Snoring-related polygenic risk and its relationship with lifestyle factors in a Korean population: KoGES study

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Abstract

Background

Few studies show the association between genetic and lifestyle factors and the risk of snoring. Polygenic risk scores (PRS) indicating genetic risks derived from genome-wide association study (GWAS) data have received much attention. Therefore, we investigated the relationships between PRS and other risk factors for snoring, including lifestyle.

Methods

To create a PRS for snoring, we combined genotyping with Korean Genome Epidemiology Study (KoGES). Associations were observed for sex, age, body mass index (BMI), alcohol consumption, smoking, physical activity, and sleep time. The PRS-KoGES was generated by PRS-Campos, derived from the European population. Using a multivariate logistic regression model, we assessed whether lifestyle factors mitigated the genetic risk of developing snoring.

Results

We included 3,526 snorers and 1,939 non-snorers in the KoGES cohort. The highest adjusted odds ratio for snoring was higher BMI, followed by male sex, older age, genetic factors as higher PRS, drinking experience, late sleep mid-time, smoking experience, and lower physical activity. The risk factors influenced by PRS were male sex, older age, alcohol consumption, smoking, lower BMI, low physical activity, and late sleep mid-time.

Conclusions

We identified the characteristics of lifestyle factors related to snoring influenced by PRS.

Introduction

Snoring is a respiratory sound (or noise) that originates during sleep and can be nocturnal or diurnal. It is a typical inspiratory sound. However, a small expiratory component can be heard or recorded, especially in patients with obstructive sleep apnea, with different spectral features [1]. Statistics on snoring are often contradictory, but at least 30% of adults and perhaps as many as 50% of people across certain demographic groups snore [2]. A survey of 5,713 American residents identified habitual snoring in 24% of men and 13.8% of women. This increased to 60% of men and 40% of women aged 60 to 65 years, suggesting an age-related increased susceptibility to snoring [3].

Previous studies have suggested that snoring can be influenced by genetics, environmental factors, and their interaction [4–8]. Early studies on the genetic factors of snoring and sleep apnea included twin and familial studies [4,9–12]. The twin study confirmed the genetic predisposition to snoring by the fact that snoring-related characteristics in identical twins were more consistent than in fraternal twins and that there were relatively fewer external factors in the correlation between characteristics in identical twins [12]. Family studies have shown that people with a family history of snoring are likelier to snore [11]. Some genetic possibilities can be mediated by other genetic lifestyle factors, such as smoking and alcohol consumption, which can also contribute to snoring [13,14].

Here, we leverage data from a Korean sample of adults, examine the prevalence of snoring, and observe the relationships between snoring and lifestyle-related factors in the Korean population. In this study, we calculated the most recent polygenic risk score (PRS) for snoring and (1) showed the difference explained by the PRS between European and Korean adults, and (2) analyzed its relationship with lifestyle factors such as smoking and alcohol consumption, physical activity, and sleeping features to investigate the degree to which inherited susceptibility to snoring is modified by these sociodemographic and lifestyle factors.

Methods

Study population

This was a retrospective cross-sectional study. The study population was derived from adults aged > 40 years from the Ansan and Ansung cohort study, a part of the Korean Genome Epidemiology Study (KoGES) [15]. Epidemiological and clinical information was collected through questionnaires and examination after obtaining consent from the participants.

As this study's target phenotype, snoring was assessed as a single question: *"Have you ever heard that you snore?*" This survey question could be answered with "*Yes*," "*No*," or "*Prefer not to answer.*" We excluded participants whose answers were "*Prefer not to answer*" (n = 28) from our analyses.

The participants' general information included sex, age, alcohol drinking, smoking experience, body mass index (BMI), physical activity calculated as metabolic equivalent of task-minute per week (MET), and sleeping time. After determining the MET value for each activity item by referring to previous studies [16,17], the average MET value for each activity was calculated and then multiplied by the weekly activity hours to calculate as MET-hour/week. Sleeping time was derived from the participants' sleep mid-time after 2 AM.

Genetic data analysis and quality control

Genotyping of the study data was performed using the KoGES Korean Chip Array. The samples were excluded based on the following criteria: 1) low call rate (< 97%) or excessive heterozygosity, 2) excessive singletons, 3) sex discrepancy, 4) cryptic first-degree relatives, and 4) withdrawals and blind replicates.

SNPs were excluded based on the following criteria: exclude all low-quality SNPs in any batch, Hardy-Weinberg equilibrium (pHWE ≥ 5×10 − 6), and call rate less than 95%. Imputation for autosomal variants was performed using Eagle v2.3 and IMPUTE4 using a reference panel constructed from 1,000 Genomes Project Phase 3, and the Korean reference genome (397 samples) was used as reference panels. Post-imputation filtering was to exclude variants with INFO < 0.8 & MAF < 1%.

Generation of Polygenic Risk Scores

We calculated PRS based on genome-wide summary statistics for snoring from European population studies [PMID: 32060260] [8]. The PRS (called PRS-Campos) was proposed and validated by Campos et al. [8]. It is based on summary statistics from a large-scale GWAS of Snoring.

To compare the performance of PRS-Campos, PRS of Korean ancestry (PRS-KoGES) was calculated using PRSice and PRS based only on genome-wide significant SNPs from discovery samples (same discovery sample as for PRS-Campos [approximately 408,000 samples] and KoGES samples [approximately 5,465 samples]).

PRS-KoGES was calculated, evaluated, and plotted using the PRSice software [18]. This software generates a PRS by summing all trait-related alleles in the target sample, weighted by the effect size of each allele in the underlying GWAS [19]. Linkage disequilibrium (LD) aggregation and p-value thresholds were used to select the optimal set of trait-related alleles. Imputed base SNPs were filtered with information scores < 0.9 and MAF < 0.01. In addition to genetic data purification, the attributed target SNPs were filtered using an information score of < 0.9. SNPs in LD were grouped such that no additional weight was assigned to a single marker. The most representative SNP with the smallest p-value was selected within a 250 kb window with r2 > 0.1. PRS-KoGES was generated from a gradually increasing p-value threshold in the default GWAS. The optimal threshold was selected to account for the largest variation in the target sample.

Previous research indicates that PRSice is well-powered to detect the cumulative effect of SNPs in target sample sizes of at least 100 subjects and base sample sizes of at least 50,000 subjects [18]. This study calculated the PRS-KoGES in our Korean population cohort (N = 5,465) using summary statistics from a large-scale GWAS (N = 408,317).

To calculate PRS in the Korean data, we first examined 42 snoring-associated SNPs that were previously established based on the European study population [PMID: 32060260] [8]. Among the 42 SNPs, 28 were identified in the Korean SNP chip data, and of the 28 SNPs, 20 SNPs showed the same direction of allelic effect between the European and Korean chip data. However, eight SNPs showed the opposite direction of allelic effect between the European and Korean chip data (Supplementary Table 1). The rs592333 SNP on the DLEU7 gene showed a p-value of less than 0.05, and the others were not significant in Korean SNP chip data.

We calculated the variance described by the PRS using the 20 SNPs present in the Korean data. When using the effect size of European data, the variance explained (Nagelkerke R2) was 0.5403%. PRS for

snoring was significantly associated with recent snoring for all but one ($p \leq 5e\text{-}14$) of the p-value inclusion thresholds (Supplementary Fig. 1).

Assessment of lifestyle variables and interactions

In this study, smoking, drinking, physical activity, and late sleep time were selected as variables that reflect an individual's lifestyle. We assessed whether these lifestyle factors mitigated the genetic risk of developing snoring. To evaluate this, we focused on the highest (top 20%) vs. lowest genetic risk quintiles (bottom 20%), as the greatest genetic risk/protection is at the extremes of risk. This analysis investigated the relationship between lifestyle and genetic factors and their tendency to snore. The odds ratio of high genetic risk to low genetic risk in lifestyle was calculated in the high- and low-lifestyle-risk groups.

Statistical analysis

Phenotype-derived estimates, such as prevalence and associations between variables and stratified plots of snoring prevalence, were performed using R. In the study population, the differences in the statistics of covariates according to snoring were tested. In this case, if the data type of the covariate was categorical, the prevalence and proportion were used as statistics, and the difference according to phenotype expression was tested using the chi-squared test. In contrast, if the data type was continuous, the mean and standard deviation were used as statistics, and differences according to the phenotype expression were tested using the t-test. Additionally, the demographic characteristics of the KoGES population and those of the UK Biobank were compared and tested for differences.

Using lifestyle factors as risk factors, the risk ratio for snoring was expressed as an odds ratio (OR). Crude OR, which treated each covariate as a univariate risk factor, and adjusted OR, which treated each covariate as a multivariate risk factor, were both calculated. Both ORs are shown through a forest plot. The explanatory power of the multivariate logistic regression model was estimated using the R-squared value. Based on the estimated coefficient, the hazard ratio of each factor was presented as OR.

Results

General characteristics of the study population

The total number of participants in the KoGES cohort was 5,465 (male:female = 2,604:2,861). The mean age of the participants was 51.7 years (SD 8.3). Snoring was reported in 3,526 (64.5%) of 5,465 participants.

Table 1 shows the general characteristics of the snorers and non-snorers. In total, 52% of snorers were identified as male, and 60% of non-snores were female. There was a statistically significant difference in the mean age between the snoring and non-snoring groups. (51.7 vs 51.3, $p < 0.001$) There were also significant differences ($p < 0.001$) in drinking and smoking habits between the two groups. In total, 57% of snores had alcohol experience, while 48% of non-snorers answered drinking experience. Regarding smoking experience, approximately 44% of snorers and 33% of non-snorers were smokers, showing

statistically significant differences ($p < 0.001$). There was also a significant difference ($p < 0.001$) in BMI between these groups, and the BMI of the snorer was 25.1, and non-snorers was 23.9. There was no significant difference in the MET ($p = 0.313$) and mid-sleep time ($p = 0.06$) between the snoring and non-snoring groups.

Table 1
General characteristics of KoGES cohort according to snoring.

Characteristics	Snorers (N = 3,526)	Non-Snorers (N = 1,939)	p-value
Sex (Male), N (%)	1,828 (52%)	776 (40%)	< 0.001[a)]
Age (years), mean (SD)	51.7 (8.32)	51.28 (8.82)	< 0.001[b)]
Drinking Experience, N (%)	2,020 (57%)	936 (48%)	< 0.001[a)]
Smoking Experience, N (%)	1,517 (44%)	656 (33%)	< 0.001[a)]
Body Mass Index, mean (SD)	25.06 (3.05)	23.85 (2.88)	< 0.001[b)]
MET[†] (min/week), mean(SD)	1,410 (1036.61)	1,440 (1058.05)	0.313[b)]
Sleep mid-time after 2 AM, N (%)	2,511 (71%)	1,331 (69%)	0.06[a)]

a) Chi-squared test used, b) t-test used, [†]Metabolic equivalent of task

Differences in the distribution of population groups according to Korean and European races

Table 2 shows the differences in sex, age, and BMI distribution between the UK and Korean populations. The sex distribution was significantly different, with more females in the Korean snoring group ($p = 0.045$). The average age of Korean snores was 51.7 years, and that of snoring in the UK Biobank was 57.01 years, indicating a statistically significant difference ($p < 0.001$). BMI was 25.06 for Koreans and 28.67 for Europeans, showing was significantly different between the two groups ($p < 0.001$).

Table 2
Sex, age, and BMI distribution differences between the UK and Korea.

		Cases (Snorers)	Controls	Total	p-value
Female, N (%)	KoGES	1,698 (48%)	1,163 (60%)	2861 (52%)	0.045 a)
	UK Biobank	63,833 (40.74%)	161,775 (61.44%)	225,608 (53.72%)	
Age, mean (SD)	KoGES	51.7 (8.32)	51.28 (8.82)	51.55 (8.5)	< 0.001
	UK Biobank	57.01 (7.70)	56.60 (8.21)	56.75 (8.03)	
BMI, mean (SD)	KoGES	25.06 (3.05)	23.85 (2.88)	24.63 (3.04)	< 0.001
	UK Biobank	28.67 (4.85)	26.64 (4.52)	27.39 (4.75)	

a) chi-squared test used

Risk factors associated with snoring

A variable analysis was performed using a multivariate logistic regression model to analyze the risk factors for snoring (Table 3). To understand the risk factors for snoring and evaluate the independent association between snoring and each risk factor, we estimated the overall explanatory power of the risk factor as an R-squared value by using both genomic and life factors as covariates. The highest crude odds ratio for snoring was higher BMI (OR = 1.96, 95% CI = 1.74–2.19), followed by male sex (OR = 1.61, 95% CI = 1.09–1.3), smoking experience (OR = 1.48, 95% CI = 1.32–1.66), drinking experience (OR = 1.44, 95% CI = 1.29–1.61]), genetic factors as higher PRS (OR = 1.19, 95% CI = 1.09–1.3), late sleep mid-time (OR = 1.12, 95% CI = 0.99–1.27), older age (OR = 1.11, 95% CI = 0.99–1.24), and lower physical activity (OR = 0.91, 95% CI = 0.99–1.27). In addition, the highest adjusted odds ratio for snoring was higher BMI (OR = 1.98, 95% CI = 1.76–2.23), followed by male sex (OR = 1.54, 95% CI = 1.28–1.86), older age (OR = 1.23, 95% CI = 1.03–1.35), genetic factors as higher PRS (OR = 1.18, 95% CI = 1.08–1.29), drinking experience (OR = 1.18, 95% CI = 1.03–1.35), late sleep mid-time (OR = 1.17, 95% CI = 1.02–1.33), smoking experience (OR = 0.99, 95% CI = 0.82–1.19), and lower physical activity (OR = 0.92, 95% CI = 0.85-1.00).

Table 3
Logistic Regression Model for Snoring.

Covariates	OR (CI 95%)	p-value
Polygenic Risk Score (low-medium-high)	1.18 (1.08–1.29)	< 0.001 ***
Sex (Male)	1.54 (1.28–1.86)	< 0.001 ***
Age (over 50)	1.23 (1.08–1.38)	0.001 **
Drinking Experience	1.18 (1.03–1.35)	0.016 *
Smoking Experience	0.99 (0.82–1.19)	0.905
Body Mass Index (over 25)	1.98 (1.76–2.23)	< 0.001 ***
Physical Activity (low-medium-high)	0.92 (0.85-1.00)	0.064
Sleep mid-time after 2 AM	1.17 (1.02–1.33)	0.022*
PRS low: bottom 20%; PRS medium: bottom 20–80%; PRS high: top 20%		
Significance codes: 0<***<0.001<**<0.01<*<0.05		
Explanatory Power: Nagelkerke pseudo R2 value is 5.98%		
Goodness of fit of the model: The likelihood-ratio test's p-value is < 0.001, so this model has statistical significance.		
Autocorrelation check: The Durbin-Watson test's p-value is 0.284, which is larger than 0.05; therefore, there is no autocorrelation multicollinearity check: the VIF values of each covariate are less than 3, and there is no multicollinearity.		

Figure 1 shows a forest plot depicting the odds ratios of each variable for snoring. Crude OR, which treated each covariate as a univariate risk factor, and adjusted OR, which treated each covariate as a multivariate risk factor, are shown. The smoking variable showed the largest difference between the univariate variable analysis (OR = 1.48, 95% CI = 1.32–1.66) and the multivariate variable analysis (OR = 0.99, 95% CI = 0.82–1.19). In contrast, PRS and physical activity showed little difference between univariate analysis (OR = 0.91, 95% CI = 0.84–0.99) and multivariate analysis (OR = 0.92, 95% CI = 0.85-1.00) (Table 4).

Table 4
Forest Plot Information

Covariates	Crude OR		Adjusted	
	OR	P-value	OR	P-value
PRS	1.19 (1.09–1.3)	< 0.001 ***	1.18 (1.08–1.29)	< 0.001 ***
Sex	1.61 (1.44–1.81)	< 0.001 ***	1.54 (1.28–1.86)	< 0.001 ***
Age	1.11 (0.99–1.24)	0.073	1.23 (1.08–1.38)	0.001 **
Drinking Experience	1.44 (1.29–1.61)	< 0.001 ***	1.18 (1.03–1.35)	0.016 *
Smoking Experience	1.48 (1.32–1.66)	< 0.001 ***	0.99 (0.82–1.19)	0.905
Body Mass Index	1.96 (1.74–2.19)	< 0.001 ***	1.98 (1.76–2.23)	< 0.001 ***
Physical Activity	0.91 (0.84–0.99)	0.029 *	0.92 (0.85-1.00)	0.064
Sleep mid-time	1.12 (0.99–1.27)	0.061	1.17 (1.02–1.33)	0.022 *

Interaction between PRS and lifestyle factors

The results of the interaction analysis between the PRS and lifestyle variables are shown in Table 5 and Fig. 2. The odds ratio of the PRS-low group was set to 1 for comparison. In the high lifestyle risk group, the variable with the highest odds ratio (OR = 1.43, 95% CI = 1.18–1.73) was physical activity ($p < 0.001$), followed by drinking experience (OR = 1.33, 95% CI = 1.17–1.50, $p < 0.001$) and sex (OR = 1.28, 95% CI = 1.12–1.46, $p < 0.001$), and there was a statistically significant difference in level. BMI showed a statistically insignificant odds (OR = 1.14, 95% CI = 0.98–1.31, $p = 0.086$). In contrast, in the low lifestyle risk group, the odds ratios of BMI (OR = 1.222, CI = 1.09–1.37, $p < 0.001$), smoking experience (OR = 1.16, CI = 1.04–1.30, $p = 0.009$), and age (OR = 1.12, CI = 1.00-1.26, $p = 0.018$) showed statistically significant results.

Table 5
Interaction analysis for snoring between PRS and lifestyle variables

Covariates	High Lifestyle Risk Group		Low Lifestyle Risk Group	
	OR for PRS high to low	P-value	OR for PRS high to low	P-value
Sex	1.28 (1.12–1.46)	< 0.001 ***	1.12 (1.00-1.26)	0.057
Age	1.22 (1.08–1.39)	0.002 **	1.16 (1.03–1.31)	0.018 *
Drinking Experience	1.33 (1.17–1.50)	< 0.001 ***	1.04 (0.92–1.19)	0.522
Smoking Experience	1.24 (1.07–1.43)	0.003 **	1.16 (1.04–1.30)	0.009 **
Body Mass Index	1.13 (0.98–1.31)	0.086	1.22 (1.09–1.37)	< 0.001 ***
Physical Activity	1.43 (1.18–1.73)	< 0.001 ***	1.13 (0.95–1.35)	0.166
Sleep mid-time	1.24 (1.11–1.38)	< 0.001 ***	1.09 (0.93–1.28)	0.286

Discussion

Although snoring is common in the general population, it has been largely understudied from an individual genetic and lifestyle perspective. In particular, the clinical relevance of PRS for snoring has not been fully elucidated in Asian populations. In this study, we calculated the most recent PRS for snoring and (1) showed the difference explained by the PRS between UK Biobank participants of European ancestry and Korean participants of Asian ancestry, and (2) analyzed its relationship with lifestyle risk factors such as smoking and alcohol use, physical activity, and sleeping time features to investigate the degree to which these individual factors modify the inherited susceptibility to snoring.

An early cohort study on the genetic characteristics of snoring was conducted in a cardiovascular disease study cohort consisting of 3,387 men aged 54–74 [9] years. A total of 3,308 participants answered the survey, and habitual snoring strongly correlated with the family history of grandparents, parents, brothers, and children. The largest difference between the group that complained of habitual snoring and the control group was the family history of self-reported snoring. Another previous study reported genetic results on snoring (n = 408,000; snorers = 152,000) using data from the UK Biobank [8]. In total, 37% of all study subjects had snoring, and snorers had a higher rate of diagnosed sleep apnea than subjects without snoring (2.88% of snoring patients vs. 0.63% of controls). Snoring was correlated with age (OR = 1.011 [1.009–1.012]) and sex (OR males = 2.264 [2.212–2.316]) and showed a positive correlation with BMI, smoking, and alcohol intake frequency, and a negative correlation with socioeconomic status. They identified 42 significant genome-wide loci with an SNP-based heritability estimate of approximately 10% on the liability scale. Genetic correlations with body mass index, alcohol intake, smoking, schizophrenia, anorexia nervosa, and neuroticism were observed in the European population. Polygenic scores predicted recent snoring and probable obstructive sleep apnea in an independent Australian sample (n = 8000). A

potential causal relationship between high BMI and snoring was suggested based on Mendelian randomization analysis results.

Several studies have compared PRSs by applying genetic analysis of specific phenotypes to other independent group data [19–24]. According to a previous study that assessed PRSs for coronary artery disease and type 2 diabetes as predictive factors for cardiovascular (CV) mortality [21], both CAD PRS (low vs. very high genetic risk groups, CAD PRS hazard ratio [HR] 2.61 [2.02–3.36]) and T2DM PRS (HR 2.08 [1.58–2.73]) were significantly correlated with CV mortality risk. These associations remained significant even after adjusting for a wide range of demographic and clinical characteristics. Adherence to an unhealthy lifestyle was also significantly linked to an elevated risk of CV mortality in the very high genetic risk group (favorable vs. unhealthy lifestyle with very high genetic risk for CAD PRS, HR 8.31 [5.12–13.49]; T2DM PRS, HR 5.84 [3.39–10.04]). In all genetic risk categories, the population attributable fraction (PAF) for CV mortality was 32.1% (95% CI 28.8–35.3%), while the PAF for smoking was 14.1% (95% CI 12.4–15.7%). Age, sex, and lifestyle factors did not significantly interact with PRSs predicting the risk of CV mortality.

Another study utilized a comprehensive health checkup database from the Korean population in conjunction with genotyping to generate PRS for BMI [24]. This study conducted a phenome-wide association (PheWAS) analysis, and a longitudinal association between BMI and PRS-BMI was observed. A model that predicted ten-year BMI based on age, sex, and baseline BMI was more accurate after including PRS-BMI ($p = 0.003$). Higher deciles of PRS were directly correlated with changes in BMI in a linear mixed model evaluating longitudinal changes in BMI with age. Significant correlations were found between PheWAS and metabolic syndrome, bone density, and fatty liver disease.

In our study, the genetic snoring risk score was calculated for 3526 snorers and 1939 non-snorers by applying the PRS based on the snoring GWAS results of a European study. Because of analyzing the various stages of significance showed, the GWAS p-value of 1.8e-08 cut-off showed the highest R2 (0.5403%). Still, it did not reach the explanatory power of the previous study. This means that the genetic explanatory power of the snoring GWAS study did not reach that of the snoring PRS calculated in the evaluation group of the same ethnic group.

Overall, the results of our study suggest that the odds ratio for snoring in the PRS high group was high. Thus, the effect of PRS can be interpreted as a genetic risk factor. Lifestyle variables interpreted as having genetic risk factors were alcohol consumption, sleeping late (derived by sleeping mid-time), and smoking. In the case of BMI, individuals with a low BMI avoid snoring, which seems to be due to genetic influences. Our results showed that the risk of snoring was high when exposed to risk factors such as PRS, sex, age, drinking experience, BMI, and sleep middle time. The risk factors that PRS influenced were male sex, older age, alcohol consumption, smoking, lower BMI, low physical activity, and late sleep mid-time.

To the best of our knowledge, this is the first study to investigate the associations between lifestyle habits and the genetic risk of snoring in the Korean population derived from European PRSs. To date, most

large-scale genetic studies have been conducted in European populations. However, in the case of snoring, the effect size was very small, with an odds ratio of 0.99 to 1.01, as seen in the European GWAS results. Hence, a large-scale cohort study is required to develop other racial populations, including the Korean PRS model.

The limitations of this study are as follows: First, there was no Korean snoring GWAS data that could be applied to the PRS model in this study. Therefore, it was impossible to conduct a preliminary analysis to verify the difference in the basic genetic structure of the European group used as a reference and the Korean group. Second, explanatory power may have decreased because of the small sample size.

Conclusion

Here, we used data from a Korean adult sample to assess the prevalence of snoring in the community and track its associations with lifestyle-related factors. To determine the extent to which these sociodemographic and lifestyle factors affect the inherited propensity to snore, we calculated the most recent PRS for snoring and (1) displayed the difference explained by the PRS between European and Korean adults and (2) analyzed its relationship with lifestyle factors such as smoking and alcohol consumption, physical activity, and sleeping features. Given the small effect size of the SNP-based association, PRS serves as an excellent diagnostic and therapeutic marker in clinical settings. Therefore, it is vital to verify the causal relationship or genetic association between characteristics by utilizing an analytical approach such as GWAS for various components known as risk factors for snoring as a method for analyzing genetic factors.

Declarations

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Author Contributions

B.Ryu and S.Lee contributed to preparing KoGES data, analyzing the data, and drafting the manuscript as first authors. E.Heo helped analyze and visualize the data. S.Yoo helped analyze the data and managed the overall study, and J.W.Kim supervised the overall study.

Conflicts of Interest

None of the authors have any conflicts of interest to declare.

Data Availability

The KoGES (Korean Genome and Epidemiology Study) genotype data that support the findings of discovery stage are available upon request under data sharing policy of National Research Institute of Health, Korea (http://www.nih.go.kr/). Other data that support our findings are available from the corresponding author upon reasonable request.

Approval and consent waiver statement

This study was performed in accordance with the relevant guidelines and regulations of the Seoul National University Bundang Hospital Institutional Review Board (SNUBH IRB). Exemption from deliberation is reasonable in accordance with Articles 13 and 33 of the Enforcement Regulations of the Bioethics and Safety Act and HRPP SOP II.A.3.

According to the research plan, it is judged to be a study that collects and uses genetic information data and survey data from Anseong/Ansan cohort, and it is not judged that the research is provided with human materials.

Since the data in this study are non-identification data that do not contain personal identification information, this study was approved based on waivers of informed consent or exemptions by the SNUBH IRB (SNUBH IRB No: B-1805-471-301, X-2112-727-901).

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Figures

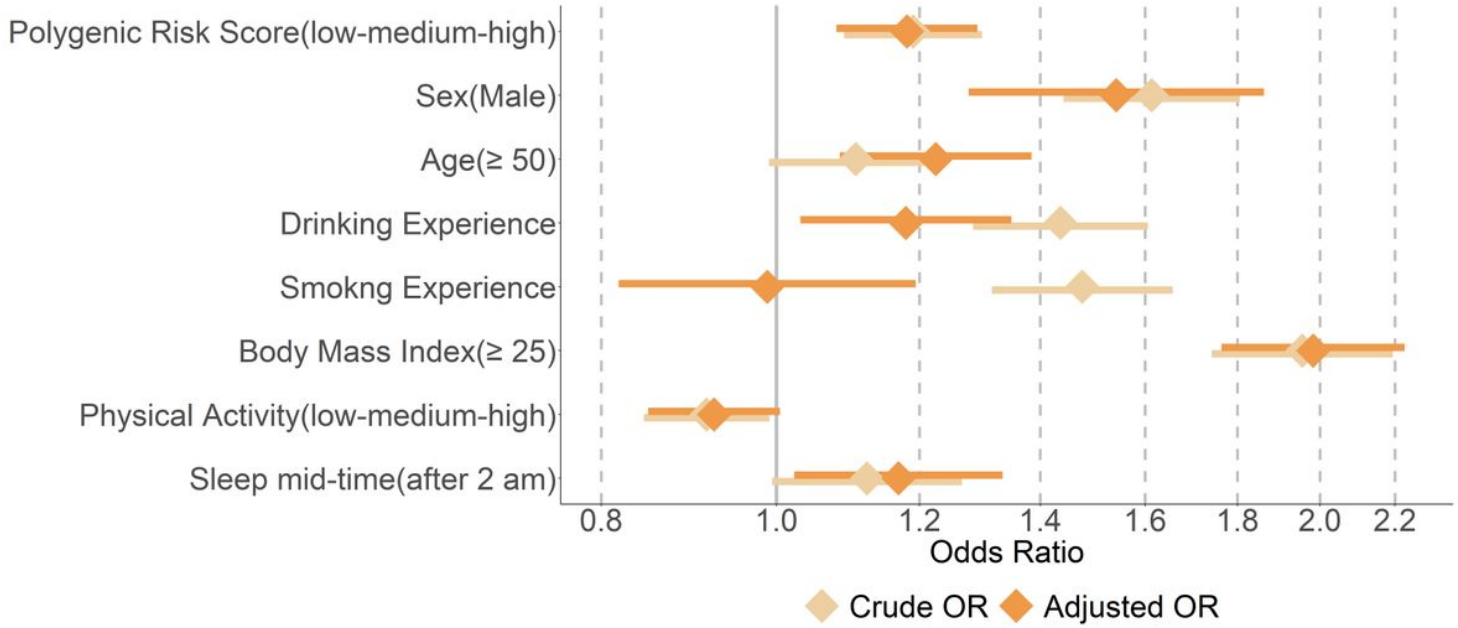

Figure 1

Forest plot depicting the odds ratios of studied variables on snoring.

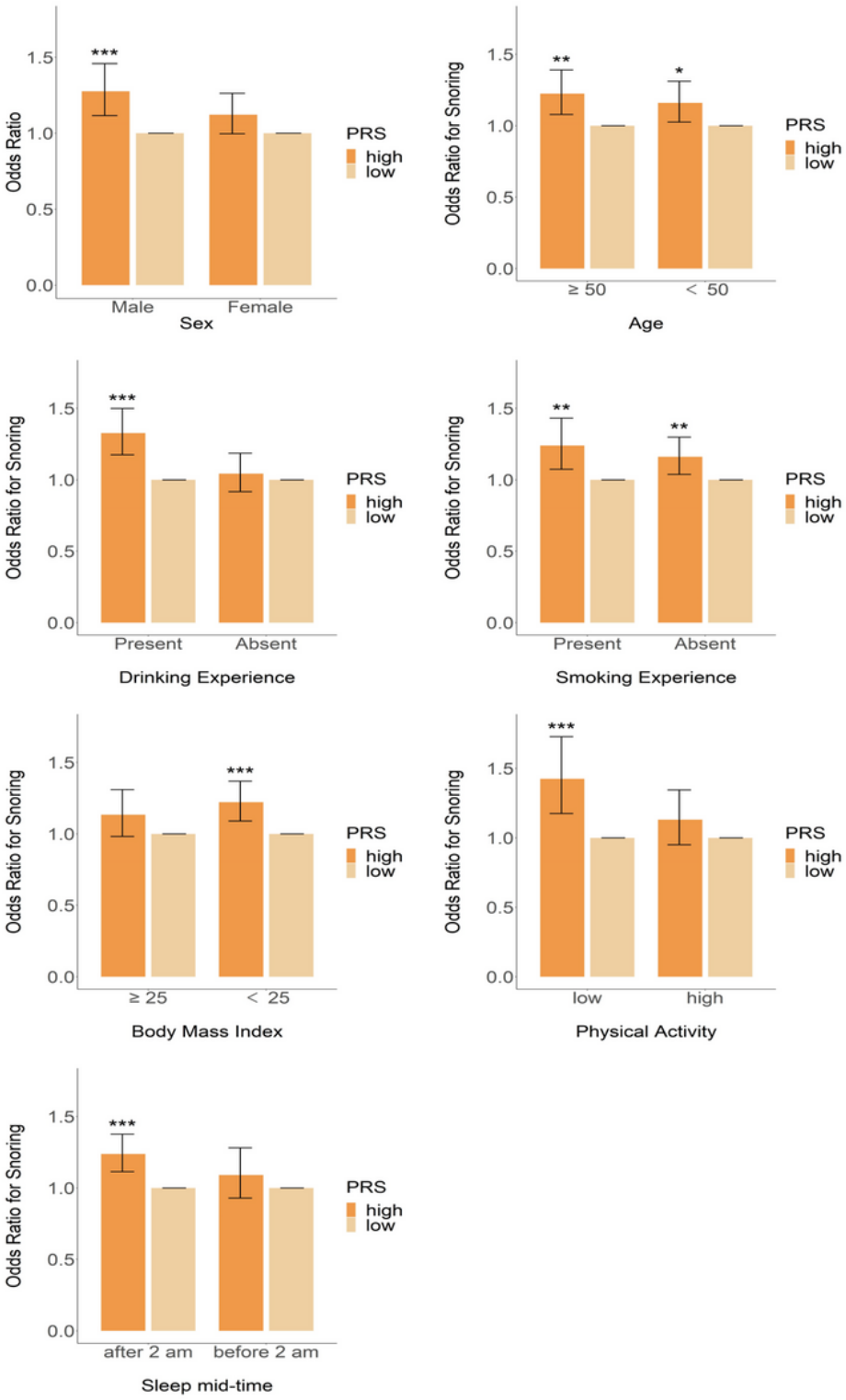

Figure 2

Interaction plot.

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