexual identity status	Azagha, S.; Shan, L.	Addict Behav	2021-06-29	BACKGROUND: Largely absent from the literature are studies examining differences in tobacco use frequency among sexual minority populations versus heterosexuals. The current study examined the frequency of tobacco product use (i.e., cigarette, e-cigarettes and cigars, smokeless tobacco, hookah, and heated tobacco products) among sexual minority students versus heterosexuals (straight). METHODS: Data from the 2020 National Youth Tobacco Survey (n = 14,531) were analyzed to examine the association between sexual identity (lesbian or gay, bisexual, not sure, and heterosexual or straight) and tobacco use frequency. Negative binomial regression and zero-inflated negative binomial models were used to assess the association between sexual identity and each tobacco use frequency among current and ever users. RESULTS: Current e-cigarettes users who identified as gay or lesbian used e-cigarette more frequently than heterosexual students. Multivariable count regression analysis showed that the e-cigarette use frequency in the past 30 days was significantly higher for gays or lesbians (IRR 1.45, 95% CI 1.19-1.76) compared to heterosexuals. Similarly, gay or lesbian students who were current hookah users on average reported 81% more days of hookah use (IRR, 1.81, 95% CI, 1.08-3.03). The frequency of cigarette smoking was also significantly higher among bisexual cigarette smokers. No significant differences were found in other tobacco product use frequencies between sexual minority and heterosexual youths. CONCLUSION: Sexual identity was associated with tobacco use frequency, especially for e-cigarettes and hookah. Elevated tobacco use among sexual minority groups deserves special consideration among a population group that is highly vulnerable to marketing and advertisement targeting.
Prevalence & Use Patterns	Use of Single, Dual, and Poly Tobacco Products in Korean Adolescents	Kwon, M.; Chung, S. J.; Lee, J.	Asia Pac J Public Health	2021-06-17	This study aimed to examine the prevalence of single, dual, and poly use of conventional cigarettes, e-cigarettes, and heated tobacco products among Korean adolescent smokers and identify factors related to dual and poly tobacco product use. Data from 4028 current smokers in the 2019 Korea Youth Behavior Web-based Survey were included. Single users accounted for 53.1%, followed by dual users at 24.8% and poly users at 22.1%. The factors influencing dual and poly tobacco product use included male, living in a metropolitan area, risky alcohol drinking, sexual experience, number of cigarettes smoked, secondhand smoke exposure, and easy-to-buy tobacco products. The findings suggest restricting the use of new types of tobacco products in the high-risk group are required to prevent dual and poly use. Furthermore, it is necessary to provide support like education for new tobacco products and smoking cessation, programs for secondhand smoke prevention, or rigorous marketing regulations for adolescents.

Prevalence & Use Patterns	A comparative study on changes in the use of heat-not-burn tobacco products based on whether apartment buildings have designated non-smoking areas	Hwang, J.; Cho, S. I.	Tob Prev Cessat	2021-06-12	<p>INTRODUCTION: Since 2016, multi-family housing developments in South Korea can designate public areas such as staircases, elevator, corridors, and underground parking lots as non-smoking areas if at least half of the households residing in the development agree. This study investigated whether there were changes in the use of heat-not-burn tobacco products (HnB) based on whether non-smoking areas were introduced in multi-family housing developments. METHODS: An online survey of 1200 apartment residents (599 men and 601 women) in seven metropolitan cities in South Korea was conducted from 10 to 18 October 2018. RESULTS: Among the 1200 people who completed the survey, 493 were smokers (351 men and 142 women), of whom 287 (195 men and 92 women) were currently using HnB. In total, 51.5% (n=148) of the HnB users reported that their smoking frequency inside (n=73) or outside (n=73) the apartment building increased after using HnB, whereas the smoking frequency of 27.5% (n=79) decreased and that of 20.9% (n=6) remained unchanged. Of the HnB users, 25.4% (n=73) were currently living in non-smoking apartments, of whom 39.7% reported that the smoking frequency outside the apartment building increased. On the other hand, of 214 people who did not currently reside in non-smoking apartments, 30.4% reported that the smoking frequency in the apartment increased. CONCLUSIONS: For smokers to quit smoking, the expansion of non-smoking areas should be accompanied by the facilitation of a smoke-free atmosphere and a smoking-cessation service for smokers.</p>
Prevalence & Use Patterns	Readiness for implementation of smoke-free work hours in private companies: A qualitative study of perceptions among middle managers	Lidegaard, Lærke P.; Kristiansen, Maria; Pisinger, Charlotta	Tobacco Prevention & Cessation	2021-05-25	<p>Introduction Workplaces are important settings for implementation of smoke-free environments. In this study, we follow a medical production company with 677 employees that implemented one of the most stringent tobacco policies legally possible in Denmark – smoke-free work hours – which means that employees are not allowed to smoke during work time. This study explores tobacco use restrictions during work hours regarding readiness of implementation, focusing specifically on middle managers' perceptions and considerations, as well as their perceived responsibility in enforcing these. Methods A case study is presented. Two focus groups of 10 middle managers were conducted, seven months before smoke-free work hours were implemented. The facilitators used open-ended questions, which consisted of a structured section with specific themes related to the implementation of smoke-free work hours. Focus groups were recorded, transcribed, and analyzed thematically. Results We identified five main themes: 1) Benefits of the new policy due to better health, lower sickness-related absences, increased productivity, and improved branding value; 2) Social interactions across smoking status; 3) Smoking is a private matter with ethical dimensions; 4) The role of middle managers and concerns about enforcement; and 5) Limited experience with resistance from the smoking employees. Conclusions The findings suggest that workplaces in the preparation phase should ensure that: 1) The middle managers gain training on how to talk with employees about smoking cessation; 2) The middle managers are equipped to handle the new policy and have a joint vision and understanding of why and how they should enforce it; and 3) Room is made for discussions on resistance and enforcement-related challenges as well as ethical issues.</p>
Prevalence & Use Patterns	Heated tobacco product use and its relationship to quitting combustible cigarettes in Korean adults	Kim, J.; Lee, S.; Kimm, H.; Lee, J. A.; Lee, C. M.; Cho, H. J.	PLoS One	2021-05-07	<p>OBJECTIVE: We assessed the prevalence of, and factors associated with, heated tobacco product (HTP) use and analysed the association between HTP use and quitting combustible cigarettes (CCs) in Korean adults. METHODS: We conducted an online survey with 7,000 adults (males, 2,300; females, 4,700; ages 20-69) out of 70,000 age-, sex- and provincial-distribution-matched individuals based on 2018 national population statistics. Females were oversampled because the prevalence of tobacco product use is very low among women in Korea. Chi-square tests were used for bivariate analyses, and odds ratios were assessed after adjusting for sociodemographic variables. RESULTS: The prevalence of current CC, electronic cigarette (EC), and HTP use was 24.8% (males, 40.4%; females, 9.3%), 6.8% (males, 10.1%; females, 3.4%), and 10.2% (males, 16.2%; females, 4.3%), respectively. Among the 574 current HTP users, 77 (13.4%) were HTP-only users and >80% were either dual users of HTP and CC/EC, or triple users of HTP, EC, and CC. Among the current CC users, the odds of having attempted to quit CCs in the past year were greater among EC-only users (aOR 2.92; 95% CI 1.81-4.69) and dual users of HTPs and ECs (aOR 8.42; 95% CI 4.85-14.62) than among non-HTP and non-EC users. Among 2,121 ever CC smokers, the likelihood of being a former CC smoker was 0.19 (95% CI 0.15-0.24) for HTP users, 0.29 (95% CI 0.20-0.42) for EC users, and 0.03 (95% CI 0.01-0.06) for users of both HTPs and ECs compared with non-HTP and non-EC users. CONCLUSION: EC-only use and dual use of HTPs and ECs were associated with increased attempts to quit CCs; however, HTP and EC use was associated with lower odds of CC smoking abstinence.</p>

Prevalence & Use Patterns	Student Tobacco Use Behaviours: A Qualitative Study of Alternative Tobacco	Zobena, Ajia	Rural Environment, Education, Personality	2021-05-07	Non-combustible alternative tobacco products such as tobacco-free nicotine pouches, heated tobacco, and electronic cigarettes (e-cigarettes) marketed as less harmful alternatives to cigarettes as smoking cessation aids are becoming increasingly popular among adolescents and young adults. This age group includes individuals still experimenting with and establishing tobacco use. The aim of the study is to investigate student tobacco use behaviours, particularly novel devices, and alternative products to understand how to decrease tobacco initiation and use among adolescents and young adults. In August 2020, two focus group discussions were organized to obtain information on young people's experience of alternative tobacco and nicotine product use. In each of them, high school students (aged over 18) and students took part. The participants of the focus group discussion were chosen by the "snowball" method. Cessation of smoking and replacing cigarettes with alternative tobacco and nicotine products reduce some of the harmful effects but are not harmless and nicotine addiction remains. By replacing cigarette smoking with the use of tobacco-free nicotine pouches, heated tobacco, or e-cigarettes, one form of nicotine use is being replaced by another. According to the study, young people have no understanding of nicotine addiction and the health risks of using alternative tobacco products. Today's adolescents and young adults often see consumption of tobacco and nicotine products as a mean to construct and project their unique identity.
Prevalence & Use Patterns	Association of heated tobacco product use with tobacco use cessation in a Japanese workplace: a prospective study	Kanai, M.; Kanai, O.; Tabuchi, T.; Mio, T.	Thorax	2021-04-19	We investigated how use of heated tobacco products (HTPs) affects tobacco cessation in a Japanese workplace. We offered cessation programmes for 158 tobacco users from November 2018 to April 2019 and surveyed the quitting rate in August 2019. Successful quitting was defined as stopping use of all kinds of nicotine-containing tobacco products. A Poisson regression analysis adjusted with inverse probability weighting showed that HTP users (either exclusive HTP users or dual users) were less likely than exclusive cigarette users to quit tobacco (risk ratio, 0.77; 95% CIs 0.61 to 0.97, p=0.024). The use of HTPs should not be recommended to assist in smoking cessation. Trial registration UMIN000034719.
Prevalence & Use Patterns	The prevalence of cigarette, e-cigarette and heated tobacco use among police employees in Poland: a 2020 cross-sectional survey	Jankowski, M.; Gujski, M.; Pinkas, J.; Opoczynska-Swiezewska, D.; Krzyzch-Falta, E.; Lusawa, A.; Wierzbna, W.; Raciborski, F.	Int J Occup Med Environ Health	2021-04-16	OBJECTIVES: Uninformed services such as police employees are exposed to acute and chronic stressful events at work that may lead to tobacco use. This study aimed to assess the prevalence of cigarette smoking, e-cigarette use and heated tobacco use among police employees in Poland, and to investigate personal characteristics associated with tobacco or e-cigarette use. MATERIAL AND METHODS: This cross-sectional study was carried out in June-July 2020 on a randomly selected sample of 8789 police employees from the Mazowieckie Province, Poland. RESULTS: Completed questionnaires were obtained from 5082 police employees (79.2% being police officers) with an overall response rate of 57.8%. Smoking \geq 100 cigarettes or similar amounts of other tobacco products was declared by 54.6% of the respondents, with significant differences ($p < 0.001$) between males (56.8%) and females (50.3%). Daily cigarette smoking was declared by 19.5% of the respondents, and 13.4% were occasional cigarette smokers. Daily e-cigarette use was declared by 3.1% of the respondents, and 3.2% were occasional e-cigarette users. Daily heated tobacco use was declared by 2.6% of the respondents, and 2.9% were occasional heated tobacco users. Higher odds of occasional cigarette smoking were observed among men compared to women (OR = 1.254, 95% CI: 1.009-1.558), and among the participants aged 20-29 years (OR = 7.982, 95% CI: 3.066-20.775) or 30-44 years (OR = 3.730, 95% CI: 1.44-9.599) vs. those aged \geq 60 years. Higher odds of occasional e-cigarette use were observed among the participants aged 20-29 years (OR = 4.554, 95% CI: 1.213-17.101) vs. those aged 60 years. Police employees with office-based work had lower odds of daily cigarette smoking vs. those with fieldwork (OR = 0.726, 95% CI: 0.55-0.946). Police officers had higher odds of daily heated tobacco use compared to civil workers (OR = 3.362, 95% CI: 1.325-8.534). CONCLUSIONS: The authors observed a marked proportion of police employees who declared occasional tobacco or e-cigarette use, which may indicate the common social smoking phenomenon in this occupational group.

Prevalence & Use Patterns	Epidemiology of tobacco use in Qatar: Prevalence and its associated factors	AlMulla, A.; Mamiani, R.; Cheema, S.; Maisonneuve, P.; Abdullah BaSuhai, J.; Mahmoud, G.; Kouyoumjian, S.	PLoS One	2021-04-15	Tobacco use is a serious public health concern as it causes various deleterious health problems. The aim of this study was to determine the prevalence of tobacco use and various types of tobacco used among a population-based sample of adults 18 years and above in Qatar (residents and expatriates). The study also attempted to assess tobacco use initiation age, tobacco dependency, and to identify factors associated with current tobacco use. This 2019 cross-sectional study was conducted among governmental employees and University students in Qatar using cluster sampling methodology. Study participants completed a self-administered, country-adapted summarized version of the Global Adult Tobacco Survey, 25.2% (n = 1741; N = 6904) of the surveyed sample reported current tobacco use. 21.5% (n = 1481) smoked tobacco (cigarettes, waterpipe, medwakh and cigar) concomitant with other forms of tobacco and only 1.0% (n = 69) were using other forms of tobacco (electronic cigarettes, smokeless tobacco and heat-not-burn tobacco products) and 2.7% (n = 191) did not mention the type of tobacco products used by them. Of the 1550 tobacco users, 42.8% were cigarette smokers, 20.9% waterpipe, 3.2% medwakh (Arabic traditional pipe) and 0.7% cigar. Moreover, 1.9% reported smokeless tobacco use (sweika), 2.0% electronic cigarette use, and 0.3% heat-not-burn tobacco use. The mean age for smoking initiation was 19.7±5.3 (Qataris 18.6±4.8 and non-Qataris 20.3±5.6). Using multivariable logistic regression, significant association was observed between tobacco use and gender, nationality, age, monthly income, living with a smoker, and self-rated health. This large population-based cross-sectional survey provides the first evidence for the prevalence of different types of tobacco use including medwakh smoking among adults (Qataris and non-Qataris) 18 years and above in Qatar. This can serve as a baseline for future research studies on the topic. Based on the review of previous and current tobacco survey findings, it is evident that the prevalence of tobacco use (current) in Qatar has declined suggesting that tobacco control measures implemented by the country have been effective in reducing tobacco consumption.
Prevalence & Use Patterns	Self-reported quit aids and assistance used by smokers at their most recent quit attempt: Findings from the 2020 International Tobacco Control Four Country Smoking and Vaping Survey	Gravely, S.; Cummings, K. M.; Hammond, D.; Borland, R.; McNeill, A.; East, K. A.; Loewen, R.; Martin, N.; Yong, H. H.; Li, L.; Liber, A.; Levy, D. T.; Quah, A. C. K.; Ouimet, J.; Hitchman, S. C.; Thompson, M. E.; Boudreau, C.; Fong, G. T.	Nicotine & Tobacco Research	2021-04-09	INTRODUCTION: This study retrospectively describes smoking cessation aids, cessation services, and other types of assistance used by current and ex-smokers at last quit attempt (LQA) in four high-income countries. METHODS: Data are from the Wave 3 (2020) International Tobacco Control Four Country Smoking and Vaping Survey in Australia, Canada, England, and the US. Eligible respondents were daily smokers or past-daily recent ex-smokers who made a quit attempt/quit smoking in the last 24-months, resulting in 3614 respondents. Self-reported quit aids/assistance included: nicotine vaping products (NVPs), nicotine replacement therapy (NRT), other pharmacological therapies (OPT: varenicline/bupropion/cytisine), tobacco (non-combustible: heated tobacco product/smokeless tobacco), cessation services (quitline/counseling/doctor), other cessation support (e.g., mobile apps/website/pamphlets etc.), or no aid. RESULTS: Among all respondents, at LQA, 28.8% used NRT, 28.0% used an NVP, 12.0% used OPT, 7.8% used a cessation service, 1.7% used a tobacco product, 16.5% other cessation support, and 38.6% used no aid/assistance. Slightly more than half of all smokers and ex-smokers (57.2%) reported using any type of pharmacotherapy (NRT or OPT) and/or an NVP, half used NRT and/or an NVP (49.9%), and 38.4% used any type of pharmacotherapy (NRT and/or OPT). A quarter of smokers/ex-smokers used a combination of aids. NVPs and NRT were the most prevalent types of cessation aids used in all four countries; however, NRT was more commonly used in Australia relative to NVPs, and in England, NVPs were more commonly used than NRT. The use of NVPs or NRT was more evenly distributed in Canada and the US. CONCLUSIONS: It appears that many smokers are still trying to quit unassisted, rather than utilizing cessation aids or other forms of assistance. Of those who did use assistance, NRT and NVPs were the most common method, which appears to suggest that nicotine substitution is important for smokers when trying to quit smoking.

Prevalence & Use Patterns	Trends and Patterns of Tobacco and Nicotine Product Use Among Youth in Canada, England, and the United States From 2017 to 2019	East, K. A.; Reid, J. L.; Rynard, V. L.; Hammond, D.	J Adolescent Health	2021-04-07	<p>PURPOSE: The tobacco and nicotine market is diversifying. Implications for public health will depend on trends in use, including overall use, and who is using these products. This study examined differences over time (2017-2019), across countries (Canada, England, the United States (US)), and by smoking and vaping, in use of other tobacco/nicotine products and overall use. METHODS: The study includes online repeat cross-sectional surveys of youth aged 16-19 years in Canada (N = 11,174), England (N = 11,170), US (N = 11,838) in 2017, 2018, and 2019. Past 30-day use of tobacco/nicotine products (any, cigarette, e-cigarette, other combusted [cigars/cigarillos/waterpipe], other non-combusted [smokeless tobacco/nicotine replacement therapies] were examined by country, year, and, for other combusted and non-combusted products, past 30-day cigarette smoking and vaping. Use of emerging products (IQOS, nicotine pouches) was explored in 2018-2019. RESULTS: From 2017 to 2019, use of any product increased in Canada (17.1%-23.2%, AOR = 1.07 [95% CI = 1.04-1.09]) and the US (18.0%-24.0%, AOR = 1.06 [1.04-1.09]) but not England (20.8%-21.7%, AOR = 1.01 [99-1.03]). Use of other combusted products (cigars/cigarillos/waterpipe) showed little change (Canada: 8.1%-7.8%; England: 6.3%-7.3%; US: 8.6%-8.5%; p >= 1.5%-3.2%, AOR = 1.02 [1.01-1.02]; England: 1.4%-2.6%, AOR = 1.02 [1.01-1.03]; US: 3.3%-4.9%, AOR = 1.02 [1.01-1.02]). Vaping increased in all countries (Canada: 8.4%-17.8%; England: 8.7%-12.6%; United States: 11.1%-18.5%; all p < .001). Smokers and vapers reported greater use of other combusted and non-combusted products than those who neither smoked/vaped (p < .001). Emerging product use was rare (<=1.5%). CONCLUSIONS: Youth past 30-day tobacco and nicotine product use increased from 2017 to 2019 in Canada and the United States, largely due to increases in vaping and other non-combusted products. "Other" tobacco/nicotine products were used predominantly by youth who smoked cigarettes and/or vaped.</p>
Prevalence & Use Patterns	Changes in Smoking Behavior Since the Declaration of the COVID-19 State of Emergency in Japan: A Cross-sectional Study From the Osaka Health App	Koyama, S.; Tabuchi, T.; Okawa, S.; Kadobayashi, T.; Shirai, H.; Nakatani, T.; Miyashiro, I.	J Epidemiol	2021-03-20	<p>BACKGROUND: In April 2020, the Japanese government declared a state of emergency due to the COVID-19 pandemic, and infection control measures, including requests to work from home and stay-at-home restrictions, were introduced. This study examined changes in smoking behavior during the COVID-19 state of emergency. METHODS: An online cross-sectional survey was conducted in Osaka, Japan. To assess differences in smoking behavior among 5,120 current smokers before and after the declaration of a state of emergency, prevalence ratios (PRs) for two outcomes, increased smoking and quitting smoking, were calculated using multivariable Poisson regression, adjusting for potential covariates. RESULTS: We found 32.1% increased the number of cigarettes smoked and 11.9% quit smoking. After adjustment for all variables, we found risk factors for COVID-19 (men and older age group) had both significantly higher PR for quitting smoking (men: PR 1.38; 95% confidence interval [CI], 1.17-1.62) and participants aged >=65 years: PR 2.45; 95% CI, 1.92-3.12) and significantly lower PR of increased smoking (men: PR 0.85; 95% CI, 0.78-0.93 and participants >=65 years: PR 0.38; 95% CI, 0.29-0.49). Additionally, respondents working from home or living alone had significantly higher PR for increased smoking (working from home: PR 1.29; 95% CI, 1.17-1.41 and living alone: PR 1.23; 95% CI, 1.10-1.38) and respondents who changed from cigarettes to heated tobacco products (HTPs) had significantly lower PR for quitting smoking (PR 0.150; 95% CI, 0.039-0.582). CONCLUSIONS: We suggest people who have high-risk factors for COVID-19 might change their smoking behavior for the better, while people who work from home or live alone might change their smoking behavior for the worse, during the COVID-19 state of emergency. Additionally, changing from smoking cigarettes to using HTPs makes smokers less likely to quit.</p>
Prevalence & Use Patterns	Nicotine dependence of cigarette and heated tobacco users in Japan, 2019: a cross-sectional analysis of the JASTIS Study	Lau, Y. K.; Okawa, S.; Meza, R.; Katanoda, K.; Tabuchi, T.	Tobacco Control	2021-03-19	<p>OBJECTIVES: Japan is currently the biggest market of heated tobacco products (HTPs) in the world. Little is known about nicotine dependence among HTP users. Thus, the objective was to assess the association of type of tobacco use and time-to-first-use, a marker of nicotine dependence. METHODS: A cross-sectional analysis of the 2019 data from an internet cohort study was conducted. The analytical sample consisted of 2147 current (>=1 day use in the past 30 days) HTP and/or conventional cigarette users, aged 25+ years. Marginal structural binomial regression was used to estimate nicotine dependence prevalence ratios (PRs) for each category of tobacco use (exclusive daily cigarette, exclusive HTP (>=1 day), dual HTP+daily cigarette, dual HTP+non-daily cigarette), relative to exclusive, non-daily cigarette smoking. RESULTS: Using a 5 min cut-off for time-to-first-use, the prevalence of nicotine dependence was higher among dual users of HTP and daily cigarettes (PR=1.38; 95% CI: 1.05 to 1.82) and exclusive, daily cigarette users (PR=1.48; 95% CI: 1.15 to 1.91), relative to exclusive, non-daily cigarette users. However, nicotine dependence among exclusive HTP users, and dual HTP+non-daily cigarette users, did not differ from that of exclusive, non-daily cigarette users. When using 15 and 30 min cut-offs, all types of users, including exclusive HTP, had higher levels of nicotine dependence relative to exclusive, non-daily cigarette users. CONCLUSIONS: Regardless of HTP use, daily cigarette users had higher prevalence of nicotine dependence compared with non-daily cigarette users. Exclusive HTP users had similar (or potentially higher) dependence compared with exclusive, non-daily cigarette users. Longitudinal studies are needed to interrogate the public health implications of growing HTP use worldwide.</p>

Prevalence & Use Patterns	Circumvention of COVID-19-related restrictions on tobacco sales by the e-cigarette industry in South Africa and comparative analyses of heated tobacco product vs combustible cigarette volume sales during 2018-2020	Agaku, I. T.; Egbe, C. O.; Ayo-Yusuf, O. A.	Prev Med	2021-03-18	As a public health measure against COVID-19, South Africa restricted the sale of "tobacco, e-cigarettes and related products" for 5 months, ending on August 17, 2020. We examined marketing activities related to novel tobacco products (e-cigarettes and heated tobacco products) during this restriction. Using web scraping, we accessed data for 2661 e-cigarette liquids marketed online by South African vendors in June 2020. We also analyzed heated tobacco product volume sales (kits) using retail scanner data from Nielsen Company. The 2661 e-cigarette liquids assessed online comprised cannabidiol liquids, 28.8%[767/2661], nicotine salts, 10.4%[276/2661], e-cigarette juice concentrates, 14.1%[376/2661], nicotine-free e-liquid, 4.0%[107/2661], and nicotine-containing e-liquid, 42.6%[1135/2661]. Cannabidiol liquids had the highest percentage of fruit (78.4%[601/767]) and tobacco flavors (9.4%[72/767]). During the restriction, many online e-cigarette vendors actively promoted cannabidiol liquid in lieu of regular e-liquid. Nielsen retail scanner data showed that volume of heated tobacco product sales in February 2020, preceding the restriction (7.76 million kits), were higher than in February 2019 (4.52 million kits). The restriction saw decreased sales of heated tobacco products; mean weekly heated tobacco product sales in the 6 weeks following the restriction (772,585 kits/week) were dramatically lower versus the 6 weeks preceding the restriction (2.26 million kits/week). Lifting the restriction saw a 131% spike in sales between the latter half of August 2020 (825,638 kits) and mid-September 2020 sales (1.90 million kits), even though total sales in September 2020 were half of what was observed in the preceding year (3.81 million units in September 2020, vs 6.33 million units, September 2019). The marketing of cannabidiol and other novel products by e-cigarette manufacturers and the tobacco industry may encourage youth use; close monitoring is required.
Prevalence & Use Patterns	Prevalence of heated tobacco product use in Japan: the 2020 JASTIS study	Odani, S.; Tabuchi, T.	Tobacco Control	2021-03-11	BACKGROUND: Japan is the leading market for heated tobacco products (HTPs). We assessed the latest prevalence of HTP use including novel products (Ploom S, glo sens, and Pulze). METHODS: Data were obtained from an internet-based, self-reported survey conducted during February-March 2020 with individuals aged 15-74 years in Japan (n=9044). Prevalence of current (past 30-day) HTP use and cigarette smoking was computed. Poison regression analysis was conducted to examine predictors of HTP use among current cigarette smokers (n=1478). All analyses were weighted to account for selection bias in the internet survey using a nationally representative sample of Japanese population. RESULTS: In 2020, prevalence of current HTP use and cigarette smoking was 10.9% and 25.9% in Japan, respectively. The most commonly used HTP brand was IQOS (5.7%) followed by Ploom TECH/Ploom TECH+ (5.4%) and glo (2.6%). Use of Ploom S, glo sens and Pulze was 1.6%, 0.8% and 0.6%, respectively. Among current cigarette smokers, 34.9% of those who were interested in quitting smoking and 30.5% of those who were not interested in quitting reported concurrent use of HTP, respectively (difference not significant). Cigarette smokers who reported having multiple chronic conditions (aPR=2.31), alcohol consumption (aPR=2.07), and e-cigarette use (aPR=1.88) were more likely to use an HTP compared to those who did not report such characteristics. CONCLUSIONS: HTP use remained prevalent in Japan. One in three current cigarette smokers used HTPs regardless of whether they were interested in quitting smoking. Continued surveillance is important to inform national and global tobacco control strategies.

Prevalence & Use Patterns	Patterns of non-cigarette tobacco and nicotine use among current cigarette smokers and recent quitters: Findings from the 2020 ITC Four Country Smoking and Vaping Survey	Li, L.; Borland, R.; Cummings, K. M.; Gravely, S.; Quah, A. C. K.; Fong, G. T.; Miller, C. R.; Goniewicz, M. L.; Le Grande, M.; McNeill, A.	Nicotine & Tobacco Research	2021-03-08	INTRODUCTION: This study explores patterns of use of non-cigarette tobacco and nicotine products among adult cigarette smokers and recent ex-smokers. Along with cigarette smoking status we explore differences as a function of countries with different product regulations, gender and age. METHODS: Data came from the ITC Four Country Smoking and Vaping Wave 3 Survey conducted between February-June 2020. The analytic sample consisted of 9112 current cigarette smokers (at least monthly) and 1184 recent ex-smokers (quit cigarettes \leq 2 years) from Australia, Canada, England, and the US. Respondents were asked about their cigarette smoking and current use of the following non-cigarette products: combustible tobacco (cigars, cigarillos, pipe, waterpipe); non-combustible tobacco (smokeless tobacco, and heated tobacco products (HTPs)); and non-tobacco nicotine products (nicotine vaping products (NVPs), nicotine replacement therapy (NRT), and nicotine pouches)). RESULTS: Overall, NVPs (13.7%) and NRT (10.9%) were the most reported nicotine products used, followed by cigars (5.3%), cigarillos (4.2%), and HTPs (3.5%). More than 21% current and recent ex-smokers of cigarettes reported using a non-tobacco nicotine product and non-combustible product, with respondents in England reporting the highest levels of use ($>26\%$). Males, younger respondents, and current non-daily cigarette smokers were more likely to use non-cigarette nicotine products. Notably, 11.6% of ex-cigarette smokers were using other combustible tobacco. CONCLUSION: Considerable percentages of current cigarette smokers and ex-smokers use non-cigarette nicotine products, and there are unexpectedly high levels of use of other combustible products by those recent ex-smokers of cigarettes which is concerning and has important implications for definitions of smoking cessation. IMPLICATIONS: The tobacco product market has evolved to include new products which add to existing non-cigarette tobacco products creating a much more diverse nicotine market. This brief report provides a snapshot of use of various combustible and non-combustible nicotine containing products among current cigarette smokers and recent ex-smokers in four western countries. Our results indicate that use of non-cigarette tobacco and nicotine products among these cigarette smokers and recent ex-smokers is not low, particularly among males, younger and non-daily cigarette smokers. Use of other combustible tobacco among respondents that recently quit cigarette smoking is concerning and has important implications for definitions of smoking cessation. Increased emphasis on researching non-cigarette nicotine product use is warranted in tobacco control generally and smoking cessation in particular.
Prevalence & Use Patterns Awareness & Perceptions	Heated Tobacco Products and Nicotine Pouches: A Survey of People with Experience of Smoking and/or Vaping in the UK	Brose, Leonie S.; McDermott, Máirtín S.; McNeill, Ann	Int J Environ Res Public Health	2021-08-22	Background: To gauge the public health impact of new nicotine products, information is needed on use among different populations. Aims were to assess in adults who smoked, vaped, did both or had recently stopped: (1) awareness, ever and current use of heated tobacco products (HTPs) and nicotine pouches (NP), (2) characteristics associated with ever use, (3) reasons for use of and satisfaction with HTPs, (4) characteristics associated with interest in use of HTPs. Methods: Online survey in the UK in 2019, n = 3883. (1) Proportion aware, ever and current (\geq monthly) use; (2) ever use regressed onto socio-demographics and smoking/vaping; (3) frequency of reasons for HTP use and satisfaction; (4) interest in trying HTPs regressed onto socio-demographics and smoking/vaping status. Results: Awareness was 34.8% for HTP and 15.9% for NP; current use was 3.2% and 2.7%. Being <45 years, higher education, living in London and currently both smoking and vaping were associated with ever having used the products. Curiosity was the most common reason for HTP use (79.8%) and 72.0% of ever HTP users found them at least as satisfying as smoking. Among those not currently using HTPs, 48.5% expressed any interest-lower among those aged over 65 and higher among those smoking and vaping. Conclusions: In this sample of adults with a history of nicotine use, very few currently used heated tobacco products or nicotine pouches. Satisfaction with and interest in HTPs were substantial. The low level of use is unlikely to substantially reduce the public health impact of smoking.
Prevalence & Use Patterns Awareness & Perceptions	Awareness and Use of Heat-Not-Burn Tobacco among Students of Egas Moniz—Cooperative of Higher Education	Pinto, Ana Sofia; Sousa-Tavares, Duarte; Cavaco-Silva, Patricia	Medical Sciences Forum	2021-07-21	Heated tobacco products (HTP) use a device that heats tobacco to generate an aerosol containing nicotine instead of burning it as it happens with combustion tobacco. This study aimed to determine the prevalence of heat-not-burn tobacco use among students of a Healthcare University Institution—Egas Moniz—and identify the factors that influence this use. A questionnaire adapted from the WHO Global Health Professional Students Survey was applied between May and July 2019 in the study population. Subsequently, an exploratory analysis of the data was carried out and a logistic regression was applied in order to determine the factors that influence students to consume heated tobacco.

Prevalence & Use Patterns Awareness & Perceptions	Heated tobacco product awareness, use, and perceptions in a sample of young adults in the U.S	Berg, C. J.; Romm, K. F.; Patterson, B.; Wysoha, C. N.	Nicotine & Tobacco Research	2021-04-01	<p>SIGNIFICANCE: The emergence of heated tobacco products (HTPs) in the US marks a critical time for identifying those most likely to use, particularly among young adults. METHODS: We analyzed Fall 2019 data from a longitudinal study of young adults (ages 18-34; n=2,375; Mage=24.66+/4.68) in 6 US cities, 24.1% of whom used cigarettes and 32.7% e-cigarettes. We assessed HTP awareness, use, and sources, as well as perceived risk, social acceptability, and likelihood of future use.</p> <p>RESULTS: In this sample, 9.7% (n=230) heard of HTPs, 3.5% (n=84) ever used them, and 2.4% (n=56) reported past-year purchases (tobacco shops, 66.1%; traditional retailers, 60.7%; online, 39.3%; IQOS specialty stores, 35.7%). In multivariable analyses, having heard of HTPs correlated with being older, male, and current cigarette and e-cigarette users; among those ever hearing of them, using HTPs correlated with being non-Hispanic and current cigarette and e-cigarette users. Greater likelihood of future use correlated with being older, male, sexual minority, non-Hispanic, and current cigarette and e-cigarette users.</p> <p>Among past-month users (n=78), the average number of days used was 5.48 (SD=5.54). Past-month cigarette and e-cigarette users, respectively, who tried HTPs were more likely to report consistent or more frequent use of their respective product than a year ago (p's<.001). HTPs were perceived as less addictive than cigarettes, smokeless tobacco, and e-cigarettes, and less harmful and more socially acceptable than other tobacco products except e-cigarettes and hookah. CONCLUSIONS: The relatively positive perceptions of HTPs and access via various channels underscores potential penetration of HTPs among US young adults.</p>
Prevalence & Use Patterns Awareness & Perceptions Aerosol Chemistry and Physics	Nicotine delivery and user ratings of IQOS heated tobacco system compared to cigarettes, Juul and refillable e-cigarettes	Phillips-Waller, A.; Przuji, D.; Pesola, F.; Myers Smith, K.; Hajek, P.	Nicotine & Tobacco Research	2021-05-13	<p>INTRODUCTION: Reduced-risk nicotine products are more likely to replace smoking if they match cigarettes in nicotine delivery and user satisfaction. We examined the nicotine delivery profile and user ratings of IQOS heated tobacco system and compared it with own-brand cigarettes (OBC), Juul, and refillable e-cigarettes (EC). METHODS: Participants (N=22) who were daily vapers smoking <1 cigarette per day on average, attended after overnight abstinence from smoking and vaping, to test at separate sessions OBC, IQOS, and Juul. Eight participants also tested two refillable EC using e-liquid with 20 mg/ml nicotine. At each session, a baseline blood sample was taken before participants used the product ad-lib for 5 minutes. Further samples were taken at 2, 4, 6, 8, 10 and 30 minutes. Maximum nicotine concentration (Cmax), time to Cmax (Tmax) and nicotine delivered over 30 minutes (AUC0->30) were calculated. Participants rated their urge to smoke and product characteristics. RESULTS: IQOS delivered less nicotine than OBC (AUC0->30: z=-2.73, p=0.006), and than Juul (AUC0->30: z=-3.08, p=0.002, Cmax: z=-2.65, p=0.008); and received less favourable ratings than Juul (effect on urges to smoke z=-3.23, p=0.001; speed of urge relief: z=-2.75, p=0.006; recommendation to friends: z=-2.45, p=0.014). Compared to refillable EC, IQOS delivered nicotine faster (Tmax: Z=-2.37, p=0.018), but received less favourable overall ratings (recommended to friends: Z=-2.32, p=0.021). CONCLUSION: IQOS pharmacokinetic profile suggests that it may be less effective than Juul for smoking cessation, but at least as effective as refillable e-cigarettes; although participants, who were experienced vapers rather than IQOS users, preferred refillable e-cigarettes. IMPLICATIONS: Because IQOS provided less efficient nicotine delivery than cigarettes and Juul in this sample, and also had a weaker effect on urges to smoke than Juul, it could be less helpful than Juul in assisting such dual users, and possibly smokers generally, to switch to an alternative product. IQOS, however, provided nicotine faster than refillable EC products, although participants preferred EC.</p>
Prevalence & Use Patterns Awareness & Perceptions	Heated tobacco product use, its correlates, and reasons for use among Mexican smokers	Cruz-Jimenez, L. Barrion-Gutiérrez, I. Zavala-Areñiega, L.; Arillo-Santillán, E.; Gallegos-Carrillo, K.; Rodríguez Bolaños, R.; Gravely, S.; Thrasher, J. F.	Drug and Alcohol Dependence	2022-01-11	<p>Background Little is known about the use of novel heated tobacco products (HTPs) in low- and middle-income countries. We examined among smokers in Mexico the prevalence and correlates of HTP use, as well as reasons for using HTPs. Methods We analyzed data from five surveys (November 2019-March 2021) of an open cohort of adult smokers (n=6,500), including an oversample of those who also use e-cigarettes. Mixed-effects multinomial logistic models were used to estimate associations between study variables and current HTP use or prior HTP trial relative to never trying HTPs. Results The weighted prevalence of current HTP use was 1.1%. Independent correlates of current HTP use included greater smoking frequency, intention to quit, e-cigarette use, having partners/family-members who use e-cigarettes or HTPs, and exposure to HTP information inside/outside tobacco shops. Having partners/family members who smoke and not knowing about the harm of HTPs relative to cigarettes were associated with lower likelihood of current HTP use. Having tried HTPs was more likely among smokers with partners/family who use e-cigarettes or HTPs and exposure to HTP information outside shops and on newspapers/magazines. Among current users, the top two reasons for using HTPs were greater social acceptability (50.2%) and lower perceived harm (40.0%) relative to cigarettes. Conclusions: Uptake of HTPs appears relatively low among Mexican smokers, and correlates of use are similar to those for e-cigarette use. Further research is needed to determine if HTPs use promotes or impedes smoking cessation, given current HTP users are also likely to use various nicotine products.</p>

Prevalence & Use Patterns Health Outcomes	Characteristics of and reasons for patients with chronic obstructive pulmonary disease to continue smoking, quit smoking, and switch to heated tobacco products	Hirai, K.; Tanaka, A.; Homma, T.; Kawahara, T.; Oda, N.; Mikuni, H.; Uchida, Y.; Saito, H.; Fukuda, Y.; Fujiwara, A.; Sato, Y.; Uno, T.; Inoue, H.; Ohta, S.; Yamaguchi, F.; Suzuki, S.; Ohnishi, T.; Sagara, H.	Tob Induc Dis	2021-11-03	INTRODUCTION: Smoking is the leading cause of chronic obstructive pulmonary disease (COPD), and smoking cessation is the most effective treatment for patients with COPD. However, few studies have investigated the continuation/cessation of smoking and heated tobacco products (HTP) in patients with COPD. The objective of this study was to examine the characteristics of patients with COPD, those who are current smokers and those who switched from cigarettes to HTP, and to examine the reason for the continuation or cessation of smoking. METHODS: This multicenter, cross-sectional study included 411 outpatients with COPD. Data for this study were part of a study conducted for a comprehensive evaluation of the smoking status and clinical factors in patients with COPD and their families. RESULTS: Logistic regression analysis revealed that a younger age, longer duration of smoking, fewer daily cigarettes, and lower modified Medical Research Council (mMRC) dyspnea score, and a lower Simplified Nutritional Appetite Questionnaire (SNAQ) score for appetite, were characteristics of current smokers (age OR=0.94; duration of smoking OR=1.07; number of cigarettes per day OR=0.94; mMRC OR=0.68; SNAQ OR=0.83; p<0.05). The logistic regression analysis model showed that a younger age and higher education level were associated with the use of HTP (age OR=0.83; higher education level OR=4.63; p<0.05). Many of the current smokers displayed smoking behaviors that are not guaranteed to be safe, such as reducing smoking or switching to lighter cigarettes or HTP. CONCLUSIONS: Patients with COPD who continue smoking tended to have low appetite as well as smoking behaviors that are not guaranteed to be safe. Physicians should provide appropriate guidance to these patients on smoking cessation.
Prevalence & Use Patterns	Effect of IQOS introduction on Philip Morris International cigarette sales in Spain: a Logarithmic Mean Divisa Index decomposition approach	Golpe, A. A.; Martín-Alvarez, J. M.; Galiano, A.; Asensio, E.	Gac Sanit	2022-02-23	OBJECTIVE: Philip Morris International, has already introduced its heated tobacco product, IQOS, in many countries and marketed it on the grounds that it is a less harmful alternative to health. The company claims that its intention is for its brand's traditional cigarette smokers to replace these with IQOS has rarely been independently tested. METHOD: Using time series data from September 2016 to June 2020, we analyze whether Heets sales have been accompanied by an improvement in the position of Philip Morris International in the market or if they have merely replaced lost sales of the rest of the brands sold by that tobacco company. RESULTS: Sales of traditional cigarettes of all the brands marketed by PMI have been replaced by IQOS since the introduction of this heated tobacco product in Spain. Almost all of the variations observed in IQOS sales are due to the positioning of this product as a substitute for the range of traditional cigarettes marketed by Philip Morris International. CONCLUSIONS: As there is still no consensus that HTPs are explicitly less harmful to health, health authorities must control messages suggesting improved health outcomes thanks to HTP usage when compared to traditional cigarettes. Such messages could generate a false sense of security and lead to an increase in the consumption of tobacco. In Spain Heets in a category that has a lower tax burden than the category of traditional cigarettes. Tax authorities must consider this migration and the impact this may have on tax collection.
Product Design	Influence of the Color and Logo Position of HNB Products on User Experience Based on Eye Tracking	Sun, Lili; Hu, Lizhong; Xiang, Lei; Wang, Xiuling; Wu, Lei; Cao, Huai	Lecture Notes in Computer Science	2021-07-03	This paper reports on two experimental psychology studies on influence of the color and logo position in the field of HNB product, which used to measure the user experience. Based on the eye tracking method, we conducted two experimental studies. The independent variables were the different colors and logo position of HNB products. The dependent variables include first fixation time, first fixation duration, total fixation duration, second fixation time and subjective evaluation. A total of 68 people participated in the experiment. The main findings of this study were as follows: (1) In terms of HNB color preference, black and white were the most acceptable colors. (2) In the selection of logo position, the lower right and upper right position were more popular with users. (3) The first fixation time and the second fixation time can reflect the most real inner experience. In addition, this study provides a method for reference value with consumer decision-making for the industrial design optimization in relate consumer electronic product fields.
Product Design	Cross-Cultural Research on Consumer Decision Making of HNB Product Modeling Based on Eye Tracking	Hu, Lizhong; Sun, Lili; Zha, Yong; Chen, Min; Wu, Lei; Cao, Huai	Lecture Notes in Computer Science	2021-07-03	This paper reports on a cross-cultural study on modeling styles in different countries in the field of HNB product, which is used to measure the consumer decision-making. Based on the eye tracking method, we conducted an experiment study. The independent variables were the HNB product in international brand and domestic brand. The dependent variables include the pupil diameter and subjective evaluation. A total of 68 subjects participated in the experiment. The main findings of this study were as follows. (1) Based on the heat map analysis, the logo, decorative ribbon and indicator light are the main of consumer's visual attention areas. (2) The mean pupil diameter of international brand was higher than domestic brands. However, the difference between the maximum and minimum pupil diameter in domestic brands was higher than international brand. (3) From the perspective of subjective evaluation, the international brand has the higher respondents score than domestic brands. In addition, this study provides a method for reference value with consumer decision-making for the design in related consumer electronic product fields.