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What Do We Know About Smoking Alternatives?
A Study on IQOS Tobacco Heaters

Filip Nadolny
University Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań
https://orcid.org/0009-0000-6433-5975
nadolnyfilip@gmail.com

Jędrzej Jabłoński
Regional Hospital in Poznań,
Juraszów 7-19, 60-479 Poznań
https://orcid.org/0009-0009-6204-407X
jedrzejkosma@gmail.com

Martyna Kania
University Hospital in Poznań
Przybyszewskiego 49, 60-355 Poznań
https://orcid.org/0009-0006-4400-0258
martyna.kania@outlook.com

Agnieszka Adamowska
Józef Struś Multispecialist Muncipal Hospital
Szwajcarska 3, 61-285 Poznań
https://orcid.org/0009-0009-1977-2522
a.adamowska12@gmail.com

Alicja Śniatała
Regional Hospital in Poznań
Juraszów 7-19, 60-479 Poznań
https://orcid.org/0009-0003-8488-3268
ala.sniatala@gmail.com

Hanna Bartkowiak
Józef Struś Multispecialist Muncipal Hospital
Szwajcarska 3, 61-285 Poznań
https://orcid.org/0009-0000-6914-4908
hannabartkowiak22@gmail.com

Damian Grubski
Józef Struś Multispecialist Municipal Hospital
Szwajcarska 3, 61-285 Poznań
https://orcid.org/0009-0003-9501-9950
damianxgrubski@gmail.com

Kacper Ziarnik
Regional Hospital in Poznan
Juraszow 7/19 60-479 Poznan
https://orcid.org/0009-0006-4676-3232
kacper.ziarnik@gmail.com

ABSTRACT

Introduction

Nicotine addiction poses a significant public health concern in Poland, exacerbated by smoking, e-cigarettes, and heated tobacco products. While tobacco companies claim their alternatives aid cessation, their vested interests warrant cautious scrutiny. This study examines tobacco harm reduction strategies.

Aim of the Study

This study examines IQOS tobacco heaters as a potential harm reduction alternative for smokers. Analyzing health data and regulatory findings, particularly from the FDA, it evaluates the effectiveness and public health impact of heated tobacco products within broader harm reduction strategies.

Materials and Methods

This study examined literature and data to assess IQOS and heated tobacco products' chemical and health risks. It analyzed findings to compare IQOS aerosol and cigarette smoke toxicant exposures, clarifying IQOS's nicotine profile and smoking cessation potential.

Conclusion

The findings indicate IQOS may reduce certain toxin exposures compared to cigarettes, but long-term health impacts are unclear. Further research is needed on IQOS's effects, including disease, addiction, and population-level consequences. Cautious regulation is warranted due to youth risks and ethical concerns surrounding nicotine alternatives.

Keywords: harm reduction, nicotine dependence, smoking alternatives, heated tobacco products, modified risk tobacco products

Introduction

Nicotine addiction remains one of the most significant public health challenges. This includes smoking cigarettes, using e-cigarettes, and heated tobacco products. Smoking is the most common addiction in Poland, with one in three adult men and one in five women smoking—around 26% of the adult population. Tobacco companies and their lobby claim that heated tobacco products or e-cigarettes are revolutionary solutions to help smokers quit. It is important to note the conflict of interest between this thesis and its authors. This article will explore the topic of tobacco harm reduction.

Tobacco Harm Reduction

According to the Polish Ministry of Health (MZ) and the National Institute of Public Health (PZH) report titled "The Health Situation of the Polish Population and Its Determinants 2022," smoking is the main risk factor responsible for the disease burden in Poland. Among addictions, it generates the highest costs for the healthcare system. Its contribution to the overall health burden is 6.03%, which translates to 4,743.8 DALYs (disability-adjusted life years) per 100,000 population [1], meaning that the effects of smoking result in nearly 4,744 lost years of productive life per 100,000 inhabitants. On a national scale of 38 million citizens, this equates to about 1.8 million lost years of life.

The risk of smoking-related diseases is dose-dependent, with various modifiable factors affecting this risk, such as the duration of smoking, the chemical composition of tobacco smoke, and the number of cigarettes smoked daily [2]. In 2000, the FDA commissioned the US Institute of Medicine to compile a report that aimed to gather existing scientific evidence on the potential for harm reduction from smoking and determine the necessary evidence to evaluate whether new tobacco and nicotine products could reduce the harm caused by tobacco use. The 2001 report "Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction" proposed that tobacco and nicotine products that significantly reduce exposure to harmful substances compared to traditional cigarettes should be developed and studied to assess any health benefits from reducing smoking risks [3]. The report emphasized that the risk profile of new products should be evaluated through the lens of public health protection, not just the health of smokers, necessitating research on reducing the harm of secondhand smoke. Several framework principles were published, analyzing the types of studies needed to evaluate the degree of risk reduction from using new products [4]. However, the term "PREP" is no longer used for tobacco products, as it is now associated with HIV pre-exposure prophylaxis internationally [5]. Proposing a globally recognized term similar to PREP might be beneficial.

Harm reduction for nicotine addiction involves a therapeutic approach aimed at mitigating the negative consequences of tobacco use without requiring complete nicotine abstinence. The primary goal is to help people minimize the impacts of nicotine addiction, rather than proposing immediate, full cessation of nicotine intake. The core strategy is substitution therapy, based on transitional solutions, which involves replacing the addictive substance with one that carries lower risk but similar pharmacological effects. Nicotine replacement therapy is a form of substitution therapy used in tobacco harm reduction. This approach is based on the concept that not all tobacco and nicotine products pose equivalent health risks, as the risks associated with cigarette smoking are more severe compared to the use of medicinal nicotine products, such as NRT. Additionally, alternative nicotine delivery methods, including e-cigarettes or heated tobacco products, may be potentially less harmful [6].

In the 2012 Family Smoking Prevention and Tobacco Control Act (FSPTCA), the FDA proposed guidelines for reporting requirements for the tobacco industry [7]. The outcome was a list of 93 harmful and potentially harmful constituents (HPHC) [8]. The HPHC list focuses on chemicals linked to the five most serious health consequences of tobacco use (cancers, cardiovascular diseases, respiratory diseases, reproductive issues, and nicotine addiction). The FDA requires tobacco product manufacturers and importers wishing to market their products in the US to report the levels of all 93 HPHC produced during use, which can potentially harm the user. When a tobacco product is introduced to the US market, a complete HPHC list must be provided. If the levels of HPHC in a new product are mostly lower than in cigarettes, the product can theoretically be classified as a tobacco harm reduction product (THR). However, merely reducing harmful substances is one thing, and proving reduced risk of tobacco-related diseases is another.

Currently, the FDA uses the term modified risk tobacco products (MRTP). Although this may appear as a uniform category, there is a critical division within MRTP. Once a product passes the application process and achieves MRTP status, the FDA publishes a "MODIFIED RISK GRANTED ORDER," indicating whether the product falls under the category of EXPOSURE MODIFICATION or RISK MODIFICATION, a very significant distinction. MRTP is divided into:

- **Exposure Modification Products** – where product documentation states "reduced exposure," indicating that the product reduces exposure to harmful and potentially harmful toxic substances (HPHC) compared to cigarettes. A potential public health

benefit from granting MRTP status is encouraging long-term smokers to switch to a reduced-exposure tobacco product.

- **Risk Modification Products** – where product documentation states "reduced risk." This means the product significantly reduces harm and/or the risk of tobacco-related diseases and/or provides population-level benefits to both users and non-users of tobacco products (i.e., passive smokers).

Although the definitions of the above categories differ significantly, FDA decisions are very precise, yet all products from these categories are collectively referred to as MRTP [9], which can be misleading.

In a 2017 announcement, the FDA acknowledged that while nicotine is highly addictive, it is delivered through a continuum of risk-varying products, with the greatest harm arising from the particulate matter in combustible cigarette smoke [10]. Moreover, epidemiological evidence demonstrates a lower risk of tobacco-related diseases among former smokers. All nicotine products carry some health risks, but the degree of harm varies. Combustible tobacco products, such as cigarettes, are the most toxic, while products that eliminate combustion, like tested heated tobacco, e-cigarettes, or nicotine replacement therapy, may pose relatively less harm [6]. Determining the risk continuum is more straightforward for products with extensive epidemiological data, such as cigarettes [11]. Given that the clinical harm of tobacco products is closely linked to inhaled smoke, products that avoid combustion, like smokeless tobacco and NRT, are inferred to present significantly lower health risks than smoking cigarettes [11]. The following table, based on a 2012 publication, does not include heated tobacco products, as they were not yet available at the time [11].

Non-combustible nicotine products	Non-combustible tobacco products	Combustible tobacco products
Pharmacotherapy NRT, E-cigarettes	Chewing tobacco, Snus	Cigarettes, Cigars, Pipes
Less harmful	→	Highly harmful

Snus, a smokeless tobacco product derived from a dry form of snuff, deserves special attention. It is administered sublingually, delivering nicotine orally without combustion, exposing users to a different profile of toxic substances compared to cigarette smokers. Snus is legally sold only in Sweden within Europe, where its popularity surpassed cigarettes in the

1990s. This shift allowed for the collection of data, revealing that Sweden has the lowest smoking-related mortality rate in Europe, at 152 per 100,000. The British Royal College of Physicians observed that the availability of snus as a lower-risk alternative could encourage many smokers to switch from traditional tobacco products [12]. As early as 2007, the College suggested that snus use does not lead to lung or oral cancer, nor is it a cause of chronic obstructive pulmonary disease, although it may be associated with a higher risk of certain cardiovascular diseases. In 2019, the FDA granted tobacco products like snus the opportunity to be classified as Modified Risk Tobacco Products under the Risk Modification category, allowing Swedish Match USA, Inc. to include information about the lower health risks of using snus compared to cigarettes [13]. Additionally, epidemiological evidence indicates that other smokeless tobacco products, such as American moist snuff and chewing tobacco, have a more favorable toxicity profile than cigarette smoking [14, 15], though further research is needed.

The author's proposed continuum of harm exposure based on the information provided is presented below as a data visualization to stimulate further discussion:

Nicotine-free drug therapy	**Drug therapy NRT**	**Snus**	**e-cigarettes, chewing tobacco**	**Tobacco heaters**	**smoking cigarettes, cigars, pipes**
Addiction therapy with proven effectiveness	**Harm reduction therapy with proven effectiveness**	**Risk-modifying tobacco product**	**Potential harm reduction***	**Potential harm reduction***	**Proven harmful effect**

*Some of my products have been proven to reduce HPHC exposure

The European Respiratory Society's 2019 report, "ERS Position Paper on Tobacco Harm Reduction," outlines several arguments against the tobacco harm reduction strategy [16]. This strategy is based on flawed beliefs about smokers' inability or unwillingness to quit [17, 18, 19], despite the availability of effective, evidence-based treatments for nicotine addiction [20]. Moreover, the assumption that alternative nicotine delivery products can help people quit smoking remains unproven [21, 22], as some studies suggest e-cigarettes may help, but many former smokers remain addicted to nicotine [23, 24]. The strategy also incorrectly assumes that smokers will replace traditional cigarettes with alternative nicotine products [25, 26], when in

reality, a portion of e-cigarette users continue to smoke cigarettes, and dual use is common among heated tobacco product users [26], providing no health benefits. Additionally, the strategy relies on unsubstantiated claims that alternative nicotine products are entirely harmless [27, 28]. Animal studies have shown that e-cigarettes can cause various health problems [29, 30, 31], while human studies have demonstrated airway obstruction and disruption of normal lung function, even after short-term use, with no evidence of improved lung function after switching from combustible to heated tobacco [32, 33, 34, 35]. Furthermore, alternative nicotine products may negatively impact public health, particularly among youth [36], by encouraging non-smokers to start using nicotine, and increasing the risk of traditional cigarette smoking [37, 38, 39].

The harm reduction strategy, based on substitution practices, may potentially alleviate the healthcare burden. Nevertheless, this approach should be reserved for a minority of high-risk smokers. Currently, e-cigarettes and heated tobacco products are available to non-smokers as well. Some countries have adopted policies aiming for the complete elimination of smoking, with Finland, New Zealand, Ireland, Denmark, Canada, and Sweden setting goals to become smoke-free by 2030-2035, meaning a reduction to less than 5% of smokers in the entire population. However, this does not imply a transition to HTPs or e-cigarettes. According to the European Respiratory Society, 40 countries have already banned e-cigarettes and/or nicotine-containing e-liquids. Meanwhile, the United Kingdom and France have implemented a harm reduction strategy. Poland's Chief Sanitary Inspectorate encourages smokers to take decisive steps to quit smoking to significantly reduce the impact of smoking on the health of Poles by 2030 [40].

FDA Decision on the IQOS Product

Under the "Family Smoking Prevention and Tobacco Control Act" in the United States, tobacco companies must receive explicit FDA approval before marketing their products as less risky for consumers. This regulation was enacted due to past instances of companies misleading the public, leading to public health harms. Consumers who could have quit smoking instead switched to products marketed as less harmful, using terms such as "light," "low," or "mild" [41]. This obscured the fact that tobacco products are inherently harmful to health, regardless of their characteristics. Claims suggesting reduced harm or lower disease risk can mislead consumers, giving them a false sense of security [42]. The FDA considers such unauthorized claims as health fraud, and false or misleading information in the promotion, labeling, advertising, distribution, or sale of tobacco products is subject to restrictions [42].

To gain FDA approval to market a tobacco product as a "Modified Risk Tobacco Product", manufacturers must provide robust scientific evidence demonstrating that the proposed MRTP will benefit the health of the entire U.S. population, including adults, children, tobacco users, and non-users. Potential health benefits may be observed when data show that consumers currently using high-harm tobacco products, such as cigarettes, exclusively switch to the MRTP. However, MRTP marketing strategies should not incentivize individuals previously disinterested in tobacco consumption to initiate use. In December 2016, Philip Morris International applied to the FDA to market the heated tobacco product IQOS as an MRTP. The FDA must enforce rigorous standards, as outlined in Section 911 of the Family Smoking Prevention and Tobacco Control Act, before approving a product as an MRTP. Specifically, the FDA may only issue MRTP decisions if the applicant demonstrates with significant and objective scientific evidence that the product, as used by consumers, significantly reduces harm and tobacco-related disease risk for individual users and provides a net benefit to the health of the general public [43].

The FDA's Tobacco Products Scientific Advisory Committee evaluated PMI's claim that "scientific studies have shown that complete switching from cigarettes to the IQOS system significantly reduces exposure to harmful or potentially harmful chemicals." While the committee voted 8 to 1 to approve this statement, the majority also concluded that PMI failed to demonstrate that the reduction in exposure leads to significant and measurable decreases in morbidity and/or mortality [44].

In April 2019, the FDA authorized the sale of the first heated tobacco product, the IQOS system with tobacco-containing cartridges. Subsequently, in February 2020, the FDA granted the IQOS product Modified Risk Tobacco Product status. This allows companies to advertise their products as having reduced exposure or reduced risk compared to existing tobacco products. Specifically, the FDA approved a marketing claim for the IQOS system indicating that it reduces exposure to harmful and potentially harmful toxic substances compared to cigarettes. This MRTP authorization could potentially encourage long-term smokers to switch from cigarettes to the IQOS heated tobacco product as a reduced-exposure alternative [45].

Philip Morris International failed to obtain approval for the "reduced risk" marketing claim due to insufficient evidence demonstrating a significant reduction in harm or risk of tobacco-related diseases from the IQOS product. Additionally, there is no evidence that this product provides population-level benefits for both users and non-users exposed to secondhand smoke [46]. While PMI's submissions suggest that a complete switch from cigarettes to IQOS would significantly reduce exposure to harmful chemicals, some substances were present in

higher amounts in Heatstick aerosol than in cigarette smoke [47]. Further research is necessary to precisely determine the potential impact of exposure to these compounds. A computational toxicological assessment of Heatstick aerosols is also recommended to predict potential adverse effects in IQOS users before their toxicity becomes evident. The FDA has outlined a list of studies that PMI should conduct to resubmit its application, including rigorous toxicological studies using genotoxicity and carcinogenicity models [47].

Despite the lack of FDA approval for a "reduced risk" claim due to insufficient evidence of significant harm reduction, Philip Morris International continues to promote IQOS. There is no data demonstrating population-level benefits for users and non-users [48]. While PMI claims a complete switch to IQOS would reduce exposure to harmful chemicals, some substances were found in higher amounts in IQOS aerosol. Further research is needed to determine the impact of these compounds. Computational toxicology assessments are recommended to predict potential adverse effects. The FDA has outlined studies PMI should conduct for resubmission [48]. The WHO has raised concerns about the growing e-cigarette and heated tobacco market [49], noting Philip Morris' "unsmoke" campaign undermines anti-smoking efforts by presenting heated tobacco as a convenient alternative. This could lead smokers to use less effective options, undermining population-level smoking reduction. The industry's marketing of new products poses challenges, as studies show Philip Morris has spread misleading information about IQOS despite FDA rejections [49]. The WHO emphasizes the need to prevent such claims as tobacco firms rapidly introduce new products globally, and notes industry-funded research undermines evidence reliability [49]. The European Respiratory Society report indicates e-cigarette companies heavily influence youth-targeted marketing [55].

The emergence of novel tobacco products presents significant challenges for comprehensive tobacco control strategies. Key stakeholders, including regulatory bodies, independent researchers, and the tobacco industry, tend to assess the toxicity and health impacts of these new products primarily by comparing them to conventional cigarettes, rather than evaluating their absolute health effects. IQOS, a novel heated tobacco product, has been the subject of extensive data generation by its manufacturers and, to a lesser degree, independent researchers [55, 56]. However, a comparative analysis of these data sources suggests a lack of consensus on the reduced-risk potential of IQOS compared to cigarettes. Regulatory authorities should exercise a high degree of caution when considering any claims of reduced risk or reduced exposure on tobacco product packaging. Studies indicate that youth often struggle to comprehend the nuanced distinctions between such claims, and any misperceptions of reduced harm can potentially lead to the initiation of tobacco use. Consequently, there is a pressing need

for more comprehensive, rigorous, and independent research on IQOS, particularly regarding the long-term health consequences for those who switch from cigarettes, dual users, and new exclusive users of the product.

1. Patient consent:

Not applicable

2. Data were obtained from

PubMed and Google Scholar.

3. Author Contributions:

- Conceptualization: Filip Nadolny
- Methodology: Filip Nadolny
- Software: Damian Grubski
- Formal Analysis: Jędrzej Jabłoński
- Investigation: Hanna Bartkowiak
- Resources: Martyna Kania
- Data Curation: Kacper Ziarnik
- Writing – Original Draft Preparation: Filip Nadolny and Alicja Śniatała
- Writing – Review & Editing: Agnieszka Adamowska
- Visualization: Alicja Śniatała
- Supervision: Damian Grubski and Jędrzej Jabłoński

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