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Running Head: HEALTH WARNINGS & REDUCED RISK MESSAGE IMPACT

Impact of different health warning label and reduced exposure messages in IQOS ads on perceptions among US and Israeli adults

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ABSTRACT

Heated tobacco products (HTPs; e.g., IQOS) are advertised as safer than cigarettes or an alternative, yet required health warning labels (HWLS) in many countries, including the US and Israel, do not consider whether HTP ads undermine HWLS, particularly those that do not explicitly address HTPs. In 2021, a randomized 4 x 3 factorial experiment among 2,222 US and Israeli adults examined IQOS ads with differing: 1) HWLS (i.e., smoking risks, prompt to quit, HTP-specific, control); and 2) ad messages (i.e., slight distancing: “cigarette-like satisfaction, no odor”, clear distancing: “looking for an alternative?”, control). Outcomes were perceived relative harm (vs. cigarettes), exposure to harmful chemicals, and disease risk and likelihood of trying or suggesting IQOS to smokers. Ordinal logistic regression was used, adjusted for covariates. One HWL effect was found: risk (vs. control) increased perceived relative harm (aOR=1.21, CI=1.03-1.41) and exposure (aOR=1.22, CI=1.04-1.42) and decreased likelihood of trying IQOS (aOR=0.82, CI=0.69-0.97). Both slight and clear distancing ads (vs. control) decreased perceived harm (aOR=0.85, CI=0.75-0.97; aOR=0.63, CI=0.55-0.72, respectively) and increased likelihood of suggesting IQOS to smokers (aOR=1.23, CI=1.07-1.41; aOR=1.28, CI=1.11-1.47); slight distancing decreased perceived disease risk (aOR=0.85, CI=0.75-0.97); and clear distancing decreased perceived exposure (aOR=0.73, CI=0.64-0.83). Clear (vs. slight) distancing decreased perceived relative harm (aOR=0.74, CI=0.65-0.85) and exposure (aOR=0.82, CI=0.71-0.93). One interaction effect was found: the quitting HWL and clear distancing led to particularly low perceived relative harm (aOR=0.63, CI=0.43-0.93). Regulatory agencies must monitor the impacts of advertising, including reduced risk/exposure messaging on perceptions of HWL messages, to inform future regulatory efforts.

Keywords: tobacco control; health communications; risk perception; alternative tobacco products; heated tobacco products; marketing; tobacco use

INTRODUCTION

Heated tobacco products (HTPs; electronic devices that heat tobacco) are among the newer products to have expanded globally in the past decade.¹ IQOS, by Philip Morris (PM), is the global HTP leader, first released in Japan in 2014 and now sold in ~70 countries. In Israel, IQOS was introduced in 2016 with no regulatory oversight, then was subject to weak regulation (2017-2018), and then to increased regulation involving advertising restrictions and plain packaging (2019-2020).² In the US, PM introduced IQOS in October 2019 after receiving Food and Drug Administration (FDA) authorization.³ In July 2020, PM received FDA Modified Risk Tobacco Product (MRTP) authorization to use “reduced exposure” (but not “reduced risk”) claims in IQOS marketing.⁴ IQOS expanded across 4 states (i.e., Georgia, Virginia, North Carolina, South Carolina) before it was discontinued in the US in November 2021 due to a patent-infringement lawsuit,⁵ but will likely re-emerge in the US.⁶

Globally, IQOS ads often claim that IQOS is a “cleaner,” “reduced-risk” product than cigarettes and a satisfactory alternative to cigarettes.⁷⁻⁹ In the US, IQOS ads have largely adhered to the FDA authorized “reduced exposure” claims in their marketing.¹⁰ Nevertheless, consumers often misunderstand this language, equating “reduced exposure” to “reduced risk”.¹¹⁻¹³

As the tobacco market has evolved, regulatory action has often lagged. For example, health warning labels (HWLs) are critical in raising consumer awareness about product risks and reducing population-level tobacco use rates.¹⁴ HWLs emphasizing severe and specific health risks (e.g., cancer, stroke/heart disease) are most effective for deterring smoking.¹⁵⁻¹⁷ In Israel, textual HWLs must cover 30% of tobacco ads and 65% of each of the 2 principal display areas on all tobacco product packaging (the front in Hebrew, the back in Arabic), except e-cigarette packaging. Thirteen different warnings are prescribed, 8 of which reference “smoking” (e.g., “Medical studies conclude that 85% of all lung cancer cases are due to smoking”) and 5 of which reference “cigarettes” (e.g., “Cigarettes cause heart disease and stroke”). In the US, there are sets of Surgeon General’s Warnings for ads and product packaging for cigarettes (e.g., “Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy”, “Quitting Smoking Now Greatly Reduces Serious Risks to Your Health”), as well as for cigar products and smokeless tobacco.¹⁸ Notably, FDA requires all ads for “covered tobacco products” (i.e., those under FDA purview, including HTPs, e-cigarettes, and others) to include: “This product contains nicotine. Nicotine is an addictive chemical.” Despite no other FDA HWL requirements for HTPs, all IQOS ads in the US have included HWL messages typically required for cigarettes.¹⁰ Neither country requires pictorial HWLs, although the US issued a 2020 rule requiring pictorial HWLs on cigarette packages, which has been repeatedly postponed due to litigation by the tobacco industry, now set for November 2023.¹⁹

How consumers interpret HWLs on product labeling and advertising of HTPs or other tobacco products, particularly those that use reduced risk/exposure messaging in their ads, has not been rigorously studied. Consumers may misperceive HWLs about the harms of smoking as not applying to IQOS, or even serving as endorsements for IQOS, especially when ad messaging distinguishes IQOS from cigarettes and/or suggests it as an alternative.²⁰ Example ad messages in Israel²¹ and the US¹⁰ include: “Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it” and “Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals.” In the context of HWLs that suggest the harms of cigarettes or the importance of quitting cigarettes, consumers may be

particularly likely to misperceive the combination of these messages, and the industry may knowingly employ strategies capitalizing on this phenomenon.²⁰

This study addresses 2 key contributions to the literature. First, while FDA requires data from manufacturers to estimate the impact of MRTP-authorized products and their marketing, manufacturers often underestimate such impact.²²⁻³⁰ Thus, comprehensive surveillance by independent researchers is needed, particularly to examine the potential interactions between advertising strategies and HWL messaging. Second, given the different tobacco markets and regulations globally, cross-country research is needed to examine the potential global impact of such advertising strategies.

This study examined the impact of IQOS advertising messages and HWL messages among 2,222 US and Israeli adults. We conducted a survey-based 4 x 3 factorial experiment that systematically manipulated the presence of: 1) HWL messages (i.e., smoking-related risks, prompt to quit smoking, HTP-specific, control); and 2) ad messages (i.e., slight distancing of HTPs from cigarettes, clear distancing, control). Outcomes included perceived harm relative to cigarettes, exposure to harmful chemicals, and risk of disease, as well as likelihood of personally trying IQOS or recommending it to cigarette smokers. We hypothesized that: 1) HWLs emphasizing severe, specific smoking health risks or HTP-specific HWLs are more effective in increasing risk perceptions and decreasing likelihood of trying or suggesting IQOS to smokers; 2) ad messages distancing IQOS from cigarettes are more effective in reducing risk perceptions and increasing likelihood of trying or suggesting IQOS; and 3) ad messages distancing IQOS from cigarettes and HWL messages promoting smoking cessation are synergistic.

METHODS

Study Sample

We conducted a randomized factorial design experiment embedded within a cross-sectional online survey of 2,222 US and Israel participants, administered in October-December 2021 and fielded by Ipsos. Eligibility criteria included: 1) able to speak English (US), or Hebrew or Arabic (Israel); and 2) 18-45 years old, as the minimum legal sales age in Israel is 18 and, despite the minimum age increase to 21 in the US in December 2019, there is utility in examining tobacco use related factors in adults ages 18-20. We aimed to recruit ~2,000 participants (1,000/country), 40% reporting any tobacco or e-cigarette use, equal males/females, and racial/ethnic group representation. The study received ethical approvals from George Washington University and Hebrew University.

US-based sample. US-based participants were recruited using KnowledgePanel®,³¹ a probability-based web panel designed to be representative, recruited via random digit dialing and address-based sampling. Participation was promoted by incentives (~5,000 KnowledgePanel® points, redeemable for ~\$5) and several prompts (6 over one-month period). Of 4,960 recruited, 2,397 (48.3%) completed eligibility screening, and 1,095 (45.7%) completed the survey.

To meet subgroup recruitment targets, Ipsos also collected an opt-in (i.e., off-panel) convenience sample of Asian tobacco users, using banner ads, web pages, and e-mail invitations.

Those who clicked on online ads completed eligibility screening (i.e., gender, race/ethnicity, tobacco use). Of 353 individuals eligible, 33 (9.3%) completed the survey.

Israel-based sample. Israel-based participants were recruited using the opt-in approach, as specified above. Of 2,970 eligible individuals, 1,094 (36.8%) completed the survey.

Experimental Design and Measures

The survey focused on tobacco use and related factors, was parallel in content across countries/languages except for specific sociodemographics (e.g., origin, religiosity), and took ~25 minutes to complete. The survey was translated from English to Hebrew and Arabic (for Israeli participants) by a professional translation company, back-translated into English, and then examined by 2 bilingual reviewers to verify comparability across translations.

Experimental design. *Table 1* provides an overview of each of the 12 experimental conditions (per our 4 x 3 factorial design), which were applied to 2 IQOS ad designs from the US market¹⁰ (*Figures 1a* and *1b*). Each participant was randomly assigned to evaluate one ad in each of the 2 sets of ads, the elements of which were presented completely in English in the US and in the language chosen by participants in Israel (either Hebrew or Arabic).

HWL messages were selected from those used by the US FDA¹⁸ that were similar in content to HWL messages in Israel, and reflected those frequently in US IQOS ads.¹⁰ These included: 1) Risks: “Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy”; 2) Quitting: “Quitting Smoking Now Greatly Reduces Serious Risks to Your Health”; and 3) HTP-specific: “Heated Tobacco Products Cause Damage to the Lungs and Heart” – a hypothetical HWL message to determine its impact on outcomes. Each of these HWLs were led with either: “Ministry of Health Warning” in Israel or “Surgeon General’s Warning” in the US. In the US, all FDA-regulated tobacco products, including IQOS, must include in their ads: “WARNING: This product contains nicotine. Nicotine is an addictive chemical;”¹⁸ thus, this statement was used in the control condition and also accompanied the HWL messages in each experimental condition.

Ad messages were based on Israel²¹ and US ads¹⁰ and included: 1) Slight distancing from cigarettes: “Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it”; 2) Clear distancing from cigarettes: “Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals”; and 3) Control: “The future of tobacco is here,” which was also included across the other ad messages.

Outcomes. Following the presentation of each ad, participants were instructed to “consider the ad above” and asked: 1) “Compared to cigarettes, how harmful to your health do you think IQOS is?” (1=much less to 5=much more); 2) “Do you think that using IQOS would expose you to: 1=almost no harmful chemicals to 4=a lot”; 3) “If you used IQOS regularly for the next 10 years, how likely do you think it is that you would eventually develop serious health problems? (If you currently smoke cigarettes, imagine that you switched completely to IQOS for the next 10 years and used it as frequently as you smoke cigarettes.) (1=not at all likely to 7=extremely likely); 4) “If one of your best friends was to offer you IQOS, would you try it?”

(1=not at all to 7=extremely); and 5) “How likely are you to recommend IQOS to a friend or family member who smokes cigarettes?” (1=not at all to 7=extremely).

Covariates. *Sociodemographic factors* included: age, gender, sexual orientation, race/ethnicity (US: White, Black, Asian, Hispanic; Israel: Jewish, Arab), nativity, educational attainment, household income, employment status, relationship status, and children in the home.

Tobacco use was assessed by asking participants to indicate lifetime use of cigarettes, e-cigarettes, HTPs, hookah, cigar products, pipe tobacco, and smokeless tobacco. Among those reporting lifetime use of each product, number of days used in the past 30 days was assessed (operationalized as any vs. none for each). For lifetime and past 30-day use, we created aggregate variables for hookah, cigars, pipe, and smokeless tobacco.

Statistical Analysis

Descriptive and bivariate analyses characterized our sample overall, by country, and by current cigarette use status. Then, bivariate analyses compared responses to the 5 outcome variables by experimental condition, using Tukey’s HSD for post-hoc comparisons. Note that there were 12 conditions (4 x 3 factorial design) and each of the 2,222 participants evaluated 2 ads; thus, each individual ad was assessed by ~185 participants, each condition (represented in 2 ads) was evaluated by ~370 participants, and a total of 4,444 responses were analyzed.

Ordinal logistic regression examined the impact of HWL messages and ad messages, respectively, on the 5 outcomes, controlling for order of presentation, country, cigarette use status, and sex. For HWL messaging, the control was the reference group. For ad messaging, slight distancing was chosen as the reference group, as for all outcomes (except perceived relative harm), it represented the condition with the midrange mean (between control and clear distancing), and thus provided the opportunity to compare slight distancing to both the control and clear distancing. We then added interaction terms for HWL and ad messages in a subsequent block for each outcome. Additional analyses assessed interactions between HWL and ad messages, respectively, by: 1) country, 2) cigarette use status, and 3) sex. Likelihood ratio tests assessed significance of interactions. Analyses were conducted using $\alpha=.05$ and Stata 15.0.

RESULTS

Participant Characteristics

Table 2 provides an overview of participant characteristics overall (n=2,222), by country (US: n=1,128; Israel: n=1,094), and by current cigarette use status (US: n=253; Israel: n=428).

Messaging Effects

Bivariate analyses examining responses to *HWL messaging* (*Supplementary Table*) indicated that the risks (vs. quitting) HWL message resulted in greater perceived harm and exposure. No other outcomes differed across conditions. In multivariable analyses (*Table 3*), one *HWL messaging* effect was found: viewing the risks (vs. control) HWL message was associated with greater perceived relative harm (aOR=1.21, CI=1.03-1.41) and exposure (aOR=1.22, CI=1.04-1.42) and lower likelihood of trying IQOS (aOR=0.82, CI=0.69-0.97).

Regarding *ad messages*, bivariate analyses (*Supplementary Table*) indicated that, compared to clear distancing messages, both slight distancing and control resulted in greater perceived relative harm and exposure, and control also resulted in lower likelihood of suggesting IQOS to smokers. In multivariable analyses (*Table 3*), both slight and clear distancing (vs. control) resulted in lower perceived harm (aOR=0.85, CI=0.74, 0.97; aOR=0.63, CI=0.55-0.72, respectively) and greater likelihood of suggesting IQOS to smokers (aOR=1.23, CI=1.07-1.41; aOR=1.28, CI=1.11-1.47); slight distancing resulted in lower perceived disease risk (aOR=0.85, CI=0.75-0.97); and clear distancing resulted in lower perceived exposure (aOR=0.73, CI=0.64-0.83). Moreover, clear (vs. slight) distancing resulted in lower perceived relative harm (aOR=0.74, CI=0.65-0.85) and exposure (aOR=0.82, CI=0.71-0.93).

Notably, one messaging interaction effect was found: viewing the quitting HWL with the clear distancing ad message (*Figure 1a, image i*) was associated with lower perceived relative harm (aOR=0.63, CI=0.43-0.93; Likelihood Ratio test $p=.039$).

Regarding covariates, Israeli (vs. US) participants, current cigarette users, and men, respectively, reported lower perceived relative harm and greater likelihood of suggesting IQOS to smokers. Current smokers and men also reported lower perceived exposure and greater likelihood of trying IQOS, and men reported lower perceived disease risk. Analyses indicated one covariate-related interaction effect: particularly low perceived exposure was found among US participants exposed to the control ad message compared to Israeli participants exposed to the slight distancing message (aOR=0.71, CI=0.54-0.93; Likelihood Ratio test $p=.016$).

DISCUSSION

Key findings were consistent with our hypotheses. Specifically, HWL messaging that emphasized smoking-related disease risks (vs. control) was more effective. Additionally, IQOS ad messages that distanced IQOS from cigarettes (vs. control) led to lower perceived harm and greater likelihood of suggesting IQOS to smokers, and certain effects were particularly pronounced for ad messaging that most clearly distanced IQOS from cigarettes. Finally, the combination of HWL messaging that promoted quitting and ad messaging that clearly distanced IQOS from cigarettes led to particularly low perceived relative harm.

Consistent with HWL research,¹⁵⁻¹⁷ HWL messaging that emphasized disease risk led to greater perceived relative harm and exposure and lower likelihood of trying IQOS relative to the control HWL message in multivariable analyses, and to greater perceived relative harm and exposure compared to the quitting HWL message in bivariate analyses. Other HWL conditions did not differ. Notably, there were no differences between the control condition and the HTP-specific message in any outcome. The reasons for this are unclear; IQOS-related perceptions may have been influenced by other aspects of the ads and/or the ads may not have clearly identified IQOS as an HTP (to which the HWL referred).

Regarding ad messages, those that distanced IQOS from cigarettes (vs. control) led to lower perceived harm and greater likelihood of suggesting IQOS to smokers. Additionally, slight distancing (“Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it”) led to lower perceived disease risk, and clear distancing (“Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful

chemicals”) led to lower perceived exposure. Moreover, clear (vs. slight) distancing led to lower perceived relative harm and exposure. These findings suggest that consumers might attend to details of ad messages in their evaluations of specific risks, and that messages that articulate that IQOS is not a cigarette (rather an alternative) and reduces exposure to chemicals impacts consumers’ specific risk perceptions. However, these findings underscore that FDA authorized reduced exposure language impacts other outcomes, including perceived harm and disease risk,^{13,32} and undermines the intent of distinct authorizations for “reduced risk” versus “reduced exposure” claims.³³ However, likelihood of trying IQOS was not impacted, similar to other research findings.¹² Additional research should examine the extent to which self-reports of perceptions and future behaviors reflect actual future behavior (e.g., uptake, cessation), which has been critical in understanding the impact of HWLs.^{16,34,35}

One noteworthy finding was that the combination of the quitting HWL message (“Quitting Smoking Now Greatly Reduces Serious Risks to Your Health”) and clear distancing messaging (“Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals”) led to particularly low perceived relative harm of IQOS. This finding suggests that these messages in combination may lead consumers to evaluate IQOS as a solution to the challenge of quitting cigarettes and induce a halo effect whereby the reduced exposure language is interpreted more broadly to include reduced risk.^{13,32} This finding might also explain the industry’s inclusion of cigarette-specific HWLs in IQOS ads.

Current findings have research and regulatory implications. How HWLs and reduced risk and exposure claims are framed influence consumers’ perceptions of products, their risks, and their benefits. Although the FDA requires surveillance to determine the impact of products that receive MRTP authorization on “consumer perception, behavior, and health...”,³⁶ insufficient research, particularly independent research, has examined the impacts of HWLs for HTPs and other newer tobacco products, especially within the context of certain advertising elements, such as ads that leverage HWL messaging – identifying a clear need. In particular, studies examining behavioral impacts of various HWLs, reduced risk/exposure messages, and different combinations of the 2 in real-world settings are needed to determine population-level impact of newer tobacco products. Results from such studies should inform the types of advertising messages regulatory agencies monitor and allow, especially for products seeking or previously granted FDA’s modified risk or exposure authorization in the US.

Strengths and Limitations

Study strengths include a rigorous 4 x 3 factorial design, real-world ad content, and data from national adult samples in 2 countries with unique regulatory settings. However, findings have limited generalizability due to participant recruitment via an online panel in the US and via blended online methods in Israel and for subgroups (Asians) in the US. Additionally, data were self-reports of participants’ perceptions rather than actual behaviors, some relevant variables (e.g., rural vs. urban) were not assessed, and the ads were only viewed once, limiting ecological validity.

Conclusions

Cross-country research is critical to advance tobacco control efforts, especially as new tobacco products emerge and evolve. In this sample of US and Israeli adults, HWL messaging emphasizing disease risk (vs. control) was more effective, IQOS ad messages that distanced IQOS from cigarettes (vs. control) decreased perceived harm and increased likelihood of suggesting IQOS to smokers, and the combination of the HWL that promoted quitting and ad messaging clearly distancing IQOS from cigarettes led to particularly low perceived relative harm. Thus, reduced exposure messaging is misinterpreted to reflect reduced risk and harm, undermining the intentions of FDA's separate authorizations for reduced exposure versus reduced risk claims. Therefore, it is crucial to monitor tobacco marketing strategies and consumer perceptions and behavior related to new tobacco products, particularly those granted FDA modified risk or exposure authorization, in order to inform future regulation by FDA and other regulatory agencies globally.

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Availability of Data: Data are available upon reasonable request.

Conflicts of Interests/Financial Disclosures: HL had received fees for lectures from Pfizer Israel Ltd (distributor of a smoking cessation pharmacotherapy in Israel) in 2017. YB-Z has received fees for lectures from Pfizer, Novartis NCH and GSK Consume Health (distributors of pharmacotherapy in Israel) in the past (2012–July 2019). LA receives royalties for the sale of Text2Quit. No other conflicts of interest are declared.

Contributors: CJB, HL, and YB-Z designed the study, obtained grant funding, and oversaw project administration. ZD, YW, JFT, LCA, AK, and KFR contributed to study design and methodology. CJB, ZD, and YW analyzed the data and wrote the draft manuscript. All authors reviewed the manuscript and confirm the approval of the submitted manuscript.

REFERENCES

1. Ratajczak A, Jankowski P, Strus P, Feleszko W. Heat Not Burn Tobacco Product-A New Global Trend: Impact of Heat-Not-Burn Tobacco Products on Public Health, a Systematic Review. *Int J Environ Res Public Health*. Jan 8 2020;17(2)doi:10.3390/ijerph17020409
2. Berg CJ, Bar-Zeev Y, Levine H. Informing iQOS Regulations in the United States: A Synthesis of What We Know. *SAGE Open*. 2020/01/01 2020;10(1):2158244019898823. doi:10.1177/2158244019898823
3. US Food and Drug Administration. Marketing Order, FDA Submission Tracking Numbers (STNs): PM0000424- PM0000426, PM0000479, IQOS System Holder and Charger and Marlboro Heatsticks, 2019. Available: <https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-orders> [Accessed 6 Aug 2020]. 2019;
4. US Food and Drug Administration. Exposure Modification Modified Risk Granted Orders, FDA submission tracking numbers (STNs): MR0000059-MR0000061, MR0000133, 2020. Available: <https://www.fda.gov/media/139797/download> [Accessed 6 Aug 2020]. 2020;
5. Associated Press. Altria: IQOS Cigarette Alternative off Market Through 2022. US News and World Report. <https://www.usnews.com/news/best-states/virginia/articles/2022-01-27/altria-iqos-cigarette-alternative-off-market-through-2022>
6. Gretler C. Philip Morris Plans U.S. IQOS-Stick Production After Import Ban. Bloomberg News. <https://www.bloomberg.com/news/articles/2022-02-10/philip-morris-plans-u-s-iqos-stick-production-after-import-ban>
7. World Health Organization. Heated tobacco products (HTPs) market monitoring information sheet
file:///T:/bsheprojs/CJ%20Berg/CJB%20Personal%208%2020%2016/Israel/WHO-NMH-PND-18.7-eng.pdf
8. Rosen L, Kislev S. The IQOS Campaign in Israel. *Tobacco Induced Diseases*. 2018;16(Suppl1):A732.
9. Hair EC, Bennett M, Sheen E, et al. Examining perceptions about IQOS heated tobacco product: consumer studies in Japan and Switzerland. *Tob Control*. May 15 2018;doi:10.1136/tobaccocontrol-2018-054322
10. Berg CJ, Romm KF, Bar-Zeev Y, et al. IQOS marketing strategies in the USA before and after US FDA modified risk tobacco product authorisation. *Tob Control*. Oct 19 2021;doi:10.1136/tobaccocontrol-2021-056819

11. McKelvey K, Baiocchi M, Halpern-Felsher B. PMI's heated tobacco products marketing claims of reduced risk and reduced exposure may entice youth to try and continue using these products. *Tob Control*. Dec 2020;29(e1):e18-e24. doi:10.1136/tobaccocontrol-2019-055318
12. Chen-Sankey JC, Kechter A, Barrington-Trimis J, et al. Effect of a hypothetical modified risk tobacco product claim on heated tobacco product use intention and perceptions in young adults. *Tob Control*. May 31 2021;doi:10.1136/tobaccocontrol-2021-056479
13. Yang B, Massey ZB, Popova L. Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS. *Tob Control*. Aug 2022;31(e1):e41-e49. doi:10.1136/tobaccocontrol-2020-056191
14. World Health Organization. *Framework Convention on Tobacco Control*: <https://fctc.who.int/who-fctc/overview>. 2022.
15. Hammond D, Reid JL, Driezen P, Boudreau C. Pictorial health warnings on cigarette packs in the United States: an experimental evaluation of the proposed FDA warnings. *Nicotine Tob Res*. Jan 2013;15(1):93-102. doi:10.1093/ntr/nts094
16. Noar SM, Hall MG, Francis DB, Ribisl KM, Pepper JK, Brewer NT. Pictorial cigarette pack warnings: a meta-analysis of experimental studies. *Tob Control*. May 2016;25(3):341-54. doi:10.1136/tobaccocontrol-2014-051978
17. O'Connor R. Warnings and packaging. *Tob Control*. Aug 2019;28(e1):e1-e2. doi:10.1136/tobaccocontrol-2019-055192
18. US Food and Drug Administration. *Retailers: Chart of Required Warning Statements on Tobacco Product Packaging and Advertising*. 2018. <https://www.fda.gov/tobacco-products/retail-sales-tobacco-products/retailers-chart-required-warning-statements-tobacco-product-packaging-and-advertising>
19. US Food and Drug Administration. Cigarette Labeling and Health Warning Requirements: <https://www.fda.gov/tobacco-products/labeling-and-warning-statements-tobacco-products/cigarette-labeling-and-health-warning-requirements>. US Food and Drug Administration. December 15, 2022.
20. Bar-Zeev Y, Berg CJ, Kislev S, et al. Tobacco legislation reform and industry response in Israel. *Tob Control*. Sep 4 2020;doi:10.1136/tobaccocontrol-2020-056041
21. Khayat A, Levine H, Berg CJ, Abrams L, Rodnay M, Bar-Zeeve Y. IQOS adspend and marketing messages in paid ads in Israel (December 2016 – August 2020). Poster at European Public Health Conference, Virtual. 2021;
22. Glantz SA. Heated tobacco products: the example of IQOS. *Tob Control*. Nov 2018;27(Suppl 1):s1-s6. doi:10.1136/tobaccocontrol-2018-054601

23. St Helen G, Jacob Iii P, Nardone N, Benowitz NL. IQOS: examination of Philip Morris International's claim of reduced exposure. *Tob Control*. Nov 2018;27(Suppl 1):s30-s36. doi:10.1136/tobaccocontrol-2018-054321
24. Glantz SA. PMI's own in vivo clinical data on biomarkers of potential harm in Americans show that IQOS is not detectably different from conventional cigarettes. *Tob Control*. Nov 2018;27(Suppl 1):s9-s12. doi:10.1136/tobaccocontrol-2018-054413
25. Chun L, Moazed F, Matthay M, Calfee C, Gotts J. Possible hepatotoxicity of IQOS. *Tob Control*. Nov 2018;27(Suppl 1):s39-s40. doi:10.1136/tobaccocontrol-2018-054320
26. Max WB, Sung HY, Lightwood J, Wang Y, Yao T. Modelling the impact of a new tobacco product: review of Philip Morris International's Population Health Impact Model as applied to the IQOS heated tobacco product. *Tob Control*. Nov 2018;27(Suppl 1):s82-s86. doi:10.1136/tobaccocontrol-2018-054572
27. Tabuchi T, Kiyohara K, Hoshino T, Bekki K, Inaba Y, Kunugita N. Awareness and use of electronic cigarettes and heat-not-burn tobacco products in Japan. *Addiction*. Apr 2016;111(4):706-713. doi:10.1111/add.13231
28. Caputi TL. Heat-not-burn tobacco products are about to reach their boiling point. *Tob Control*. Sep 2017;26(5):609-610. doi:10.1136/tobaccocontrol-2016-053264
29. McKelvey K, Popova L, Kim M, et al. IQOS labelling will mislead consumers. *Tob Control*. Nov 2018;27(Suppl 1):s48-s54. doi:10.1136/tobaccocontrol-2018-054333
30. El-Toukhy S, Baig SA, Jeong M, Byron MJ, Ribisl KM, Brewer NT. Impact of modified risk tobacco product claims on beliefs of US adults and adolescents. *Tob Control*. Nov 2018;27(Suppl 1):s62-s69. doi:10.1136/tobaccocontrol-2018-054315
31. The GfK Group. *Knowledge Panel Design Summary*: <https://silo.tips/download/knowledgepanel-design-summary>. 2017.
32. Seidenberg AB, Popova L, Ashley DL, Wackowski OA. Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims. *Tob Control*. Oct 12 2020;doi:10.1136/tobaccocontrol-2019-055560
33. Popova L, Lempert LK, Glantz SA. Light and mild redux: heated tobacco products' reduced exposure claims are likely to be misunderstood as reduced risk claims. *Tob Control*. Nov 2018;27(Suppl 1):s87-s95. doi:10.1136/tobaccocontrol-2018-054324
34. Hall MG, Sheeran P, Noar SM, Ribisl KM, Boynton MH, Brewer NT. A brief measure of reactance to health warnings. *J Behav Med*. Jun 2017;40(3):520-529. doi:10.1007/s10865-016-9821-z
35. Noar SM, Francis DB, Bridges C, Sontag JM, Ribisl KM, Brewer NT. The impact of strengthening cigarette pack warnings: Systematic review of longitudinal observational studies. *Soc Sci Med*. Sep 2016;164:118-129. doi:10.1016/j.socscimed.2016.06.011

36. U.S. Food & Drug Administration. MODIFIED RISK GRANTED ORDERS. September 21, 2021. <https://www.fda.gov/media/139797/download>

Table 1. IQOS ad experimental conditions

HWL Message	Ad Message ^d		
	Control	Slight distancing from cigarettes	Clear distancing from cigarettes
Control ^{a, b}	- The future of tobacco is here.	- Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it.	- Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals.
	- WARNING: This product contains nicotine. Nicotine is an addictive chemical.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical.
Risks ^a	- The future of tobacco is here.	- Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it.	- Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals.
	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.

Quitting^a	- The future of tobacco is here.	- Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it.	- Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals.
	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
HTP-Specific^c	- The future of tobacco is here.	- Cigarette-like satisfaction without the odor. IQOS heats tobacco but does not burn it.	- Looking for an alternative to cigarettes? IQOS significantly reduces the production of harmful and potentially harmful chemicals.
	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Heated Tobacco Products Cause Damage to the Lungs and Heart.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Heated Tobacco Products Cause Damage to the Lungs and Heart.	- WARNING: This product contains nicotine. Nicotine is an addictive chemical. - [Israel: MINISTRY OF HEALTH WARNING/ US: SURGEON GENERAL'S WARNING]: Heated Tobacco Products Cause Damage to the Lungs and Heart.

^aHWL messages used by the US FDA¹⁸ and similar to those used by the Israel Ministry of Health. ^b Message required of all FDA covered tobacco products.¹⁸

^c Hypothetical HWL message to examine potential utility of referencing HTPs in HWL messages. ^d Adapted from ad content in the US and Israel.^{10,21}

Table 2. US and Israel participant characteristics and bivariate analyses examining correlates of current cigarette use, N=2,222

[illegible]

White, Non-Hispanic	493 (22.2)	493 (43.7)	360 (42.5)	122 (48.2)	.253	--	--	--	
Black, Non-Hispanic	284 (12.8)	284 (25.2)	224 (26.4)	55 (21.7)		--	--	--	
Asian, Non-Hispanic	177 (8.0)	177 (15.7)	130 (15.3)	42 (16.6)		--	--	--	
Hispanic	174 (7.8)	174 (15.4)	134 (15.8)	34 (13.4)		--	--	--	
Jewish	954 (42.9)	--	--	--		954 (87.2)	581 (87.5)	371 (86.7)	.693
Arab	140 (6.3)	--	--	--		140 (12.8)	83 (12.5)	57 (13.3)	
Foreign born, N (%)	234 (10.5)	105 (9.3)	86 (10.1)	17 (6.7)	.101	129 (11.8)	79 (11.9)	50 (11.7)	.914
Education < College degree, N (%)	1,114 (50.1)	644 (57.1)	450 (53.1)	176 (69.6)	<.001	470 (43.0)	283 (42.6)	186 (43.5)	.785
Income, N (%)									
≤\$24,999 or ≤30,000 NIS	387 (17.4)	183 (16.2)	112 (13.2)	65 (25.7)	<.001	204 (22.1)	128 (24.4)	75 (18.9)	.007
\$25,000-\$149,999 or 30,001-192,000 NIS	1,304 (58.7)	735 (65.2)	556 (65.6)	162 (64.0)		569 (61.6)	301 (57.3)	268 (67.5)	
≥\$150,000 or ≥192,001 NIS	360 (16.2)	210 (18.6)	180 (21.2)	26 (10.3)		150 (16.3)	96 (18.3)	54 (13.6)	
Employed, N (%)	1,589 (71.5)	825 (73.1)	637 (75.1)	166 (65.6)	.003	764 (69.8)	441 (66.4)	322 (75.2)	.002

Married/living with partner, N (%)	1,186 (53.4)	601 (53.3)	461 (54.4)	127 (50.2)	.244	585 (53.5)	329 (49.5)	255 (59.6)	.001
Children, N (%)	1,125 (50.6)	529 (46.9)	393 (46.3)	123 (48.6)	.525	596 (54.5)	360 (54.2)	235 (54.9)	.823
<i>Ever use, N (%)</i>									
Cigarettes	1,202 (54.1)	592 (52.5)	312 (36.8)	253 (100)	<.001	610 (55.8)	180 (27.1)	428 (100)	<.001
E-cigarettes	831 (37.4)	396 (35.1)	206 (24.3)	173 (68.4)	<.001	435 (39.8)	157 (23.6)	276 (64.5)	<.001
IQOS	307 (13.8)	76 (6.7)	30 (3.5)	41 (16.2)	<.001	231 (21.1)	73 (11.0)	157 (36.7)	<.001
Other tobacco (hookah, cigars, pipe, smokeless)	1,209 (54.4)	564 (50.0)	346 (40.9)	198 (78.3)	<.001	645 (59.0)	299 (45.0)	344 (80.4)	<.001
<i>Current (past 30-day) use, N (%)</i>									
E-cigarettes	445 (20.3)	170 (15.5)	77 (9.2)	90 (36.3)	<.001	275 (25.2)	64 (9.7)	210 (49.1)	<.001
IQOS	172 (7.8)	36 (3.2)	3 (0.4)	31 (12.3)	<.001	136 (12.5)	26 (3.9)	110 (25.7)	<.001
Other tobacco (hookah, cigars, pipe, smokeless)	487 (22.3)	168 (15.4)	66 (7.9)	99 (39.4)	<.001	319 (29.2)	109 (16.5)	210 (49.1)	<.001

* Missing current smoking status on 27 participants in the US and 2 in Israel.

Table 3. Ordinal logistic regression results of experiment exposing US and Israeli adults to IQOS ads with 4 different health warning label (HWL) messages and 3 types of advertising messages in relation to perceived relative harm, exposure, and disease risk and likelihood of personally trying or suggesting IQOS to smokers

	Perceived Relative Harm	Perceived Exposure	Perceived Disease Risk	Likelihood to Personally Try	Likelihood to Suggest to Smokers
Variables	aOR (CI)	aOR (CI)	aOR (CI)	aOR (CI)	aOR (CI)
Order (Ref: 2)	1.00 (0.90 - 1.12)	0.96 (0.86 - 1.07)	1.00 (0.90 - 1.11)	1.03 (0.91 - 1.16)	1.03 (0.92 - 1.15)
Sociodemographics					
Country US (Ref: Israel)	1.57 (1.41 - 1.76)	1.48 (1.33 - 1.66)	1.00 (0.90 - 1.11)	0.55 (0.48 - 0.62)	0.42 (0.37 - 0.47)
Current (past 30-day) cigarette use (Ref: Nonuse)	0.72 (0.64 - 0.81)	0.47 (0.41 - 0.53)	1.06 (0.95 - 1.18)	8.00 (7.02 - 9.12)	3.27 (2.90 - 3.69)
Male (Ref: Female)	0.79 (0.71 - 0.89)	0.76 (0.68 - 0.85)	0.79 (0.71 - 0.88)	1.29 (1.15 - 1.45)	1.21 (1.08 - 1.35)
Experimental Conditions					
<i>HWL message (Ref: Control)</i>					

Risks	1.21 (1.03 - 1.41)	1.22 (1.04 - 1.42)	1.06 (0.92 - 1.24)	0.82 (0.69 - 0.97)	0.87 (0.74 - 1.02)
Quitting	0.94 (0.80 - 1.10)	0.97 (0.83 - 1.14)	1.00 (0.86 - 1.16)	0.96 (0.82 - 1.14)	1.07 (0.91 - 1.25)
HTP-specific	1.14 (0.98 - 1.33)	1.06 (0.91 - 1.24)	0.99 (0.85 - 1.14)	0.86 (0.73 - 1.02)	0.90 (0.77 - 1.06)
<i>Ad message (Ref: Slight distancing*)</i>					
Clear distancing**	0.74 (0.65 - 0.85)	0.82 (0.71 - 0.93)	1.05 (0.93 - 1.20)	1.02 (0.88 - 1.17)	1.04 (0.91 - 1.20)
Control	1.18 (1.03 - 1.34)	1.12 (0.98 - 1.28)	1.17 (1.03 - 1.33)	0.89 (0.77 - 1.03)	0.81 (0.71 - 0.94)

One messaging interaction: Quitting by Clear distancing – perceived relative harm: OR=0.63, 95%CI=0.43, 0.93. Likelihood ratio test p-value=.039.

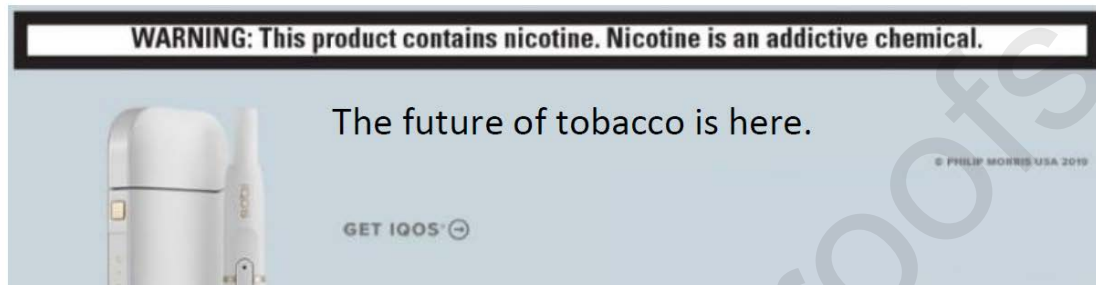
* Slight distancing vs. Control (aOR, CI) as follows: Perceived relative harm aOR=0.85, CI=0.74, 0.97; Perceived exposure aOR=0.89, CI=0.78, 1.02; Perceived disease risk aOR=0.85, CI=0.75, 0.97; Likelihood to personally try aOR=1.12, CI=0.97, 1.30; Likelihood to suggest to smokers aOR=1.23, CI=1.07, 1.41.

** Clear distancing vs. Control (aOR, CI) as follows: Perceived relative harm aOR=0.63, CI=0.55, 0.72; Perceived exposure aOR=0.73, CI=0.64, 0.83; Perceived disease risk aOR=0.90, CI=0.79, 1.02; Likelihood to personally try aOR=1.14, CI=0.99, 1.32; Likelihood to suggest to smokers aOR=1.28, CI=1.11, 1.47.

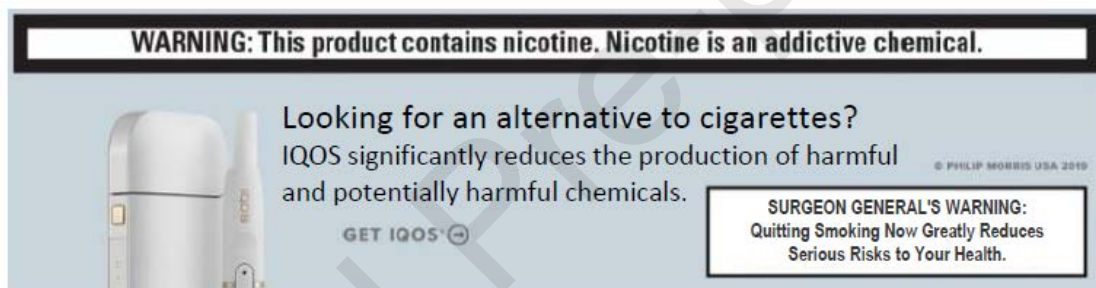
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Figure 1. Example IQOS ads and ad messaging

Figure 1a. First ad design



i. Control HWL message x Control ad message



ii. Quitting HWL message x Clear distancing from cigarettes ad message*

Figure 1b. Second ad design



i. Control HWL message x

Control ad message

ii. Disease risks HWL message x

*Slight distancing from cigarettes ad message**

* In Israel, all ads were presented in Hebrew or Arabic, based on the participant's selected language; additionally, "Surgeon General's Warning" was replaced by "Ministry of Health Warning" in Hebrew or Arabic.

Supplementary Table. Bivariate analyses characterizing responses to ad stimuli across outcomes

	Perceived Relative Harm ^a	Perceived Exposure ^b	Perceived Disease Risk ^c	Likelihood to Personally Try ^c	Likelihood to Suggest to Smokers ^c
<i>Messages</i>	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)

<i>HWL message</i>	**	*			
Risks	2.88 (1.02)	2.95 (0.87)	4.27 (2.22)	2.48 (1.95)	2.60 (1.92)
Quitting	2.74 (1.03)	2.85 (0.89)	4.23 (2.13)	2.67 (2.05)	2.82 (2.01)
HTP-specific	2.84 (1.00)	2.89 (0.87)	4.19 (2.17)	2.54 (1.97)	2.64 (1.94)
Control	2.78 (1.00)	2.86 (0.87)	4.22 (2.17)	2.63 (2.03)	2.71 (1.93)
<i>Ad message</i>	***	***			**
Slight distancing	2.84 (1.01)	2.90 (0.88)	4.15 (2.17)	2.58 (2.00)	2.72 (1.94)
Clear distancing	2.71 (1.07)	2.81 (0.88)	4.21 (2.15)	2.64 (2.04)	2.79 (1.99)
Control	2.89 (0.95)	2.95 (0.86)	4.32 (2.20)	2.52 (1.97)	2.56 (1.91)

Notes: ^a 1=much less, 2=somewhat less, 3=equally/same, 4=somewhat more, 5=much more; ^b 1=almost no harmful chemicals, 2=a few harmful chemicals, 3=some harmful chemicals, 4=a lot of harmful chemicals; ^c 1=not at all likely to 7=extremely likely.

* $p < .05$; ** $p < .01$; *** $p < .001$ for ANOVA tests. Post-hoc pairwise tests (Tukey's HSD): *HWL messages*: Perceived relative harm: Risks>Quitting. Perceived exposure: Risks>Quitting. *Ad messages*: Perceived relative harm: Slight distancing>Clear distancing; Control>Clear distancing. Perceived exposure: Slight distancing>Clear distancing; Control>Clear distancing. Likelihood to suggest to smokers: Clear distancing>Control.

HIGHLIGHTS

- The US FDA authorized a heated tobacco product IQOS to use reduced exposure claims.
- Alternative tobacco products rarely have specific health warning labels (HWLs).
- Disease risk HWLs increased perceived harm and decreased likelihood to try IQOS.
- Ads distancing IQOS from cigarettes decreased perceived harm.
- HWLs on quitting cigarettes with these distancing ads were particularly effective.

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