ABSTRACT BOOK

3rd Scientific Summit

Tobacco Harm Reduction: Novel products, Research & Policy

24 & 25 SEPTEMBER 2020

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3rd Scientific Summit

Tobacco Harm Reduction:
Novel products, Research & Policy

24 & 25 SEPTEMBER 2020

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24 & 25 SEPTEMBER 2020

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IQOS UPTAKE AND HISTORY OF TOBACCO PRODUCT USE: FINDINGS FROM CROSS-SECTIONAL SURVEYS IN JAPAN, ITALY, AND GERMANY

Steve Roulet, Peter Langer, Julien Almodovar, Karina Fischer, and Pierpaolo Magnani

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PMI R&D, Philip Morris Products S.A., Neuchâtel, Switzerland

Background: With the increasing availability of tobacco products that do not burn tobacco but heat it and have the potential to present less risk of harm, it becomes increasingly important to assess the impact of the emergence of this product category at a population level. Philip Morris Products initiated repeated cross-sectional surveys in Japan, Italy, and Germany to monitor the uptake of its own heated tobacco product (marketed under the *IQOS*® brand name) after its commercialization.

Methods: Surveys with probability samples of the adult general population were used to estimate tobacco use prevalence. In parallel, surveys with random samples of *IQOS* users drawn from *IQOS* Owner databases were used to estimate indicators of tobacco initiation.

Results: In 2018, the prevalence of *IQOS* use among current adult tobacco or nicotine-containing product (TNP) users in the general population in Japan, Italy, and Germany was 16.9%, 2.7%, and 0.7%, respectively. Furthermore, the *IQOS* user survey in these countries indicated that the majority of *IQOS* users in Japan (98.7%), Italy (99.3%), and Germany (99.4%) had a history of TNP use before starting to use *IQOS*.

Conclusions: The data from Japan, Italy, and Germany showed a different extent of switching from cigarettes to *IQOS* among adult smokers. Factors such as regulatory frameworks, harm reduction strategies, product availability and awareness, and consumer acceptance might explain the differences in *IQOS* uptake across these countries.

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Christopher Russell, Gabriel Barnard and Neil McKeganey

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Background: This study examined concordance in self-reported past 30-day use of the JUUL ENDS in response to survey measures of verbal recognition of the JUUL brand name versus visual recognition of the JUUL device.

Methods: A cross-sectional online survey assessed use of 15 brands of pod-based ENDS in non-probability, U.S. nationally representative samples of adolescents (n=1,000), young adults (n=1,000) and older adults (n=1,000) who responded "yes" to the question, "Have you used/vaped a brand of e-cigarette called "JUUL" in the past 30 days?". Respondents then viewed unlabeled images of 27 ENDS that are marketed in the United States, one of which was the JUUL ENDS, and were asked to indicate which, if any, of these ENDS they had used in the past 30 days.

Results: 41.8% (95% CI=38.7% to 44.9%) of adolescents, 60.9% (95% CI=57.9% to 63.9%) of young adults, and 41.7% (95% CI=38.6% to 44.8%) of older adults who reported past 30-day JUUL ENDS use in response to the JUUL brand name recognition-based question subsequently identified an image of the JUUL ENDS as a device they had used in the past 30 days. Of those who reported past 30-day JUUL ENDS use in response to both the name and image recognition questions, 70.5% of adolescents (95% CI=66.1% to 74.8%), 78.0% of young adults (95% CI=74.7% to 81.3%), and 73.5% of older adults (95% CI=69.3% to 77.7%) correctly identified an image of the JUUL ENDS as "a JUUL".

Conclusions: The visual similarity of the JUUL ENDS to an increasing number of 'JUUL-like' ENDS may be contributing to the individuals' confusion about the brands of pod-based ENDS they have used. Surveys may more accurately estimate the population's use of the JUUL ENDS by coupling verbal survey items with at least one image of the JUUL ENDS.

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SMOKING HABITS IN PATIENTS WITH ACUTE CORONARY SYNDROME, AFTER THEIR DISCHARGE FROM THE HOSPITAL

Antria Neokleous, Kallirhoe Kourea, **Gavriela Kostelli,** and Ignatios ikonomidis

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Introduction: The negative effects of smoking in patients with Acute Coronary Sydrome (ACS) and their attitude towards smoking after discharge were investigated. The association of passive smoking and ACS has also been studied.

Methods: The study was based on 103 smokers and 61 passive smokers. A questionnaire was used as a research tool for collecting data during patient hospitalization. Subsequently, smokers were assessed for their smoking habits by telephone after 3 and 6 months. The degree of dependence of patients on nicotine with the help of the Fagerstrom test was also measured.

Results: Of the 103 smokers, there were 82 men and 21 women. The average starting age for smoking was 19 years. In the follow-up after 3 months, 70.9% of patients reported having quit smoking. In the second follow-up at 6 months, 37.9% had resumed smoking. The 55.3% of the population had a high dependence and lack of self-control related to smoking behavior. The association of smoking cessation at 3 and 6 months with age, the number of cigarettes smoked and the Fagerstrom score showed that patients who quit smoking for 6 consecutive months, had a lower average Fagerstrom score than those who discontinued at 3 but resumed up to 6 months 6.4 ($t=2.97$, $p=0.004$). 61 passive smokers with an average age of 67 years took part. The majority of people were in public places where others smoked (65.6%). A 100% of the participants in this group said that passive smoking is harmful to health and suffered from Acute Coronary Syndromes.

Conclusions: Age did not appear to be associated with the recurrence of smoking behavior. The factors that appeared through this study to be directly related to relapse are the number of cigarettes smoked by patients before their arrival in the hospital and their addiction to nicotine.

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TOXICOLOGICAL ASSESSMENT OF FLAVORED E-LIQUIDS IN SPRAGUE DAWLEY RATS IN AN OECD SUBCHRONIC INHALATION STUDY COMPLEMENTED BY SYSTEMS TOXICOLOGY ENDPOINTS

Jenny Ho[1], **Davide Sciuscio[2]**, Ulrike Kogel[2], Blaine W. Phillips[1], Bjoern Titz[2], Patrice Leroy[2], Gregory Vuillaume[2], Marja Talikka[2], Stefan Lebrun[2], Wenhao Xia[1], Yang Xiang[2], Ashraf Elamin[2], Keyur Trivedi[2], Nikolai V. Ivanov[2], Julia Hoeng[2], Manuel C. Peitsch[2], and Patrick Vanscheeuwijck[2]

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Introduction: A few studies have evaluated the toxicity of e-liquid flavors when inhaled.

Methods: The toxicity of a mixture of flavors in an e-liquid was characterized in a 90-day inhalation study following OECD Test Guideline 413 by using 28 flavor group representatives (FGR) selected by grouping 178 flavors into 26 distinct groups on the basis of chemical structure. A scoring approach was used to create flavor groups. Substances predicted to be of potential toxicological concern were also included in each group to create representative hypothetical mixture (probable worst-case scenario). Sprague Dawley rats were exposed for 6 h/day, 5 days/week, for at least 13 weeks to aerosols of a vehicle, an e-liquid (propylene glycol [PG], vegetable glycerin [VG], and nicotine), an e-liquid with three concentrations of FGR mixture, or PG/VG with a medium concentration of FGR mixture, 6 arms in total. The test atmosphere concentrations of nicotine, PG, and VG were 23, 1520, and 1890 µg/L, respectively. The concentrations of the 28 flavors were derived from the maximum levels used in our products at the time of the conduct of this study.

Results & Conclusions: The results indicated that inhalation of the flavored e-liquid caused minimal local and systemic toxic effects. None of the groups showed significant changes in the number of inflammatory cells or chemokine levels in bronchoalveolar lavage fluid. The effects of exposure to the FGR mixture were limited and nicotine-mediated, including changes in hematological and blood chemistry parameters and organ weights. There were minimal histopathological findings. Macro- and microscopic findings in the spleen, adrenal, and thymus were attributed to procedure-related stress. The FGR mixture added to the e-liquid did not induce a measurable response at the nose, lung and liver transcriptome level—except a nicotine-mediated effect on metabolic processes. Those results showed mainly nicotine exposure-associated effects and limited synergistic effects attributable to the flavors.

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COMPARATIVE HEALTH RISK ASSESSMENT OF JUUL SYSTEM AND COMBUSTIBLE CIGARETTE

Roxana Weil, Charlene Liu, Perla Valencia Landestoy, Vincent Cheah, Christina Sulaiman, Bryant Hiraki, Clarissa Yang, Mike Oldham, Jie Zheng, and Felix Ayala-Fierro

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JUUL Labs, Inc.

Background: Tobacco smoke is a highly complex mixture of carbon-based solid particulate matter containing over 5000 constituents, 93 of which have been identified in tobacco products and tobacco smoke or aerosol by the U.S. Food and Drug Administration (FDA) as harmful and potentially harmful constituents (HPHCs) linked to the most serious health effects of tobacco use (cancer, cardiovascular and respiratory diseases, and reproductive effects). The JUUL System heats a nicotine-containing liquid within a pre-defined temperature range designed to minimize HPHCs formed as heat degradation by-products of the e-liquid ingredients. With the premarket tobacco product application (PMTA) as the pathway to market for electronic nicotine delivery systems (ENDS) in the US, there is a need to determine the potential health risks of ENDS products not only in relation to combustible cigarettes, but also as an independent product considered as an alternative to smoking. The objective of this study was to assess the relative noncancer hazards and cancer risk from use of the JUUL System (Virginia Tobacco 5.0% and Menthol 5.0%) compared to combustible cigarettes.

Methods: JUUL System aerosol samples collected under non-intense and intense puffing conditions were analyzed using targeted chemical analyses for the FDA recommended HPHCs and compared to constituent levels in smoke from combusted cigarettes. HPHC yields in mainstream smoke generated under non-intense and intense machine smoking regimens were obtained from the published literature for the 3R4F reference cigarette.

Results: The aerosol produced from heating the JUUL System showed a marked reduction in the overall number and levels of HPHCs, including greater than 92 to 99% reduction of the most potent toxicants and carcinogens identified by the World Health Organization (WHO) Study Group on Tobacco Product Regulation as playing a major role in combustible cigarette smoke toxicity and mandated for reduction.

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Conclusions: The decrease in the number and levels of HPHCs in JUUL System aerosols demonstrate likely substantial reductions in toxicant exposures and the overall associated health hazards (i.e., cancer risks and noncancer hazards) compared to cigarette smoking.

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REAL-TIME ASSESSMENT OF E-CIGARETTES AND CONVENTIONAL CIGARETTES EMISSIONS: AEROSOL SIZE DISTRIBUTIONS, MASS, AND NUMBER CONCENTRATIONS

Spyros Lampos[1], Evangelia Kostenidou[2,#], Konstantinos Farsalinos[1], Zoi Zagoriti[1], Aristeidis Ntoukas[1], Demetrios Kouretas[3], **George Lagoumintzis[1],** and Konstantinos Poulas[1,4]

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Cigarette smoke is a complex mixture of chemical compounds which are emitted during the processes of tobacco combustion. Electronic cigarettes (e-cigs) are expected to produce less harmful compounds due to the absence of tobacco leaf combustion. However, potential risks of the passive exposure to the aerosol exhaled by e-cig users have been raised in the last decade. In this study, the aerosols with diameter less than 1 μm (PM_1) produced by vaping of various e-cig liquids were compared to those generated by smoking conventional cigarettes in real-time. The mass and number concentration along with the number size distribution were measured in a closed room of 35 m^3 volume. Our results showed that aerosol emitted from e-cig liquids had a different profile compared to the conventional cigarettes. Although e-cigs initially produced higher particle mass and number concentrations, they had much shorter life time of approximately 10-20 seconds, in comparison with the conventional and hand-rolling cigarette particulate emissions which had a dissipation time of approximately 1.4 h in a 35 m^3 room. E-cigs emitted aerosols which volatilized rapidly, as they probably consist almost only of propylene glycol and/or vegetable glycerin.

ABSTRACT BOOK

EVALUATING THE IMPACT OF ELECTRONIC CIGARETTE FLAVORING AGENTS IN ALDEHYDE EMISSIONS

Mohamed A. El Mubarak[1], Charikleia Danika[1], Nikos Vlachos[2], George Lagoumintzis[2], Gregory Sivolapenko[1], and Konstantinos Poulas[2]

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Toxic aldehyde emissions, such as formaldehyde, acetaldehyde and acrolein, formed from heating mixtures of propylene glycol and vegetable glycerin, as well as flavoring compounds—typical carrier solvents for electronic cigarette liquids—is one of the main health concerns about electronic cigarette usage, since these aldehydes are potential irritants, toxicants and/or carcinogens. Recent studies have shown that e-liquid flavors are the major factor for aldehyde emissions.

The aim of this study was to explore the effect of flavoring compounds in acetaldehyde, acrolein, crotonaldehyde and formaldehyde emissions in commercially top selling flavored categories of e-liquids. The e-liquids used, can be categorized in three groups: Sweets, Tobacco and Fruits flavors. A Nautilus 2, 0.7 Ω resistance was used and the atomizer was tested at 3.7 V. Our results show that as far as for acetaldehyde, Fruit flavors produced in general the lower emissions, with the Sweets and Tobacco flavors producing the highest emissions. However, in case of formaldehyde, Fruit flavors dominate in formaldehyde emissions, followed by Sweets and then Tobacco flavors. As for acrolein and crotonaldehyde, the opposite propensity of formaldehyde was observed. Yet, it is worth mentioned, that even among flavors of the same category, intense variations were observed. Our study—in line with previous reports for aldehyde emissions from e-cigarettes—adds to the growing concerns regarding long-term health effects of carbonyl emissions from e-cigarettes that warrants continuous monitoring and further investigation.

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ALDEHYDE EMISSIONS IN RELATION WITH RESISTANCE TEMPERATURE AND AGING IN E-CIGARETTES

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One of the main health concerns about electronic cigarette use is the potential for toxic aldehyde emissions, such as formaldehyde, acetaldehyde and acrolein, which are known to be formed from heating mixtures of propylene glycol and vegetable glycerin, typical carrier solvents for electronic cigarette liquids, as thermal decomposition products. The levels of the aldehyde emissions are highly dependent on the temperature of the heating coil.

The objective of this study was: a) to explore the aldehyde emissions of a mixture of propylene glycol and glycerin (50:50) in different voltage settings and consequently to higher vaping temperatures, and b) to investigate how resistance temperature and resistance aging influences the emission levels of the aldehydes. A Nautilus 2, 0.7 Ω resistance was used and the atomizer was tested at 3.7 V, 4.3 V and 5 V. Aldehyde emission levels are found to raise in higher voltage settings and accumulate proportionally over serial vaping cycles. In addition, high voltage settings appeared to be detrimental to the resistance's lifetime. At 3.7 V and 4.3 V a sharp increase in aldehyde emission was observed at approximately 1200 puffs, while at 5 V a similar raise was observed approximately at 300 puffs. Our results indicate a considerable different lifespan of electronic cigarettes' resistance due to high temperatures in the resistance, possibly because of high voltage settings.

ABSTRACT BOOK

THE ROLE OF ENDOTHELICAL GLYCOCALYX IN SMOKERS WITH ACUTE CORONARY SYNDROME

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Introduction: Smoking is the most common cause of cardiovascular diseases. Endothelial glycocalyx has been shown to be a regulator of vascular permeability and inflammation, but its role in acute coronary syndrome (ACS) remains unknown.

Aim: To investigate the effect of smoking on endothelial glycocalyx in patients with ACS.

Methods: 80 patients, 40 active smokers and 40 non-smokers with ACS were studied. During their hospitalization, a questionnaire was completed, and blood samples were taken to determine the value of troponin (T), creatine phosphokinase (CK-MB), and other markers of inflammation such as CRP and leukocytes (WBC). In the Laboratory of Preventive Cardiology (4 days later) the parameters of aortic function were measured, such as aortic pulse wave velocity (PWVa), augmentation index (Aix), central and peripheral blood pressure with Complior and Arteriograph devices. The evaluation of the endothelial glycocalyx (PBR) was performed using a camera with the SFD method. The nicotine dependence was assessed using the Fagerstrom Test. Exhaled monoxide (CO) levels were measured.

Results: Smokers showed multiple vascular damage (stem and 3 vessels) and increased values compared to non-smokers of PBR indicators, which means greater deterioration. Also, the group of smokers showed a statistically significant difference in the values of Aix and the central pressures. The mean value of the PWV, although higher in smokers, the difference was statistically insignificant compared to non-smokers. The prices of T, CK-MB, CRP, and WBC were increased (almost three times) also in smokers. The majority of patients underwent angioplasty.

Conclusion: The endothelial glycocalyx can be a potential key indicator of vascular permeability and inflammation, which helps in the prognosis of risk of ACS.

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PRECLINICAL EVALUATION

THE FLAVORING AND NOT THE NICOTINE CONTENT IS A DECISIVE FACTOR FOR THE EFFECTS OF REFILL LIQUIDS OF ELECTRONIC CIGARETTE ON THE REDOX STATUS OF ENDOTHELIAL CELLS

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Electronic cigarettes are constantly gaining ground as they are considered less harmful than conventional cigarettes, and there is also the perception that they may serve as a potential smoking cessation tool. Although the acute effects of electronic cigarette use have been extensively studied, the long-term potential adverse effects on human health remain largely unknown. It has been well-established that oxidative stress is involved in the development of various pathological conditions. So far, most studies on e-cigarettes concern the effects on the respiratory system while fewer have focused on the vascular system.

In the present study, we attempted to reveal the effects of electronic cigarette refill liquids on the redox state of human endothelial cells (EA.hy926 cell line). For this purpose, the cytotoxic effect of three e-liquids with different flavors (tobacco, vanilla, apple/mint) and nicotine concentrations (0, 6, 12, 18 mg/ml) were initially examined for their impact on cell viability of EA.hy926 cells. Then, five redox biomarkers [reduced form of glutathione (GSH), reactive oxygen species (ROS), total antioxidant capacity (TAC), thiobarbituric acid reactive substances (TBARS) and protein carbonyls (CARBS)] were measured. The results showed a disturbance in the redox balance in favor of free radicals in tobacco flavored e-liquids while vanilla flavored e-liquids exhibited a more complex profile depending on the nicotine content. The most interesting finding of the present study concerns the apple/mint flavored e-liquids that seemed to activate the cellular antioxidant defense and, thus, to protect the cells from the adverse effects of free radicals. Conclusively, it appears that the flavorings and not the nicotine content play a key role in the oxidative stress-induced toxicity of the e-liquids.

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NICOTINE, RISK AND SAFETY FACTORS - A SYSTEMATIC REVIEW OF PRECLINICAL STUDIES OF ITS TOXICOLOGY

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TOBACCO CIGARETTE, BUT NOT ELECTRONIC CIGARETTE AND HEATED TOBACCO PRODUCT, IMPAIRS 3T3-L1 PRE-ADIPOCYTE DIFFERENTIATION TO BEIGE ADIPOCYTES

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Electronic cigarettes (ECIG) and heated tobacco products (HTP) are alternative nicotine delivery systems used as cigarette smoking (CS) cessation tools. They are also promoted as less harmful than CS because known carcinogens and toxic constituents generated by tobacco combustion in CS are detected in substantially lower levels in ECIG and HTP aerosols. *In vitro* studies, mainly in airway epithelial cells, have reported reduced cytotoxic, inflammatory, and oxidative impact of ECIG and HTP compared to CS. However, the impact of ECIG and HTP on the energy-dissipating brown and "beige" adipocytes has not yet been compared side-by-side to that of CS.

In this study, we sought to examine and compare the effects of CS, ECIG and HTP on 3T3-L1 pre-adipocyte differentiation towards a beige adipocyte fate. For the administration of CS, HTP and ECIG aerosols, extract-enriched media were prepared, and the concentration of nicotine was determined in each extract by LC-MS/MS, as an equalizing factor. CS was found to be more cytotoxic to 3T3-L1 pre-adipocytes in a dose- and exposure time-dependent manner. Additionally, non-cytotoxic concentrations of CS extract significantly impaired pre-adipocyte differentiation towards a "beige" adipocyte phenotype as seen by a) the significantly decreased relative lipid accumulation and number of mature differentiated cells containing multilocular lipid droplets and b) the reduced mRNA levels of the brown/"beige" adipocyte-selective marker *Pgc-1α* and of the general adipogenic markers *Ppar-γ* and *Resistin*. In contrast, only minimal such effects were observed in cells exposed to HTP aerosol, while exposure to ECIG aerosol did not significantly modify these parameters.

We conclude that the CS extract, but not the HTP and ECIG extracts, negatively impacts pre-adipocyte differentiation to beige adipocytes and may thus modify the metabolic capacity of adipose tissue.

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COMPARATIVE ANALYSIS OF NICOTINE AND COTININE LEVELS BY LC-MS/MS IN MOUSE PLASMA AND BRAIN FOLLOWING EXPOSURE TO CIGARETTE SMOKE, HEATED TOBACCO PRODUCT AEROSOL AND E-CIG VAPOR

Mohamed A. El Mubarak[1], Zoi Zagoriti[2], Korina Atsopardi[3], Konstantinos Farsalinos[2], Marigoula Margarity[3], Stavros Topouzis[4], Konstantinos Poulas[2], and Gregory B. Sivolapenko[1]

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Nicotine is the major ingredient of tobacco, which is responsible for the addictive properties of smoking in humans. Cotinine constitutes the principal metabolite of nicotine and is considered a valid indicator of cigarette smoke (CS) exposure. Electronic cigarettes (e-cig) and heated tobacco products (HTP) have been designed to deliver nicotine through an inhaled aerosol and have been used as smoking cessation alternatives.

The objective of this study was to develop a sensitive, selective and reproducible LC-MS/MS method for the simultaneous determination of nicotine and cotinine and to evaluate and compare the effect of CS, HTP and e-cig exposure on nicotine and cotinine levels in mouse plasma and brain homogenate. The preclinical exposure protocol included 20 BALB/c male mice exposed to CS, HTP aerosol, e-cig vapor or ambient air, daily for a week. Plasma samples were collected during the exposure period, while the brain was isolated at the 7th day. Chromatographic separation was achieved using a Gemini NX-C18 column 150×2.0 mm, 3μm, proguard, 2.0 to 4.0 mm (Phenomenex) operating at 40°C. The mobile phase was consisted of ammonium bicarbonate 10 mM, (solvent A) and acetonitrile (solvent B) with a gradient elution at flow rate of 0.3 mL/min. Protein precipitation was achieved with 1% ammonia in acetonitrile and gave the highest nicotine and cotinine recovery (~70%).

The developed method showed high sensitivity with lower limit of quantification of 0.5 and 0.25 ng/mL for nicotine and cotinine, respectively. Increased plasma levels of both nicotine and cotinine were reported during the 1-week exposure period. The highest concentrations of nicotine and cotinine were detected in the plasma of animals exposed to HTP (23 ng/mL and 29 ng/mL, respectively), compared to CS and e-cig-exposed mice. In brain, ~28, 19 and 16 ng/mL of nicotine were identified in HTP, CS and e-cig-exposed mice, respectively, while cotinine was found to be <10 ng/mL.

ABSTRACT BOOK

THE IMPACT OF BANNING ENDS PRODUCTS ON COMBUSTIBLE CIGARETTE SALES: INITIAL EVIDENCE FROM U.S. STATE-LEVEL POLICIES

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Objectives: In fall 2019, several states in the US passed short-term bans on the sale of Electronic Nicotine Delivery Systems (ENDS), partially in response to an outbreak of illnesses tied to THC vaping products that received national news coverage. As ENDS products are an alternative for adult smokers to switch away from cigarettes, there may be unintended consequences for them in banning ENDS. This study provides preliminary evidence of the impact of state-level ENDS bans on cigarette sales.

Methods: Generalized Synthetic Control (GSC) models were used to predict counterfactual cigarette sales for states that passed an ENDS ban in fall 2019, based on synthetic weights derived from states that did not pass such bans. The outcome was weekly cigarette sales per capita, based on commercial data, from Jan. 2018 - Dec. 2019. Factors that affect tobacco product sales, including smoking prevalence, tobacco taxes, inflation, unemployment, population size, and lagged ENDS market share, were included as control variables. Fixed and random effects accounted for state and time-level variation.

Results: Cigarette sales in states banning ENDS were significantly higher than would have been observed otherwise. A full ban on ENDS products increased weekly per capita cigarette sales by 8.3% in Massachusetts ($p<0.001$); banning just flavored ENDS products resulted in higher than expected sales in Washington (4.6%) and Rhode Island (5.0%) ($ps<0.001$). States that passed a ban that was later revoked (Oregon, Michigan) showed no difference in observed cigarette sales in the same period. Results were robust to a number of validation and specification checks.

Conclusions: This study provides some of the first evidence that banning ENDS products may have unintended consequences, such as potentially higher cigarette sales than would have been seen otherwise in the time following the bans. Future research is needed to understand the longer-term impact of these policies.

ABSTRACT BOOK

UNDERSTANDING THE NEED TO (RE) INNOVATE TOBACCO HARM REDUCTION STRATEGIES FOR THE INDIAN SUBCONTINENT

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Tobacco harm reduction (THR) initiatives have had relatively good success in the West by introducing alternatives such as Snus, Electronic Nicotine Delivery Systems (ENDS) and Nicotine Replacement Therapy (NRT) while driving down demand of harmful tobacco products based on guidelines from Article 14 of the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC). Similar initiatives are now being adapted in South Asian countries like India and Bangladesh. However, THR for these countries need to overcome challenges mainly concerning affordability, acceptability, and usability of alternatives for tobacco consumers. Further, disease and substance use data can be vital for establishing region-specific THR objectives. This study presents historical data on the prevalence of a) smoking and lung cancer, and b) smokeless tobacco and oral cancer which are closely correlated with direct causation. With more than twice the number of smokers, SLT products form the most popular tobacco form in India. Should we then expect that oral cancer might present a bigger health risk than lung cancer, and that THR should be primarily targeted to reduce SLT consumption?

Challenges for THR aimed at SLT use in India remain incomprehensible accountable to socio-cultural and economic complexities. Although reduced risk products such as Snus, ENTs, NRTs along with cessation initiatives based on smartphone use provide some clues, THR for countries like India has to be strategically driven by first understanding existing challenges. Preliminary data suggests that oral cancer might be the elephant in the room as illustrated in Fig. 1 requiring hybrid cessation models. Further, this data emphasizes the urgent need to re-innovate THR products, early interventional and detection technologies for South Asia, especially considering that underprivileged population sub-groups form majority of patients diagnosed with oral cancer which is a direct health burden from SLT consumption.

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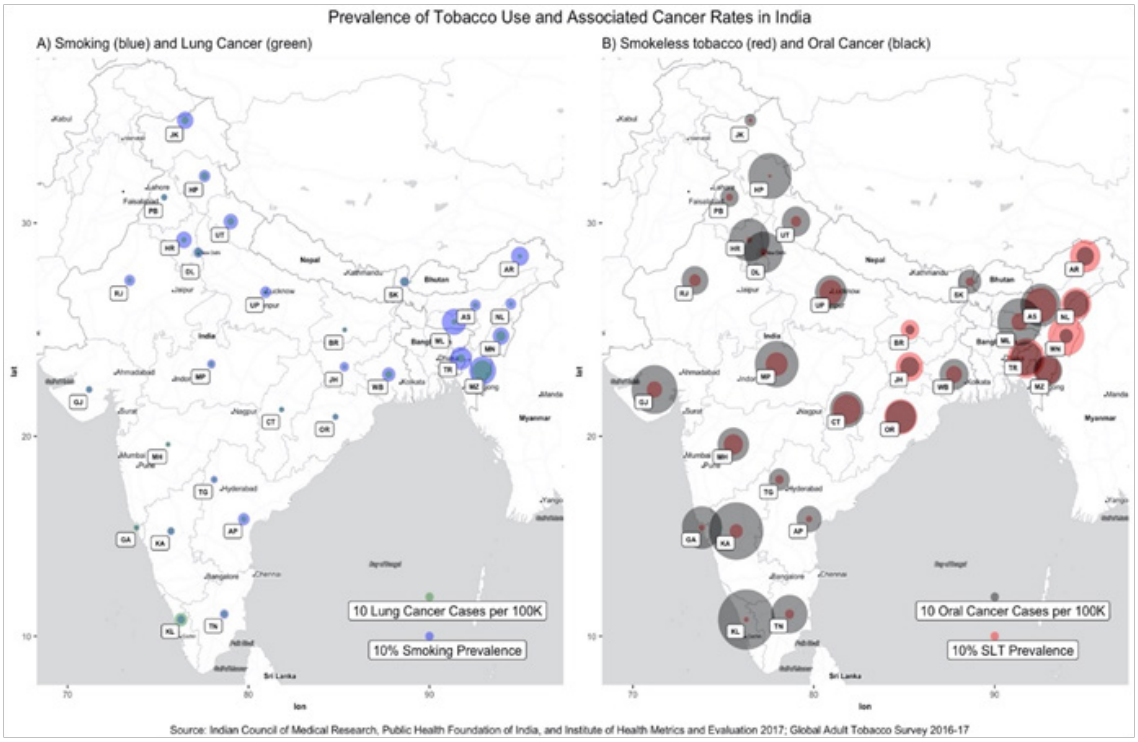

Figure 1. *Prevalence of smoking and smokeless tobacco in Indian states shown together with rates of lung cancer and oral cancer, respectively.*

ABSTRACT BOOK

SWITCHING AMONG ADULT SMOKERS WHO PURCHASED THE JUUL SYSTEM: 12-MONTH FOLLOW-UP RESULTS FROM TWO LARGE LONGITUDINAL STUDIES

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Objective: Evaluating complete switching away from combustible cigarettes is a key component of assessing the potential population health benefit of ENDS. Switching was assessed in two parallel longitudinal studies of adult smokers who purchased the JUUL System.

Methods: Adult smokers (age ≥21 years, smoked in the past 30 days at baseline, smoked ≥100 cigarettes in lifetime and currently smoke 'some days' or 'every day') who purchased the JUUL System (JS; Juul Labs, Inc.) in 2018 were recruited into two prospective cohort studies. Past 30-day smoking (yes/no) was assessed via online surveys 12 months after JS purchase. Point prevalence of past 30-day complete switching (no cigarette smoking in the past 30 days, not even a puff) was calculated, and logistic regression models assessed factors associated with switching at 12 months.

Results: Among respondents, self-reported complete switching at 12 months was 51.2%, in Study 1 (N=11,919) and 58.6% in Study 2 (N=8,511). Covariate-adjusted odds for reporting past 30-day switching at 12 months was significantly higher for daily (vs. non-daily) users of JS, and among participants with lighter smoking histories. Participants who reported purchasing JS to help "quit smoking" (vs. those who did not purchase to quit smoking) were more likely to report switching at 12-months (Study 1: OR [95% CI]=1.36 [1.21, 1.53]; Study 2: OR [95% CI]=1.32 [1.16, 1.51]).

Conclusions: Results were consistent across both studies: more than 50% of smokers reported complete switching at 12-months. Switch rates were high among all smokers, although lighter smoking history, increased frequency of JS use, and intention to quit smoking (switch) were significantly associated with switching at 12-months. These results concord with and extend published data that suggests use of JS among adult smokers is associated with switching.

ABSTRACT BOOK

MODELING POTENTIAL HEALTH GAINS AND HEALTH SYSTEM SAVINGS ASSOCIATED WITH VAPORIZED NICOTINE PRODUCTS IN CANADA

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Objectives: To model population-wide health and cost impacts of vaporized nicotine products (VNPs) use among Canadian adults 20 years and older from 2015-2095.

Materials & Methods: The AppEco multi-state lifetable model was used to project potential changes in life expectancy and health-system costs, overall and by province/territory, using a 0% discount rate. The simulated population was divided into 68 cohorts by sex, ethnicity, and 5-year age groups. Each year, individuals could either remain in their current state, or transition to one of six smoking/vaping states. Input data including smoking/vaping prevalence by state, transition matrices, and relative risks of tobacco-related (TR) diseases by smoking/vaping state were extracted or estimated using data from Statistics Canada and literature. For each TR disease, incidence, prevalence, and direct healthcare and indirect costs were calculated. Three scenarios were modeled to reflect a range of uncertainty: Status Quo ("SQ", VNPs commercialized as they are currently in Canada); No-Vaping ("NV", assuming VNPs never entered the Canadian market); and a Pro-Switching Policy ("PSP", assuming increased VNP prevalence).

Results: The model performed well against validation with publicly available data. Compared to NV, SQ projected to increase life-years by 922,547, while PSP increased them further (+718,137). SQ projected a C$39.0 billion reduction in cumulative lifetime costs compared to NV; PSP would further reduce them by C$30.4 billion. Statistical variability was assessed using sensitivity analyses on input parameters, and Monte-Carlo simulations.

Conclusions: Accessibility to VNPs in Canada was projected to generate net public-health gains and health-system cost savings. These projected health and economic consequences are sensitive to assumptions about accessibility and use by adult smokers and may vary by type of policy environment.

ABSTRACT BOOK

HELP HER QUIT: A WOMEN-CENTERED STRATEGY FOR UP-SKILLING OBGYNS IN TOBACCO HARMFULNESS KNOWLEDGE AND SMOKING CESSATION

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***Team of 60 European Scientists supporting the project as HHQ Ambassadors**

Women smokers compared to non-smokers demonstrate higher risk of cancers including many forms of gynecologic cancers, coronary and vascular diseases, chronic obstructive lung disease (COPD), reproductive health, embryo development and osteoporosis. Tobacco use has harmful effects on women of all ages. Greek women remain the world's leading smokers. The obstetrician-gynecologist when trained is well positioned to counsel women on tobacco consumption and cessation. IASO is one of the top European private women's hospitals and IOL a leader institute in IVF. As smoking is very common among women, we decided to create our strategy for the benefit of women smokers of all ages, pathologies, fertility and pregnancy.

HELP HER QUIT (HHQ) is IASO and IOL strategic partnership to up-skill doctors and healthcare personnel in smoking cessation and knowledge of harm reduction (URL: www.hhquit.eu).

HELP HER QUIT Milestones:

a) Mapping the level of awareness and capacities of OBGYNs in" tobacco and women's health".

b) Building OBGYNs/ midwives/ nurses' capacities to help women in smoking cessation.

c) Developing a toolkit for MD-OBGYNs on women's health/fertility/cancer and smoking, including smoking cessation guidelines, scientific, medical, and epidemiological issues on modified risk products and all issues on harm reduction.

d) Informing women on smoking harmfulness.

References
1. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2011/09/tobacco-use-and-womens-health
2. https://clivebates.com/documents/BeagleholeLancet.pdf
3. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31884-7/fulltext

ABSTRACT BOOK

DIFFERENTIAL EFFECTS OF HEAT-NOT-BURN AND CONVENTIONAL CIGARETTES ON CORONARY FLOW, MYOCARDIAL AND VASCULAR FUNCTION

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Background: Heat-not-burn cigarette (HNBC) constitutes a non-combustible smoke product. However, its cardiovascular effects have not been defined.

Objectives: We compared the effects of HNBC to those of tobacco cigarette (TCig), on arterial stiffness, oxidative stress, and platelet activation, acutely and after 1 month of switching to HNBC, as well as on endothelial, myocardial, and coronary function after 1 month of switching to HNBC.

Methods: In the acute study, 50 smokers were randomised into smoking a single Tcig or an HNBC and after 60 minutes were crossed over to the alternate smoking (HNBC or Tcig). For the chronic phase, 75 smokers were examined. Of those, 50 were switched to HNBC and 25 continued Tcig for 1 month. Pulse wave velocity (PWV) and biomarkers [malondialdehyde (MDA), protein carbonyls (PC), and thromboxane B2 (TXB2)] were assessed in the acute and chronic study. Myocardial deformation [global longitudinal strain (GLS), myocardial work index (GWI) and wasted myocardial work (GWW)], coronary flow reserve (CFR) by echocardiography, total arterial compliance (TAC), and flow-mediated dilation (FMD) were additionally assessed in the chronic study.

Results: Compared to baseline, TCig smoking acutely increased exhaled CO, PWV, MDA, and TxB2 ($p<0.05$), while no changes were observed after HNBC. Compared to resuming Tcig smoking, switching to HNBC for 1 month improved CO (mean change: -55% vs -2.4%), FMD (+55% vs +15%), CFR (+46% vs +4%), TAC (+9% vs -0.5%), GLS (+6% vs +1%), GWW (-19% vs +0.5%), MDA (-19% vs 1 %), and TxB2 (-12% vs 4%) ($p<0.05$ for all comparisons).

Conclusions: HNBCs exert a less detrimental effect on vascular and cardiac function than tobacco cigarettes.

ABSTRACT BOOK

ASSESSING THE HEALTH EFFECTS OF SWITCHING TO THE TOBACCO HEATING SYSTEM RELATIVE TO SMOKING CESSATION ON BIOMARKERS OF POTENTIAL HARM: ADDITIONAL EVIDENCE ON THE POTENTIAL TO REDUCE THE RISK OF SMOKING-RELATED DISEASES

Christelle Haziza, Marija Bosilkovska, S. Michael Ansari, Loyse Felber Medlin, Wee Teck Ng, Guillaume de La Bourdonnaye, and Annie Heremans

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Background: The Institute of Medicine considers biomarkers of potential harm (BoPH) appropriate for estimating reduced risk for cigarette alternatives. Such approach could offer smokers, who would otherwise continue smoking, faster access to potentially less harmful than cigarettes.

A core of eight BoPH, reversible upon smoking cessation (SC) and associated with smoking-related diseases, were selected based on Hill's criteria, to estimate the reduced risk potential associated with tobacco heating system (THS) switching in smokers in clinical studies. As SC is the best path to risk reduction, changes in these BoPH were evaluated in THS switchers against smokers who stopped smoking.

Methods: The exposure response study (ERS) was a 6-month study (NCT02396381), extended by 6 months (NCT02649556), in adult healthy smokers, not willing to quit, randomized to THS or to cigarettes. Concurrently, a 12-month smoking cessation study (SCR) was conducted with adult healthy smokers, willing to quit for 12 months (NCT02432729).

Baseline comparability of data across THS, cigarette, and quitter groups was evaluated using a propensity score (PS) approach. The effect magnitude in the THS group was benchmarked against quitters for each BoPH.

Results: THS users (n=248), with over 70% of THS use, showed favorable BoPH changes versus smokers (n=398), congruent with quitters (n=327). At least 40% of the SC effect was preserved for 5 out of the eight BoPH. In THS users with CEMA (BoExp to acrylonitrile) <40 ng/mg creatinine (n=93), more than 66% of the SC effect was preserved for: igh-density-lipoprotein-C; white blood cell; forced-expiratory-volume-in-one-second FEV1; carboxyhemoglobin; total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; 8-epi-prostaglandinF2α; s-intercellular adhesion molecule-1. Overall, the preserved SC effect ranged between 44.3% and 100% across the 8 BoPHs for THS users.

Conclusions: The preserved SC effect when switching to THS provides evidence that THS potentially reduces the risk of developing smoking-related diseases in smokers who would otherwise continue smoking.

Funding:
Philip Morris International is the sole source of funding and sponsor of this research.

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TOBACCO HEATING SYSTEM 2.2 IN MILD TO MODERATE CHRONIC OBSTRUCTIVE PULMONARY DISEASE SUBJECTS: AN EXPLORATORY ANALYSIS

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Background: Tobacco Heating System (THS) 2.2, a novel product that electronically heats tobacco at temperatures significantly lower (<350) than those generated when burning cigarettes (CC), produce substantially lower levels of harmful and potentially harmful constituents, with 90% mean decrease. A randomized, two-arm parallel group, multicenter exposure study (NCT02396381) demonstrated statistically significant changes in five-of-eight biomarkers of effect (BoEff) at 6 months among adults switching to THS compared to who continued smoking, meeting primary objective, with all BoEffs moving in the direction of smoking cessation (SC). The study was extended by additional 6 months (NCT02649556). These favorable changes were maintained 12 months.

Methods: This analysis explored the THS switching effect (n=17) compared with continued smoking (n=28) in a subgroup of subjects (from the two aforementioned exposure studies) with baseline spirometry indicating mild-to-moderate COPD (GOLD 2018). The results from a subset of subjects (n=18) with mild COPD from 1-year continuous smoking abstinence study (NCT02432729) were used as reference. The analysis was also conducted on a broadened subgroup with obstruction defined by $FEV_1/FVC \leq 0.75$, based on Lung Health Study's review(*) of mild-to-moderate COPD, which defined obstruction with the precedent ATS guidelines. Main respiratory and cardiovascular endpoints were WBC count, sICAM-1 and 8-epi-$PGF_{2\alpha}$ levels.

Results: After 12-month follow-up, COPD subjects showed favorable shifts in the direction of changes observed in SC for most BoEffs after predominant (≥70%) THS use. This magnitude was more pronounced than those in the exposure studies general population (majority were enrolled healthy subjects), with THS–CC: 72mL difference in FEV_1 among COPD, 1.95Gl/L reduction in WBC, 6.8% in sICAM-1 levels, 28% in 8-epi-$PGF_{2\alpha}$ levels for THS relative to CC.

Reference
(*)Scanlon P, Connett J, et al. Smoking Cessation and Lung Function in Mild-to-Moderate Chronic Obstructive Pulmonary Disease -The Lung Health Study. American Journal of Respiratory and Critical Care Medicine; Vol. 161, No. 2; 2000.

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Conclusions: These preliminary analysis results are consistent with the main study findings, with marked changes observed among COPD. These results suggest reduced harm potential for THS vs. smoking in mild-to-moderate COPD subjects.

Difference between THS and CC use	LS mean	95% CI
%pred FEV_1		
Month 6		
General Study Population	0.990	–0.0226, 2.00
COPD (Precedent ATS)*	1.47 (5.98)	–0.525, 3.46
COPD (GOLD 2018) subjects	0.710 (5.83)	–2.97, 4.39
Month 12		
General Study Population	1.16	–0.0625, 2.39
COPD (Precedent ATS)*	1.92 (6.39)	–0.490, 4.32
COPD (GOLD 2018) subjects	3.48 (5.96)	–1.12, 8.07
Best FEV_1 (mL)		
Month 6		
General Study Population	30.1	–6.99, 67.1
COPD (Precedent ATS)*	46.4 (222)	–27.5, 120
COPD (GOLD 2018) subjects	11.1 (209)	–125, 147
Month 12		
General Study Population	40.7	–2.15, 83.5
COPD (Precedent ATS)*	60.2 (236)	–27.9, 148
COPD (GOLD 2018) subjects	71.8 (231)	–101, 244

Note:
Adjusted least squares (LS) means and confidence intervals (CI) from a mixed model derived from original values with visit, baseline value and its interaction with visit, sex, Caucasian origin, product use pattern category and its interaction with visit, and baseline smoking intensity as fixed effect factors and site as a random effect factor.
Analysis of spirometry endpoints were adjusted for diet; no age adjustment of FEV_1 parameters expressed as %pred.
General Study Population encompasses the study population of the exposure response studies (NCT02396381 and NCT02649556).
**Precedent ATS Guidelines for obstruction with 0.70 < FEV_1/FVC < 0.75.*

Table 1. *Differences between groups in FEV_1 (%pred and absolute values).*

ABSTRACT BOOK

NICOTINE PHARMACOKINETIC AND SUBJECTIVE ASSESSMENT OF THE JUUL SYSTEM WITH THREE NICOTINE CONCENTRATIONS RELATIVE TO COMBUSTIBLE CIGARETTES IN ADULT SMOKERS

Nicholas I. Goldenson[1], Ian M. Fearon[2], August R. Buchhalter[3], and Jack E. Heningfield[3]

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[2]**whatIF? Consulting Ltd, Harwell, U.K.**
[3]**PinneyAssociates, Inc., Bethesda, Maryland, USA**

Objective: This randomised, open-label, cross-over clinical study evaluated nicotine pharmacokinetics (PK) and subjective effects of the JUUL system (JS; Juul Labs, Inc.) with 59 mg/mL, 18 mg/mL and 9 mg/mL nicotine concentrations (all tobacco-flavored) compared to usual brand (UB) cigarettes in 24 adult smokers.

Methods: At each of five study visits, participants used one of four JS products or smoked their UB cigarette during controlled (10 standardized puffs) and then *ad libitum* (5 minutes) use sessions. Blood samples were taken at specified timepoints for 60 minutes in each session. The modified Product Evaluation Scale assessed subjective effects 30-minutes post-use in the controlled use session.

Results: Maximum plasma nicotine concentration ($C_{max\ BL}$), total nicotine exposure ($AUC_{0\ 60\ BL}$) and rate of plasma nicotine rise (i.e., speed of nicotine delivery or absorption) were significantly lower for all JS compared to participants' UB cigarette in controlled and *ad libitum* use sessions. In both use sessions these PK parameters were significantly higher for JS 59 mg/mL compared to 18 mg/mL and 9 mg/mL. Subjective measures of both cigarette craving and withdrawal relief (e.g., "Did it immediately relieve your craving for a cigarette?", "Did it relieve withdrawal symptoms?") and "Was it enough nicotine?" for JS 59 mg/mL did not significantly differ from UB cigarettes, but JS 18 mg/mL and 9 mg/mL were rated significantly lower than JS 59 mg/mL and UB cigarettes on these measures.

Conclusions: Nicotine delivery from all JS evaluated was significantly lower than combustible cigarettes. Nicotine exposure and subjective relief were directly related to the nicotine concentration of the JS: higher nicotine concentrations gave rise to significantly greater plasma nicotine levels and relief from craving. Heavier and more dependent smokers may require the greater nicotine delivery of the JS 59 mg/mL to successfully transition away from cigarettes.

ABSTRACT BOOK

ANALYSIS OF THE LUNG OVERALL CONDITION IN SMOKERS AND VOLUNTEERS, THAT USE ALTERNATIVE NICOTINE DELIVERY PRODUCTS

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In a few private clinics of Kyiv city was announced a free screening of the lung conditions in smokers. Research was made with 394 volunteers. Questionnaire included chronic respiratory diseases and harmful work conditions. Screening was performed during COVID-19 pandemic.

Materials and methods. Low-dose computer lung tomography with standard protocol was used, as well as spirometry with Spirobank II spirometer (device calculates 32 parameters of external breath functions and automatically interprets it according to ATS \ ERS standards, no calibration needed).

Results and discussion. All volunteers were divided into 4 groups. First group were healthy volunteers –100 people between 18 and 40 years. Second group were 170 people –smokers with smoking history for 8 to 10 years. Third group included 99 volunteers, that had previous smoking experience less than 8 years and started to use tobacco heating system or/ and electronic cigarettes for last three years. Fourth group consisted of 25 patients, who had smoking history for 8-10 years, but quit smoking during the last year.

Results of the low-dose computer lung tomography showed the following changes in the lungs: Group 1: stochastic findings (adhesions) - 25 (25%), other – no changes. Group 2: fibrotic ganglions, chronic bronchitis, fibrous adhesions, multiple bronchiectasis, bullous emphysema, calcification, encrusted pleura, progonomas - 158 (93%), other – no changes. Group 3: frosted glass-type changes – 2 (2,4%); chronic bronchitis, fibrous adhesions – 36 (30%), other – no changes. Group 4: sporadic fibrotic ganglions, chronic bronchitis, fibrous adhesions – 10 (40%), other – no changes.

Conclusions: 1. Non-specific symptoms in lungs were observed in all groups. No signs on presence of malignant processes or COVID-19 infections observed in all volunteers. 2. Users of alternative nicotine delivery systems (electronic cigarettes, tobacco heating systems) have substantially better results of lung CT comparing to smokers. 3. Two patients who used tobacco

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heating systems had places with frosted glass-type changes observed on CT and non-pronounced lymphadenopathy. Both males switched to alternative products very recently (2-3 month). Follow-up screening is recommended after 3 months (Table).

In patients with average cigarette per day number of 15.6 ± 6.9 and smokers' index 186.9 ± 83.4 (high risk of smoking disease development) respiratory function changes, characterized as obstructive, was observed (2nd group). It was related to the disruption of air flow in bronchi. In patients who switched to tobacco heating system or electronic cigarettes, light restrictive/obstructive changes of respiratory function were observed (3rd group). In patients who quit smoking (smoking history 8-10 years) light obstructive changes were observed.

	Group 1	Group 2	Group 3	Group 4
		Lung volumes		
RR / min.	17.1±1.1	18.7±1.8	17.8±1.2	17.7±1.2
TVe, ml	597.4±72.2	551.9±32.4	524.6±43.8	581.7±61.2
LVV, l	9171±4±94.6	9168.7±51.4	9204.6±60.8	9177.1±74.6
IRV, ml	1946.2±44.6	1717.4±88.1	1525.9±84.6	1592.2±72.8
ERV, ml	1238.2±41.2	970.4±39.6	1094.6±72.8	1014.6±62.1
		Lung capacities		
VC, ml	3540.4±101.6	3124.4±52.8	2778.4±87.2	2893.1±71.9
		Velocity indicators		
Forced VC, ml	3226.1±61.7	2951.7±68.2	2074.2±54.6	2271.8±42.4
FEV1, l/sec	2658.2±32.7	1416.8±47.2	1607.2±44.6	1830.1±52.4
FVC index	75.1%	45.3%	58.2%	63.2%

Table: *Spirometry results.*

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DIFFERENCES IN RATES OF ADULT SMOKERS SWITCHING AWAY FROM SMOKING USING JUUL SYSTEM PRODUCTS, ACROSS JURISDICTIONS WITH DIFFERENT MAXIMUM NICOTINE CONCENTRATIONS (NORTH AMERICA AND THE UNITED KINGDOM)

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Background: Electronic nicotine delivery systems (ENDS), such as the JUUL System (JS; Juul Labs, Inc.), can potentially improve public health by helping adult smokers switch away from cigarettes. Conceptually, switching should be facilitated when ENDS provide adequate nicotine delivery. We compare switching rates with JS in the UK, where regulations limit nicotine concentration to 20 mg/mL versus North America («N.Am.»; US and Canada), where higher concentrations are available.

Methods: Adult smokers who newly purchased a JUUL Starter Kit or Device were recruited into a longitudinal study. We analyzed the percent of established smokers (age ≥21, smoked ≥100 cigarettes in lifetime, smoking at least some days) who reported having switched (no smoking for ≥30 days) when assessed 1, 3, or 6 months later, respectively (Ns with follow-up data: UK 1,247; N.Am.: 8,840 [US 6,798; Canada 2,042]).

Results: In both jurisdictions, ≥85% of participants reported using the highest JS nicotine concentration available (UK: 18 mg/mL; N.Am.: 59 mg/mL). Unadjusted switching rates were similar across jurisdictions at 1 month (17-18%), but significantly higher in N.Am. (28%) than the UK (24%) at 3 months (OR=1.30, p<0.01) and 6 months (N.Am.: 34%; UK 28%, OR=1.33; p<0.01). Variation was not explained by jurisdiction differences in smoking quantity and frequency, duration of smoking, cigarette dependence, or perceived risks of JS, all of which were *lower* in the UK, which should have predicted *higher* switching rates in the UK. After propensity score matching on demographics and baseline smoking characteristics, switching rates were significantly higher in N.Am. at 1, 3, and 6 months (ORs: 1.40, 1.51, 1.52, all p<0.01).

Conclusions: These results suggest that making available ENDS with nicotine concentrations greater than 20 mg/mL may be associated with a higher likelihood of switching among adult smokers. However, between-country differences can be influenced by many factors, including social norms and other government policies.

Sponsorship:
This research was sponsored by Juul Labs, Inc. Data were collected by the Centre for Substance Use Research.

SS disclosure
SS is Senior Scientific Advisor to PinneyAssociates, which provides consulting services on tobacco harm reduction on an exclusive basis to Juul Labs, Inc. Within the last two years, PinneyAssociates has consulted for British American Tobacco and Reynolds American Inc and subsidiaries on tobacco harm reduction. SS co-holds a patent for a novel nicotine medication that has not been developed or commercialized.

ABSTRACT BOOK

SMOKING AND MULITPLE SCLEROSIS (MS): EFFECT ON DISEASE DEVELOPMENT AND DISABILITY PROGRESSION

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Introduction: Aim of this study was to investigate the effect of smoking on the development of MS and the progression of disability through a systematic review of the literature.

Methods: PUBMED database was searched for studies published from 01/01/2009 to 31/12/2018 using the keywords: «multiple sclerosis», «smoking», «passive smoking», «cigarette», «nicotine», «risk», «progression» and «disability». Selection criteria captured only primary adult studies who compared the risk of developing MS or/and the disease progression as well as the associated disability between patients exposed to smoking (active/passive) and non-smokers.

Results: The initial search yielded 641 articles but only 23 were included in the review after applying the search criteria and after reading the titles, the abstracts, and the whole text. 10 studies showed that smoking is a risk factor for developing MS with the odds ratio of smokers for MS ranging from 1.49 to 4.2 compared to never-smokers. Furthermore, in 7 studies, it was found that the risk of developing MS increases with the number of smoking pack-years, thus presenting a dose-dependent association. Two studies revealed that exposure to passive smoking was a risk factor for MS too, but in another study, this exposure rate did not differ significantly between patients and controls. Concerning the impact of smoking on disease progression and disability accumulation, the results were conflicting. Four studies showed that smokers had significantly higher EDSS scores as well as significantly faster disability progression compared with non-smokers. However, four other studies failed to prove any association between smoking habit and disability progression. Finally, as far as the risk of transforming into a secondary progressive course of MS is concerned, it seems to be higher in smokers.

Conclusions: Smoking, both active and passive, increases the risk of acquiring MS. However, its effect on disease progression requires further investigation. Since smoking is a modifiable health behavior, this investigation becomes increasingly important as its cessation/reduction could be extremely beneficial for MS patients.

ABSTRACT BOOK

DEPENDENCE ON JUUL SYSTEM ENDS IS LOWER THAN CIGARETTE DEPENDENCE: ADULTS AND YOUTH

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It is important to understand dependence on ENDS, including nicotine-salt-based ENDS, in comparison to cigarette dependence. Data from four studies and two dependence scales compared dependence on JUUL System products (JS, a nicotine-salt-based ENDS) to dependence on cigarettes. A cross-sectional US study used the 4-item version of the PROMIS dependence scale (scaled 0 to 4) to compare dependence in adult (age 25+) samples of 1,261 exclusive smokers and 96 exclusive users of JS. Psychometric analyses indicated the scale was valid for assessment and comparison in smokers and JS users, but not in dual users. Dependence was significantly lower among exclusive JS users than among exclusive smokers (1.68±0.97 vs 2.08±0.97, p <0.001). Similarly, among US youth (13-17), JS users (n=1,017) scored lower than smokers (n=441) (1.28±1.00 vs 1.43±1.07, p<0.015). A longitudinal study of US adult smokers who newly purchased a JS Starter Kit used the 16-item scale developed by the PATH study group (scaled 1-5), and validated for comparing dependence across products, including dual users. One month after starting JS, respondents' dependence on JS was significantly lower than their baseline dependence on cigarettes, among both smokers who had switched completely away from smoking (n=4,655, 2.45±0.87 vs 2.59±1.12, p<0.001) and among those still smoking (dual users) at follow-up (n=10,530, 2.31±0.85 vs. 3.12±1.06, p<0.001). Results were similar in a longitudinal study of US and Canadian smokers who switched to exclusive JS use one month later, based on the PROMIS-4 scale (n=958, decrease from 2.82±1.10 cigarette dependence to 2.59±0.86 JS dependence, p<0.001). Further, the declines in dependence when switching to JSs did not significantly differ among those primarily using the 5.0% nicotine concentration JS as in those primarily using the 3.0% concentration (p>0.75). In sum, dependence on JS is consistently lower than dependence on cigarettes, and smokers' dependence decreases as they transition to JSs.

Disclosures
Juul Labs authors had no access to data collected from youth, which is firewalled from JLI. PinneyAssociates provides consulting services on tobacco harm reduction on an exclusive basis to Juul Labs, Inc. Within the last two years, PinneyAssociates has consulted for British American Tobacco and Reynolds American Inc and subsidiaries on tobacco harm reduction. SS co-holds a patent for a novel nicotine medication that has not been developed or commercialized.

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