Impact of the use of heated tobacco products (HTP) on indoor air quality

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Abstract: **Introduction**: Heated tobacco products (HTP) have gained popularity in recent years. However, questions have been raised about the damage they cause to health, especially the impacts resulting from exposure to their emissions. This study aims to evaluate the impact of the use of HTPs indoors on air quality and/or the health of passively exposed people, through a systematic review of original studies. **Methods**: A bibliographic search was carried out in the Medical Literature Analysis and Retrieval System (MEDLINE), Excerpta Medica Database (EMBASE), Latin American and Caribbean Health Sciences (LILACS) and SCOPUS databases. **Results**: 21 studies were selected and included in this review. The results indicate that heated tobacco products are a source of environmental pollution due to the emission of particulate matter. The stages of selection, data extraction and risk of bias assessment of the studies were performed in pairs, independently, and disagreements were resolved by consensus. **Conclusion**: Heated tobacco products produce emissions that can expose people to toxic substances emitted indoors, just like other tobacco products.

➤ **Keywords:** Electronic Nicotine Delivery Systems. Indoor Air Pollution. Tobacco Smoke Pollution. Systematic review.

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Introduction

Smoking is a chronic and epidemic disease caused by nicotine addiction present in tobacco products. It is stated in the 11th International Classification of Diseases (ICD-11) for mortality and morbidity statistics, in the group "mental, behavioral or neurodevelopmental disorders", in "disorders caused by nicotine use" (WHO, 2022).

The World Health Organization (WHO) states that tobacco kills more than 8 million people per year. More than 7 million of these deaths result from direct use of the product, while close to 1.2 thousand are the result of non-smokers exposed to secondhand smoke. WHO affirms, furthermore, that about 80% of the world's two more than one billion smokers live in low-income and medium-income countries, where the weight of tobacco-related illnesses and deaths is higher (WHO, 2019).

In accordance with the Resolution of the Collegiate Directorate (RDC) nº 46/2009, of the Brazilian Health Regulatory Agency (ANVISA), the Electronic Devices to Smoking (EDS) mimic the act of smoking and encompass a series of products with various functionalities, various formats, and flavors, as well as different ways of generating emissions. Considering the function, the content and the emissions, they are smoking products, which may or may not be derived from tobacco (ANVISA, 2009).

EDS can be divided into three groups: products that use a liquid matrix, such as electronic cigarettes; those that use a solid matrix, such as heated tobacco products; and hybrids, that we can use both matrixes. In a short time, new models will emerge, with great technological appeal and modern design, such as fourth-generation electronic cigarettes, which use nicotine cartridges (PODs), such as Juul, and the renaissance of heated tobacco products (HTP), such as IQOS and Glo. Likewise, the design of electronic cigarette atomizing units is in constant evolution (WILLIAMS; TALBOT, 2019; BERTONI; SZKLO, 2021; TOBACCO TACTICS, 2023).

However, this technology is calling attention, especially among young people and never smokers. This fact can be observed in the rapidly increasing prevalence of e-cigarette use in the United States, for example. Scholars have stated that, in 2011, the prevalence of use among high school students was 1.5%, and in 2014 it jumped to 13.4%. Alert remains that, in 2019, the prevalence of conventional cigarettes has surpassed (27.5% versus 5.8%) (BERTONI; SZKLO, 2021).

Among EDS, HTPs require the use of an electronic device to heat a tobacco rod or capsule to a temperature high enough to generate a nicotine aerosol (mostly) to be inhaled. HTPs systems are fully integrated, so that the heating device and the rods or capsules of each must be used together. Usually, the systems are proprietary for each manufacturer, since the components are not interchangeable. Furthermore, various types of refills are used with additives that facilitate experimentation, thus leaving the products more palatable (GLANTZ, 2018; ACTBr, 2019; STOP, 2022).

By 2021, HTPs will represent 3% of the global market for tobacco products; All in all, we have seen a significant growth in sales in recent years. Regarding the estimated participation in the global HTPs market, Philip Morris International (PMI) has 71.5% of the market with the IQOS brand, followed by British American Tobacco (BAT), with 15.3%, with its Glo brand, and Japan Tobacco International (JTI), with 4.3%, with the Ploom brand. Korean Tobacco & Ginseng (KTG) owns the brand Lil and owns 2.9% of the market (in markets outside of South Korea, this brand is sold under license by PMI). There are still other brands marketed in Europe by Imperial Brands, in Asia by China National Tobacco, such as Pulse and Mok, among others (STOP, 2022).

Still, it should be noted that heated tobacco products are not a novelty. The tobacco industry developed technology for two tobacco products aged in the 1960s, being launched on the market in the late 1980s, but with no commercial return. Likewise, these products, despite having updated their technologies, basically present the same concept of two previously launched products, relaunched as novelty and presenting allegations, for example, of being a "cleaner" tobacco product (ELIAS *et al.*, 2018).

In Italy, the sales of two HTPs jumped from 11 tons per year in 2015, to 519 tons in 2017 (LIU *et al.*, 2018), where the goal of two HTP users (45%) and more than two people interested in products had never smoked traditional cigarettes (LIU *et al.*, 2019).

Studies attest that these products emit particulate matter and dozens of toxic substances. Among the measures indicated by the WHO to reverse the tobacco epidemic, the need to implement tobacco-free environments stands out. This measure contributed to making smokers stop smoking and contributed to avoiding passive exposure to product emissions (WHO, 2023).

In Brazil, the use of EDS in collective indoor environments is banned. On December 14, 2011, Law No. 12,546 was approved, prohibiting smoking indoors throughout the country. The Art. 2 of Law No. 9,294, of July 15, 1996, came into force with the following wording: "It is prohibited to use cigars, cigarettes, pipes or any other smoking product, derived or not from tobacco, in indoor, private or public collective premises." Include as indoor collective environments: public offices, hospitals and health posts, classrooms, libraries, collective work venues and theaters and cinemas (BRASIL, 2011).

Thus, this study aims to analyze the effects of aerosol/vapor/smoke/aerodispersoids from HTP in the indoor quality of air, through a systematic process of review of the scientific literature.[1]

Methodology

This is a systematic review of literature in the databases Medical Literature Analysis and Retrieval System (MEDLINE), Excerpta Medica Database (EMBASE), Latin American and Caribbean Literature in Health Sciences (LILACS) and Scopus. The structured PECO acronym refers to: P (population): people exposed to HTP aerosol/smoke in indoor environments; E (exposition): aerosol/smoke emitted by HTPs; C (control or comparer): internal free air of aerosol/smoke of HTPs; O (outcome): internal air pollution and/or impacts on the health of passively exposed people. For each component of the PECO strategy, a set of descriptors and free terms was selected, extracted from two controlled vocabularies Descriptors of Health Sciences (DeCS), Medical Subject Headings (MeSH) and Embase Subject Headings (Emtree). Based on these components, the following research question was presented: what is the impact of the use of HTPs in internal/indoor environments on the quality of the health of passively exposed people?

Development of search strategies

The search strategies were elaborated (Chart 1) on May 10, 2022, correlating search terms for each PECO component, by means of two Boolean operators AND and OR. No data, language and/or study design filters are applied, so as not to limit the results, and all the strategies will follow the recommendations of the Peer Review of Electronic Search Strategies (PRESS).

Chart 1. Search strategies

	SEARCH STRATEGIES	NUMBER OF ARTICLES
PUBMED	((Heat-Not-Burn[tiab] OR Heated Tobacco[tiab] OR Heating Tobacco[tiab] OR Tobacco Heating Product*[tiab] OR HNB[tiab] OR HTP[tiab] OR IQOS[tiab] OR Ploom[tiab] OR Glo[tiab] OR THS2.2[tiab] OR THP1.0[tiab]) AND (Environmental Pollution[mj] OR Environment Pollution[tiab] OR Environmental Pollution[tiab] OR Air Pollution, Indoor[mj] OR Indoor Air Pollution[tiab] OR Air Quality[tiab] OR Tobacco Smoke Pollution[mj] OR Secondhand[tiab] OR Passive Smok*[tiab] OR Passive Tobacco[tiab] OR Passive Exposure*[tiab] OR Involuntary Smok*[tiab] OR Involuntary Tobacco[tiab] OR Involuntary Exposure*[tiab] OR Exposure[ti] OR Workplace*[tiab] OR Smoke-free[tiab] OR Indoor[tiab] OR Home*[ti])) NOT (GLOBOSA[ti] OR Gene*[ti] OR Ground-Level Ozone[ti] OR 5-HTP[tiab] OR 5-HT[tiab])	144
EMBASE	('heated tobacco':ti,ab OR 'heat-not-burn':ti,ab OR 'heating tobacco':ti,ab OR 'tobacco heating product*':ti,ab OR 'iqos':ti,ab OR 'hnb':ti,ab OR 'ploom':ti,ab OR 'glo':ti,ab OR 'ths2.2':ti,ab OR 'thp1.0':ti,ab) AND ('environment pollution':ti,ab OR 'environmental pollution':ti,ab OR 'indoor environment'/exp OR 'indoor environment':ti,ab OR 'indoor air pollution'/exp OR 'air pollution':ti,ab OR 'indoor air pollution':ti,ab OR 'air quality'/exp OR 'air quality':ti,ab OR 'passive smoking'/exp OR 'environmental tobacco smoke':ti,ab OR 'environmental tobacco smoking':ti,ab OR 'passive cigarette smoke':ti,ab OR 'passive cigarette smoking':ti,ab OR 'passive smok*':ti,ab OR 'passive tobacco smoke':ti,ab OR 'passive tobacco smoking':ti,ab OR 'secondhand':ti,ab OR 'tobacco smoke pollution':ti,ab OR 'passive exposure*':ti,ab OR 'involuntary smok*':ti,ab OR 'involuntary tobacco':ti,ab OR 'involuntary exposure*':ti,ab OR 'workplace*':ti,ab OR 'smoke free':ti,ab OR indoor:ti OR home:ti) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)	33
SCOPUS	(TITLE-ABS-KEY("Heat-Not-Burn" OR "Heated Tobacco" OR "Heating Tobacco" OR "Tobacco Heating Products" OR hnb OR htp OR iqos OR "Ploom" OR "Glo" OR ths2.2 OR thp1.0) AND TITLE("Environment Pollution" OR "Environmental Pollution" OR "Indoor Air Pollution" OR "Indoor Air Pollution" OR "Air Quality" OR secondhand OR "Passive Smoke" OR "Passive Smoking" OR "Passive Tobacco" OR "Passive Exposure" OR "Involuntary Smoke" OR "Involuntary Smoking" OR "Involuntary Tobacco" OR "Involuntary Exposure" OR indoor OR home* OR "Smoke-free") AND NOT TITLE(homeless* OR globosa OR 5-htp OR 5-ht OR "Ground-Level Ozone" OR Gene* OR Homeostasis))	63
LILACS	tw:("Heat-Not-Burn" OR "Heat-not-Burn Tobacco Products" OR "Heated Tobacco" OR "Heating Tobacco" OR "Tobacco Heating Products" OR "tabaco aquecido" OR "tabaco calentado" OR IQOS OR Ploom) AND (db:("LILACS"))	5

Source: The authors, 2022.

Additionally, the references were consulted in two studies selected for reading the full text, being recovered six references that had not been considered in the initial search. The retrieved references are exported to the EndNote Online reference manager, to exclude duplicates between the databases. After this process, a file was generated, in RIS format, to export and make it possible to select two studies in Rayyan software.

Studies selection

The selection of studies was done independently by two reviewers and occurred in three stages: (1) reading of the title and abstract, to include studies that answered the research question; (2) reading in full two studies selected in the previous phase; (3) analyze the references of the two studies included to capture and include possible studies not recovered by searching the databases. Any discrepancies during the stages are resolved by consensus between the reviewers or by reading it by a third reviewer.

Eligibility criteria

As inclusion criteria, the original studies that attend the established PECO are selected. Exclusion criteria were in vitro studies, studies with animals, reviews, abstracts from congresses, editorials, letter to the editor and theoretical essays.

Data extraction

For the analysis and subsequent synthesis of two recovered documents, a data extraction sheet was used, prepared in Microsoft Excel, with the following information: author, year, study title, aim, study destination; description of the place where the experiment was carried out; description of the experiment; waste measures; results; conflict of interest; and source of financing. The plan was reviewed by two reviewers independently and any discrepancies were resolved by consensus. The information collected in this extraction phase is stored in an electronic data bank created in the Microsoft Excel for Windows® version 2019 program.

Classification of electronic cigarettes, heated tobacco and hybrid products

There are different models of electronic smoking devices on the market. To perform an analysis of two studies, it was necessary to differentiate them. The following table presents a summary of the main characteristics of these products.

Chart 2. Characteristics of electronic cigarettes, heated tobacco and hybrid products

DEFs	Electronic cigarettes	Heated tobacco	Hybrid products
Mechanism and components	Device in which a battery heats a liquid solution (e-liquids), with or without nicotine (in different concentrations) and produces an aerosol that the user inhales. Electronic cigarettes usually contain: water, flavoring, nicotine, propylene glycol and glycerin.	Rechargeable electronic warming device that uses processed tobacco sticks (cigarette) or capsules.	In this case, there are two types of devices: those that can use both solid and liquid matrices. There is even a type of product that uses a stick like those of HTPs along with a chamber with nicotine-free e-liquids to generate vapor similar to electronic cigarettes.
Tobacco	It uses a liquid tobacco extract.	Yes, they heat Tobacco.	Yes. There are hybrid products that may use liquid extracts, tobacco, cannabis, herbs or other plants.
Nicotine	Electronic Nicotine Delivery Systems with and without nicotine. There are "e-liquids" with or without nicotine.	Yes	There are "e-liquids" that may or may not contain nicotine. There are products that use tobacco. Other types of plants can also be used in these products.

Source: The authors, 2022.

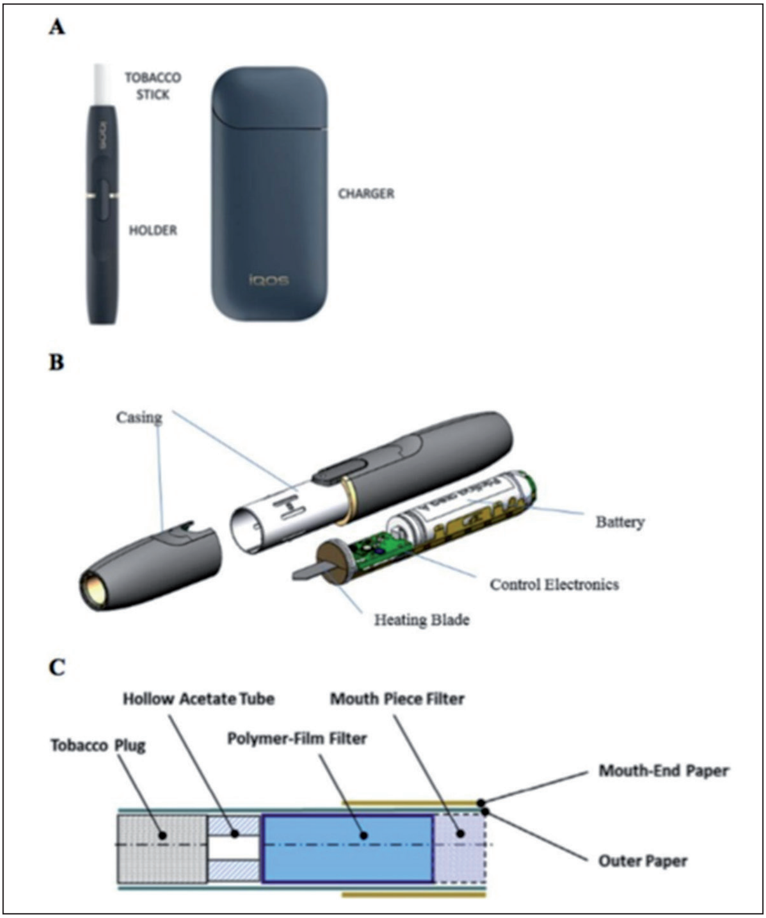
It is important to note that, in addition to two common HTPs, there are still other hybrid products. These are models of portable vaporizers for double use. They can vaporize chopped tobacco, dry herbs and even Cannabis, i.e., they can be used by their owners for different purposes. Furthermore, some manufacturers also call for hybrid products, heated tobacco products that present a kind of chamber with propylene glycol or another substance to generate vapor in a similar way to electronic cigarettes. For the purposes of this article, these products are considered HTP.

Results

There are different types of electronic devices, on the market, that heat tobacco and exclusive accessories suitable for the model marketed by each tobacco company. Likewise, there are also various denominations for the tobacco refill used in HTPs, such as tobacco stick, sheets, neostiks, heatsticks and others, depending on the model and manufacturer of the product.

The following image shows the structure of a product that burns or tobacco. It is possible to observe the operating mechanism of the device, as well as the tobacco stick and heatstick suitable for it.

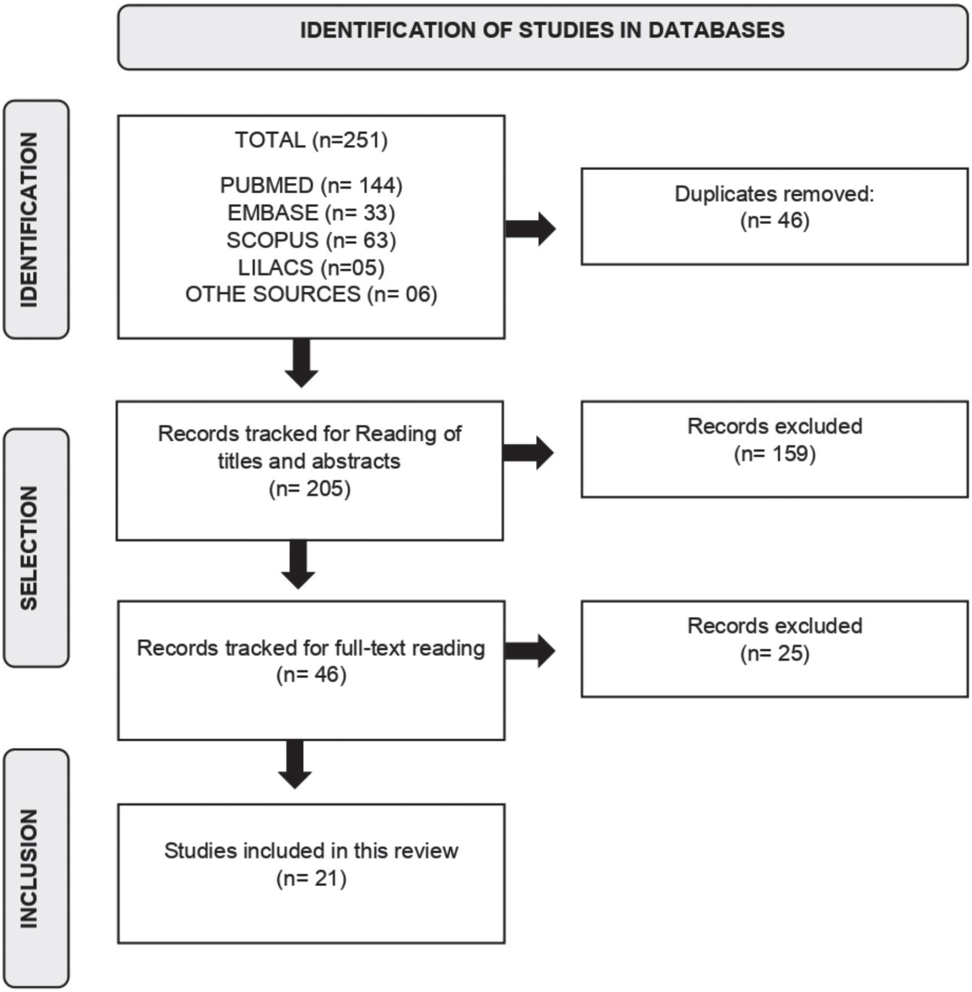
Figure 1. Structure of the IQOS device – heated tobacco



Subtitle: (A) The charger, support and HeetStick from Philip Morris International IQOS (tobacco stick). (B) Schematic drawing of the holder. (C) Schematic of the HeetStick tobacco stick.
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6252052/

We identified 251 records and removed 46 duplicates, subtracting 205 records for title and abstract reading. Once the eligibility criteria were applied, two reviewers selected 46 studies for full reading. In the end, 21 studies were included in the report. The systematization of the search, identification and selection phases of the two studies is represented through the Prisma Flowchart (Figure 2).

Figure 2. PRISMA flowchart of the selection process of two items



Source: Adapted from Prisma Flow Diagram, 2020.

The studies identified are quite heterogeneous, especially in terms of methodology, products used in the experiments and substances tested not to be rejected. Of the 21 selected studies, a third, i.e., seven will have some type of financing from the tobacco industry. For this reason, the results of the study on the impact of the use of HTPs on the quality of air in indoor environments are organized in three categories: Studies financed by the tobacco industry; Independent studies; and Independent studies of impacts on health. Such categorization was necessary due to the historical, already reported, investment in the tobacco industry in studies and dissemination, both in scientific journals, with results that favor them, and which are often used to disqualify evidence from scientific studies without conflicts of interest (VELICER *et al.*, 2018).

Brazilian legislation prohibits the use of smoking tobacco products of any kind indoors or partially indoors, and these products, to be released for consumption, must prove the absence of impacts on the quality of the environment, and not in comparison of their emissions with conventional cigarettes. Thus, in this study only the results are presented on the products of heated tobacco, even if the original studies made such comparisons. We also took into consideration the possibility that these comparisons, depending on the context, could lead to wrong perceptions, interpretations, and conclusions in relation to the risks of these products.

In the research question of this study, this option is clear when it is made explicit that the comparison will be made with the basal level or the background level, that is, without the use of any product.

Category I: Tobacco industry-funded studies

Enomoto *et al.* (2022) evaluated the impact of the use of heated tobacco products on the air quality of environments simulating residences and restaurants. They point out that there was an increase in total volatile organic compounds, glycerol, tobacco-specific nitrosamines, acetaldehyde, propionaldehyde, n-butyraldehyde, benzene, pyridine, and propylene glycol, in relation to the environment without the use of such products.

In a study by Foster *et al.* (2018) in which exposure was simulated in three types of environments – residence, office and hospitality –, an increase in formaldehyde (in the residence), acetaldehyde (in the 3 environments), nicotine and particulate matter of the three investigated diameters (in the office and hospitality) and in the total number of particles (in the 3 environments) was observed.

Kauneliene *et al.* (2019) simulated the variation in air quality after using a heated tobacco product in a non-operating nightclub and during operation, concluding that the use of IQOS brought a significant increase in the concentration of the number of particulate matter in relation to the background environment (control). They also pointed out that the simultaneous use of IQOS may be associated with an increase in nicotine, acetaldehyde, and particulate matter.

Meišutovič-Akhtarieva *et al.* (2019) found that use of heated tobacco product in a simulated indoor environment resulted in increased nicotine, acetaldehyde, particulate matter compared to "background" and particle concentration.

Mitova *et al.* (2016) conducted a study simulating three environments: office, home, and hospitality. According to the findings, acetaldehyde and nicotine concentrations were increased after using heated tobacco product in the three sites. In Mitova *et al.* (2019), it was reported that after investigating the use of heated tobacco in a simulated environment of a residence, an increase in nicotine, acetaldehyde and glycerin was observed. And finally, Mitova *et al.* (2021), this time using simulated home, shop, and restaurant environments, found that the use of heated tobacco increased levels of nicotine, acetaldehyde, glycerine, and (if menthol products are used) menthol relative to background levels, with a corresponding increase in total volatile organic compound values.

Category II: Independent studies

Camalleri *et al.* (2020) carried out an experiment in a university library, in which they evaluated pollution, in an open environment, resulting from the use of tobacco products, including heated tobacco; and the contribution of the use of tobacco products, smoked outside, on the air quality of a nearby indoor location. They found that, in the external area, there was an increase in particulate matter. The authors also point to a worsening of the indoor air quality, due to the proximity of the use of these products in the nearby outdoor area. They suggest that there should be legislation and measures to protect passive smoking in external areas as well.

Cancelada *et al.* (2019) identified and quantified chemicals released during the use of IQOS in a chamber – an experimental environment. They found more than 100 volatile compounds, of which 33 were identified and quantified. According to a prediction model, in an environment of $48m^2$, air change rate of 1.54h-1 and a maximum of 14 heatsticks consumed in 3h, the concentration of formaldehyde would be 0.14µgm-3, of acetaldehyde 6.6µgm-3 and of acrolein 0.19µgm-3. Prediction results suggest that indoor air quality can be affected in both homes and public spaces, with non-users being exposed to potentially harmful concentrations of carbonyls and volatile organic compounds.

Assessing the impact of the use of heated tobacco (Ploomtech, Glo and IQOS) in two environments simulating a shower box and a room, Hirano *et al.* (2020) found that the maximum concentrations of nicotine, in the shower box test, varied between the different types of devices studied.

Khalaf *et al.* (2020) analyzed the emission of particulate matter after the use of IQOS in a test room, finding an increase in concentration for all three investigated diameters (≤1 µm, ≤2.5 µm, ≤10 µm).

Peruzzi *et al.* (2020) compared particulate matter emissions from the use of different tobacco products indoors. There was an increase in particulate matter of all diameters and also in total particulate matter during use of all heated tobacco products compared to baseline (before use) levels. Comparisons between all types of heated tobacco products investigated demonstrated that different flavors/additives impact indoor particulate matter emissions, both due to smoke characteristics and different usage patterns (e.g., frequency, depth, nasal or oral exhalation).

Protano *et al.* (2020) also evaluated the emission of particulate matter from the use of different IQOS, Glo and Juul sticks and capsules. All electronic alternatives determined a worsening of PM1 concentration in an indoor environment, with median values varying between devices. The high variability of particle loads was attributed to both the type of stick used and the different way users smoked during the experiments. The results showed that all tested products worsen indoor air quality during use.

In a study published in 2017, Protano *et al.* evaluated the emission of submicron particles from the use of different tobacco products, including heated tobacco. The study demonstrated an increase in the concentration of particles in the air after using IQOS. They also estimated the accumulation of particle doses in the respiratory system after using IQOS, pointing out that this accumulation would be greater in infants and children. And yet, that the highest percentage of particles would be deposited in the alveolar region, where they could induce inflammation and, once accessing the bloodstream, reach other organs. The authors emphasized that even if an individual smokes alone in an indoor environment, the environment remains polluted and contributes to the exposure of others who live with the smoker. This is particularly worrying for infants and children, who, in addition to being more susceptible than adults to adverse effects, are the age group in the study that absorbed the greatest amounts of submicron particles per kilogram of body weight, of which a large number of very small particles can easily reach the alveolar region.

Protano *et al.* (2016) evaluated profiles of passive exposure to submicromic particles emitted by heated tobacco products (IQOS) and found that, after their use, submicromic particles are released that can be deposited in the airways of a passively exposed subject. In all the experiments carried out, approximately half of the deposited submicron particles were so small that they could reach the alveolar region of passively exposed subjects; an hour spent indoors in which a single IQOS is smoked determines exposure to submicron particles equivalent to that which would occur by spending 10 minutes in a high traffic area.

Ruprecht *et al.* (2017) found, in their experiment based on the analysis of the smoke emitted by the IQOS into the environment, that the emission of organic matter particles from these devices is significantly different depending on the organic compound. In the smoke from this device, certain n-alkanes, organic acids such as suberic acid, azelaic acid and n-alkanoic acids with carbon numbers between 10 and 19, as well as levoglucosan, were detected, which were emitted at substantial levels from the IQOS. Another important finding is the presence of carcinogenic aldehyde compounds, including formaldehyde, acetaldehyde and acrolein, in IQOS smoke.

Savdie *et al.* (2020) investigated the effect of different tobacco products on air quality in a home and a car, assessing the concentrations of particulate matter, black carbon, carbon monoxide, and carbon dioxide. There was an increase in all evaluated substances, in relation to the control, after the use of the heated tobacco product.

In yet another study that investigated pollution in cars (SCHOBER *et al.*, 2019), the authors state that smoking inside cars is worrying because the concentrations of potentially harmful substances can be very high in such small spaces.

Yu *et al.* (2022) concluded that various types of volatile organic compounds, aldehydes, particulate matter and nanoparticles were produced from the use of heated tobacco products in an experimental indoor environment. The results indicate that such substances affect indoor air quality.

Category III: Independent studies on health impacts

Two independent studies investigated, albeit through simulation or a preliminary exploratory analysis, the possible effects on health from passive exposure to emissions from heated tobacco products. Hirano and Takei (2020) calculated that the excess risk of cancer for individuals exposed to smoke from heated tobacco products would be 2.7x10-6. Imura and Tabuchi (2021), through a cross-sectional study, found that 39.5% of those exposed to smoke from heated tobacco products had some subjective symptom. Non-smoking tobacco product users had the following symptoms when exposed to heated tobacco product aerosol: sore throat (23%), cough (22.5%), asthma attack (10.9%), chest pain (11.8%), eye pain (19.3%), nausea (31.9%), headache (17.7%). Based on these findings, they suggest that respiratory and cardiovascular abnormalities may be related to passive exposure to HTP aerosol.

Synthesis matrix of selected studies

Chart 3 presents the synthesis matrix of selected studies grouped according to author/year, experiment description, evaluated compounds/substances and results.

Chart 3. Synthesis matrix of selected studies

Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Cammalleri *et al.* (2020)	The indoor air (no smoking) and outdoor air (where people usually smoke) were measured simultaneously for 10 hours in a university library to assess particulate matter (PM) emitted by traditional cigarettes, hand-rolled cigarettes, electronic cigarettes and heated tobacco products. (IQOS, JUUL, GLO).	Air pollution measured by PM of different diameters (≤ 10, 4, 2.5, 1 μm = PM*10, PM4, PM2.5, PM1) indoors and outdoors. Unit of measurement = μg m-3.	Increase in particulate matter (PM1) with the use of Glo (check the accuracy of the registration symbol) in an outdoor area: Before use: average PM1 level (in μg m-3) of 35.85 (SD: 1.09); After use: mean PM1 level (in μg m-3) of 106.30 (SD: 191.92). There was no significant difference after using IQOS. PM1 peaks in the external environment about 4 and 34 times greater than the baseline level, respectively for the use of IQOS and GLO.	No

continua...

Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Cancelada *et al.* (2019)	IQOS and 3 types of heatsticks were consumed by one machine in puff volumes of 55mL, puff durations of 2s (1650 cm3 min-1) and puff intervals of 30s. The heating blade was powered for a period of 6min, generating a total of 12 individual puffs. Temperature measurements were taken every 10-20s during the 6min of operation and repeated 3x to assess reproducibility.	More than 100 volatile compounds were detected in the emission of heated tobacco products, of which 33 were identified and quantified. Air pollution measured by µg of identified volatile compound.	Nitrogen compounds: nicotine (<0.09), pyridine (0.32 to 0.62); , 3-ethenylpyridine (0.03 to 0.05), pyrrole (0.26 to 0.42), N-methylformamide (<0.04), acrylonitrile (<0.03), 3-ethylpyridine (<0. 04), 2,3-dimethylpyridine (<0.04); Carbonyls: acetaldehyde (18.6 to 24.2), diacetyl (1.3 to 1.4), butanal (2.3 to 3), acetone (3.2 to 4.3), propanal (1.0 to 1, 2), benzaldehyde (0.4 to 1.5), methacrolein (0.8 to 1.1), acrolein (0.6 to 0.8), crotonaldehyde (0.3 to 0.4), formaldehyde (0. .7 to 1.0), 2-butanone (1.0 to 1.5), m-tolualdehyde (0.40 to 0.52), hexaldehyde (0.08 to 0.2); Other oxygenated compounds: acetol (hydroxyacetone) (1.3 to 3.4), furfural (1.0 to 1.7), glycidol (0.1 to 0.2), 2-furanmethanol (0.5 to 0.8); Terpenoids: isoprene (0.47 to 0.8), menthol (10.5); and Aromatic compounds: phenol (0.09 to 0.51), p-cresol +m-cresol (<0.07), o-cresol (<0.04), benzene (0.08 to 0.12), quinoline (<0.04), naphthalene (<0.02 to 0.024). Mean daily intakes predicted by users for benzene, formaldehyde, acetaldehyde and acrolein were 39 µg, 32 µg, 2.2 mg and 71 µg, respectively. Concerning acrolein levels (greater than 0.35 µg m−3).	No
Enomoto *et al.* (2022)	They simulated 2 environments (restaurant and residence), with an experiment time of 1h, and evaluated the use of 3 types of heated tobacco systems (T1.0a, IT2.0a, and DT2.2a) and a commercial cigarette. For the restaurant simulation, 2 adult smokers entered the chamber and smoked alternately every 8 minutes, a total of 7 cigarettes, with 15 to 16 puffs per cigarette. To simulate a residence, 1 smoker entered the room and smoked 1 cigarette every 30 minutes, for a total of 2.	48 constituents were measured as tobacco-specific nitrosamines; carbonyls, VOC, TVOC, polycyclic aromatic hydrocarbons, polycyclic aromatic amines, mercury, lead, cadmium, chromium, nickel, beryllium, arsenic, ETS markers, specific components of the tobacco heating system, CO, CO_2, ammonia and NO_x, NO_2, combined nitrogen oxides.	In the “residence” simulation, the use of IT1.0a and IT12.0a increased the concentration of TVOC and glycerol in the air, compared to the control: TVOC (µg/m3) - IT1.0a 83.2 +-9.2; IT2.0a 84.2+-7.5; Control 42.1+-13.2; Glycerol (µg/m3) - IT1.0a 54.2 +-10.4; IT2.0a 90.9+-20.5; Control - 13.4+-2.3. In the "restaurant" the use of DT2.2a increased the concentration in the air of acetaldehyde, propionaldehyde, n-butyraldehyde, glycerol, benzene, pyridine, NNN, NAT and NNK, compared to control: NNN (ng/m3) - 2.85 ; Control LOD; NAT (ng/m3) - <LOQ; Control – LOD; NNK (ng/m3) - <LOQ; Control – LOD; Acetaldehyde (µg/m3) - DT2.2a 10.4 +-1.1 ; Control - 4.62+-0.26; Propionaldehyde (µg/m3) - DT2.2a 1.17 +-0.07; Control - 0.618+-0.040; n-butyraldehyde (µg/m3) - DT2.2a 2, 08+-0.30; Control - 0.900+-0.087; Glycerol (µg/m3): 37.3+-6.9; Control 13.4+-2.3; Benzene (µg/m3): <LOQ; Control: <LOD; Pyridine (µg/m3): 1.59+-0.14; Control - <LOQ.	Yes

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Foster *et al.* (2018)	Four participants were present in the test room at all times, accompanied by an independent non-smoker moderator, and 5 test situations were carried out, each lasting 4 hours, conducted per week in 3 stages, according to the 3 conditions of ventilation (office, residence and hospitality). 1 heated tobacco product and 2 regular cigarettes - Luck Strike regular (7mg tar) and Du Maurier Silver (9mg tar) were used.	O2, CO, NOx, ozone (O3) and PM1, PM2.5 and PM10 mm, individual and total volatile organic compounds, carbonyl compounds (formaldehyde, acetaldehyde, acrolein and crotonaldehyde); polycyclic aromatic hydrocarbons; nicotine; glycerol; 3-Ethehil Pyridino; and tobacco-specific nitrosamines.	Levels of formaldehyde, acetaldehyde, nicotine, particulate matter and number of particles were higher after using THP compared to control in the following situations: Formaldehyde (µg/m3): (Residence) THP - 18 and control - 16; Acetaldehyde (µg/m3): (Residence) THP - 10; Control - 5; (Office) THP - 16; Control - 7; (Hospitality) THP - 6; Control – 3; Nicotine (µg/m3): (Office) THP - 1.4; Control - 0.6; (Hospitality) THP - 0.4; Control - <0.2; PM1 (µg/m3): (Office) THP - 10.3; Control - 2.4; (Hospitality) THP - 6.5; Control - 3.8; PM2.5 (µg/m3): (Office) THP - 10.7; Control - 2.6; (Hospitality) THP - 6.6; Control - 3.9; PM10 (µg/m3): (Office) THP -13.8; Control - 5; (Hospitality) THP - 8.4; Control – 6; No. of particles (1/cm3): (Residence) THP -1.0E+04; Control - 9.6E+03; (Office) THP - 8.5E+03; Control - 9.9E+02; (Hospitality) THP - 4.7E+03; Control - 2.3E+03.	Yes
Hirano *et al.* (2020)	Tests in the shower box were carried out alternately with each of the products, with an interval of 1 hour, in which the room was ventilated. A single subject used the products. Fifty puffs were given on each product, with an interval of 30s. In the tests carried out in the room, the same man used all the products, and in the case of ploomTech, one more man used the product. Number of puffs: 50 for IQOS, 130 for glo, 265 ploomTech and 54 regular cigarettes. The per minute average of particulate matter was measured up to 120 minutes after the test started in the box and 60 minutes in the room. Data were collected for 2 heights (1m and 1.8m).	Nicotine concentration and PM 2,5 (ug/m3).	The maximum nicotine concentrations, in the shower test, for 1.0 and 1.8m were 29.3 and 25.9 µg/m3 for ploomTECH, 160 and 111 µg/m3 for Glo and 257 and 212 µg/m3 for IQOS [all greater than tolerated for adverse health events - 3.0 µg/m3]. Regarding PM2.5, the lowest values were observed for ploomTECH, 21 and 10 µg/m3 (SD=55.6.6) for 1.0 and 1.8 m, followed by 330 and 99 µg/m3 (SD = 564, 119) for Glo and 492 and 413 µg/m3 (SD = 667, 466) for IQOS. In the room test the nicotine concentrations with the 3 types of HTP did not exceed 3 µg/m3. PM2.5 concentrations measured at 1.5 and 2.5 m away from the user were lower for ploomTECH and IQOS, 6.5 and 7.0 µg/m3 (SD = 5.8, 2.7), and 7.0 and 6.9 µg/m3 (SD = 11.6, 4.0), respectively, and higher for Glo, reaching 102 and 56 mg/m3 (SD = 95, 56), respectively.	No

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Hirano & Takei (2020)	They used the values obtained in the previous study in relation to nicotine concentration and related them to IARC measurements for type 1 and 2 carcinogens for cigarette smoke. This was used as a parameter to calculate the cancer risk of using HTP compared to smoking.	Excessive cancer risk	Excess cancer related to passive exposure to HTP smoke is: $2.7x10^{-6}$	No
Imura & Tabuchi (2021)	Self-reported internet questionnaire survey of 8,784 eligible respondents aged 15-73. They examined the frequency (%) of subjective symptoms related to passive exposure to regular cigarettes and HTP (sore throat, cough, asthma attack, chest pain, eye pain, nausea, headache, and other symptoms).		39.5% of those exposed to HTP aerosol had some subjective symptom. Non-cigarette or HTP users had the following symptoms when exposed to HTP vapor: sore throat (23%), cough (22.5%), asthma attack (10.9%), chest pain (11.8 %), eye pain (19.3%), nausea (31.9%), headache (17.7). It suggests that respiratory and cardiovascular abnormalities may be related to secondary exposure to HTP aerosol.	No
Kaunelienė *et al.* (2019)	The 1st campaign was carried out outside the nightclub, for 3 days and 5 sessions: "background", "background" with 10 people not using the product, 10 people using IQOS simultaneously, "background" with 30 people not using IQOS, and 30 people using IQOS. Each session took 30 minutes with natural ventilation. The 2nd "campaign" also took place in 3 days and on each day, 1 hour before the house opened (background) and 3 hours with the club in operation. On the last day, the measurement of the actual operating situation was extended to an additional 4 hours.	Particle number concentration in real time (PNC), CO_2 concentration, relative humidity and temperature, offline carbonyls (acetaldehyde and formaldehyde), nicotine and 3-ethenylpyridine concentration also offline. The measured distributions were based on PNC (single particles cm–3 or # cm–3)	The use of 10 IQOS increased the particle concentration. The maximum peak recorded was 1.2E+5 # cm–3, with a median concentration of 3.6E+4 # cm–3 and 3.5E+4 # cm–3 in Zones 1 and 2, respectively. This was a significant increase over the background indoor environment or with 10 people not using the product. Thirty IQOS users resulted in another significant increase in particle number concentration with a peak value of 1.5E+5 # cm–3, and an average of 1.2E+5 # cm–3 in Zone 1 and 1.3E+5 # cm– 3 in Zone 2. The use of 30 IQOS devices did not result in a significant increase in particulate matter concentration compared to the control (background indoor environment), with the median PM2.5 ranging from 2.7 µg m–3 in Zone 1 and 2.8 µg m–3 in Zone 2 in the background environment to 11.4 µg m–3 (Zone 1) and 12.3 µg m–3 (Zone 2) after using 30 IQOS.	Yes

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Khalaf *et al.* (2020)	Electronic cigarette, common cigarette and IQOS were used separately for 10 minutes each, by the same person. Particle concentrations were measured by aerosol diffusion spectrometer.	PM1, PM2.5 and PM10 (ug/m3)	The results were presented in graphs where it is not possible to know the exact values. It can be said that the highest values were observed after 5 minutes of using the IQOS, with PM1 close to 250 (µg/m3); PM2.5 below 100(µg/m3) and PM10 below 250 (µg/m3); and also, that there was a growth in relation to the baseline level, that is, before the use of this product. The surface area value of the particles reached approximately 1000 µm2/cm3 with 5 minutes of using IQOS.	Unable to identify
Meišutovič-Akhtarieva *et al.* (2019)	Thirty sessions of HRT and 3 of cigarettes were performed to analyze the quantitative effects of environmental variables, including ventilation intensity (V) such as air exchanges per hour (0.2, 0.5 or 1), intensity of use of THS as number of parallel users (1, 3 or 5), relative humidity (RH, 30, 50 or 70%) and distance from the observer (D, 0.5, 1 or 2 m) for pollutant concentration variations in a camera.	Real-time particle number (PNC) concentration, CO and CO_2 concentration, offline concentration of acetaldehyde, formaldehyde, nicotine and 3-ethenylpyridine were measured during and after active use. The measured distributions were based on the concentration of the number of particles (unit particles/cm3 or #/cm3). The number of particles per volume of air with a size between Dp and dDp, expressed mathematically as Dp ¼ dN/dlogDp (#/cm3).	The use of HRT resulted in a significant increase in nicotine, acetaldehyde, PM10, PM2.5 and PNC compared to "background". The maximum concentration of 30min of fine particulate matter - PM2.5 (635.7 mg/m3) and PNC (4.8 105 #/cm3), as well as the maximum concentration of 1s of PM2.5 (109.8 mg/cm3) m3) and PNC (9.3 106 #/cm3) suggest that intensive use of HRT in a confined space with limited ventilation can cause elevated particle concentrations.	Yes

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Mitova *et al.* (2016)	The simulation was performed in a controlled walk-in room (size: 24.1 m2, 72.3 m3) with recommended ventilation conditions to simulate an office, residential and hospital environment, and was compared with smoking a cigarette (Marlboro Gold) under identical experimental conditions. Occupant density was set at 8 m2/person for the office and residence, and 4.8 m2/ person for the hospital. Evaluated products: nicotine, carbonyls and volatile organic compounds.	They studied the concentrations of 18 constituents in indoor air.	Statistical evaluation of the data showed that the concentrations of suspended respirable particles, ultraviolet particulate matter, fluorescent particulate matter, solanesol, 3-ethenylpyridine, formaldehyde, acrolein, crotonaldehyde, acrylonitrile, benzene, 1,3-butadiene, isoprene, toluene, CO, NO and NOx in the evaluations with THS 2.2 in three environmental conditions were equivalent to the concentrations found in the background internal air. Only acetaldehyde and indoor air nicotine concentrations were increased in the THS 2.2 assessments in the 3 simulated environments compared to the background indoor air as follows: Office - acetaldehyde: 9.42 x 5.77 and nicotine: 1.61 x 0.51; Residence - acetaldehyde: 12.5 and 7.44 and nicotine: 2.66 and 0.855; Hospitality - acetaldehyde: 4.05 and 2.65 and nicotine: 1.09 and 0.438.	Yes
Mitova *et al.* (2019)	The THS 2.2 device was used for 2 hours by the control (participant present in the room, without using any product) and by the smoker, with a 60-minute break with no one inside. The density of occupants was set at 8m2/ person. The ventilation rate of 37m3/h (0.5 air changes/h -ACH) was based on the European ventilation performance standard EN 15251.	Environmental tobacco smoke particulate phase markers (in µg/ m3): breathable suspended particles, ultraviolet particulate matter, fluorescent particulate matter, solanesol and carbonyls (µg/ m3): acetaldehyde, acrolein, crotonaldehyde, formaldehyde. Volatile organic compounds (in µg/ m3): acrylonitrile, benzene, 1,3-butadiene, isoprene, toluene. Tobacco-specific gas phase markers: CO (ppm), NOx (ppb), TVOC, specific nitrosamines (NNK and NNN), glycerine, propylene glycol, and online measurement of PM 1 and 2.5.	After using heated tobacco, nicotine, acetaldehyde, and glycerin were the only substances found in the air with higher concentrations than in the control. Nicotine (mean): 1.48 (SD: 0.685) after THS and 0.330 (SD: 0.047); Acetaldehyde (mean): 6.76 (SD: 0.760) after THS and 3.32 and (SD: 0.280); Glycerin(mean): 13.3 (SD: 3.39) after HRT and <6.23 in control.	Yes

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Mitova *et al.* (2021)	Comprehensive evaluation of THS 2.2 environmental aerosol compared to background under three ventilation conditions representative of simulated residential category III (0.5 h−1), shop (2.4 h−1), and restaurant (4.3 h−1) 1). The density of occupants was set at 6 m2/person. Ventilation rates were based on the European Ventilation Performance Standard EN 15251 and ASHRAE 62-1 and 62-2. Each set of experiments was performed on a separate day, starting at approximately 9:30 am, with a 2h background assessment. Four repetitions were planned for each type of evaluation, and air sampling was performed for 2 hours, starting at time t = 0 min. The indoor air quality control room was air flushed at the maximum flow rate of fresh filtered air (750 m3/h) for 15 minutes after the background session and overnight between individual assessments.	Environmental tobacco smoke particulate phase markers (in µg/m3): breathable suspended particles, ultraviolet particulate matter, fluorescent particulate matter, solanesol, Carbonyls (in µg/m3): acetaldehyde, acrolein, crotonaldehyde, formaldehyde; Volatile organic compounds (µg/m3): acrylonitrile, benzene, 1,3-butadiene, isoprene, toluene; Tobacco-specific gas phase markers: CO (ppm), NOx (ppb), total volatile organic compounds, specific nitrosamines (NNK and NNN), glycerin, propylene glycol, and online measurement of PM 1 and 2.5.	Internal use of HRT 2.2 increased levels of nicotine, acetaldehyde, glycerin and (if menthol products are used) menthol from background levels, with a corresponding increase in total volatile organic compound (TVOC) values. Furthermore, a temporary increase in ultrafine particles was observed when two or more tobacco sticks were used simultaneously or with a short time interval between uses, but concentrations returned to levels close to background levels almost immediately. This is because THS 2.2 generates an aerosol of liquid droplets, which quickly evaporate. Acetaldehyde, TVOCs, and UFP concentrations decreased with increasing ventilation rates, while airborne glycerin levels were only slightly influenced, and nicotine levels were not influenced.	Yes

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Peruzzi *et al.* (2020)	Seven smokers received one of the smoking products as a set of 2 blocks of 15 sessions each, for a total of 30 sessions (thus giving 15 device/flavor combinations repeated twice). GLO2 was smoked by Smoker 1, IQOS3 by Smoker 2, GLO4 by Smoker 3, IQOS6 by Smoker 4, IQOS1 by Smoker 5, GLO3 by Smoker 6, JUUL4 by Smoker 7, and so on. Emissions of particulate matter with a diameter ≤ 10 µm (PM10), ≤ 4 µm (PM4), ≤ 2.5 µm (PM2.5) and ≤ 1 µm (PM1) were continuously measured under actual use conditions 5 min before, during and 5 min after smoking each product in a room measuring 53m3, with temperature and relative humidity varying between 20 and 23◦C and 36 and 40%, respectively. Measurements were carried out in the "cumulative" mode, including the mass of all particles smaller than or equal to the defined size.	Total particulate matter (in µg/m3) and in the following diameters: PM1, PM2.5, PM4 and PM10	There was an increase in particulate matter of all diameters and also in total particulate matter during use of all heated tobacco products compared to baseline (before use) levels. During use, emissions of PM≤1 µm (PM1) were 28(16;28) µg/m3 for GLO, 25(15;57) µg/m3 for IQOS. Total particulate matter concentrations measured during use were 39 (24; 127) µg/m3 for Glo, 31 (20; 63) µg/m3 for Iqos (compared to pre-use levels, which were respectively 19 (12; 29) and 16 (12;23) µg/m3). Comparisons between all types of heated tobacco products investigated demonstrated that different flavors/additives impact indoor PM emissions, both due to smoke characteristics and different patterns of use (e.g., frequency, depth, nasal or oral exhalation). In the case of Glo, the variation, for example, of PM10 concentration between two flavors was 33 (22; 59) a. 82 (31; 277) µg/m3, p = 0.027). Regarding IQOS, for example, PM2.5 concentration during use ranged from 14 (11; 25) to 79 (22; 1370) µg/m3, depending on the flavor.	One of the authors stated that he consulted for a medical company.
Protano *et al.* (2020)	Particulate matter (PM) with an aerodynamic diameter smaller than 10, 4, 2.5 and 1 µm (PM10, PM4, PM2.5, PM1) was measured before and during the use of IQOS®, GLO®, JUUL®, with different types of sticks/sachets, as well as during the smoking of a conventional tobacco cigarette.	Particulate matter (µg/m3) in varied diameters: PM 1, PM2,5, PM4 and PM 10.	The aerosol was mostly in the PM1 size range (>95%). All DEFs determined a worsening of the PM1 concentration in a closed environment, which ranged from very mild for JUUL® - depending on the capsule used - to considerably severe for IQOS® and GLO®. Median values ranged from 11.00 (IQOS3 and JUUL2) to 337.5 µg m−3(IQOS4). The high variability of particle loads was attributed both to the type of stick used and to the different way of smoking of the volunteers who smoked/vaped during the experiments. The results showed that all tested DEFs worsen indoor air quality during use.	No

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Protano *et al.* (2017)	Aerosol measurements were performed in a model room with combustion devices (conventional and cigarettes, cigars and pipes) and non-combustion devices (electronic cigarettes and IQOS®). The data were used to estimate the dose of particles deposited in the respiratory system of subjects aged 3 months to 21 years using the multipath particle dosimetry (MPPD) model.	Submicron particles, with diameters ranging from 5 to 560 nm. Estimation of exposure of individuals to secondhand smoke using investigated products, with specific profiles according to age: infants, children, adolescents, adults.	The study demonstrated an increase in the concentration of particles in the air after using IQOS. It also demonstrated the accumulation of particle doses in the respiratory system after the use of IQOS, and that this accumulation is greater in infants and children. And yet, that the highest percentage of particles was deposited in the alveolar region. Approximately 60% to 80% of the particles deposited on the heads of 3-month-old babies were smaller than 100nm. Results refer to a single air exchange rate; these results, although representative of those that occur in domestic environments, do not take into account the possible variability in the air exchange rate that would affect particle concentration levels.	No
Protano *et al.* (2016)	Submicron particles were measured using a spectrometer in a 52.7 m3 room with a door and a window (room air changes: 0.67 air changes/h). To simulate the subjects' passive exposure, the air sampler was placed 2 meters away from the smoker and 1.5 meters from the floor. For each experiment, lasting 1 h, we also modeled the dose of submicron particle deposition in the human respiratory tree. Each experiment was performed three times; Arithmetic mean values were calculated for each 1s time measurement and used for data comparison.	Submicron particles, with diameters ranging from 5 to 560nm. Estimation of exposure of individuals to secondhand smoke through the use of investigated smoking products	The main results of the experiments are: 1. After the use of IQOS, submicromic particles are released that are deposited in the airways of a passively exposed subject; 2. After using IQOS submicron particle values immediately return similar to background levels; it is presumable that submicron particles generated by non-burning tobacco smoke unite with each other quickly and in large numbers, increasing their average diameter and sedimenting immediately; 3. In all experiments, approximately half of the deposited submicron particles were so small that they managed to reach the alveolar region of passively exposed subjects; 4. An hour spent indoors in which a single IQOS® is smoked provides exposure to submicron particles equivalent to that which would occur in spending 10 minutes in a high traffic area.	No

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Ruprecht *et al.* (2017)	Experiments with the IQOS, in a room occupied by two to three people and equipped with real-time analyzers (2m away from the smokers), samplers and three fans were in operation during the smoking sessions. Continuous and time-integrated measurements were performed in an indoor environment, followed by the calculation of the emission rates of the substances.	Carbon black, metallic particles, organic compounds and mass of particles segregated by size and numerical concentrations emitted by the devices	Analysis of the smoke emitted by the IQOS indicated that the emission of organic matter particles from this device is significantly different depending on the organic compound. While polycyclic aromatic hydrocarbons were mostly undetectable in IQOS smoke, certain n-alkanes, organic acids (such as suberic acid, azelaic acid, and n-alkanoic acids with carbon numbers between 10 and 19), as well as levoglucosan, were still emitted at substantial levels of IQOS (up to 2–6 mg/hr during a regular regimen of use). Metal emissions were similar to background levels. Another important finding is the presence of carcinogenic aldehyde compounds, including formaldehyde, acetaldehyde and acrolein.	No
Savdie *et al* (2020)	Particulate matter measurements were performed in two settings: home and in the car. The living room (73 m3) was furnished and occupied by 2 people. The equipment for monitoring air quality was placed 1.5 m away from the smoker with probes and absorption tubes pointing upwards, at a height of approximately 1 m from the floor. Car measurements were carried out inside a medium volume car (Diesel Opel Corsa, 2007) traveling on a low traffic intensity route of 4.95 km at an average speed of 34 km/h. The probes or absorption tubes of the various devices were positioned in the area corresponding to a child's breathing zone. The study was carried out with 2 occupants in the car: a driver (the smoker) and a non-smoker passenger. Three types of electronic devices (Slate JUUL, IStickTC40W and IQOS) and two common cigarettes (Chesterfield blue and menthol) were used.	Particulate matter (in µg/m3): PM1, PM2.5, PM10; Ultrafine particles (particles/m3); Black carbon (µg/m3); CO (mg/m3); CO2 (mg/m3).	At home, there was an increase in all substances evaluated, in relation to the control, after using the heated tobacco product. The concentration of PM10 (87.8 + 51.7 µg/m3) was 4 times higher, of ultrafine particles (35,700 + 11,500 particles/m3) was 7.6 times higher, of carbon black (1.2 + 0.7 µg/m3) was 5.6 times higher and CO2 (2640 + 680 mg/m3) was 1.5 times higher after using heated tobacco when compared to the control. The use of heated tobacco did not cause an increase in CO. In the car, there was an increase in particulate matter of all evaluated diameters after using a heated tobacco product. The concentration of ultrafine particles (22,100 + 16,800 particles/m3) was 2.8 times higher, of carbon black (0.5 + 0.3 µg/m3) was 0.7 times higher, after the use of heated tobacco when compared to the control. The use of heated tobacco did not cause an increase in CO. The carbon dioxide concentration found was 1020 + 60 mg/m3. CO2 showed no increase directly associated with nicotine delivery systems, but a trend linked to a higher breathing rate with smoking.	No

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Author/Year	Experiment description	Compounds / evaluated substances	Results	Funded by TI or with conflict of interest declaration
Schober *et al.* (2019)	Comprehensive assessment of environmental pollution in 7 passenger cars while tobacco cigarettes and new electronic smoking products (IQOS, e-cig) were being smoked. Seven drivers (one man, six women) were recruited, who were asked to bring their own car to smoke while driving. Data on indoor climate and indoor air pollution with fine and ultrafine particles and volatile organic compounds were collected while the cars were being driven.	CO, CO2, PM2,5, volatile organic compounds, aldehydes/ketones .	Smoking an IQOS had almost no effect on the concentration of the mean number of fine particles (> 300 nm) or the concentration of PM2.5 inside the vehicle. In contrast, the particle number concentration with a diameter of 25–300nm increased in all vehicles (1.6–12.3 ×104 /cm3) and averaged 9 to 232% above background levels (control). With the use of IQOS the nicotine concentration increased to 4-12μg/m3 in 3 out of 7 cars. However, no increase over background level of volatile organic compounds was observed after its use in any vehicle. Use of IQOS did not affect concentration of carbonyls (aldehydes and ketones)	No
Yu *et al.* (2022)	Two experiments were carried out with three heated tobacco products (IQOS, GLO and Lil) to analyze the concentrations of substances emitted by HTP and compare them with those of conventional cigarettes. A smoking machine was used to generate these compounds from heated tobacco products.	Concentrations of nicotine, propylene glycol, vegetable glycerin, volatile organic substances, aldehydes, particulate matter and nanoparticles	Nicotine levels transferred by heated tobacco products (0.8-1.2 mg cigarette -1). The concentrations of propylene glycol emitted by heated tobacco products ranged from 0.2-0.3 mg cigarettes -1. The levels of vegetable glycerin emitted were 3.1-5.9mg -1 cigarettes. Among the volatile organic compounds investigated, the highest concentration found was toluene: ~2.1ppb. However, toluene and m,p-xylene were not found in IQOS and ethylbenzene was only found in Lil. On the other hand, all VOCs were detected in Glo. Several aldehydes were detected at low concentrations: Formaldehyde: 0.001-0.009 ppb; Acetone: ~0.004ppb; Acetaldehyde: ~0.002ppb. The size distribution of the main nanoparticles ranged from 38.5-91.4 nm and the numerical concentration of all products was around 137000 cm^{-3}.	No

Source: The authors, 2022.

Subtitle: NNN = N-nitrosonornicotine; NAT = N′-nitrosoanatabine; NNK = nicotine-derived nitrosamine ketone; LOQ = Limit of quantification; LOD = Limit of detection; TVOC = Total Volatile Organic Compounds; VOC = Volatile Organic Compounds.

Final considerations and conclusion

Electronic devices to smoking are a major challenge for global public health, especially for tobacco control. The real impacts on the health of individuals, society and the environment are still not fully known. Regarding heated tobacco products, studies are even more limited. However, evidence is already beginning to accumulate on the toxicity of its components, which allows inferences about the damage to health. Studies indicate that there are substances classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group I), such as formaldehyde, acetaldehyde and acrolein.

The findings of this study indicate that the emissions emitted by heated tobacco products are a source of environmental pollution and point to a worsening of air quality with their use, with special emphasis on the emission of particulate matter, consistently identified in most studies. Other substances, such as nicotine and acetaldehyde, were identified in more than one study, and the list of pollutants investigated and identified at least once is significant. Heated tobacco products produce emissions that can expose people to toxic substances emitted indoors.

Several of these pollutants are recognized as causing disease. However, there is still no evidence, nor conclusive work on the causal relationship between exposure to emissions and the emergence of health problems. The studies identified here already point to possible damage to health, either by simulating the deposit of particles in the respiratory system and excess risk of cancer, or by initial exploratory data on the effects after exposure. So there is a need for more studies by independent researchers to understand the damage caused, since studies on this topic are often funded by the tobacco industry.

Another important issue is that the evaluated emissions of these products are usually done in comparison with cigarette emissions or using a list of priority toxic agents such as, for example, the one used by the FDA in its authorization process for reduced risk products. In this case, the studies do not consider the more than 80 chemical substances, including carcinogenic ones, present in heated tobacco products, as well as the substances that are found in higher concentrations than in cigarettes. Thus, more studies are needed to assess not only the environmental contamination generated by these products, but also their impacts on health.

Another point to be considered concerns the immense diversity of models and products (including hybrid devices), additives, with different toxic substances being used, as well as the great heterogeneity of published works, which can result in different outcomes.

Despite the gaps about the real extent of environmental contamination and damage caused by these products to non-users, the evidence evaluated is sufficient to point out that HTP are capable of degrading ambient air quality with potentially harmful substances. Therefore, they should not be used under any circumstances in an indoor environment, so as to avoid contamination of non-users of these products. It is also important to highlight the need to adopt additional measures to curb the illegal trade of these products and to reinforce the inspection of the use of electronic devices indoors, accompanied by information campaigns for the population.

It should also be noted that there is no safe level of exposure to environmental tobacco smoke and that the implementation of smoke-free environments contributes to reducing the prevalence of smoking and passive smoking in Brazil.[2]

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Notes

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Resumo

Impacto do uso de produtos de tabaco aquecido (HTP) na qualidade do ar em ambientes fechados

Introdução: Os produtos de tabaco aquecido (HTP) têm ganhado popularidade nos últimos anos. No entanto, tem-se questionado sobre os danos que provocam na saúde, em especial aos impactos decorrentes da exposição a suas emissões. O objetivo deste estudo é avaliar o impacto do uso de HTPs em ambientes internos/fechados na qualidade do ar e/ou na saúde das pessoas expostas passivamente, por meio de uma revisão sistemática de estudos originais. **Métodos:** Realizou-se busca bibliográfica nas bases de dados Medical Literature Analysis and Retrieval Sistem (MEDLINE), Excerpta Medica Database (EMBASE), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e SCOPUS. As etapas de seleção, extração dos dados e avaliação do risco de viés dos estudos foi realizada em dupla, de forma independente, e as divergências foram resolvidas por consenso. **Resultados:** Foram selecionados 21 estudos, incluídos nesta revisão. Os resultados indicam que os produtos de tabaco aquecido são fonte de poluição ambiental decorrente da emissão de material particulado. **Conclusão:** Os produtos de tabaco aquecido produzem emissões que podem expor as pessoas às substâncias tóxicas emitidas no ambiente fechado, assim como outros produtos de tabaco.

➤ **Palavras-chave:** Sistemas eletrônicos de liberação de nicotina. Poluição do ar em ambientes fechados. Poluição por fumaça de tabaco. Revisão sistemática.