Impact of Alcohol-Induced Facial Flushing Phenotype on Alcohol Consumption among Korean Adults: A Two-Year Cross-Sectional Study

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Abstract

Background: Alcohol-induced facial flushing phenotype (flushing) is commonly observed among East Asians. Despite a small intake of alcohol, they experience heightened levels of acetaldehyde, a group-1 carcinogen, which in turn causes unpleasant symptoms such as flushing, acting as a robust protective mechanism against consuming alcohol. However, some individuals with this genetic trait exhibit weakened alcohol restraint, which increases the risk of developing alcohol-related cancers, such as esophageal and head/neck cancer, by more than ten times. Thus, identifying the population characteristics of those who have the flushing trait but cannot refrain from drinking is crucial. However, there is a paucity of studies that have comprehensively investigated the effect of flushing or its genotype on alcohol consumption in a large group of East Asians while controlling for various sociodemographic and health-related variables at a country level. Our aim was to address this research gap.

Objective: This cross-sectional study aimed to explore the effect of flushing on drinking behavior in Koreans and to examine whether the effect varies across sociodemographic and health-related factors.

Methods: We used data from the Korean National Health and Nutrition Examination Survey 2019–2020 conducted by the Korea Disease Control and Prevention Agency. Our sample comprised 10,660 Korean adults. We investigated the association of 26 variables, including flushing, with drinking frequency and amount. The effect of flushing was investigated with and without adjusting for the other 25 variables using multinomial logistic regression analysis. Additionally, we tested the interaction effect with flushing and conducted a simple effect analysis.

Results: In the flushing group, the odds of each drinking frequency/amount versus “never drank in the past year” (reference) were significantly lower than in the non-flushing group after adjusting for potential confounders at all levels except the lowest contrast (all of OR < 1 and 95% CI did not include the value of one); the odds ratio tended to decrease as the drinking frequency/amount increased. Flushing had notable interactions with other variables. A simple effect analysis showed a diminished alcohol-suppressive effect of flushing on alcohol consumption for specific groups (e.g., those with a low level of education, limited family support, physical labor, or health-related issues).

Conclusions: Our findings suggest that flushing suppresses drinking in Koreans overall but has little or no effect in certain vulnerable populations. Therefore, health authorities should conduct targeted epidemiological studies to assess drinking patterns and disease profiles, particularly regarding alcohol-related cancers, and establish effective preventive measures tailored to this population. Generalizability of these findings to other East Asian communities should also be determined.

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Impact of Alcohol-Induced Facial Flushing Phenotype on Alcohol Consumption among Korean Adults: A Two-Year Cross-Sectional Study

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Author contributions

CK, BK, and SHS performed the study conceptualization and study design. BK conducted literature search. BK and SHS conducted data collection and created tables and figures. SHS undertook data curation, formal analysis, methodology, software, and visualization. CK, BK, and SHS conducted data analysis and interpretation, and composed the initial manuscript draft. CK, BK, SHS, YJ, and HS reviewed and revised the manuscript.

June 9, 2023

Travis Sanchez
Editor-in-Chief
JMIR Public Health and Surveillance

Dear Editor:

I wish to submit an article titled “Impact of Alcohol-Induced Facial Flushing Phenotype on Alcohol Consumption among Korean Adults: A Two-Year Cross-Sectional Study” for publication in the *JMIR Public Health and Surveillance.*

The alcohol-induced facial flushing (flushing) phenotype is commonly observed among East Asians. Despite consuming only small amounts of alcohol, they experience heightened levels of acetaldehyde, a group-1 carcinogen, which in turn causes unpleasant symptoms acting as a robust protective mechanism against consuming alcohol. However, some individuals with this genetic trait exhibit weakened alcohol restraint, which increases the risk of developing alcohol-related cancers, such as esophageal or head/neck cancer, by more than ten times.

Identifying the population characteristics of those who have the flushing trait but cannot refrain from drinking is crucial when identifying high-risk groups. However, there is a paucity of studies that have comprehensively investigated the effect of flushing or its genotype on alcohol consumption in a large group of East Asians, while controlling for various sociodemographic and health-related variables at a country level. Our aim was to address this research gap.

Our study, based on a substantial sample of representative Koreans, provides evidence that flushing still has a significant alcohol-deterrence effect, even after controlling for various confounders. Furthermore, the findings reveal that this robust biological defense mechanism is diminished in some population groups, thereby identifying new vulnerable characteristics of Korean drinkers. This is the first time that such attenuation has been confirmed.

We believe that our manuscript is appropriate for submission to the *JMIR Public Health and Surveillance* as the study provides new insight into unveiling cancer risk candidates. The findings are relevant to social and preventive medicine as they identify a newly vulnerable population (East Asians) toward the harmful effects of alcohol consumption due to their heightened exposure to group 1 carcinogens. We hope that our paper will contribute to developing targeted health policies.

This manuscript has not been published before and is not under consideration by another journal. We have read and understood your journal’s policies and believe that neither the manuscript nor the study violates any of these. There are no conflicts of interest to declare.

We thank you for your consideration and look forward to hearing from you.

Sincerely,
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Original Paper

Impact of Alcohol-Induced Facial Flushing Phenotype on Alcohol Consumption among Korean Adults: A Two-Year Cross-Sectional Study

Abstract

Background: Alcohol-induced facial flushing phenotype (flushing) is common among East Asians. Despite a small intake of alcohol, they experience heightened levels of acetaldehyde, a group-1 carcinogen, which in turn causes unpleasant symptoms such as redness, acting as a robust protective mechanism against consuming alcohol. However, some individuals with this genetic trait exhibit weakened alcohol restraint, which increases the risk of developing alcohol-related cancers, such as esophageal and head/neck cancer, by more than ten times. Although this flushing phenomenon is crucial for public health, there is a paucity of studies that have comprehensively investigated the effect of flushing or its genotype on alcohol consumption in a large group of East Asians while controlling for various sociodemographic and health-related variables at a country level.
Objective: This two-year cross-sectional study aimed to explore the effect of flushing on drinking behavior in Koreans and to examine whether the effect varies across sociodemographic and health-related factors.
Methods: We used data from the Korea National Health and Nutrition Examination Survey 2019–2020 conducted by the Korea Disease Control and Prevention Agency. Our sample comprised 10,660 Korean adults. The study investigated the association of 26 variables, including flushing, with drinking frequency and amount. The effect of flushing was examined with and without adjusting for the other 25 variables using multinomial logistic regression analysis. Additionally, we tested the interaction effect with flushing and conducted a simple effect analysis. To ensure unbiased results, we employed complex sample design elements, including strata, clusters, and weights, to obtain unbiased results for the Rao-Scott $\chi 2$ test, t-test, and multinomial logistic regression analysis.
Results: The suppressive effect of flushing was significant across all pronounced categories of alcohol consumption at the significance level of .001 in 2019. The ranges of the standardized regression slopes and odds ratios were -6.70 ≥ β ≥ -11.25 and 0.78 ≥ OR ≥ 0.50 for frequency; -5.37 ≥ β ≥ -17.64 and 0.73 ≥ OR ≥ 0.36 for amount, respectively. The effect became somewhat stronger when adjusted for confounders. The effect also exhibited an overall stronger trend as the severity of alcohol consumption increased. The betas and odds ratios were consistently smaller in 2020 compared to the previous year. A simple effect analysis revealed a diminished alcohol-suppressive effect of flushing on alcohol consumption for specific groups (e.g., those with low levels of education, limited family support, physical labor, or health-related issues).
Conclusions: Our findings suggest that flushing suppresses drinking in Koreans overall but has little or no effect in certain vulnerable populations. Therefore, health authorities should conduct targeted epidemiological studies to assess drinking patterns and disease profiles, particularly regarding alcohol-related cancers, and establish effective preventive measures tailored to this population.

Keywords: facial flushing; alcohol consumption; drinking behavior; alcohol; acetaldehyde; aldehyde dehydrogenase 2 polymorphism; East Asian

Introduction

Alcohol-induced facial flushing phenotype (hereafter flushing), characterized by facial redness even with a small intake of alcohol, is a prevalent genetic trait among East Asians. This distinctive response is attributed to a reduced metabolic capacity of aldehyde dehydrogenase 2 (ALDH2) variant, which leads to elevated levels of acetaldehyde—a Group 1 carcinogen [1–5]. Such a genetic variation is rare in individuals of European or African origin [2,3]. Alongside facial redness, individuals with this trait typically experience other unpleasant symptoms including tachycardia, headache, and nausea, which collectively serve as a robust biological defense mechanism deterring alcohol intake [3,6-8]. However, recent limited observations indicate that some individuals with this genetic trait exhibit weakened alcohol restraint [1,9,10].

Prolonged alcohol consumption among individuals with the ALDH2 variant significantly amplifies the risk of developing alcohol-related cancers, such as esophageal and head/neck cancer, by more than tenfold compared to those with active ALDH2 [11-14]. Therefore, it is imperative to identify the population characteristics of individuals who exhibit flushing but have reduced drinking inhibitions, as they are particularly vulnerable to the detrimental effects of alcohol consumption due to heightened exposure to group 1 carcinogens [3-6]. However, to the best of our knowledge, comprehensive research investigating the impact of flushing trait or its genotype on alcohol consumption behavior, while accounting for various sociodemographic and health-related factors, has not yet been conducted, particularly within a large East Asian population.

Hence, we hypothesized that flushing exerts a stronger influence on drinking behavior among East Asian individuals compared to other factors, and specific vulnerable subgroups may exhibit a mitigated effect. To test this hypothesis, we investigated the impact of flushing on alcohol consumption among a representative sample of Korean adults, drawn from the entire population. Additionally, we explored the potential mediating influence of socioeconomic and health-related variables.

Methods

Study Design and Population

This two-year cross-sectional study included data from the annual Korea National Health and Nutrition Examination Survey (KNHANES) for 2019–2020 administered by the Korea Disease Control and Prevention Agency (KDCPA). Using a two-stage stratified cluster sampling method, the survey sample was selected based on geographic region and housing type. Approximately 8,000 individuals are recruited for the KNHANES each year. Although the KNHANES has been conducted since 1998, the health survey on flushing was only added in 2019. Thus, the data from the 2019 and 2020 surveys were included in this study. To address the potential impacts of COVID-19, the two-year merged dataset was analyzed to assess the interaction effect between year and flushing. Subsequently, unadjusted and adjusted logistic models were separately applied to the data for each individual year.
People aged ≤18 years and lifetime abstainers were excluded because they were children or did not know whether they experienced facial redness after drinking alcohol.

Assessment of Variables

A total of 28 variables, including 25 sociodemographic and health-related variables, flushing, and two drinking behavior variables (frequency and amount of drinking), were used for the study. The drinking behavior data were obtained from the following survey questions: (1) How often did you drink over the past year (answered in six categories: did not drink in the past year, less than once a month, once a month, 2–4 times per month, 2–3 times per week, and ≥4 times per week)? (2) How many glasses did you drink when you drank over the past year (did not drink in the past year, 1–2 glasses, 3–4 glasses, 5–6 glasses, 7–9 glasses, and ≥10 glasses)? One glass is defined as 50 cc of soju

(Korean traditional liquor, 20% alcohol by volume percentage [ABV]) or 220 cc of beer, the volume of the most common Korean beer glass size (5% ABV).

Flushing was determined by the following questions, developed by Yokoyama [12,15]: (a) Do you currently have a constitution of your face turning red quickly after drinking as little as one glass of beer (soju) (never, sometimes, often, or always)? The individuals who answered “always,” “often,” or “sometimes” to Question (a) were defined as currently exhibiting flushing. Next, Question (b) was asked to those who responded “never” or “not applicable” (did not drink within the past year) to Question (a). (b) Did you experience your face turning red quickly after drinking as little as one glass of beer (or soju) during the 1–2 years after you started drinking (yes or no)? The individuals who responded “yes” to Question (b) were regarded as formerly having exhibited flushing. These current and former individuals with flushing experience were assigned to the flushing group.

The survey data on the other 25 variables, selected from a literature review regarding the participants’ sociodemographic factors and health status, were obtained through in-person interviews or self-administration [16-20]. Details of each variable and response options are included in Table 1. Age, body mass index, and sleep time were continuous variables while the rest were discrete. For some discrete variables, no responses were classified into a category.

Statistical Analysis

Frequency and Mean Analyses

To comprehensively explore the baseline characteristics of the study sample, mean and frequency analyses were conducted. Differences between the two study years were examined utilizing the Rao-Scott χ2 test and t-test for complex survey data. Additionally, a frequency analysis, accounting for strata, cluster, and weight, was performed to estimate the nationwide proportions of individuals exhibiting flushing among adults who had consumed alcohol.

Multinomial Logistic Regression Analysis

A two-phase multinomial logistic regression analysis was employed to investigate potential variations in the impact of flushing on alcohol consumption behavior across different years. This analysis considered the influence of the COVID-19 pandemic and associated social distancing regulations. The model with drinking frequency or amount as the outcome variable included flushing, year, and their interaction to assess variations across years. Subsequently, multinomial logistic regression models were applied to each year's data when the interaction effect was or close to significant. For each year, two models were formulated for each outcome variable: a simple model including only flushing as a predictor, and a complex model incorporating additional sociodemographic and health-related factors.

Joint Analysis of Interaction and simple effects

Furthermore, interaction effects with flushing were tested for significant predictor variables in the complex models to investigate whether the effect of flushing on drinking behavior remained consistent across different levels of other predictor variables. When the interaction effect was significant at $P < .05$, a simple effect analysis was performed to examine the impact of flushing at each level of the other variable, separately. Predicted individual probabilities were computed for continuous variables with an interaction effect of $P < .05$.

Statistical Methods and Software

All statistical analyses were performed using SAS (version 9.4 TS Level 1M7; SAS Institute Inc). Given the limitations of the proportional odds assumption with numerous predictors, a more comprehensive multinomial logistic regression model was employed. Standardized regression coefficients (β), odds ratios (OR), and 95% confidence intervals (CI) for predictor variables were presented to enhance direct comparability among the 26 predictor variables. Following the recommendation of KNHANES, complex sample design elements including strata, clusters, and weights were utilized, ensuring nationally representative population-based results for all inferential statistics generated in this study. Since the 2019 and 2020 datasets were combined within the same 8th survey cycle, a new weight was calculated for analysis by multiplying 0.5 with the basic association weight variable, *wt_itvex*, for each year's dataset. Furthermore, to prevent any bias in standard errors that may arise when analyzing only the data of the target group after excluding the rest of the dataset, a group variable was created to distinguish the individuals under investigation from those aged ≤18 years and lifetime abstainers. This variable was specified in the SAS statements for frequency and mean analyses, as well as for multinomial logistic regression analysis.

Institutional Review Board Approval

The original data collection was approved by the Institutional Review Board (IRB) of KDCPA, and this study received exemption from review by our institution's IRB.

Results

Baseline Characteristics

A total of 15,469 individuals participated in the KNHANES 2019–2020 survey. Of these, 10,660 were used in the analysis, excluding children (aged ≤18) and lifetime abstainers. 5,506 cases from 2019 and 5,154 cases from 2020 were used in the complex multinomial logistic regression models. The baseline characteristics of participants are shown in Table 1. In 2019, the number of people categorized into the flushing group was 2,489 (45.25%), while in 2020, it was 2,083 (40.46%). The corresponding population proportions were estimated to be 44.42% for 2019 and 40.11% for 2020, respectively.

Table 1. Baseline characteristics of the study sample and population: Korean adults from 2019-2020 Korea National Health and Nutrition Examination Survey

Variable	2019		2020		*p*
		N		*N*	
Age (years), mean (SD)	50.12(16.5)	5,506	50.49(16.9)	5,154	.68
BMI, mean (SD)	23.93(3.6)	5,485	24.21(3.8)	5,094	<.001
Sleeping hours per day on days off, mean (SD)	7.40 (1.7)	5,502	7.44(1.7)	5,149	.47
Sex, n(%)		5,506		5,154	.39
Male	2,621 (47.6)		2,522 (48.9)		
Female	2,885 (52.4)		2,632 (51.1)		
Spouse, n (%)		5,506		5,154	.09
Never married	1,028(18.7)		1,119 (21.7)		
Living with a spouse	3,819 (69.3)		3,360 (65.2)		
Living without a spouse	659 (12.0)		675 (13.1)		
Education, n (%)		5506		5154	.03
≤Elementary school diploma	789(14.3)		665 (12.9)		
Middle school diploma	477(8.7)		433 (8.4)		
High school diploma	1,830(33.2)		1,758 (34.1)		
≥University diploma	2,186 (39.7)		1,948 (37.8)		

Other, including no response	224(4.1)		350 (6.8)		
Family size (number of members), n (%)					
1	666 (12.1)	5,506	646 (12.5)	5,154	.18
2	1,736 (31.5)		1,529 (29.7)		
3	1,417 (25.7)		1,325 (25.7)		
4	1,292 (23.5)		1,198 (23.2)		
5	322 (5.9)		345 (6.7)		
≥6	73 (1.3)		111 (2.2)		
Area type, n (%)					
City district	4,465 (81.1)	5,506	4,178 (81.1)	5,154	.71
Town/village	1,041(18.9)		976 (18.9)		
Occupation, n (%)					
Administrator, professional	786 (14.3)	5,506	724 (14.1)	5,154	.23
Office worker	646 (11.7)		545 (10.6)		
Service or sales worker	680 (12.4)		684 (13.3)		
Farmer, fishermen	153 (2.8)		159 (3.1)		
Mechanic, technician	586(10.6)		474 (9.2)		
Simple labor worker	466 (8.5)		404 (7.8)		
Unemployed (housewife, student)	1,943 (35.2)		1,802 (34.9)		
Other, including no response	246(4.5)		362 (7.0)		
Household income, n (%)					
Low	721 (13.1)	5,486	624 (12.1)	5,140,	.95
Low-Middle	953 (17.4)		868 (16.9)		
Middle	1,124 (20.5)		1,096 (21.3)		
Middle-High	1,312 (23.9)		1,242 (24.2)		
High	1,376 (25.1)		1,310 (25.5)		
Number of houses owned, n (%)					
0	1,950 (35.4)	5,505	1,661 (32.2)	5,153	.18
1	2,918 (53.0)		2,783 (54.0)		
≥2	637(11.6)		709 (13.8)		
Type of health insurance, n (%)					
National health insurance residence-based	1,503 (27.3)	5,506	1,549 (30.1)	5,154	.06
National health insurance work-based	3,813 (69.3)		3,392 (65.8)		
Medical care	190 (3.4)		213 (4.1)		
Private health insurance, n (%)					
Have	4,544 (82.9)	5,480	4,272 (83.4)	5,120	.59
Does not have	936 (17.1)		848 (16.6)		
Smoking, n (%)					
Daily	896 (16.3)	5,502	820 (15.9)	5,150	.75
Occasionally	154 (2.8)		139 (2.7)		
Smoked before but not presently	1,383 (25.1)		1,317(25.5)		
Never	3,069 (55.8)		2,874(55.9)		
Weight control effort within the past 1 year, n (%)					
To lose weight	2,283 (41.5)	5,505	2,148 (41.7)	5,153	.01
To maintain weight	1,096 (19.9)		1,108 (21.5)		
To gain weight	302 (5.5)		226 (4.4)		

Never tried	1,824 (33.1)		1,671 (32.4)		
Limitation on life activities due to health or disability, n (%)					
Have	358 (6.5)	5,506	321 (6.2)	5,154	< .01
Do not have	4,928 (89.5)		4,492 (87.2)		
Other, including no response	220 (4.0)		341 (6.6)		
Feeling stressed, n (%)					
Very frequently	257 (4.7)	5,502	264 (5.1)	5,146	.59
Frequently	1,236 (22.5)		1,187(23.1)		
Occasionally	3,204 (58.2)		2,956(57.4)		
Seldomly	805 (14.6)		739(14.4)		
Suicide attempt within the past 1 year, n (%)					
Yes	20 (0.4)	5,503	25 (0.5)	5,149	.96
No	5,483 (99.6)		5,124 (99.5)		
Psychiatric consultation within the past 1 year, n (%)					
Yes	175 (3.2)	5,503	177 (3.4)	5,149	.81
No	5,328 (96.8)		4,972 (96.6)		
Number of major fatal illness[a], n (%)					
1	464 (8.4)	5,506	428 (8.3)	5,154	.45
≥2	51 (0.9)		38 (0.7)		
Other, including no response	4,991 (90.7)		4,688 (91.0)		
Osteoarthritis/rheumatoid arthritis diagnosis, n (%)					
Present	582 (10.6)	5,506	524 (10.2)	5,154	.24
Other, including no response	4,924 (89.4)		4,630 (89.8)		
Hypertension diagnosis, n (%)					
Present	1,267 (23.0)	5,506	1,242 (24.1)	5,154	.54
Other, including no response	4,239 (77.0)		3,912(75.9)		
Dyslipidemia diagnosis, n (%)					
Present	989 (18.0)	5,506	1,082 (21.0)	5,154	.03
Other, including no response	4,517 (82.0)		4,072 (79.0)		
Osteoporosis diagnosis, n (%)					
Present	327 (5.9)	5,506	316 (6.1)	5,154	.42
Other, including no response	5,179 (94.1)		4,838 (93.9)		
Diabetes diagnosis, n (%)					
Present	496 (9.0)	5,506	530 (10.3)	5,154	.16
Other, including no response	5,010 (91.0)		4,624 (89.7)		
Drinking frequency within the past 1 year, n (%)					
Never	1,070 (19.4)	5,503	1,103 (21.4)	5,153	.08
<Once per month	1,106 (20.1)		1,076 (20.9)		
Once per month	690 (12.5)		581 (11.3)		
2–4 times per month	1,330 (24.2)		1,215 (23.6)		
2–3 times per week	897 (16.3)		847(16.4)		
≥4 times per week	410 (7.5)		331(6.4)		
Drinking amount within the past 1 year (No. of glasses), n (%)					
0	1,070 (19.4)	5,503	1,103 (21.4)	5,153	.17

1–2	1,570(28.5)		1,469 (28.5)		
3–4	940(17.1)		822 (16.0)		
5–6	629(11.4)		507 (9.8)		
7–9	686(12.5)		655 (12.7)		
≥10	608(11.1)		597 (11.6)		
Alcohol-induced facial flushing[b],					
Present	2,489(45.3)	5,501	2,083 (40.5)	5,148	
Absent	3,012(54.7)		3,065 (59.5)		
Present[c]	8,589,410(44.4)	19,337,305	7,867,415(40.1)	19,612,917	< .001
Absent[c]	10,747,895(55.6)		11,745,502 (59.9)		

[a] The number of diagnoses by doctors for stomach, liver, colon, breast, cervical, lung, thyroid, and other cancers; stroke; and myocardial infarction or angina. [b] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section. [c] The weighted statistics obtained to estimate population parameters.

Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption. *P*-values for discrete variables were obtained from the Rao-Scott χ^2 test, while those for continuous variables were obtained from the t-test. To ensure unbiased results, complex sample design elements, including strata, clusters, and weights, were incorporated in both the Rao-Scott χ^2 test and t-test.

Impact of Flushing on Alcohol Consumption Behavior by year

The results of the multinomial logistic regression analysis using the two-year merged dataset revealed significant or close-to-significant interaction effects between flushing and year on drinking behavior. The test statistics and *P* values were as follows: $F(5,341) = 3.02$, $P = .011$ for drinking frequency, and $F(5,341) = 2.01$, $P = .077$ for drinking amount. For further details, see Tables S1 and S2 in Multimedia Appendix 1. It's worth noting that COVID-19 and strict social distancing regulations were prevalent in 2020. It is likely that the effects of the 25 confounders on alcohol consumption behavior, as well as their relationships with flushing, varied across the two years due to extreme social changes. Therefore, further analyses were conducted separately for each year.

Impact of Flushing on Alcohol Consumption Behavior Among Koreans

Frequency of Alcohol Consumption

The effects of the simple and complex multinomial logistic regression models with drinking frequency as the dependent variable are presented in Table 2. The presence of flushing showed a significantly negative correlation with the frequency of alcohol consumption at all contrasts (all ORs were <1, and CIs did not include the value of one) except for the lowest category of “<1 per month” versus “did not drink within the past year”. For instance, the odds of “drinking 2–3 times per week” versus “did not drink in the past year” were 0.56 times lower in the flushing group than in the non-flushing group (OR=0.56, CI=[0.45,0.69]). The odds further decreased to 0.47 times lower (CI=[0.37,0.59]) when other confounding variables were taken into account in the complex model. The OR tended to decrease overall as the drinking frequency increased, and they became smaller in the same contrasts in 2020, when the COVID-19 pandemic and social distancing regulations prevailed (Table 2).

Table 2. Effect of alcohol-induced facial flushing[a] on drinking frequency among Korean adults from 2019-2020 Korea National Health and Nutrition Examination Survey

Predictor variable	Category vs. reference category	Statistics	Drinking frequency (Reference = did not drink in the past year)				
			<Once per month	Once per month	2 – 4 times per month	2 – 3 times per week	≥ 4 times per week
Alcohol-induced facial flushing[a] (2019)	Presence vs. Absence of simple model	β^{b}	0.77	−2.97*	−6.70***	−6.88***	−8.12***
		OR	1.07	0.78	0.56	0.56	0.50
		[95%CI]	[0.85,1.34]	[0.62,0.98]	[0.47,0.68]	[0.45,0.69]	[0.39,0.64]
	Presence vs. Absence of complex model	β	1.09	−3.06*	−7.32***	−8.83***	−11.25***
		OR	1.10	0.77	0.54	0.47	0.38
		[95%CI]	[0.87,1.39]	[0.61,0.98]	[0.44,0.65]	[0.37,0.59]	[0.29,0.51]
Alcohol-induced facial flushing[a] (2020)	Presence vs. Absence of simple model	β	-1.46	−5.93***	−9.80***	−13.56***	−10.23***
		OR	0.88	0.60	0.43	0.31	0.41
		[95%CI]	[0.73,1.07]	[0.47,0.76]	[0.36,0.52]	[0.25,0.39]	[0.30,0.56]
	Presence vs. Absence of complex model	β	-1.62	−7.07***	−12.02***	−17.22***	−15.54***
		OR	0.87	0.54	0.35	0.23	0.26
		[95%CI]	[0.70,1.08]	[0.42,0.70]	[0.28,0.44]	[0.17,0.29]	[0.18,0.37]

[a] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section.
[b] The statistic β represents a standardized regression coefficient, the absolute value of which reflects the degree of association between the predictor variable and the outcome variable (drinking frequency), which enhances direct comparability among multiple predictor variables in the multinomial logistic regression analysis.
Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption. Multinomial logistic regression analysis was conducted, incorporating complex sample design elements, including strata, clusters, and weights, to ensure unbiased results.
* *P* < .05. ** *P* < .01. *** *P* < .001.

Amount of Alcohol Consumed

The results from the simple and complex multinomial logistic regression models with drinking amount as their dependent variable are presented in Table 3. The effect of flushing on the amount of drinking showed a similar but slightly stronger pattern (all slopes were significantly negative, ORs were <1, and CIs did not include the value of one, except for the lowest category of “drinking 1–2 glasses each time” versus “did not drink within the past year” in 2019). The OR decreased consistently as the drinking amount increased (Table 3).
When sociodemographic and health-related variables were included in the model as explanatory variables in addition to flushing (complex model), the OR decreased. The ORs were smaller in the same contrasts in 2020 compared to 2019 (Table 3).

Table 3. Effect of alcohol-induced facial flushing[a] on drinking amount among Korean adults from 2019-2020 Korea National Health and Nutrition Examination Survey

Predictor variable	Category vs. reference category	Statistics	Drinking amount (glasses per drinking occasion) (reference = did not drink in the past year)				
			1 – 2	3 – 4	5 – 6	7 - 9	≥ 10
Alcohol-induced facial flushing[a] (2019)	Presence vs. Absence of simple model	β^{b}	0.44	−3.61**	−5.37***	−7.54***	−11.84***
		OR	1.04	0.73	0.63	0.52	0.36
		[95%CI]	[0.86,1.26]	[0.60,0.89]	[0.50,0.79]	[0.40,0.69]	[0.28,0.47]
	Presence vs. Absence of complex model	β	1.25	−5.33***	−8.33***	−12.01***	−17.64***
		OR	1.11	0.63	0.49	0.36	0.22
		[95%CI]	[0.91,1.36]	[0.52,0.78]	[0.38,0.63]	[0.26,0.49]	[0.16,0.30]
Alcohol-induced facial flushing[a] (2020)	Presence vs. Absence of simple model	β	-3.11**	−7.89***	−8.73***	−12.01***	−12.42***
		OR	0.77	0.51	0.47	0.36	0.34
		[95%CI]	[0.64,0.92]	[0.41,0.62]	[0.37,0.60]	[0.28,0.45]	[0.27,0.44]
	Presence vs. Absence of complex model	β	-3.10**	−10.24***	−12.36***	−17.26***	−18.40***
		OR	0.77	0.41	0.34	0.23	0.20

	[95%CI]	[0.63,0.94]	[0.33,0.52]	[0.26,0.46]	[0.17,0.30]	[0.15,0.28]

[a] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section.
[b] The statistic β represents a standardized regression coefficient, the absolute value of which reflects the degree of association between the predictor variable and the outcome variable (drinking amount), which enhances direct comparability among multiple predictor variables in the multinomial logistic regression analysis.
Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption. Multinomial logistic regression analysis was conducted, incorporating complex sample design elements, including strata, clusters, and weights, to ensure unbiased results.
$^{*}P < .05$. $^{**}P < .01$. $^{***}P < .001$.

Sociodemographic and Health-Related Variables Affecting Alcohol Consumption Behavior

Frequency of Alcohol Consumption

In the complex model, 5 sociodemographic and 7 health-related characteristics besides flushing were significantly associated with drinking frequency in 2019 (Table S3 in Multimedia Appendix 1). Age, education level, limitation on life activities, and the number of major fatal illness showed a negative association in two or more contrasts, albeit to varying degrees whereas smoking, feeling stressed, and hypertension diagnosis were positively associated with drinking frequency. Males tended to drink more frequently than females. Individuals covered by work-based national health insurance drank more frequently than medical-care beneficiaries, as observed in the contrast of less than once per month. People living without a spouse consumed alcohol less frequently than those who were never married in the contrast of once per month. BMI exhibited a significantly negative association with drinking frequency in a single contrast of once per month. There were no statistically significant contrasts in occupation, although the overall test for this variable was significant according to the Type 3 analysis of effects (Table S3 in Multimedia Appendix 1).

Meanwhile, in the complex model using the 2020 dataset, the number of major fatal illness was no longer statistically significant. Instead, family size, household income, number of houses owned, private health insurance, and weight control effort were newly identified as significant predictor variables. Family size was negatively associated with drinking frequency, whereas household income, number of houses owned, and private health insurance were positively associated. They were all statistically significant in two or more contrasts. Additionally, individuals making efforts to lose weight drank more frequently than those who never tried weight control efforts in the single contrast of '2–4 times per month' (Table S4 in Multimedia Appendix 1).

Amount of Alcohol Consumed

The complex model, using drinking amount as the outcome variable with the 2019 dataset, yielded results generally comparable to those obtained from its counterpart using drinking frequency with the same dataset. In total, 13 variables showed statistical significance, except for flushing. Out of the twelve confounding variables initially identified as significant in the model with drinking frequency, three—spouse, type of health insurance, and feeling stressed—were no longer significant. Additionally, four new variables—private health insurance, weight control efforts, suicide attempt, and off-day sleep hours—emerged as significant predictor variables. (Table S5 in Multimedia Appendix 1).

Age, education level, and limitations in life activities exhibited negative associations across multiple contrasts with varying degrees, while smoking, private health insurance, and hypertension diagnosis were positively associated with alcohol consumption. Males tended to consume more alcohol than their counterparts. Individuals making efforts to gain weight drank less than those who never attempted weight control efforts in the two contrasts of consuming 3–4 glasses or 7-9 glasses per drinking occasion. Office workers and mechanics/technicians tended to consume more alcohol, while unemployed individuals such as housewives or students consumed less alcohol compared to administrators/professionals.

Regarding the results based on the 2020 dataset, ten out of thirteen variables identified as significant in the analysis of the 2019 dataset remained significant. Three variables—weight control efforts, off-day sleep hours, and suicide attempt—were no longer significant. However, three new variables—household income, type of health insurance, and dyslipidemia diagnosis—emerged as significant confounding variables. Household income was positively associated in multiple contrasts, while dyslipidemia diagnosis was negatively associated in one contrast with alcohol consumption. Individuals covered by work-based national health insurance drank more than medical-care beneficiaries in the contrast of 7-9 glasses (Table S6 in Multimedia Appendix 1).

Changes in the Effect of Flushing on Alcohol Consumption Behavior at Different Levels of Sociodemographic and Health-Related Variables

The interaction effects between flushing and other explanatory variables were investigated to determine whether the restraining effect of flushing on drinking behavior would vary across different levels of the sociodemographic and health-related characteristics. Only the variables whose associations with drinking behavior were significant were tested for this analysis. As a result, five variables exhibited a significant interaction effect with flushing in the analysis with drinking frequency as the outcome variable, while one variable showed significance in the analysis with drinking amount as the outcome variable, using the 2019 dataset. (Tables 4 and 5). The results from the 2020 dataset are displayed in Tables S7 and S8 in Multimedia Appendix 1. Subsequently, a simple effect analysis was conducted to evaluate the impact of flushing on drinking behavior for each category of discrete variables with significant interaction.-

Table 4. Changes in the impact of alcohol-induced facial flushing [a] on drinking frequency at different levels of demographic and health-related variables among Korean adults from 2019 Korea National Health and Nutrition Examination Survey (simple effects analysis)

Predictor variable	Statistics	Drinking frequency (Reference = did not drink in the past year)				
		<Once per month	Once per month	2–4 times per month	2–3 times per week	≥4 times per week
Age[b]*Flushing[a]	(F = 3.12**)					
Sex*Flushing[a]	(F = 2.86*)					
Male	OR [95% CI]	1.13 [0.77,1.64]	0.61** [0.43,0.87]	0.45*** [0.33,0.60]	0.39*** [0.28,0.53]	0.35*** [0.25,0.50]
Female		1.04 [0.81,1.35]	0.85 [0.64,1.14]	0.58*** [0.45,0.76]	0.70* [0.53,0.93]	0.67 [0.37,1.21]
Spouse*Flushing	(F = 2.29*)					
Never married	OR [95% CI]	1.18 [0.62,2.25]	0.59 [0.32,1.08]	0.43** [0.23,0.79]	0.65 [0.35,1.19]	0.53 [0.23,1.23]
Living with a spouse		0.92 [0.71,1.20]	0.84 [0.63,1.13]	0.61*** [0.49,0.75]	0.48*** [0.37,0.63]	0.46*** [0.34,0.61]
Living without a spouse		1.63* [1.02,2.60]	0.77 [0.41,1.42]	0.58* [0.34,0.98]	1.00 [0.54,1.85]	0.79 [0.36,1.76]

Education*Flushing	(*F* = 1.75*)					
≤Elementary school diploma	OR [95% CI]	0.87 [0.57,1.32]	1.02 [0.52,2.01]	1.33 [0.84,2.09]	1.18 [0.64,2.19]	0.79 [0.45,1.38]
Middle school diploma		1.14 [0.58,2.22]	0.76 [0.34,1.70]	0.40** [0.22,0.73]	0.67 [0.34,1.33]	0.43* [0.21,0.88]
High school diploma		1.17 [0.80,1.71]	0.75 [0.52,1.07]	0.51*** [0.37,0.71]	0.44*** [0.30,0.64]	0.46*** [0.29,0.72]
≥University diploma		0.99 [0.70,1.39]	0.67* [0.47,0.96]	0.53*** [0.39,0.72]	0.55** [0.38,0.80]	0.42** [0.25,0.73]
Hypertension diagnosis*Flushing	(*F* = 2.25*)					
Present	OR [95% CI]	1.08 [0.70,1.67]	0.98 [0.56,1.70]	0.76 [0.53,1.09]	0.86 [0.59,1.25]	0.48** [0.30,0.76]
Other including no response		1.03 [0.79,1.33]	0.72* [0.56,0.92]	0.51*** [0.42,0.63]	0.49*** [0.38,0.62]	0.51*** [0.37,0.70]

[a] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section.
[b] Although age had a significant interaction with flushing, a simple effect analysis could not be performed because age was a continuous variable. Instead, the interaction effect between flushing and age could be visually observed by comparing the difference in expected probability between the flushing group and the non-flushing group over age at each level of drinking frequency (Figure 1).
Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption in 2019. Multinomial logistic regression analysis was conducted, followed by simple-effect analysis for variables showing a significant interaction effect with flushing. To ensure unbiased results, complex sample design elements, including strata, clusters, and weights, were incorporated in the multinomial logistic regression analysis. The *F* value in parentheses represents the test statistic for Type 3 analysis of the interaction effect between the two variables under investigation. A significant interaction effect was observed for the variable 'Number of major fatal illness,' but omitted due to unstable results caused by zero or near-zero observations in certain categories reflecting the rarity in the population.
* $P < .05$. ** $P < .01$. *** $P < .001$.

For instance, referring to Table 4, the suppressive effect of flushing on drinking behavior significantly decreases as the level of education decreases, particularly evident in the three most pronounced contrasts in alcohol intake (2–4 times per month to ≥4 times per week vs. the reference). The odds of consuming alcohol '2–4 times a month,' '2–3 times a week,' and '≥4 times a week' compared to 'did not drink in the past year' were 0.51, 0.44, and 0.46 times lower for the flushing group than the non-flushing group, respectively, among those with a high school diploma. However, these restraining effects completely disappeared in the flushing group with an elementary school diploma or lower (OR=1.33, CI=[0.84,2.09]; OR=1.18, CI=[0.64,2.19]; and OR=0.79, CI=[0.45,1.38]). This pattern of attenuation was also observed for the drinking frequency of the 2020 dataset (Table S7 in Multimedia Appendix 1). The suppressive effect of flushing on drinking amount noticeably diminished among individuals with a middle school diploma or lower (Table S8 in Multimedia Appendix 1). Similarly, as the level of household income decreased, the flushing effect tended to somewhat diminish (Table S7).

Further, the flushing effect diminished among individuals who were not living with a spouse or never married compared to those living with a spouse, as seen in the three largest contrasts (Table 4). The flushing effect completely disappeared among individuals whose family size was ≥ 6, while it persisted in categories with fewer than 6 members (Table S7). Among different occupational groups, the alcohol-restraining effect of flushing noticeably disappeared in farmers and fishermen in the three largest contrasts of drinking frequency, while the effect remained relatively stable among administrators or professionals (Table S7). Male individuals exhibited a more pronounced suppressive effect of flushing compared to females, as indicated by notably smaller odds ratios observed at the last four levels of drinking frequency in both years (Table 4, Table S7). This gender disparity in the impact of flushing on drinking frequency is further illustrated in Table S9 of Multimedia Appendix 1, which was based on a gender-stratified analysis conducted using the 2019 dataset, presumed to be unaffected by the pandemic. Initially, a significant interaction effect between gender and flushing was observed solely during the examination of drinking frequency.

Table 5. Changes in the impact of alcohol-induced facial flushing[a] on drinking amount at different levels of demographic and health-related variables among Korean adults from 2019 Korea National Health and Nutrition Examination Survey (simple effects analysis)

Predictor variable	Statistics	Drinking amount (glasses per drinking occasion) (Reference = did not drink in the past year)				
		1–2	3–4	5–6	7–9	≥10
Smoking *Flushing[a]	(F = 2.20**)					
Daily	OR [95% CI]	2.57* [1.25,5.29]	0.74 [0.40,1.38]	0.33*** [0.18,0.61]	0.37** [0.20,0.68]	0.20*** [0.12,0.33]
Occasionally		0.95 [0.14,6.48]	0.67 [0.10,4.37]	1.36 [0.21,8.90]	0.68 [0.11,4.28]	0.32 [0.06,1.77]
Smoked before but not presently		1.12 [0.72,1.74]	0.67 [0.45,1.02]	0.43*** [0.26,0.69]	0.42*** [0.27,0.66]	0.31*** [0.18,0.53]
Never		1.05 [0.83,1.32]	0.65** [0.50,0.85]	0.75 [0.53,1.06]	0.38*** [0.25,0.58]	0.32*** [0.20,0.51]

[a] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section.
Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption in 2019. Multinomial logistic regression analysis was conducted, followed by simple-effect analysis for the variable showing a significant interaction effect with flushing. To ensure unbiased results, complex sample design elements, including strata, clusters, and weights, were incorporated in the multinomial logistic regression analysis. The F value in parentheses represents the test statistic for Type 3 analysis of the interaction effect between the two variables under investigation. Significant interaction effects were observed for the variables 'Number of major fatal illness' and ‘Suicide attempt‘, but omitted due to unstable results caused by zero or near-zero observations in certain categories reflecting the rarity in the population.
$^{*}P < .05$. $^{**}P < .01$. $^{***}P < .001$.

In terms of health-related issues, the alcohol-suppressing effect of flushing on drinking behavior appeared weaker among hypertension patients compared to others (Table 4). The flushing effect completely disappeared among occasional smokers (Tables 5 & Table S7), or diminished among individuals without private health insurance except for the most severe level of alcohol consumption (Table S8).

Figure 1 shows how the flushing effect varied as a function of age.

Discussion

Flushing was estimated to manifest in 40.11% or 44.42% of the Korean population aged 19 years or older who have experienced drinking alcohol. People with this phenotype tended to consume significantly less alcohol in terms of drinking frequency and amount than people without it. The suppressive effect of flushing was significant in all categories of alcohol consumption except for the lowest one (< Once per month or 1-2 glasses per occasion) in 2019 (0.78 ≥ OR ≥ 0.50 for frequency;

0.73 ≥ OR ≥ 0.36 for amount). This restraining tendency grew stronger as the drinking frequency and amount increased. When sociodemographic and health-related variables were added to the models, the restraining effect of flushing on drinking behavior remained statistically significant, and its effect size remained relatively large or even slightly larger (0.77 ≥ OR ≥ 0.38 for frequency; 0.63 ≥ OR ≥ 0.22 for amount). Put differently, with various contextual characteristics such as age, sex, economic status, education, family size, occupation, smoking, activity limitation, and various illnesses held constant, those with flushing had a significantly lower drinking frequency and amount than those without it. The effect also showed an overall stronger trend as the severity of alcohol consumption increased. Meanwhile, when comparing results year by year, the suppressive impact of flushing became more pronounced in 2020 compared to 2019; the odds ratios consistently showed a decrease in 2020 compared to the previous year. This suggests that the impact of the COVID-19 pandemic and associated social distancing measures on alcohol consumption suppression appeared to be relatively greater in the flushing group. All of these were illustrated by the magnitude of their standardized regression slopes and odds ratios; this phenotype exhibited one of the most substantial effect sizes, alongside age, sex, and smoking.

Although many studies have reported similar findings, our results are unique and important in the following aspects: First, the findings of this study may reflect the characteristics of East Asians in general because a sufficient and representative sample of the Korean population was used in the analysis. Prior studies focused on subgroups of the general population, such as college students, young adults, and middle-aged men, and were generally limited to fewer than 500 participants [7,22-25]. The studies conducted by Baik et al. and Au Yeung et al. examined over 2,800 and 4,800 participants, respectively, but both targeted specific male age ranges, thus potentially limiting generalizability [8,26]. Second, in addition to flushing, 25 sociodemographic and health-related factors known to possibly affect drinking behavior were included in the analysis, making it possible to interpret the flushing effect with sufficient adjustment for the effects of contextual factors. Previous studies involved a single variable (ALDH2 deficiency) or included several other predictors [7,8,22-26]. Third, the study measured the magnitude of the impact of flushing on alcohol consumption behavior by directly comparing it with those of other competing factors in terms of standardized regression coefficients.

Further, this study demonstrated that the magnitude of the flushing effect on alcohol-drinking behavior could differ substantially and is contingent on the level of sociodemographic and health-related variables. This outcome can provide valuable information to public health policymakers. Initially, we observed a significant suppressing effect of flushing on alcohol consumption in simple and complex models. However, the subsequent joint-analysis of interaction and simple effects revealed attenuation of this effect in various categories, including adults with low education levels, low levels of household income, living without a spouse, six or more family members, farmers/fishermen, and individuals with certain health-related issues (e.g., hypertension diagnosis, absence of private insurance, and occasional smoking). This attenuation may be attributed to two factors. First, the flushing group's alcohol intake increased, aligning it with a similar drinking level as the non-flushing group. Second, the non-flushing group consumed less alcohol due to the overall lower level of drinking in those specific categories. When examining the level of drinking in these categories as the strength associated with the dependent variables (Tables S3-S6 in Multimedia Appendix 1), as indicated by the standardized regression coefficient beta, individuals with low educational levels, no spouse, six or more family member, farmers/fishermen, hypertension diagnosis, and occasional smokers did not exhibit low levels of drinking, indicating that the attenuation of the alcohol-suppressing effect of flushing in these categories was caused by the first factor. Conversely, the other categories showed relatively low drinking levels, suggesting that the attenuation in these categories may belong to the second factor.

Previous reports on university students or office workers in Korea and Japan have mentioned that the effect of restraining themselves from drinking alcohol weakens, even if they have ALDH2 deficiency, under pressure from their peers or seniors at drinking gatherings (East Asian drinking culture of forcing alcohol); similarly, Irons et al. documented this phenomenon concerning parental alcohol consumption and misuse [1,9,10]. All these aspects are closely related to the categories in which attenuation occurred in this study. Our result is the first to confirm that the suppressing effect of flushing on alcohol consumption can be significantly attenuated for certain groups of people in a large population representing East Asians at a comprehensive country level. The study findings suggest that public health stakeholders in alcohol consumption behavior should identify such attenuation factors and vulnerable groups to seek out preventive practices and policies.

In this study, the multinomial logistic regression allowed us to thoroughly examine the research phenomenon by providing a comprehensive set of pairwise comparison results with respect to the established reference categories. However, this model was more complex compared to the binary logistic regression model, making the interpretation of the analysis results more challenging. Furthermore, this investigation utilized data from the 2019–2020 KNHANES. The second-year survey (2020) coincided with the onset of the COVID-19 pandemic. While Korea did not implement a lockdown during this period, measures such as gathering bans led to a decrease in monthly drinking rates from 73.4% in 2019 to 70.2% in 2020. These public health policies may have imposed mental health burdens, potentially driving individuals towards substance use as coping mechanisms [30]. Despite the influence of the pandemic, our findings suggest that there were no remarkable differences between 2019 and 2020 in terms of key outcomes.

Limitations

This study has several limitations. First, although ALDH2 deficiency prediction by the flushing questionnaire is known to be highly accurate overall and advantageous for large-scale group surveys in which it is difficult to apply genetic tests, the 40.11% or 44.42% of alcohol flushing rate in this study was somewhat higher than the 29–37% variant ALDH2 genotype rate of Koreans [27,28]. In Yokoyama's 1997 study, people whose faces "sometimes" turn red after less drinking were also regarded as having ALDH2 deficiency, even if they never experienced flushing when they started drinking [15]. However, even those with active ALDH2 may encounter flushing with minimal alcohol consumption depending on their current physiological state or advancing age. Furthermore, a few individuals may also experience flushing due to the variant alcohol dehydrogenase enzyme. These factors may have slightly compromised the accuracy of the KNHANES flushing questionnaire to distinguish inactive ALDH2 [6,29].

Conclusions

Flushing, a prevalent genetic trait among East Asians, significantly inhibits alcohol consumption at a national level among Koreans, even after accounting for sociodemographic and health-related factors. However, this robust biological defense mechanism is limited or negligible in demographically vulnerable Koreans, potentially increasing their susceptibility to group 1 carcinogens, acetaldehyde. Health authorities should conduct targeted epidemiological studies to assess drinking patterns and disease profiles, particularly regarding alcohol-related cancers, and establish effective preventive measures tailored to this population. Generalizability of these findings to other East Asian communities should also be determined.

Conflicts of Interest

None declared.

Author Contributions

CK, BK, and SHS performed the study conceptualization and design. BK conducted literature search. BK and SHS conducted data collection and created tables and figures. SHS undertook data curation, formal analysis, methodology, software, and visualization. CK, BK, and SHS conducted data analysis and interpretation and composed the initial manuscript draft. CK, BK, SHS, YJ, and HS reviewed and revised the manuscript.

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Data Sharing Statement

The 2019-2020 KNHANES data utilized in this study is publicly accessible via the following URL: https://knhanes.kdca.go.kr/knhanes/sub03/sub03_02_05.do.

Generative AI usage statement

ChatGPT was utilized to review the draft manuscript for grammatical errors and language mechanics. However, the authors retained the autonomy to make final decisions regarding the incorporation of suggested revisions into the final writing.

Abbreviations

ABV: alcohol by volume percentage
ALDH2: aldehyde dehydrogenase 2
CI: confidence interval
KNHANES: Korea National Health and Nutrition Examination Survey
KDCPA: Korea Disease Control and Prevention Agency
OR: odds ratio

Multimedia Appendix 1: supplementary Tables

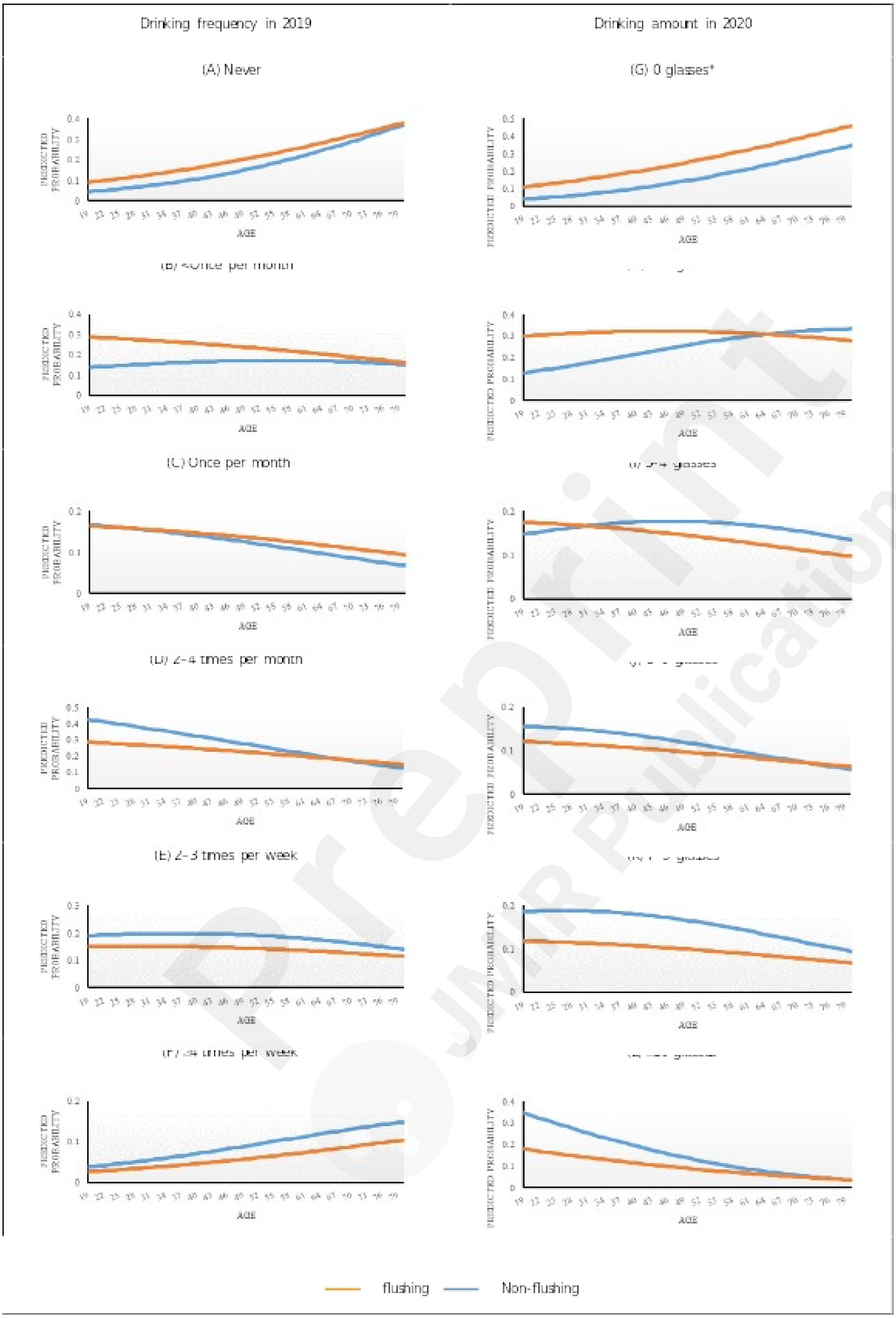
References

1. Brooks PJ, Enoch MA, Goldman D, Li TK, Yokoyama A. The alcohol flushing response: an unrecognized risk factor for esophageal cancer from alcohol consumption. PLoS Med 2009;6(3):e50. PMID:19320537
2. Chen CH, Ferreira JC, Gross ER, Mochly-Rosen D. Targeting aldehyde dehydrogenase 2: new therapeutic opportunities. Physiol Rev 2014;94(1):1-34. PMID:24382882
3. Gross ER, Zambelli VO, Small BA, Ferreira JC, Chen CH, Mochly-Rosen D. A personalized medicine approach for Asian Americans with the aldehyde dehydrogenase 2*2 variant. Annu Rev Pharmacol Toxicol 2015;55:107-127. PMID:25292432
4. IARC working group on the evaluation of carcinogenic risks to humans. Personal habits and indoor combustions. IARC Monogr Eval Carcinog Risks Hum 2012;100(Pt E):1-538. PMID:23193840
5. Peng GS, Chen YC, Wang MF, Lai CL, Yin SJ. ALDH2*2 but not ADH1B*2 is a causative variant gene allele for Asian alcohol flushing after a low-dose challenge: correlation of the pharmacokinetic and pharmacodynamic findings. Pharmacogenet Genomics

2014;24(12):607-617. PMID:25365528

6. Yokoyama A, Omori T, Yokoyama T. Alcohol and aldehyde dehydrogenase polymorphisms and a new strategy for prevention and screening for cancer in the upper aerodigestive tract in East Asians. Keio J Med 2010;59(4):115-130. PMID:21187698
7. Tanaka F, Shiratori Y, Yokosuka O, Imazeki F, Tsukada Y, Omata M. Polymorphism of alcohol-metabolizing genes affects drinking behavior and alcoholic liver disease in Japanese men. Alcohol Clin Exp Res 1997;21(4):596-601. PMID:9194910
8. Au Yeung SL, Jiang C, Cheng KK, Liu B, Zhang W, Lam TH, et al. Is aldehyde dehydrogenase 2 a credible genetic instrument for alcohol use in Mendelian randomization analysis in Southern Chinese men? Int J Epidemiol 2013;42(1):318-328. PMID:23243119
9. Irons DE, Iacono WG, Oetting WS, McGue M. Developmental trajectory and environmental moderation of the effect of ALDH2 polymorphism on alcohol use. Alcohol Clin Exp Res 2012;36(11):1882-1891. PMID:22563891
10. O'Shea T, Thomas N, Webb BT, Dick DM, Kendler KS, Chartier KG. ALDH2*2 and peer drinking in East Asian college students. Am J Drug Alcohol Abuse 2017;43(6):678-685. PMID:28471244
11. Yokoyama A, Muramatsu T, Omori T, Yokoyama T, Matsushita S, Higuchi S, et al. Alcohol and aldehyde dehydrogenase gene polymorphisms and oropharyngolaryngeal, esophageal and stomach cancers in Japanese alcoholics. Carcinogenesis 2001;22:433–439. PMID:11238183
12. Yokoyama T, Yokoyama A, Kato H, Tsujinaka T, Muto M, Omori T, et al. Alcohol flushing, alcohol and aldehyde dehydrogenase genotypes, and risk for esophageal squamous cell carcinoma in Japanese men. Cancer Epidemiol Biomarkers Prev 2003;12(11):1227–1233. PMID:14652286
13. Mizumoto A, Ohashi S, Hirohashi K, Amanuma Y, Matsuda T, Muto M. Molecular Mechanisms of Acetaldehyde-Mediated Carcinogenesis in Squamous Epithelium. Int J Mol Sci 2017;18:1943. PMID:28891965
14. Boccia S, Hashibe M, Galli P, De Feo E, Asakage T, Hashimoto T, et al. Aldehyde dehydrogenase 2 and head and neck cancer: A meta-analysis implementing a mendelian randomization approach. Cancer Epidemiol Biomarks Prev 2009;18:248–254. PMID:19124505
15. Yokoyama A, Muramatsu T, Ohmori T, Kumagai Y, Higuchi S, Ishii H. Reliability of a flushing questionnaire and the ethanol patch test in screening for inactive aldehyde dehydrogenase-2 and alcohol-related cancer risk. Cancer Epidemiol Biomarkers Prev. 1997;6(12):1105–1107. PMID:9419411
16. Heath AC, Bucholz KK, Madden PA, Dinwiddie SH, Slutske WS, Bierut LJ, et al. Genetic and environmental contributions to alcohol dependence risk in a national twin sample: consistency of findings in women and men. Psychol Med 1997;27:1381-1396. PMID:9403910
17. Lemke S, Schutte KK, Brennan PL, Moos RH. Gender differences in social influences and stressors linked to increased drinking. J Stud Alcohol Drugs 2008;69(5):695-702. PMID:18781244
18. Bobo JK, Husten C. Sociocultural influences on smoking and drinking. Alcohol Res Health 2000;24(4):225-232. PMID:15986717
19. Brown SL, Rinelli LN. Family structure, family processes, and adolescent smoking and drinking. J Res Adolesc 2010;20(2):259-273. PMID:20543893
20. Wall TL, Luczak SE, Hiller-Sturmhöfel S. Biology, genetics, and environment: underlying factors influencing alcohol metabolism. Alcohol Res 2016;38:59-68. PMID:27163368
21. Derr, B. (2013). "Ordinal Response Modeling with the LOGISTIC Procedure." In Proceedings of the SAS Global Forum 2013 Conference. Cary, NC: SAS Institute Inc. https://support.sas.com/resources/papers/proceedings13/446-2013.pdf

22. Hendershot CS, Neighbors C, George WH, McCarthy DM, Wall TL, Liang T, et al. ALDH2, ADH1B and alcohol expectancies: integrating genetic and learning perspectives. Psychol Addict Behav 2009;23:452-463. PMID:19769429
23. Duranceaux NC, Schuckit MA, Luczak SE, Eng MY, Carr LG, Wall TL. Ethnic differences in level of response to alcohol between Chinese Americans and Korean Americans. J Stud Alcohol Drugs 2008;69:227-234. PMID:18299763
24. Kim SK, Lee SI, Shin CJ, Son JW, Ju G. The genetic factors affecting drinking behaviors of Korean young adults with variant aldehyde dehydrogenase 2 genotype. Psychiatry Investig 2010;7(4):270-277. PMID:21253411
25. Dickson PA, James MR, Heath AC, Montgomery GW, Martin NG, Whitfield JB, et al. Effects of variation at the ALDH2 locus on alcohol metabolism, sensitivity, consumption, and dependence in Europeans. Alcohol Clin Exp Res 2006;30:1093-1100. PMID:16792555
26. Baik I, Cho NH, Kim SH, Han BG, Shin C. Genome-wide association studies identify genetic loci related to alcohol consumption in Korean men. Am J Clin Nutr 2011;93:809-816. PMID:21270382
27. Eng MY, Luczak SE, Wall TL. ALDH2, ADH1B, and ADH1C genotypes in Asians: a literature review. Alcohol Res Health 2007;30(1):22-27. PMID:17718397
28. Korean Disease Control and Prevention Agency (KDCA). National distribution of rs671 (ALDH2) genotypes and the effect of alcohol on chronic disease in each genotype. [Updated February 14, 2023] Available from: https://www.kdca.go.kr/board/board.es?mid=a20602010000&bid=0034&list_no=713979&act=view
29. Yokoyama A, Yokoyama T, Kimura M, Matsushita S, Yokoyama M. Combinations of alcohol-induced flushing with genetic polymorphisms of alcohol and aldehyde dehydrogenases and the risk of alcohol dependence in Japanese men and women. PLoS One 2021;16(7):e0255276. PMID:34310648
30. Montiel Ishino F, Villalobos K, Williams F. Substance use from social distancing and isolation by US nativity during the time of COVID-19: cross-sectional study. JMIR Public Health Surveill 2023;9:e38163. PMID: 36265162



Drinking frequency in 2019
Drinking amount in 2020
(A) Never
(G) 0 glasses*
(B) <Once per month
(C) Once per month
(D) 2-4 times per month
(E) 2-3 times per week
(F) ≥4 times per week
PREDICTED PROBABILITY
AGE
flushing
Non-flushing

Fig 1. Changes in the effect of alcohol-induced facial flushing[a] on alcohol consumption behavior over age among Korean adults from 2019-2020 Korea National Health and Nutrition Examination Survey

[a] A genetic predisposition linked to aldehyde dehydrogenase 2 deficiency, manifesting as facial redness even with small amounts of alcohol. The identification of this phenotype relies on a two-step questionnaire outlined in the Method section.

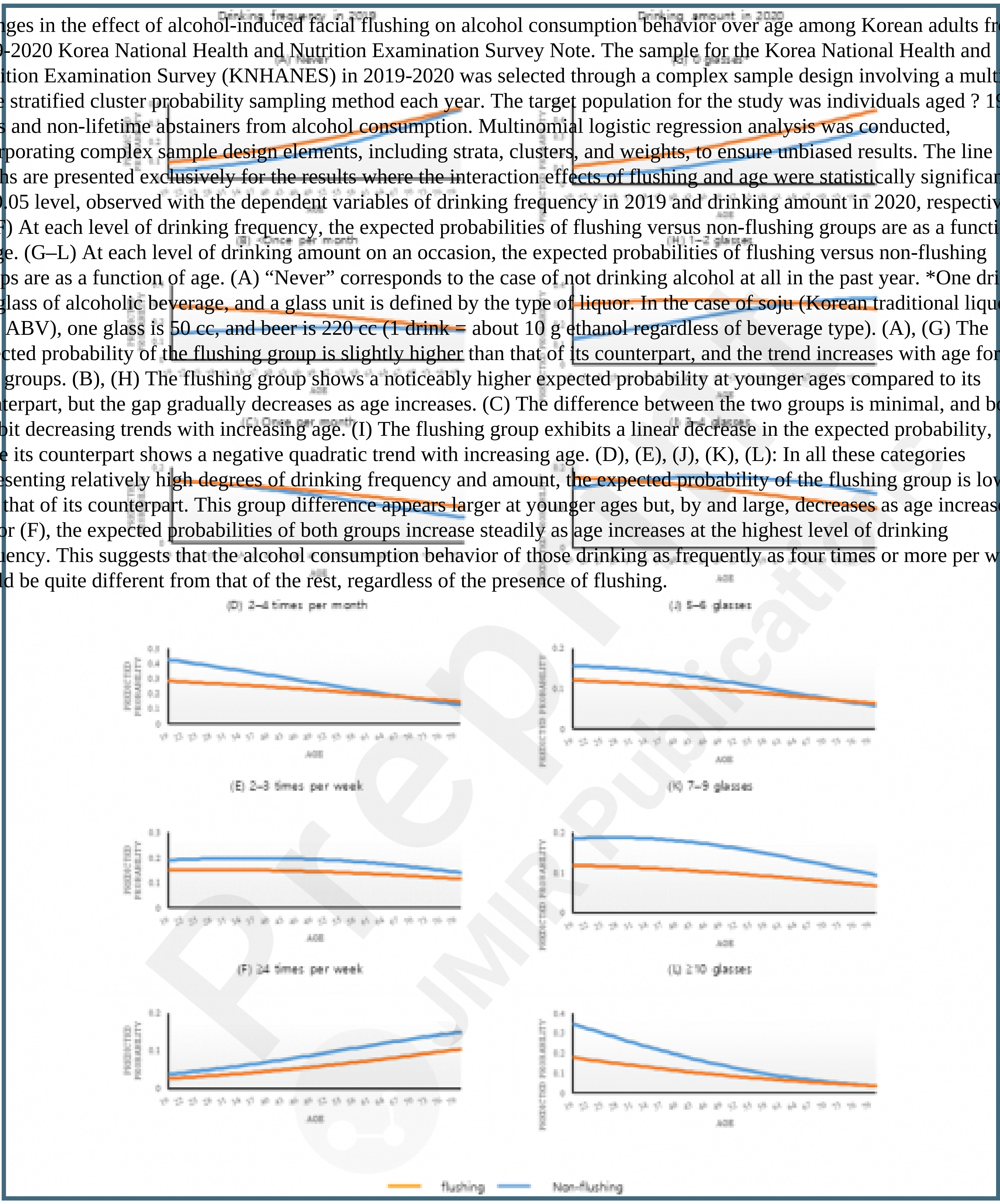
Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ≥ 19 years and non-lifetime abstainers from alcohol consumption. Multinomial logistic regression analysis was conducted, incorporating complex sample design elements, including strata, clusters, and weights, to ensure unbiased results. The line graphs are presented exclusively for the results where the interaction effects of flushing and age were statistically significant at the 0.05 level, observed with the dependent variables of drinking frequency in 2019 and drinking amount in 2020, respectively. (A–F) At each level of drinking frequency, the expected probabilities of flushing versus non-flushing groups are as a function of age. (G–L) At each level of drinking amount on an occasion, the expected probabilities of flushing versus non-flushing groups are as a function of age. (A) “Never” corresponds to the case of not drinking alcohol at all in the past year. *One drink is a glass of alcoholic beverage, and a glass unit is defined by the type of liquor. In the case of soju (Korean traditional liquor, 20% ABV), one glass is 50 cc, and beer is 220 cc (1 drink = about 10 g ethanol regardless of beverage type). (A), (G) The expected probability of the flushing group is slightly higher than that of its counterpart, and the trend increases with age for both groups. (B), (H) The flushing group shows a noticeably higher expected probability at younger ages compared to its counterpart, but the gap gradually decreases as age increases. (C) The difference between the two groups is minimal, and both exhibit decreasing trends with increasing age. (I) The flushing group exhibits a linear decrease in the expected probability, while its counterpart shows a negative quadratic trend with increasing age.

(D), (E), (J), (K), (L): In all these categories representing relatively high degrees of drinking frequency and amount, the expected probability of the flushing group is lower than that of its counterpart. This group difference appears larger at younger ages but, by and large, decreases as age increases. As for (F), the expected probabilities of both groups increase steadily as age increases at the highest level of drinking frequency. This suggests that the alcohol consumption behavior of those drinking as frequently as four times or more per week would be quite different from that of the rest, regardless of the presence of flushing.

Supplementary Files

Figures

Changes in the effect of alcohol-induced facial flushing on alcohol consumption behavior over age among Korean adults from 2019-2020 Korea National Health and Nutrition Examination Survey Note. The sample for the Korea National Health and Nutrition Examination Survey (KNHANES) in 2019-2020 was selected through a complex sample design involving a multi-stage stratified cluster probability sampling method each year. The target population for the study was individuals aged ? 19 years and non-lifetime abstainers from alcohol consumption. Multinomial logistic regression analysis was conducted, incorporating complex sample design elements, including strata, clusters, and weights, to ensure unbiased results. The line graphs are presented exclusively for the results where the interaction effects of flushing and age were statistically significant at the 0.05 level, observed with the dependent variables of drinking frequency in 2019 and drinking amount in 2020, respectively. (A–F) At each level of drinking frequency, the expected probabilities of flushing versus non-flushing groups are as a function of age. (G–L) At each level of drinking amount on an occasion, the expected probabilities of flushing versus non-flushing groups are as a function of age. (A) “Never” corresponds to the case of not drinking alcohol at all in the past year. *One drink is a glass of alcoholic beverage, and a glass unit is defined by the type of liquor. In the case of soju (Korean traditional liquor, 20% ABV), one glass is 50 cc, and beer is 220 cc (1 drink = about 10 g ethanol regardless of beverage type). (A), (G) The expected probability of the flushing group is slightly higher than that of its counterpart, and the trend increases with age for both groups. (B), (H) The flushing group shows a noticeably higher expected probability at younger ages compared to its counterpart, but the gap gradually decreases as age increases. (C) The difference between the two groups is minimal, and both exhibit decreasing trends with increasing age. (I) The flushing group exhibits a linear decrease in the expected probability, while its counterpart shows a negative quadratic trend with increasing age. (D), (E), (J), (K), (L): In all these categories representing relatively high degrees of drinking frequency and amount, the expected probability of the flushing group is lower than that of its counterpart. This group difference appears larger at younger ages but, by and large, decreases as age increases. As for (F), the expected probabilities of both groups increase steadily as age increases at the highest level of drinking frequency. This suggests that the alcohol consumption behavior of those drinking as frequently as four times or more per week would be quite different from that of the rest, regardless of the presence of flushing.



Multimedia Appendixes

Supplementary Tables.
URL: http://asset.jmir.pub/assets/a270f6d3b919046625dbfa4fd24ab3d1.pdf