A New Ingenious Enemy: Heat-Not-Burn Products

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ABSTRACT: While cigarette smoking is still a major source of morbidity and mortality, e-cigarette usage is skyrocketing, and the tobacco industry is finding new ways to market nicotine. With updated published research highlighting the dangers of cigarette smoking and now vaping, the industry has been developing new techniques and devices that circumvent this research to hook users on tobacco and nicotine. The FDA allowed Philip Morris International (PMI) to sell their heat not burn tobacco products known as iQOS in 2019. By 2019, 49 countries had permitted the sale of iQOS. This commentary summarizes the recent research on heat not burn cigarettes, also known as heated tobacco products and their effects on public policy. We urge policy makers to consider the research published regarding these new products and prevent the widespread use of these products that will harm public health.

KEYWORDS: tobacco industry, nicotine, tobacco, tobacco products, tobacco use, tobacco, smokeless

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Introduction

The tobacco industry began research into heat-not-burn (HnB), also called heated tobacco products (HTP), in the 1980s and the first HnB, Premier, developed by RJ Reynolds, hit the markets in 1988, although it was unpopular due to its taste.[1] In 1998, Philip Morris International (PMI) launched their first HnB, *Accord*, but it was discontinued after 8 years on the market due to poor sales.[2] The tobacco industry's initial goals for developing HnB were not health-driven, but rather to evade smoke-free regulations and to complement cigarettes.[3] Subsequently, the tobacco industry has been involved in marketing other technologies, such as e-cigarettes, especially JUUL,[4] which have dominated the market. As the vaping and tobacco smoking epidemic continues[5] and the public has been increasingly made aware of the detrimental effects of using new nicotine-containing products, tobacco companies have been developing products that will appeal to the public. In the last decade, the heat-not-burn (HnB) tobacco cigarette hit the worldwide market, which ultimately is a modernized type of the original HnB products.[6] The HnB tobacco product heats tobacco (rolled cast leaf sheets of tobacco soaked in propylene glycol) to temperatures around 350 Celsius rather than burn it at roughly 600 Celsius. This creates an aerosol that contains nicotine which can be inhaled by users and is reportedly less toxic and harmful than e-cigarette vapor or smoke from combusted cigarettes.[7]

Market for Heated Tobacco Products

Since 2014, the HnB market has grown rapidly; in 2019, sales had increased 12 700%.[8] HnB products have been marketed in Korea, Japan, and have been gaining traction both among cigarette smokers and e-cigarette users.[9] By 2015, PMI's product, iQOS, dominated over 80% of the HnB products on the market and will be the focus of this commentary.

PMI initially entered the HnB market with the unsuccessful product, Accord, but in 2014, they released a new product, iQOS. iQOS is described by the company as "a revolutionary technology that heats tobacco without burning it, giving the users the true taste of tobacco, with no smoke, no ash and less smell".[10] It has been successfully marketed in over 49 countries including 3 flagships iQOS stores in Atlanta, Georgia, Richmond, Virginia, and Charlotte, North Carolina and is gaining traction among people, with roughly one in five people being aware of the new product in one survey in Italy where it was first introduced.[11] A 2019 longitudinal study of young adults in the US, 24.1% of whom used cigarettes and 32.7% used e-cigarettes, showed overall awareness was fairly low at 9%. Yet, HnB products were perceived as less addictive than cigarettes, smokeless tobacco, and e-cigarettes, and less harmful and more socially acceptable than other tobacco products except for e-cigarettes and hookah.[12] Alarmingly, PMI has been very successful in marketing their products as "safe" alternatives, especially to younger generations.[13]

iQOS Claims

Researchers at PMI claim that iQOS has the potential to present less risk of harm compared to continued smoking for adult smokers who switch to it completely (Table 1). Strikingly, many countries have laws that protect people from passive

smoke, but since this product claims to have no smoke it is often exempt from the same tobacco and nicotine laws required for other tobacco products.[11] In the media, iQOS is being promoted as a potentially less harmful alternative not only compared to smoking traditional cigarettes but also compared to vaping electronic cigarettes.[14] A survey in London found that iQOS was perceived as less harmful than smoking, but not risk-free.[15] Some studies show that these products significantly reduce levels of harmful carcinogens.[16] However, most of these studies are funded by tobacco companies, so we need to proceed with caution when interpreting this data.[17]

On June 29, 2021, PMI took out a full-page ad in the Wall Street Journal quoting Dr Moira Gilchrest, Vice President, Strategic and Scientific Communications, in which she talked about "misinformation and disinformation" apparently referring to those who express caution about adopting HnB. Only near the end of the ad did Dr Gilchrest mention that PMI is on a path to replace cigarettes with scientifically substantiated alternatives for those adults who would otherwise continue to smoke, referring to, but not naming iQOS. Our commentary focuses on providing evidence-based independent information on HnB.

Independent research (not funded by tobacco companies) on HnB products

Simonavicius et al.[18] performed a systemic literature review of HnB products in 2019. They found that 20 out of 31 studies were affiliated with the tobacco industry and that HnB products exposed users and bystanders to toxicants, although at substantially lower levels than cigarettes.

The original work done by Auer et al[19] is pivotal to the early combat of these products. The Auer group found that volatile organic compounds, polycyclic aromatic hydrocarbons, and carbon monoxide were present in iQOS aerosol.[19] Research has shown that polycyclic aromatic hydrocarbons from tobacco smoke are carcinogenic.[20] Carbon monoxide has been shown to have both acute and chronic effects on smokers' health.[21] Furthermore, the Auer group[19] found that iQOS smoke had nearly as much nicotine found in conventional cigarette smoke (roughly 84%), and iQOS smoke contains elements from pyrolysis and thermogenic degradation; same as conventional cigarettes. Work done by Li et al[22] also found that pyrolysis of tobacco from iQOS products released not only harmful constituents but also similar levels of nicotine and tar when compared to cigarettes.

Farsalinos et al[23] showed that the levels of nicotine delivered to the aerosol of the HnB products were lower than tobacco cigarette, higher than e-cigarettes at low puff duration but lower than high-power e-cigarettes at longer puff duration (see Table 1). Breland et al[24] found that the iQOS product actually delivered more nicotine than JUUL, which in 2018 was the most popular e-cigarette brand with a market share of 49.6%.[25] This research suggests that iQOS use will likely lead to nicotine addiction. Nicotine binds to the nicotinic acetylcholine receptors in the brain and other tissues which causes increased dopamine release in certain regions of the brain, leading to dependency on dopamine release that leads to nicotine addiction, especially in the youth.[26] Adriaens et al[27] showed that users preferred iQOS products because they were more satisfying and provided more enjoyable throat sensations.

Davis et al[28] found that iQOS was well manufactured and had similar performance properties when compared to different units and different heat sticks. This is unlike other electronic nicotine delivering devices including vapes, which are highly variable among different brands and units.[29] They also stated

Table 1. PMI claims versus peer-reviewed published research.

CLAIMS FROM PMI	FACTS
Does not generate combustion or smoke	iQOS smoke contains elements from pyrolysis and thermogenic degradation[19]
Contains aerosol that has an average of 95% lower levels of harmful constituents and is much less toxic than cigarette smoke	iQOS aerosol was found to have volatile organic compounds, polycyclic aromatic hydrocarbons, and carbon monoxide. It may or may not be less toxic than cigarette smoke as side-by-side studies have not been done
Reduces exposure to harmful constituents to users who switch to iQOS	Calculated lifetime cancer risk of HnB products is higher when compared to e-cigarettes[39]
Will have a positive impact on a smoker's health	With high levels of nicotine delivery and other harmful constituents, it is unlikely that there will be a positive impact on smokers
Does not adversely affect indoor-air quality according to indoor air-quality tests and is not a source of second-hand smoke	iQOS should fall under the same indoor smoking bans as conventional cigarettes and e-cigarettes
Encourages the potential for full switching among adult smokers, but does not encourage people who have never smoked[10]	Studies have shown that users who have not smoked before are more willing to try these products than ex-smokers[11]
Nicotine levels are "lower" in HnB products	Nicotine levels in HnB are 15.2 mg/g[23], which is similar to levels of nicotine in cigarettes. Nicotine levels are more than doubled in HnB than in e-cigarettes in short puffs[40]

Table 2. Awareness and use of iQOS in Italy, 2017 (Data extracted from Liu, et al).[11]

	N	AWARE OF IQOS, %	HAVE TRIED IQOS, %	INTEND TO TRY IQOS, %
Total	3086	19.5	1.4	2.3
Never smokers	2009	17.5	1.0	1.7
Ex-smokers	389	17.7	0.8	0.5
Current-smokers	688	26.4	3.1	5.0
Never users of E-cigs	2924	18.6	1.2	1.7
Ex-user of E-cigs	86	34.3	2.9	12.1
Current-user of E-cigs	76	37.2	7.7	14.0

iQOS' properties facilitated high risk habits and addiction for its users. iQOS can only be operated for about 6 min at a time before needing to be recharged. This time constraint may push users to decrease the time between puffs to get the most nicotine from each stick, thereby increasing the amount of nicotine inhaled with each puff. Increased usage in a short amount time caused tobacco pyrolysis with charring around the heating element after use. PMI recommends that the iQOS be cleaned after being used for 20 tobacco sticks. The Davis group found that without regular cleaning (at the recommended 20 sticks), the temperature in the heating chamber increased leading to more pyrolysis and charring of the tobacco leading to increased release of toxic constituents. Lastly, Davis et al[28] found that the polymer-film filter that is used to cool the aerosol before it is inhaled in the product melted during use. This plastic melting leads to the release of many chemicals including formaldehyde cyanohydrin. The Environmental Protection Agency has listed this toxic chemical as "extremely toxic" and warned that inhalation of this chemical may cause asphyxiation, similar to that caused by hydrogen cyanide.[28]

Leigh et al[30] found that aerosol from iQOS induced levels of cytotoxicity. They measured 6 cytokines (interleukin (IL)-1β, IL-6, IL-10, CXCL1, CXCL2, and CXCL10) which are indicators of inflammatory cell responses in human lung cells and found that all cytokines were elevated after use. These changes are also shown to correlate with several clinically relevant outcomes and diseases.[31] The levels were actually higher when compared to vapor from e-cigarettes.[30]

Public Health Implications

PMI has stated that their products will not create any new generations of smokers or vapers, rather they will help people quit smoking. However, Liu et al[11] found that iQOS in Italy is already taking a grasp on adult smokers and never smokers. In a study of 3086 subjects, participants were asked about their awareness and use of iQOS (see Table 2). The data shows 739,000 have already tried iQOS in Italy, including 329,000 never smokers and that e-cigarette users, both current and ex-users, are at high risk of trying and using HnB products. This supports the claim of Liu et al[11] that iQOS usage will create new generations of nicotine-addicted users.

A 2018 ITC survey in Japan found that 549 of 658 HnB product users were using them concurrently with cigarette smoking (dual users). If smokers are using HnB products to complement their cigarettes, the harm reduction potential of HnBs is diminished. Furthermore, 90.6% of HnB product users stated that they use these products because they believed they were safer than smoking cigarettes,[32] although a survey in London found that iQOS was perceived as less harmful than smoking but not risk-free.[15]

McKelvey et al[13] investigated PMI's modified-risk tobacco product (MRTP) application seeking authorization from the FDA to market their product as an MRTP. PMI failed to provide any evidence that youth will not find iQOS appealing, will not initiate use of iQOS, and will not perceive these products as risk-free. They found that iQOS will result in adolescent and young adult non-users initiating tobacco use with iQOS and will increase poly-use of iQOS with other tobacco products. Furthermore, these products are sleek, "high-tech" devices designed and marketed in ways known to attract youth.[33] In spite of these concerns, on July 7, 2021, the FDA authorized marketing of IQOS with "reduced exposure".[9] The FDA determined that authorizing these products for the U.S. market was appropriate for the protection of the public health because, among several key considerations, the products produce fewer or lower levels of some toxins than combustible cigarettes.[34] The authorization for iQOS required the company to conduct post-market surveillance and studies to determine whether the MRTP orders continue to be appropriate, including assessing the potential for increased use among youth.

Conclusions and Implications

The work that researchers have put forth is substantial enough to disprove most of the claims by PMI, and iQOS should fall under the same indoor-smoking bans as conventional tobacco cigarettes.[19] There is a continued need for independent research to study the harmful chemicals that are released during the pyrolysis of the tobacco sticks. We know from previous research

that the claimed original function of e-cigarettes to help smokers stop smoking may have actually had the opposite effect and in certain circumstances encouraged conventional cigarettes and actually pushed users to become dual users.[35] We expect the same trend to occur with iQOS users, with nicotine addiction pushing those trends and habits. Unless practicable and sustainable actions are taken, these products will inevitably lead to new generations of nicotine addiction unless action is taken.

Fortunately, there is good news, although it may be temporary. The U.S. International Trade Commission ruled that PMI and its parent company Altria must stop the sales and imports of their iQOS tobacco device in the US as of November 29, 2021 and stop advertising these products online and on social media.[36] The decision is the result of a patent case filed by rival R.J. Reynolds. The trade agency found that the cigarette alternative infringed on two of Reynolds' patents. PMI said it plans to appeal the trade agency's decision.

In 2019, President Donald Trump signed the US Tobacco 21 law restricting the sale of all e-cigarette products to those aged 21 and over after pushback from the community.[37] Successful measures within the communities and implementation of measures and programs set forth by the WHO Framework Convention on Tobacco Control (WHO FCTC)[38] were pivotal in the passing of US Tobacco 21. This law has the potential to save a large number of lives and reduce tobacco/nicotine usage in the USA. If we continue the work previously started to publicize the detrimental effects of HnB products along with tobacco in general, and use media literacy, community-based efforts, and education in schools about the dangers of HnB products, we can potentially prevent them from becoming the next public health crisis.

Author contributions

Samuel CJ Kim wrote the manuscript with support from Theodore C Friedman.

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