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ORIGINAL RESEARCH

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Effect of Advertising Exposure on Responses of Young Non-e-Cigarette Users to Banning Flavors in China: A Cross-Sectional Study

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ABSTRACT

Background: E-cigarettes, particularly those with flavors, have become increasingly popular among young people. Many countries have implemented flavor bans, though limited research has explored how non-users react to flavor bans. This research investigates the influence of advertising exposure on changes in intention to use e-cigarettes among young Chinese non-users in response to a hypothetical flavor ban.

Methods: A probability-based online survey conducted from September to November 2021 included 2989 participants aged 20–34. We assessed the association between advertising exposure and change in intention to use e-cigarettes after a hypothetical flavor ban. We used propensity score weighting (PSW) to reduce potential selection bias.

Results: The intention to use e-cigarettes next year among young non-users was rated highly (3.99 out of 5 points), with the flavor ban, this intention decreased by 5.8%. Females showed a greater decline in intention than males ($p = 0.011$). After adjusting for covariates, young adults with higher advertising exposure exhibited a more pronounced decline in their intention to try e-cigarettes. The interaction between advertising exposure and sex was statistically significant ($B = 0.217$, $p < 0.05$), suggesting that females are more likely than males to initiate e-cigarette use with increased advertising exposure.

Conclusions: A flavor ban may have the potential to significantly reduce young people's intention to use e-cigarettes, particularly among females and those exposed to more advertising. These findings highlight the need for sex-specific approaches in tobacco control policies.

1 | Introduction

Electronic cigarettes (e-cigarettes) are battery-powered devices that heat a liquid containing nicotine, generating an aerosol for

inhalation by the user [1, 2]. Although often marketed as a tobacco cessation aid and harm reduction [3], they have been demonstrated to be associated with both respiratory and cardiovascular diseases [4]. Over the past decade, these products

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have become popular globally among young people. The proportion of US young adults who used e-cigarettes on a daily basis sharply increased by 50% from 2017 to 2020 [5]. In China, e-cigarette use has remained relatively low, yet on a steady rise. The Chinese Center for Disease Control and Prevention reported that the percentage of adults who had used an e-cigarette within the past 30 days increased from 1.3% in 2015 to 1.6% in 2019 and from 2.0% to 2.7% among young people aged 18–29 [6]. Another more recent national study found that up to 20% of Chinese adolescents and young adults reported being ever users, 8% current users, and 3% daily users [7]. Their experimentation and transition to regular use and addiction to nicotine is driven in part by access to appealing flavors of e-liquids, especially fruit and sweet for females [8].

The surge in e-cigarette use is also partially due to the fact that these products have been extensively marketed through various channels targeting young people, including retail stores, billboards, and social media platforms [9]. Prior investigations have demonstrated that advertising exposure is positively correlated with e-cigarette usage, intention to use, and susceptibility in young adults [10–13], as information conveyed by advertisements can shape their perception and attitude towards e-cigarettes. A recent study of 2304 participants found that exposure to advertisements may increase young adults' likelihood of e-cigarette use by 1.34 times after 12 months [12]. Having grown up in the era of widespread internet usage, young adults are also likely to be repeatedly exposed to online advertising messages and thus potentially become long-term e-cigarette users [14, 15]. Young adults who have tried e-cigarettes are also more likely to notice advertising promoting new flavored products, which can reinforce their use [16]. Advertising for sweet, fruit, and menthol/ice/cool flavored e-cigarettes appears to be particularly effective among young adults relative to tobacco flavors [17, 18].

Existing literature has documented the modification effects of sex on the relationship between traditional tobacco use and advertising exposure [19–22]. Tobacco advertising that includes relaxing themes appealing to females increases their intention to smoke [20]. A 5-year longitudinal study of US adolescents suggested that advertising exposure at baseline predicted subsequent smoking initiation only among females [23]. Researchers have recently proposed that sex must be taken into consideration when formulating policies for not only combustible tobacco products but also e-cigarettes [24]. However, research about e-cigarette use and advertising exposure by sex has remained relatively scant. Similar to tobacco products, e-cigarette advertisements highlight appealing flavors [25] and seek to link these products to themes that have traditionally appealed to women, such as independence, modernity, and glamour [26], aiming to increase their likelihood of use. One US study found female participants more likely than male participants to report increased e-cigarette appeal when they noticed menthol, mint, or fruit flavors in advertising [27].

Many US jurisdictions and European Union member states have prohibited the sales of flavored e-cigarettes [28]. Canada demands no “dessert” or “confectionery” flavors be promoted on product packaging [29]. Beginning to include e-cigarettes into the national tobacco regulation framework in 2021, the

State Tobacco Monopoly Administration of China also announced the ban on all but tobacco-flavored e-cigarette products, including both rechargeable/disposable vaping pens and mods, on May 1, 2022. To date, little research has investigated the effect of the flavor ban in China. However, the potential for benefits is notable. Prior research indicates that flavored products are commonly used by youth at e-cigarette initiation, and the majority of users are likely to quit or switch to tobacco-flavored e-cigarettes when other flavors are banned [29, 30]. A prior study reported that after flavors were prohibited in the city of San Francisco, California, the prevalence of flavored nicotine e-cigarette product use decreased among those aged 18–34 years old [31]. Prior work also indicates that e-cigarette shop customers who like flavors were significantly less willing to purchase non-flavored e-cigarettes and exhibited a reduced intention to continue e-cigarette use when faced with a hypothetical flavor ban [32]. Furthermore, individuals' reactions to a flavor ban may vary by e-cigarette use status. Researchers have so far primarily focused on evaluating the policy effect among people who use e-cigarettes or cigarettes [30, 32–34]; however, to our best knowledge, no prior study has examined how non-users would respond to flavor bans and investigated factors associated with their decisions relating to experimental use. In addition, experimental use of e-cigarettes is dependent on individual characteristics and environmental factors across age groups. Stroup et al. found that curiosity and exposure to advertisements were associated with increased intention to use among adolescents who had never tried e-cigarettes. Similarly, Trumbo et al. reported that college students' positive views of e-cigarettes and exposure to advertisements were linked with their higher intention to use e-cigarettes. These findings suggested advertisement exposure as a key determinant of intention to try e-cigarettes across age groups.

Our research aims to address this critical gap by measuring the extent to which advertising exposure influences change in intention to use e-cigarettes among young adult non-users in China in response to a flavor ban, and whether the relationship, if any, is moderated by sex. We hypothesize that advertising exposure is associated with a greater desire to try e-cigarettes due to flavors among females; thus, their intention to try e-cigarettes would decrease more than that of males once flavored e-cigarettes are removed from the marketplace [8, 35]. This study will generate evidence informing the development of sex-specific interventions to prevent e-cigarette use.

2 | Methods

2.1 | Study Design and Participants

We conducted a national, probability-based online survey via Questionnaire Star, a leading enterprise technology platform that has been widely used in China [36, 37]. Through quota sampling, we recruited participants stratified by sex, age (20–24, 25–29, and 30–34), and geographic area (East, Central, and West) to match their percentages in census data. The data were collected from a total of 5215 young adults aged 20–34 between September and November 2021. We first removed 113 participants, accounting for 2.2% of the sample, including those

who filled out the questionnaire repeatedly based on IP addresses or had logic errors in responses (for instance, their age of smoking initiation was greater than their current age). We further restricted our analytical sample to 2989 participants who had never tried e-cigarettes before the survey. The Institutional Review Board of Peking University approved the study (Approval number: IRB00001052-21125). Participants provided active written informed consent by reading and then clicking “agree” to start the online survey.

2.2 | Measures

2.2.1 | Primary Outcome: Intention to Use E-Cigarettes

Our primary outcome of interest was the change in self-reported intention to use e-cigarettes after a hypothetical flavor ban [32]. Participants were asked whether they would try e-cigarette products: (a) next year under current conditions (with all available flavors) and (b) hypothetically, if only tobacco-flavored e-cigarettes were available in the market, excluding youth-appealing flavors such as fruit or candy flavors. Based on the existing literature, responses were measured on a 5-point Likert scale ranging from “definitely not,” “possibly not,” “not sure,” “possible will,” to “definitely will,” with higher values indicating stronger intention to use e-cigarettes in the future [38, 39]. We subtracted the value of the first response (under current conditions) from that of the second response (with the hypothetical flavor ban) as the outcome. Larger differences indicated greater increases in intention to use after the flavor ban, while smaller ones suggested decreases or no change in intention to use.

2.2.2 | Advertising Exposure

For advertising exposure, participants were asked about the frequency with which they saw e-cigarette advertisements in the past 6 months. Response options ranged from “never,” “less than once a month,” “once a month,” “more than once a month,” “once a week,” to “more than once a week.” We categorized them into three levels of exposure: no exposure, low exposure (approximately “once a month” or less), and high exposure (“more than once a month” or higher), with higher levels of exposure reflecting greater frequency of encountering e-cigarette advertisements [40].

2.2.3 | Demographic, Socioeconomic, and Health Behavior Characteristics

We used several demographic, socioeconomic, and health behavior characteristics as covariates in multivariable analyses: age (20–24, 25–29, or 30–34 year old), sex (male or female), residential area (if living in one of four most economically developed cities, including Beijing, Shanghai, Guangzhou, and Shenzhen, also known as first-tier cities), educational attainment (high school and below, junior college, undergraduate, or postgraduate), occupation type (health-related or not), annual household income (< 50,000, 50,000–200,000, or > 200,000

Chinese yuan), and smoking status (non-, former, or current smokers).

2.2.4 | Influence of Social Factors and E-Cigarette Knowledge

We further adjusted for family and peer influence (if any family members or friends use e-cigarettes) and e-cigarette knowledge level. Participants’ e-cigarette knowledge was assessed by whether they know the following three correct statements to be true, including e-cigarette products (1) often contain the addictive substance nicotine, (2) contain harmful chemicals, and (3) affect the brain development of adolescents. A greater number of correct answers, ranging from 0 to 3, indicated a higher level of knowledge. A greater number of correct answers to these questions indicated a higher level of knowledge [41].

2.3 | Data Analysis

We first performed univariate analyses to describe the distribution of change in intention to use e-cigarettes and other sociodemographic characteristics by sex, with either two-independent sample *t*-test or χ^2 test to examine the differences between the groups. The QQ plot was used to evaluate whether our outcome followed a normal distribution (Supporting Information S1: Figure S1 in the appendix showed the normality). We then used multivariable linear regression models to assess the association between change in intention to use e-cigarettes and advertising exposure, adopted stepwise regression strategies to sequentially control demographic, socioeconomic, and health behavior characteristics variables, and further conducted sex-stratified analyses. We further performed the moderation analysis with an interaction term between advertising exposure and sex being added to the regression model to assess whether the effect of advertising exposure on intention to use e-cigarettes varied by sex. To address differential selection bias, pairwise comparisons out of the three advertising exposure categories were performed for both sexes using propensity score weighting (PSW). In each pairwise comparison, we calculated the propensity scores and then employed the inverse probability of treatment weighting using those scores to achieve comparability between exposed and control groups. To evaluate whether the propensity score weights obtained have eliminated the imbalance between different groups, we checked the quality of balancing performance after the weighting process. All the analyses were conducted using the statistical analysis software STATA 17 (StataCorp, College Station, TX) with $p < 0.05$ being considered statistically significant.

3 | Results

Table 1 provides the characteristics of 2989 young non-e-cigarette users across sex. On average, the intention to use e-cigarettes next year is 3.99 out of 5 points, and the intention decreased by 5.8% among all participants if the flavor ban were to be implemented. Specifically, females and males exhibited

TABLE 1 | Descriptive statistics of demographic, socioeconomic, health behavior, and change in intention to use E-cigarettes among young non-e-cigarette users aged 20–34 years by sex.

Characteristic	Female <i>n</i> = 1799 (60.2%)	Male <i>n</i> = 1190 (39.8%)	Total <i>n</i> = 2989	<i>p</i> value
Intention to use next year (mean, SE)	4.10 ± 0.03	3.83 ± 0.04	3.99 ± 0.02	< 0.001
Change in intention to use (mean, SE)	0.26 ± 0.02	0.19 ± 0.02	0.23 ± 0.02	0.011
E-cigarette advertising exposure				
Never	184 (10.2%)	179 (15.0%)	363 (12.1%)	< 0.001
Low	1115 (62.0%)	660 (55.5%)	1775 (59.4%)	
High	500 (27.8%)	351 (29.5%)	851 (28.5%)	
Age				
20–24	516 (28.7%)	325 (27.3%)	841 (28.1%)	0.289
25–29	652 (36.2%)	414 (34.8%)	1066 (35.7%)	
30–34	631 (35.1%)	451 (37.9%)	1082 (36.2%)	
Residential area				
Does not live in a first-tier city	1523 (84.7%)	1001 (84.1%)	2524 (84.4%)	0.690
Live in a first-tier city	276 (15.3%)	189 (15.9%)	465 (15.6%)	
Health-related occupations				
No	1546 (85.9%)	1017 (85.5%)	2563 (85.7%)	0.716
Yes	253 (14.1%)	173 (14.5%)	426 (14.3%)	
Educational attainment				
High school and below	100 (5.6%)	109 (9.2%)	209 (7.0%)	0.001
Junior college	294 (16.3%)	195 (16.4%)	489 (16.4%)	
Undergraduate	1251 (69.5%)	771 (64.8%)	2022 (67.6%)	
Postgraduate	154 (8.6%)	115 (9.7%)	269 (9.0%)	
Annual household income				
< ¥50,000	490 (27.2%)	310 (26.1%)	800 (26.8%)	0.435
¥50,000–¥200,000	961 (53.4%)	664 (55.8%)	1625 (54.4%)	
> ¥200,000	348 (19.3%)	216 (18.2%)	564 (18.9%)	
Smoking status				
Never	1654 (91.9%)	830 (69.7%)	2484 (83.1%)	< 0.001
Current	135 (7.5%)	318 (26.7%)	453 (15.2%)	
Former	10 (0.6%)	42 (3.5%)	52 (1.7%)	
Family members or peers use e-cigarettes				
No	791 (44.0%)	554 (46.6%)	1345 (45.0%)	0.164
Yes	1008 (56.0%)	636 (53.4%)	1644 (55.0%)	
E-cigarette knowledge level (mean, SE)	1.34 ± 0.03	1.44 ± 0.03	1.38 ± 0.03	0.031

a decrease of 0.26 and 0.19 points in intention to use, respectively, with the difference being statistically significant ($p = 0.011$). Close to 60% of participants had a low exposure to advertising within the past 6 months, followed by those with high exposure (28.5%) and no exposure (12.1%). Approximately one in 10 female participants had never seen any advertisements, while 15% of males had no such exposure.

Participants aged 20–24, 25–29, and 30–34 each accounted for approximately one-third of the sample. Overall, 39.8%

were male, and 15.6% resided in a first-tier city. Three quarters of the participants had attained at least a college degree, and just more than half reported their annual household income to be in the middle range ¥50,000–¥200,000 (approximately 7000–28,000 US dollars). Most (83.1%) reported being non-cigarette smokers, and over half (55.0%) had family members or friends using e-cigarettes. Females demonstrated lower levels of knowledge about e-cigarettes and were less likely to believe in their benefits than males.

TABLE 2 | Multivariate-adjusted relationship between advertising exposure and changes in intention to use E-cigarettes.

	Only sex adjusted ^a	Sociodemographic adjusted ^b	All covariates adjusted ^c		
			Total (n = 2989)	Female (n = 1799)	Male (n = 1190)
E-cigarette advertising exposure					
Low	0.12** (0.03, 0.22)	0.10* (0.01, 0.19)	0.08 (−0.01, 0.17)	0.15* (0.01, 0.28)	0.03 (−0.10, 0.16)
High	0.21** (0.11, 0.31)	0.18** (0.07, 0.28)	0.14** (0.04, 0.25)	0.24** (0.08, 0.39)	0.03 (−0.11, 0.18)

Note: The 95% confidence intervals (CIs) are in parentheses.

* $p < 0.05$; ** $p < 0.001$.

^aModel only controlled for sex.

^bModel control for respondents' age, sex, residential area, health-related occupations, educational attainment, total annual household income, and smoking status.

^cModel additionally controls the variables related to e-cigarettes: whether family members or peers use e-cigarette products, and e-cigarette knowledge level.

We presented the association between advertising exposure and young adults' changes in intention to use e-cigarettes in response to the flavor ban in Table 2. Advertising exposure had a significant and positive effect on the change in intention to use in the model adjusted for sex only. Specifically, compared to no exposure, both low and high exposure were associated with reductions of 0.12 (95% CI: 0.03, 0.22) and 0.21 (95% CI: 0.11, 0.31) points, respectively. Controlling for other sociodemographic characteristics and smoking status, the estimated coefficients of advertising exposure attenuated but were still significant. With additional adjusting for impacts of family and peers and e-cigarette knowledge level, the findings revealed that the estimated effect of high advertising exposure remained robust and significant, but low exposure did not.

Stratified by sex, the coefficients for low and high advertising exposure among females were 0.15 (95% CI: 0.01, 0.28) and 0.24 (95% CI: 0.08, 0.39), which were both statistically significant, while those for males were not. Based on marginal effects for the interaction term included in the final model, additionally adjusting for the impacts of family and peers, and e-cigarette knowledge level, we further plotted the predicted average changes in intention to use e-cigarettes for males and females at different levels of advertising exposure. As illustrated in Figure 1, females' changes in intention varied significantly, and those with higher levels of advertising exposure showed a more pronounced decline in their reported likelihood of trying e-cigarettes, while males showed no significant changes in their intentions across levels of advertising exposure. Sex was found to moderate the relationship between advertising exposure and intention to use e-cigarettes changed by the hypothetical flavor ban.

We additionally conducted sensitivity analysis using the PSW to check whether the regression results were robust. The differences in covariates between the pairwise comparison groups were no longer significant after the weighting process, thus validating the good balance of subjects across the groups (Table S1). Table 3 illustrates the effects on the potential change among participants with varying levels of advertisement exposure after PSW, largely consistent with those in the multivariate-adjusted regressions. On average, compared to those with no advertising exposure in the past 6 months, the females with low advertising exposure ($B = 0.144$, $p < 0.05$) and high advertising exposure ($B = 0.211$, $p < 0.05$) exhibited a more

pronounced decline in their intended use. However, no statistically significant association was observed between advertising exposure and a shift in intention to use among males.

4 | Discussion

Our study examined how intention to use e-cigarettes changes among Chinese young adult non-users in response to a hypothetical flavor ban and levels of advertising exposure. The results suggest that intention to initiate use declines when nontobacco flavored products are no longer accessible. Notably, young adults with a higher level of advertising exposure exhibited a more pronounced decline in their reported intention to try e-cigarettes if the flavor ban were to be implemented. Furthermore, we measured the moderating effect of sex and found that the negative association of advertising exposure with intention to use was only significant among females.

The current research supports banning flavored e-cigarettes as an effective regulatory approach to deter e-cigarette non-users from experimental use, and extends prior research that primarily focused on current users [30, 32–34]. Soule and colleagues measured the potential impact of a flavor ban among current e-cigarette users [34]. Their findings indicated that users expressed a reduced intention to continue purchasing e-cigarettes after a hypothetical flavor ban, suggesting that removing flavors could play a role in discouraging current users. Our study is the first to examine the effect of this policy on non-users, and as such, there is no directly comparable research within this population. However, our findings complement existing studies by providing a fresh perspective on how flavor bans may influence young adults who are potential users.

However, the 2020 International Tobacco Control Surveys of 851 people who regularly use e-cigarette or former cigarette smokers from Canada, England, and the United States reported that if preferred flavors of nicotine e-cigarette products were forbidden, 28.8% of participants would switch to other available flavors, and 17.1% would discontinue e-cigarette use but switch to smoking, and only 12.9% would quit using both e-cigarettes and all other tobacco products [30]. This suggests that a proportion of current users might be negatively impacted by this regulation, as they will look for substitutes, including flavored

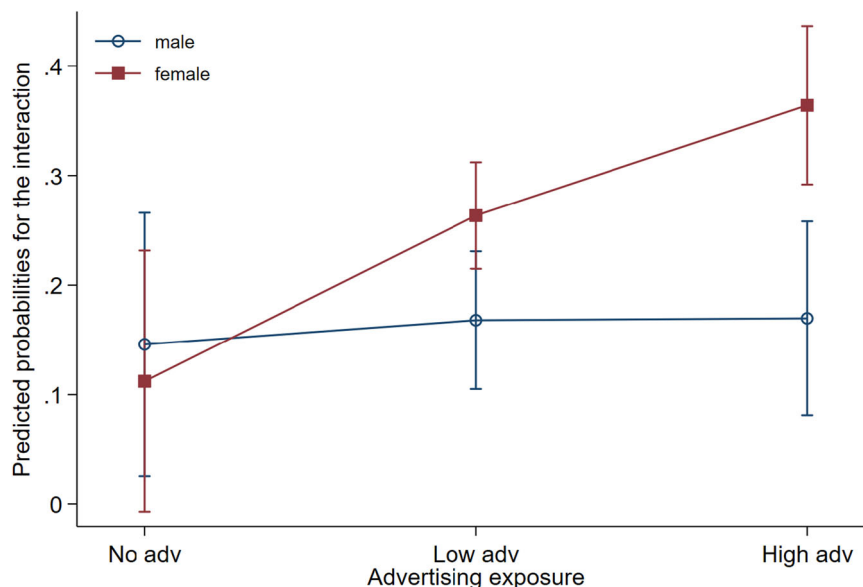


FIGURE 1 | The predictive margins plot of the interaction between sex and advertising exposure for change in intention to use E-cigarettes.

TABLE 3 | Advertising exposure effect estimations for change in intention to use E-cigarettes after PSW.

	No versus low ^a	No versus high ^a	Low versus high ^b
Female	0.144* (0.02, 0.26)	0.211* (0.04, 0.38)	0.076 (−0.02, 0.17)
Male	0.010 (−0.11, 0.13)	−0.038 (−0.20, 0.13)	0.014 (−0.09, 0.12)

* $p < 0.05$. The 95% confidence intervals (CIs) are in parentheses.

^aReference is the no-exposure advertising group.

^bReference is the low-exposure advertising group.

e-cigarette products containing unknown ingredients from illicit markets [42]. These products, such as “milk tea cups” and “Coke cans” (Supporting Information S1: Figure S2), have been frequently reported to be circulating in the Chinese market and continue to attract young generations regardless of past experiences in use and their illicit status [43]. Therefore, strict enforcement of the flavor ban will be needed to protect youth health by extensively eradicating the illegal flavor products.

In China, smoking has long been deemed a socially unacceptable behavior for women; however, with changing social norms related to gender equality [44], females' interest in e-cigarettes has grown. In our study, we observed that the response of young adults to the flavor ban varied across sex. The greater decrease in intended use among females supports the argument that the candy- and fruit-flavored e-cigarette products dominating the global market are more appealing to them compared to males [45]. This susceptibility may stem from women's more positive perceptions of sweetness [46] and preferences for sugary foods [47]. Research also suggests that the pleasant flavors of e-cigarettes function to satisfy the desire for food, and thus may be used by some for weight management through suppressing their appetite [48]. Analyzing nationally representative data, Zhao et al. found that though current users were predominantly male, the proportion of female users in China had increased by approximately 15% from 2015 to 2018 [6].

This study further showed that a change in intention to use e-cigarettes due to the flavor ban was positively associated with advertising exposure, but only among females, suggesting differential impacts of advertising in reinforcing customer attraction to flavors by sex. Many prior studies on tobacco use have investigated sex-specific preferences and explained how advertisements attract females [11, 20, 23]; however, similar research on e-cigarettes remains rare, especially in developing countries. Tobacco advertising has long featured themes and product characteristics that specifically target and appeal to females [20, 26]. Our findings suggest that similar marketing strategies have been successfully adopted by e-cigarette manufacturers through emphasizing nontobacco flavors to appeal to females in China. Chinese e-cigarette manufacturers have long promoted both flavors and e-cigarettes marketed as being designed for females [49]. The decrease in intention to use e-cigarettes following the flavor ban suggests that advertising has generated a strong interest among females who do not use e-cigarettes specifically for trying nontobacco flavored e-cigarettes rather than for trying e-cigarettes more generally. Accordingly, banning flavored products can help reduce e-cigarette use among females.

Though the data sampling stratified by age, sex, and geographic area enhanced national representativeness of our results, we acknowledge the following limitations. The cross-sectional nature of our study hinders causal inferences, further research is thus warranted to collect longitudinal data to quantify the actual impact of the regulation on e-cigarette use. Furthermore, our survey did not explicitly ask whether flavor-related content appeared in advertisements seen by participants, resulting in indirect evidence for the hypothesis.

5 | Conclusion

In conclusion, this research advanced our understanding of how e-cigarette advertising exposure influences intention to use across sex and investigated how non-users would react to the newly implemented flavor ban in China. The study results

suggest that future research on e-cigarettes may investigate sex differences in susceptibility to use. Moreover, the findings have important implications for public health policy. While the flavor ban will help reduce the appeal of e-cigarette use among women, the continued illicit market for flavored products necessitates targeted preventive measures [44]. Studies on the effectiveness of these interventions, including monitoring illicit markets to enforce the flavor ban, are critical to understanding how such policies can mitigate e-cigarette use. Additional research is also warranted to assess the long-term effects of flavor bans on behavior, such as whether the policies reduce overall e-cigarette consumption or merely shift consumer preferences to other products. Public education efforts through public warnings and social media campaigns should be dedicated to informing women about the health risks of flavored e-cigarette liquids and increasing their awareness of the harms associated with nicotine products.

Author Contributions

Xiaoyang Lv: writing – original draft, data curation, formal analysis. **Duo Yan:** visualization, writing – review and editing. **Linnea Laestadius:** writing – review and editing, supervision, methodology. **Fernando A. Wilson:** writing – review and editing, supervision. **Miaoqing Yang:** writing – review and editing, supervision. **Adam Martin:** writing – review and editing, supervision. **Yang Wang:** conceptualization, funding acquisition, investigation, writing – review and editing, supervision, methodology, project administration.

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Ethics Statement

The Institutional Review Board of Peking University approved the study (Approval Number: IRB00001052-21125).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Transparency Statement

The lead author, Yang Wang, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Supplementary Figures S1 and S2 revised. Supplementary Table S1 revised.