

Associations of Adverse Childhood Experiences with Patterns of Tobacco and Alcohol Use among Middle-Aged and Older Adults in China: A Population-Based Study

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Abstract

Background

Adverse childhood experiences (ACEs) have been associated with tobacco and alcohol use, yet little is known about their associations with combined patterns of use in later life. Drawing on a life-course perspective, this study investigated how threat- and deprivation-related ACEs were associated with tobacco and alcohol use patterns among middle-aged and older adults in China.

Methods

This population-based cross-sectional study included 13,926 adults aged ≥ 45 years from the China Health and Retirement Longitudinal Study. ACEs were grouped into threat-related ACEs (physical abuse, household substance abuse, domestic violence, unsafe neighborhood, and bullying) and deprivation-related ACEs (emotional neglect, household mental illness, incarcerated household member, parental separation or divorce, and parental death). Exposure to each dimension was categorized as 0 or ≥ 1 ACE. Latent class analysis identified tobacco and alcohol use patterns based on current smoking and drinking status, age at initiation (< 18 vs. ≥ 18 years), the Heaviness of Smoking Index (≤ 2 vs. > 2), and heavy alcohol use (≥ 14 units/week for men; ≥ 7 for women). Multinomial logistic regression estimated adjusted relative risk ratios (aRRR) and 95% confidence intervals (CIs).

Results

Five tobacco and alcohol use patterns were identified: non-use (53.15%), adult-onset smoking only (12.49%), adult-onset drinking only (8.58%), adult-onset higher-risk co-use (17.29%), and early-onset higher-risk co-use (8.49%). Relative to the non-use pattern, neither ACE dimension was significantly associated with the smoking-only or drinking-only patterns. Threat-related ACEs were associated with both adult-onset higher-risk co-use (aRRR 1.27, 95% CI 1.05 to 1.53) and early-onset higher-risk co-use (aRRR 1.35, 95% CI 1.08 to 1.70). Deprivation-related ACEs were associated with early-onset higher-risk co-use (aRRR 1.27, 95% CI 1.04 to 1.55) but not with adult-onset higher-risk co-use.

Conclusions

ACEs were associated with higher-risk tobacco and alcohol co-use among middle-aged and older adults in China, after adjustment for sociodemographic factors. These findings underscore the importance of a life-course perspective in understanding substance co-use in later life, although longitudinal studies are warranted to clarify the temporal relationships underlying these associations and to inform the development of targeted strategies for substance-use risk reduction in aging populations.

1. Background

Tobacco smoking and harmful alcohol use are major preventable contributors to premature mortality and disability worldwide [1, 2]. These behaviors are of particular public health concern in China, which consumes approximately 40% of the world's cigarettes [3] and has experienced a substantial increase in alcohol consumption over recent decades [4]. Tobacco and alcohol use also frequently co-occur, with approximately 14.1% of Chinese adults reported to use both substances [5]. Both behaviors are leading contributors to disability-adjusted life-years lost in China [6], and their co-occurrence may be associated with greater health risks than either behavior alone [7, 8].

Tobacco and alcohol use may have particular implications for middle-aged and older adults, among whom multimorbidity, polypharmacy, functional limitations, and reduced psychological resilience are increasingly common [9]. Continued smoking and high-risk alcohol consumption may add to the burden of chronic disease, complicate disease management, and increase the risks of disability and premature mortality [10]. The co-occurrence of these behaviors may identify a subgroup with a greater cumulative behavioral risk burden than would be captured by examining smoking or drinking separately. Identifying heterogeneous patterns of tobacco and alcohol use is therefore relevant not only to substance-use prevention but also to chronic disease management, functional independence, and healthy aging. Although research on substance use in later life has largely focused on current socioeconomic circumstances, social influences, and mental health [11–13], a life-course perspective could provide additional insight into the early-life vulnerabilities associated with these behaviors.

Adverse childhood experiences (ACEs) encompass stressful or potentially traumatic experiences during childhood and may have lasting implications for health-related behaviors [14]. Increasingly, ACEs have been conceptualized along two partially distinct dimensions: threat, involving experiences of actual or threatened harm, such as physical abuse and domestic violence; and deprivation, involving the absence of expected cognitive, emotional, or social inputs, such as emotional neglect [15, 16]. These dimensions may be associated with later health

behaviors through partly different psychosocial and developmental pathways. Potential pathways include altered stress regulation, maladaptive coping, mental health difficulties, socioeconomic disadvantage, and limited access to supportive resources. Tobacco and alcohol use could be adopted as coping responses and develop into long-standing behavioral patterns that persist into later adulthood. Such established behaviors may become increasingly difficult to modify as chronic disease burden and age-related vulnerability increase.

Existing evidence generally supports associations between ACE exposure and tobacco and alcohol use later in life [17, 18]. However, previous studies have predominantly relied on cumulative ACE scores, examined smoking and drinking separately, or focused on younger populations. A cumulative score may obscure potentially meaningful differences between threat- and deprivation-related experiences [19], while the separate assessment of smoking and drinking could overlook the clustering of these behaviors. Examining ACE dimensions in relation to combined tobacco and alcohol use patterns among middle-aged and older adults may therefore help identify life-course vulnerabilities underlying current health-risk behaviors and inform more tailored prevention and health-promotion strategies.

Age at initiation provides additional information for understanding substance-use patterns in later life. Adolescence is a period of substantial neurobiological and psychosocial development characterized by increased risk-taking and susceptibility to substance initiation [20]. Earlier initiation has been associated with a greater likelihood of persistent and higher-risk use in adulthood [20–22]. Current use alone may therefore provide an incomplete representation of an individual's behavioral history and cumulative exposure. Integrating initiation age with current smoking intensity and alcohol consumption may distinguish subgroups with different developmental and behavioral profiles that conventional measures of current or ever use fail to capture. Nevertheless, limited evidence is available on how threat- and deprivation-related ACEs are associated with combined patterns of initiation timing and tobacco and alcohol use among middle-aged and older adults.

Using data from the China Health and Retirement Longitudinal Study (CHARLS), a population-based study of Chinese adults aged 45 years and older, we applied latent class analysis to identify distinct tobacco and alcohol use patterns based on current use status, age at initiation, smoking intensity, and heavy alcohol consumption. We then examined the associations of threat- and deprivation-related ACEs with membership in these patterns. By integrating childhood adversity, substance-use initiation, and current behavioral characteristics, this study aimed to identify higher-risk behavioral subgroups and provide evidence relevant to targeted health-risk assessment, chronic disease prevention, and healthy-aging interventions among middle-aged and older adults.

2. Methods

2.1 Study design and participants

The present study used data from CHARLS, a longitudinal survey of adults aged ≥ 45 from over 10,000 households across 150 counties in China. Baseline data from 2011 and ACEs information from the 2014 life-history survey were analyzed. CHARLS employs rigorous quality control and standardized face-to-face interviews covering sociodemographics, lifestyle, and health. Further details of the survey design are provided elsewhere [23]. Ethical approval was granted by Peking University (No. IRB00001052-11015), with written informed consent obtained from all participants. This secondary analysis did not require separate ethical approval. Reporting was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

A total of 17,594 participants were recruited in the CHARLS 2011 survey, and 20,452 participated in the 2014 life history survey (Fig. 1). We performed 1:1 matching to identify 14,375 respondents who completed both surveys. After excluding 302 participants aged < 45 years and 147 participants who had missing data for any of the smoking and alcohol use indicator variables, 13,926 participants were included in the final analysis.

2.2 Measures

2.2.1 Adverse Childhood Experiences (ACEs)

ACEs occurring before age 17 were assessed using face-to-face interviews administered as part of the 2014 Life History Survey. Consistent with prior studies [24–26], the ACE measure comprised 10 indicators: five threat-related adversities (physical abuse, household substance abuse, domestic violence, unsafe neighborhood conditions, and bullying) and five deprivation-related adversities (emotional neglect, household mental illness, an incarcerated household member, parental separation or divorce, and parental death). Operational definitions for each indicator are provided in Supplementary Table 1. Each ACE indicator was coded dichotomously as 0 (absent) or 1 (present). Cumulative threat-related and deprivation-related scores were calculated by summing the number of endorsed indicators within each dimension. For each dimension, participants were categorized into two groups: 0 indicated no exposure, and 1 indicated exposure to at least one ACE indicator.

2.2.2 Tobacco and alcohol use

Participants' smoking status was categorized into current smokers, former smokers and never smokers. Current smokers included individuals who used any form of tobacco products (such as cigarettes, cigars, pipes, or self-rolled cigarettes) either daily or intermittently (e.g., non-daily or occasional use). Former smokers were those who had smoked previously but had since quit, while never smokers reported no lifetime use of any tobacco products. Nicotine dependence among current smokers was measured using the Heaviness of Smoking Index (HSI) [27], which comprises two items: (a) time to first cigarette after waking (≤ 5 , 6–30, 31–60, or > 60 minutes) and (b) number of cigarettes smoked per day (≤ 10 , 11–20, 21–30, or > 30). Each item was scored from 0 to 3, yielding a total HSI score of 0–6. Dependence levels were defined as light (0–2), moderate (3–4), and heavy (5–6). Due to a limited number of heavy smokers, the moderate and heavy categories were combined for latent class analysis.

Drinking status was divided into current drinkers, former drinkers, occasional drinkers, and never drinkers. Alcohol consumption in the preceding 12 months was evaluated based on self-reported drinking frequency: never, less than once per month, or at least once per month. Participants consuming alcohol at least monthly within the past year were designated current drinkers. Those with less frequent or no recent drinking were further queried about lifetime alcohol use and frequency using the same categories. Individuals reporting no lifetime consumption were classified as never drinkers. Those who drank at least monthly prior to the past year but abstained during the last 12 months were considered former drinkers. Participants with infrequent drinking (less than once per month) both before and during the past year were classified as occasional drinkers.

For current drinkers, additional details were collected regarding their most recent drinking occasion: beverage type (spirits, beer, or wine), amount consumed, and drinking frequency over the previous 12 months (once per month; 2–3 times per month; once per week; 2–3 times per week; 4–6 times per week; once per day; twice per day; or more than twice per day). Beverage quantities were recorded as 220 mL mugs or 550 mL bottles for beer and 50 mL “liang” for wine and spirits. Drinking frequency and portion size were then converted to weekly pure alcohol intake by estimating weekly ethanol consumption using alcohol contents of 3.9% (beer), 12% (wine), and 53% (spirits) (percent by volume) [28]. One unit (drink) was defined as 14 g of pure alcohol. Heavy drinking was defined as ≥ 14 units per week for men and ≥ 7 units per week for women [29]. In this study, alcohol consumption was converted into weekly pure alcohol intake and classified as heavy drinking or not.

Smoking and drinking patterns were identified using several indicators: smoking and drinking status, age at initiation (< 18 vs. ≥ 18 years), current nicotine dependence (Heaviness of Smoking Index ≤ 2 vs. > 2), and heavy alcohol consumption (≥ 14 units/week for men, ≥ 7 for women) among current users. The age at initiation for both smoking and drinking was dichotomized at 18 years, consistent with previous studies that classify initiation at 18 or older as adult onset, distinguishing it from adolescent initiation [21].

2.2.3 Covariates

Sex, age, educational attainment, marital status, and childhood area of residence were collected through face-to-face interviews.

2.3 Statistical analysis

Latent class analysis (LCA) was used to identify distinct patterns of smoking and drinking onset age and dependence status among middle-aged and older adults. Model fit for determining the optimal number of classes was evaluated using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and sample-size adjusted BIC (aBIC), with lower values indicating better fit. The Vuong–Lo–Mendell–Rubin likelihood ratio test (VLMR) and the Bootstrap Likelihood Ratio Test (BLRT) were used to assess whether a model with k classes fit significantly better than a model with $k-1$ classes [30]. Class size and entropy were also examined to evaluate class separation and classification accuracy. To facilitate the visual interpretation of response patterns across latent classes, the conditional probability matrix was presented as a heatmap generated using GraphPad Prism (version 11.1). Latent classes were displayed on the x-axis, while the observed indicators were displayed on the y-axis.

Multinomial logistic regression was used to examine the associations between ACEs (threat and deprivation dimensions) and the five identified smoking and drinking patterns. Both crude and adjusted models were fitted, with adjustments for sex, age, educational attainment, marital status, and childhood area of residence. Relative risk ratios (RRRs), adjusted relative risk ratios (aRRRs) and 95% confidence intervals (95% CIs) were reported. A sensitivity analysis was conducted by modeling ACEs as a continuous variable to examine the robustness of the associations between ACEs and smoking and drinking patterns. All statistical analyses were performed using Stata Version 16.0 (StataCorp, College Station, TX, USA) and Mplus version 8.0. All tests were two-sided, and statistical significance was set at $P < 0.05$.

3. Results

3.1 Characteristics of study participants

The analytic sample included 13,926 participants aged 45 years or older. Among them, 3,671 participants (26.36%) reported at least one threat-related ACE and 6,256 (44.92%) reported at least one deprivation-related ACE. Participant characteristics according to ACE exposure are presented in Table 1. Compared with participants who reported no threat-related ACEs, those exposed to at least one threat-related ACE were more likely to be male (58.42% vs. 53.33%), have lower educational attainment (60.52% vs. 55.28%), and have lived in a rural area during childhood (78.96% vs. 75.47%). They also had a higher prevalence of concurrent tobacco and alcohol use (22.01% vs. 19.06%). Participants exposed to at least one deprivation-related ACE were more likely to have lower educational attainment (71.59% vs. 62.48%) and being unmarried (12.17% vs. 10.32%) compared with those reporting no deprivation-related ACEs.

3.2 Latent class solution and characteristics of identified patterns

Fit indices for the latent class models are presented in Table 2. The five-class solution provided the most interpretable representation of the data, considering the AIC, BIC, aBIC, high entropy, and well-distributed class sizes. Although fit statistics should not be considered in isolation, the five-class solution showed adequate class separation and no substantively small class. Figure 2 presents a heatmap of the conditional probabilities for the five-class solution. Latent classes are displayed on the x-axis, and manifest indicators on the y-axis. Cell colors represent conditional probabilities ranging from 0 to 1, with warmer colors denoting higher probabilities and cooler colors denoting lower probabilities.

Latent classes were labeled according to their most distinctive smoking and alcohol use characteristics, as reflected in the class-specific conditional response probabilities. Labels described substance use status, age at initiation (early onset: <18 years; adult onset: ≥18 years), and risk-related characteristics, including smoking intensity and heavy drinking. The term “higher-risk co-use” described classes characterized by both tobacco and alcohol use and higher probabilities of heavier smoking and heavy drinking, rather than clinically assessed dependence. Five patterns were identified: non-use (n = 7,401; 53.15%), adult-onset smoking only (n = 1,739; 12.49%), adult-onset drinking only (n = 1,195; 8.58%), adult-onset higher-risk co-use (n = 2,408; 17.29%), early-onset higher-risk co-use (n = 1,183; 8.49%).

Table 3 presents the socioeconomic characteristics of the study sample stratified by distinct smoking and drinking patterns. Significant differences were observed across all characteristics (all Ps < 0.001). The non-use pattern was predominantly female (83.94%), whereas men comprised the majority of the adult-onset smoking only (75.56%) and the early- and adult-onset higher-risk co-use patterns (95.60% and 95.72%, respectively). Age also differed significantly across classes (P < 0.001). The adult-onset smoking only

Table 1
Characteristics of participants grouped by threat- and deprivation-related ACEs (CHARLS 2011 Survey, N = 13,926)

Characteristics	Overall n (%)	Threat-Related ACEs			Deprivation-Related ACEs		
		No (n = 5,822)	Yes (n = 3,671)	P value	No (n = 6,706)	Yes (n = 6,256)	P value
		n (%)	n (%)		n (%)	n (%)	
Age, y (mean ± SD)	59.16 ± 9.49	57.31 ± 8.22	56.96 ± 8.67	0.05	57.87 ± 8.97	59.39 ± 9.10	< 0.001
Sex				< 0.001			0.21
Male	6,749(48.00)	3,102(53.33)	2,143(58.42)		3,250(48.49)	2,961(47.38)	
Female	7,312(52.00)	2,715(46.67)	1,525(41.58)		3,453(51.51)	3,288(52.62)	
Educational attainment				< 0.001			< 0.001
Primary school or below	9,587(68.19)	3,215(55.28)	2,221(60.52)		4,188(62.48)	4,473(71.59)	
Middle school or above	4,473(31.81)	2,601(44.72)	1,449(39.48)		2,515(37.52)	1,775(28.41)	
Marital status				0.14			0.001
Married	12,356(87.81)	5,344(91.79)	3,338(90.93)		6,014(89.68)	5,494(87.83)	
Other ^a	1,716(12.19)	478 (8.21)	333(9.07)		692(10.32)	761(12.17)	
Childhood area of residence				0.003			0.28
Rural	6,534(79.89)	2,553(75.47)	1,708(78.96)		3,107(80.26)	2,895(79.27)	
Urban	1,645(20.11)	830(24.53)	455(21.04)		764(19.74)	757(20.73)	
Smoking status				< 0.001			0.91
Never smokers	8,434(61.78)	3,357(59.50)	1,920(54.15)		4,021(61.85)	3,745(61.46)	
Former smokers	1,149(8.42)	486(8.61)	335(9.45)		537(8.26)	508(8.34)	
Current smokers	4,069(29.81)	1,799(31.89)	1,291(36.41)		1,943(29.89)	1,840(30.20)	
Smoking initiation age, y (mean ± SD)	22.33 ± 8.10	22.23 ± 7.34	21.78 ± 7.44	0.07	22.05 ± 7.45	22.58 ± 8.55	0.03
Nicotine dependency (HSI) ^b				0.92			0.73
Light (0–2)	1,645(43.37)	753(42.86)	507(42.11)		784(42.72)	742(43.70)	
Moderate (3–4)	1,650(43.50)	769(43.77)	533(44.27)		811(44.20)	728(42.87)	
Heavy (5–6)	498(13.13)	235(13.38)	164(13.62)		240(13.08)	228(13.43)	
Drinking status				< 0.001			0.016
Never drinkers	8,512(60.62)	3,396(58.43)	1,975(53.90)		4,074(60.85)	3,742(59.93)	
Former drinkers	844(6.01)	335(5.76)	242(6.60)		355(5.30)	414(6.63)	
Occasional drinkers	1,134(8.08)	480(8.26)	328(8.95)		552(8.24)	498(7.98)	
Current drinkers	3,552(25.30)	1,601(27.55)	1,119(30.54)		1,714(25.60)	1,590(25.46)	
Drinking initiation age, y (mean ± SD)	25.93 ± 11.26	25.63 ± 10.40	25.23 ± 10.28	0.28	25.95 ± 10.75	25.97 ± 11.61	0.97

Characteristics	Overall n (%)	Threat-Related ACEs			Deprivation-Related ACEs		
		No (n = 5,822)	Yes (n = 3,671)	P value	No (n = 6,706)	Yes (n = 6,256)	P value
		n (%)	n (%)		n (%)	n (%)	
Heavy drinking ^c				0.66			0.06
No	1,308(49.49)	594(49.71)	434(50.70)		645(50.83)	570(47.11)	
Yes	1,335(50.51)	601(50.29)	422(49.30)		624(49.17)	640(52.89)	
Tobacco and alcohol use				< 0.001			0.88
None	7,482(54.85)	2,951(52.33)	1,664(46.95)		3,556(54.72)	3,318(54.49)	
Smoking only	1,724(12.64)	724(12.84)	510(14.39)		804(12.37)	783(12.86)	
Drinking only	2,093(15.34)	889(15.77)	590(16.65)		1,000(15.39)	932(15.31)	
Both (dual use)	2,343(17.17)	1,075(19.06)	780(22.01)		1,138(17.51)	1,056(17.34)	

Sample size varied owing to missing data.

^a Other: Never married/Separated/divorced/widowed.

^b Nicotine dependency was assessed using the Heaviness of Smoking Index (HSI), which consists of two items: time to first cigarette after awaking (response options: ≤5, 6–30, 31–60 and > 60 minutes) and the number of cigarettes smoked per day (response options: ≤10, 11–20, 21–30, > 30). Each response is scored from 0–3. The total HSI score ranges from 0–6, with 0–2 indicating light dependence, 3–4 indicating moderate dependence and 5–6 indicating heavy dependence.

^c Only include current drinkers.

Table 2
Results of statistical fit indices of latent class analysis models (N = 13,926)

Model	LL	AIC	BIC	aBIC	Entropy	BLRT P value	VLMR P value	Composition
Two classes	-30113.883	60261.766	60389.972	60335.947	0.981	< 0.001	< 0.001	61.73/38.27
Three classes	-27554.694	55161.388	55357.468	55274.842	0.960	< 0.001	< 0.001	25.96/12.32/61.72
Four classes	-25299.616	50669.232	50933.185	50821.958	0.955	< 0.001	< 0.001	12.32/53.15/8.58/25.95
Five classes	-25052.613	50193.226	50525.053	50385.225	0.938	< 0.001	< 0.001	17.29/53.15/8.58/12.48/8.50
Six classes	-25047.147	50200.293	50599.993	50431.564	0.912	0.001	0.001	12.48/3.22/8.50/17.29/5.36/53.15

The two classes model represents improvement over a 1 class (baseline) model; the first BLRT and VLMR p-values correspond to this comparison. LL = Log Likelihood; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = adjusted Bayesian Information Criterion; BLRT = Bootstrapped Likelihood Ratio Test (P value); VLMR = Vuong-Lo-Mendell-Rubin (P value).

pattern had the highest mean age (60.46 ± 9.50 years), whereas the early-onset higher-risk co-use pattern had the lowest (58.85 ± 9.17 years). In terms of education, the adult-onset higher-risk co-use pattern had the lowest proportion of primary school or below education (57.19%), while the non-use pattern had the highest (72.95%). Marital status was largely similar across patterns, but the co-use patterns (both adult- and early-onset) showed slightly higher rates of being married (91.45% and 90.79%, respectively) compared to the non-use (86.16%) and adult-onset smoking only (85.97%) patterns. Participants in all patterns were predominantly from rural areas, with the highest rural proportions observed in the adult-onset higher-risk co-use (83.37%) and the adult-onset smoking-only (82.90%) patterns.

3.3 Associations of participant characteristics with smoking and alcohol use patterns

Adjusted relative risk ratios (aRRR) for membership in each tobacco and/or alcohol use pattern, relative to the non-use pattern, are presented in Table 4. Sex showed the strongest and most consistent association with pattern membership. Compared to males, females had substantially lower adjusted relative risk ratios across all four patterns, particularly for co-use patterns (aRRR 0.01, $P < 0.001$ for both early-onset higher-risk co-use and adult-onset higher-risk co-use). Higher education (middle school or above) was associated with a lower risk of the adult-onset smoking only pattern (aRRR 0.82, 95% CI 0.68 to 0.99, $P < 0.05$) and, most notably, the early-onset higher-risk co-use pattern (aRRR 0.54, 95% CI 0.43 to 0.67, $P < 0.001$). Being unmarried, divorced, separated, or widowed (vs. married) was associated with a 25% higher risk of adult-onset smoking only pattern (aRRR 1.25, 95% CI 1.03 to 1.53, $P < 0.05$). Urban versus rural residence was not significantly associated with any of the four patterns, although the association with the adult-onset higher-risk co-use pattern approached marginal significance (aRRR 0.81, 95% CI 0.66 to 1.00).

3.4 Associations of ACE dimensions with smoking and alcohol use patterns

Table 5 presents the associations of threat- and deprivation-related ACEs with membership in the four tobacco and/or alcohol use patterns, using the non-use pattern as the reference. In crude models, exposure to at least one threat-related ACE was associated with greater likelihood of membership in all four tobacco and/or alcohol use patterns (RRR range: 1.23–1.43, all P s < 0.01). After adjustment for demographic covariates, threat-related ACE exposure remained associated with higher-risk co-use patterns. Specifically, participants exposed to at least one threat-related ACE had a higher relative risk of membership in the adult-onset higher-risk co-use pattern (aRRR

Table 3
The patterns of smoking and drinking by socioeconomic characteristics (N = 13,926)

Age, y (mean $\pm$ SD)	Overall	Non-use (n = 7,401)	Adult-onset smoking-only (n = 1,739)	Adult-onset drinking-only (n = 1,195)	Adult-onset higher-risk co- use (n = 2,408)	Early-onset higher-risk co- use (n = 1,183)	P
	59.16 $\pm$ 9.49	58.77 $\pm$ 9.66	60.46 $\pm$ 9.50	59.07 $\pm$ 9.65	59.62 $\pm$ 8.85	58.85 $\pm$ 9.17	< 0.001
Sex							< 0.001
Male	6,749(48.00)	1,187(16.06)	1,314(75.56)	684(57.29)	2,303(95.72)	1,131(95.60)	
Female	7,312(52.00)	6,205(83.94)	425(24.44)	510(42.71)	103(4.28)	52(4.40)	
Educational attainment							< 0.001
Primary school or below	9,587(68.19)	5,393(72.95)	1,159(66.65)	769(64.35)	1,376(57.19)	805(68.05)	
Middle school or above	4,473(31.81)	2,000(27.05)	580(33.35)	426(35.65)	1,030(42.81)	378(31.95)	
Marital status							< 0.001
Married	12,356(87.81)	6,377(86.16)	1,495(85.97)	1,076(90.04)	2,202(91.45)	1,074(90.79)	
Other ^a	1,716(12.19)	1,024(13.84)	244(14.03)	119(9.96)	206(8.55)	109(9.21)	
Region							< 0.001
Rural	6,534(46.94)	3,270(44.19)	916(52.49)	534(44.77)	1,193(49.58)	591(50.34)	
Urban	1,645(11.76)	938(12.75)	189(10.71)	153(12.73)	238(9.72)	119(10.06)	

^a Other: Never married/Separated/divorced/widowed.

Table 4
Adjusted relative risk ratio (aRRR) and 95% CI of smoking and drinking patterns by demographic characteristics (N = 13,926)

Age, y (mean ± SD)	Adult-onset smoking only vs. Non-use	Adult-onset drinking only vs. Non-use	Adult-onset higher-risk co-use vs. Non-use	Early-onset higher-risk co-use vs. Non-use
	1.01(1.00,1.02)*	1.00(0.99,1.01)	1.01(1.00,1.02)*	0.99(0.98,1.00)
Sex				
Male	Ref	Ref	Ref	Ref
Female	0.06(0.05,0.07)***	0.15(0.13,0.18)***	0.01(0.01,0.01)***	0.01(0.01,0.01)***
Educational attainment				
Primary school or below	Ref	Ref	Ref	Ref
Middle school or above	0.82(0.68,0.99)*	0.98(0.80,1.20)	0.97(0.82,1.17)	0.54(0.43,0.67)***
Marital status				
Married	Ref	Ref	Ref	Ref
Other ^b	1.25(1.03,1.53)*	0.84(0.66,1.06)	0.93(0.74,1.16)	1.03(0.79,1.34)
Region				
Rural	Ref	Ref	Ref	Ref
Urban	0.87(0.71,1.06)	1.09(0.88,1.34)	0.81(0.66,1.00)	1.00(0.77,1.29)

^a aRRR: Adjusted relative risk ratio.

^b Other: Never married/Separated/divorced/widowed.

*P < 0.05, **P < 0.01, ***P < 0.001.

Table 5
Association of smoking and drinking patterns with threat- and deprivation-related ACEs (N = 13,926)

	Adult-onset smoking only vs. Non-use		Adult-onset drinking only vs. Non-use		Adult-onset higher-risk co-use vs. Non-use		Early-onset higher-risk co-use vs. Non-use	
	RRR (95% CI)	aRRR ^a (95% CI)	RRR (95% CI)	aRRR ^a (95% CI)	RRR (95% CI)	aRRR ^a (95% CI)	RRR (95% CI)	aRRR ^a (95% CI)
Threat-related ACEs (Any exposure vs. no exposure)	1.26 (1.11,1.44) ***	1.14 (0.94,1.38)	1.27 (1.09,1.48) **	1.06 (0.85,1.31)	1.23 (1.10,1.37) ***	1.27 (1.05,1.53) *	1.43 (1.24,1.65) ***	1.35 (1.08,1.70) **
Deprivation-related ACEs (Any exposure vs. no exposure)	0.98 (0.88,1.10)	1.08 (0.92,1.27)	1.09 (0.96,1.24)	1.14 (0.95,1.36)	1.00 (0.91,1.10)	1.13 (0.96,1.34)	1.14 (1.00,1.30) *	1.27 (1.04,1.55) *

^a Adjusted for sex, age, educational attainment, and marital status.

1.27, 95% CI 1.05 to 1.53), and the early-onset higher-risk co-use pattern (aRRR 1.35, 95% CI 1.08 to 1.70) compared with the non-use pattern. Adjusted associations with the adult-onset smoking only and late-onset drinking only patterns were not statistically significant. Deprivation-related ACEs showed a more specific pattern of association. Exposure to at least one deprivation-related ACE was associated with membership in the early-onset higher-risk co-use pattern after adjustment (aRRR 1.27, 95% CI 1.04 to 1.55), whereas no statistically significant association was observed for the adult-onset smoking only, late-onset drinking only, or adult-onset higher-risk co-use patterns.

Overall, threat-related ACEs were associated with both early-onset and adult-onset higher-risk co-use patterns, whereas deprivation-related ACEs were significantly associated only with the early-onset higher-risk co-use pattern. Sensitivity analyses modeling ACE counts within each dimension as continuous variables yielded results broadly consistent with the primary analyses (Supplementary Table 2).

4. Discussion

In this study of middle-aged and older Chinese adults, we identified heterogeneous patterns of tobacco and alcohol use and found that ACEs were associated with membership in higher-risk use patterns. Threat-related ACEs were associated with both adult-onset and early-onset high-risk co-use patterns, whereas deprivation-related ACEs were specifically associated with the early-onset high-risk co-use pattern. These findings extend previous research that has generally considered smoking and alcohol consumption separately and suggest that early-life adversity may remain relevant to the clustering and persistence of health-risk behaviors into middle and older age. From a healthy-aging perspective, identifying such behavioral heterogeneity is important because tobacco and alcohol co-use may mark a subgroup facing greater challenges in risk-factor modification, chronic disease management, and the maintenance of health and functioning.

Previous studies have reported associations between ACEs and adolescent substance use [31]. Our study extends this evidence to patterns incorporating age at initiation and intensity of tobacco and alcohol use among middle-aged and older adults. Statistically significant associations were observed primarily for the higher-risk co-use patterns. One possible explanation is that ACEs are associated with difficulties in emotion regulation, altered stress responses, and maladaptive coping, which may represent shared vulnerabilities underlying both smoking and drinking [32]. Previous research also suggests that adversity-related alterations in stress-response and self-regulatory systems may contribute to substance use behaviors [33, 34]. However, these mechanisms were not directly assessed in this study, and our findings cannot establish whether co-use reflects greater adversity-related vulnerability than single-substance use. The nonsignificant associations for single-substance use patterns may also reflect limited precision, within-class heterogeneity, or other unmeasured factors and should not be interpreted as evidence of no association.

The observed associations across threat and deprivation dimensions warrant further investigation. Threat-related ACEs were significantly associated with both early-onset and adult-onset higher-risk co-use, a finding broadly consistent with previous research linking threat exposure to stress responses and emotion regulation [35]. Deprivation-related ACEs were significantly associated only with early-onset higher-risk co-use. Previous studies suggest that emotional neglect or limited environmental stimulation may be associated with the development of executive functioning and self-regulatory capacities [16]. Although these findings offer possible theoretical explanations, they do not establish that threat and deprivation influence tobacco and alcohol use through distinct developmental pathways. In particular, a statistically significant association for one dimension and a nonsignificant association for another do not demonstrate a statistically significant difference between them. Moreover, patterns derived from retrospectively reported initiation ages and use characteristics cannot capture complete histories of continued use, cessation, and relapse. Future studies incorporating more detailed temporal information, repeated behavioral assessments, and formal comparisons between dimensions are needed to investigate these observed patterns of association.

The Chinese sociocultural context may also help contextualize these findings. Smoking and social drinking, particularly among men, are influenced by social interactions and gender norms [36, 37]. Tobacco and alcohol use may therefore reflect a range of social influences beyond childhood adversity. However, the social acceptability of these behaviors does not imply low health risk, nor does it establish that single-substance use is unrelated to ACEs. Consistent with previous studies [38, 39], men and participants with lower educational attainment were more likely to belong to some tobacco and alcohol use classes. Gender differences may reflect behavioral norms and social contexts, whereas educational differences may reflect inequalities in access to health information, preventive services, and cessation support [40]. Previous research also indicates that childhood socioeconomic disadvantage may co-occur with maltreatment and other adverse experiences [41]. Childhood adversity and adult social circumstances should therefore be considered within an interconnected context, although this study did not directly examine the cumulative or mediating effects of socioeconomic disadvantage.

The principal implications for older adult care concern the co-occurrence of tobacco and alcohol use and the life experiences that may be relevant to these behaviors. Assessing smoking and drinking together in chronic disease management and routine health assessments may provide a more comprehensive description of behavioral risks. For middle-aged and older adults with histories of childhood adversity, communication that respects autonomy, protects privacy, and avoids stigmatization may help clinicians understand current psychological distress, coping strategies, and barriers to changing tobacco and alcohol use. However, this study did not assess the incremental clinical value of ACE screening or whether trauma-informed care improves smoking cessation, alcohol reduction, or other health outcomes. These findings therefore provide a rationale for further research rather than direct support for universal ACE screening or specific interventions. Future studies should evaluate the acceptability, feasibility, and effectiveness of incorporating an adversity-informed perspective into existing services for middle-aged and older adults. Preventing childhood adversity remains an important public health priority, but whether such prevention reduces tobacco- and alcohol-related burdens in later life requires further longitudinal and intervention research.

5. Limitations

Several limitations should be acknowledged. First, the cross-sectional design limits causal inference, and the retrospective assessment of both ACEs and age at substance-use initiation may introduce recall bias and uncertainty in temporal sequencing. Although all ACEs were defined as occurring before age 17, retrospective reports may not fully capture the timing, frequency, or severity of childhood adversity. Nevertheless, retrospective ACE measures have shown acceptable reliability and remain a useful complement to prospective assessments [42]. Second, dichotomizing ACE exposure as 0 versus ≥ 1 may have reduced sensitivity to potential dose–response relationships and heterogeneity in adversity burden. However, sensitivity analyses using continuous ACE scores produced broadly consistent results (Supplementary Table 2). Third, despite adjustment for key sociodemographic covariates, residual confounding from unmeasured genetic, familial, psychosocial, and contextual factors cannot be excluded. Fourth, estimating weekly alcohol intake from past-year drinking frequency and the most recent drinking quantity may not fully capture usual consumption, potentially misclassifying heavy drinking. However, incorporating drinking frequency may partly mitigate reliance on a single occasion. Fifth, tobacco and alcohol use were self-reported and may be affected by recall and social desirability bias, potentially leading to exposure or outcome misclassification. Future studies incorporating biomarkers, clinical assessments, or other external sources of validation are warranted. Finally, because the sample was restricted to adults aged 45 years and older, the findings may not be generalizable to younger populations. Cohort effects should also be considered, as participants were exposed to different historical periods of tobacco and alcohol availability, regulation, and social norms. Prospective longitudinal studies across multiple generations are needed to clarify temporal pathways and examine whether these associations persist across changing social contexts.

6. Conclusion

ACEs were associated with higher-risk tobacco and alcohol co-use among middle-aged and older Chinese adults. Threat-related ACEs were associated with both adult-onset and early-onset higher-risk co-use, whereas deprivation-related ACEs were significantly associated only with early-onset higher-risk co-use. These findings highlight the relevance of considering multiple dimensions of childhood adversity alongside the timing of initiation and risk profiles of tobacco and alcohol use. In chronic disease management, greater attention to co-use and early-life experiences may help contextualize individual care needs. However, these associations do not establish causality or demonstrate distinct developmental pathways across ACE dimensions. Further research is needed to assess whether trauma-informed approaches to co-use management are feasible, acceptable, and effective in this population.

Declarations

Ethics approval and consent to participate

Ethical approval for the CHARLS was obtained from the institutional review board at Peking University (No. IRB00001052-11015), with written informed consent obtained from all participants. The data were anonymized, and participants were assured of confidentiality. This secondary analysis did not require separate ethical approval.

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Authors' contributions

YY conceptualized the study. YY and XW designed the study. YY and CC curated the data. YY and NG performed the statistical analyses. YY drafted the manuscript. MPW and CS critically revised the manuscript for important intellectual content. CS supervised the study. All authors critically reviewed subsequent drafts and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to concerns regarding participant privacy and confidentiality, but are available from the corresponding author on reasonable request.

Clinical trial number

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

References

1. World Health Organization. Alcohol use. 2024. <https://www.who.int/europe/news-room/fact-sheets/item/alcohol-use>. Accessed 5 June 2026.
2. World Health Organization. Tobacco. 2025. <https://www.who.int/news-room/fact-sheets/detail/tobacco>. Accessed 5 June 2026.
3. Chan KH, Wright N, Xiao D, Guo Y, Chen Y, Du H, et al. Tobacco smoking and risks of more than 470 diseases in China: a prospective cohort study. *Lancet Public Health*. 2022;7:e1014–26. [https://doi.org/10.1016/S2468-2667\(22\)00227-4](https://doi.org/10.1016/S2468-2667(22)00227-4).
4. Manthey J, Shield KD, Rylett M, Hasan OSM, Probst C, Rehm J. Global alcohol exposure between 1990 and 2017 and forecasts until 2030: a modelling study. *Lancet*. 2019;393:2493–502. [https://doi.org/10.1016/S0140-6736\(18\)32744-2](https://doi.org/10.1016/S0140-6736(18)32744-2).
5. Cui Z. The Prevalence of tobacco dependence, alcohol dependence, and the association between smoking and drinking alcohol in China. Doctoral Dissertation. Peking Union Medical College; 2023.
6. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1223–49. [https://doi.org/10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2).
7. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet*. 2017;389:1885–906. [https://doi.org/10.1016/S0140-6736\(17\)30819-X](https://doi.org/10.1016/S0140-6736(17)30819-X).
8. GBD 2016 Alcohol Collaborators. *Lancet*. 2018;392:1015–35. [https://doi.org/10.1016/S0140-6736\(18\)31310-2](https://doi.org/10.1016/S0140-6736(18)31310-2). Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016.
9. Han BH, Moore AA, Sherman SE, Palamar JJ. Prevalence and correlates of binge drinking among older adults with multimorbidity. *Drug Alcohol Depend*. 2018;187:48–54. <https://doi.org/10.1016/j.drugalcdep.2018.01.038>.
10. Madero-Cabib I, Bambs C. Association between lifetime tobacco use and alcohol consumption trajectories and cardiovascular and chronic respiratory diseases among older people. *Int J Environ Res Public Health*. 2021;18:11275. <https://doi.org/10.3390/ijerph182111275>.
11. van den Ende MWJ, Freichel R, van der Maas HLJ, Wiers RW, Epskamp S. Societal spirits in the silver streak: Unraveling complexity in drinking habits of the mature adult population. *Alcohol Clin Exp Res (Hoboken)*. 2025;49:217–25. <https://doi.org/10.1111/acer.15486>.
12. Magalhães LS, Moura WEA, Silva GO, Dias MB, Silva E, Pereira BVD. Alcohol consumption in later life: prevalence and associated risk factors. *BMC Geriatr*. 2026;26:546. <https://doi.org/10.1186/s12877-026-07227-x>.
13. Lee J, Kim Y, Cho W-K. Secondary cross-sectional analysis of smoking and drinking factors among older Korean men: A 13-year national survey. *Tob Induc Dis*. 2025;23. <https://doi.org/10.18332/tid/211500>.
14. Elder GH, Johnson MK, Crosnoe R. The emergence and development of life course theory. In: Mortimer JT, Shanahan MJ, editors. *Handbook of the Life Course*. Boston, MA: Springer US; 2003. pp. 3–19. https://doi.org/10.1007/978-0-306-48247-2_1.
15. McLaughlin KA, Sheridan MA, Lambert HK. Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. *Neurosci Biobehav Rev*. 2014;47:578–91. <https://doi.org/10.1016/j.neubiorev.2014.10.012>.
16. Sheridan MA, McLaughlin KA. Dimensions of early experience and neural development: deprivation and threat. *Trends Cogn Sci*. 2014;18:580–5. <https://doi.org/10.1016/j.tics.2014.09.001>.
17. Zhu J, Racine N, Devereux C, Hodgins DC, Madigan S. Associations between adverse childhood experiences and substance use: A meta-analysis. *Child Abuse Negl*. 2025. <https://doi.org/10.1016/j.chiabu.2023.106431>. 168 Pt 1:106431.
18. Joannès C, Castagné R, Kelly-Irving M. Associations of adverse childhood experiences with smoking initiation in adolescence and persistence in adulthood, and the role of the childhood environment: Findings from the 1958 British birth cohort. *Prev Med*. 2022;156:106995. <https://doi.org/10.1016/j.ypmed.2022.106995>.
19. Duffy KA, McLaughlin KA, Green PA. Early life adversity and health-risk behaviors: proposed psychological and neural mechanisms. *Ann N Y Acad Sci*. 2018;1428:151–69. <https://doi.org/10.1111/nyas.13928>.

20. National Institute on Drug Abuse. Drugs, Brains, and Behavior: The Science of Addiction: Drugs and the Brain | NIDA. 2020. <https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain>. Accessed 10 June 2026.
21. Reidpath DD, Davey TM, Kadirvelu A, Soyiri IN, Allotey P. Does one cigarette make an adolescent smoker, and is it influenced by age and age of smoking initiation? Evidence of association from the U.S. Youth Risk Behavior Surveillance System (2011). *Prev Med*. 2014;59:37–41. <https://doi.org/10.1016/j.ypmed.2013.11.011>.
22. World Health Organization. WHO report on the global tobacco epidemic. 2017: monitoring tobacco use and prevention policies. 2017. <https://www.who.int/publications/i/item/9789241512824>. Accessed 8 June 2026.
23. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol*. 2014;43:61–8. <https://doi.org/10.1093/ije/dys203>.
24. Wolf S, Suntheimer NM. A dimensional risk approach to assessing early adversity in a national sample. *J Appl Dev Psychol*. 2019;62:270–81. <https://doi.org/10.1016/j.appdev.2019.03.004>.
25. Lin L, Wang HH, Lu C, Chen W, Guo VY. Adverse childhood experiences and subsequent chronic diseases among middle-aged or older adults in China and associations with demographic and socioeconomic characteristics. *JAMA Netw Open*. 2021;4:e2130143. <https://doi.org/10.1001/jamanetworkopen.2021.30143>.
26. Lin L, Cao B, Chen W, Li J, Zhang Y, Guo VY. Association of adverse childhood experiences and social isolation with later-life cognitive function among adults in China. *JAMA Netw Open*. 2022;5:e2241714. <https://doi.org/10.1001/jamanetworkopen.2022.41714>.
27. Borland R, Yong H-H, O'Connor RJ, Hyland A, Thompson ME. The reliability and predictive validity of the Heaviness of Smoking Index and its two components: findings from the International Tobacco Control Four Country study. *Nicotine Tob Res*. 2010;12(Suppl):S45–50. <https://doi.org/10.1093/ntr/ntq038>.
28. Wang Q, Zhang Y, Wu C. Alcohol consumption and associated factors among middle-aged and older adults: results from China Health and Retirement Longitudinal Study. *BMC Public Health*. 2022;22:322. <https://doi.org/10.1186/s12889-022-12718-8>.
29. Centers for Disease Control and Prevention. National Health Interview Survey. 2024. https://archive.cdc.gov/www_cdc_gov/nchs/nhis/alcohol/alcohol_glossary.htm. Accessed 1 June 2026.
30. Nylund K, Asparouhov T, Muthén B. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Struct Equ Model*. 2007;14:535–69. <https://doi.org/10.1080/10705510701575396>.
31. Rakovski C, Lalli M, Gu J, Hobson M, Wollenhaupt-Aguiar B, Minuzzi L, et al. Childhood maltreatment as a predictor of substance use/misuse among youth: A systematic review and meta-analysis. *Neurosci Biobehav Rev*. 2024;166:105873. <https://doi.org/10.1016/j.neubiorev.2024.105873>.
32. Stellern J, Xiao KB, Grennell E, Sanches M, Gowin JL, Sloan ME. Emotion regulation in substance use disorders: a systematic review and meta-analysis. *Addiction*. 2023;118:30–47. <https://doi.org/10.1111/add.16001>.
33. Stephens MAC, Wand G. Stress and the HPA axis: role of glucocorticoids in alcohol dependence. *Alcohol Res*. 2012;34:468–83. <https://doi.org/10.35946/arc.v34.4.11>.
34. Enoch MA. The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology*. 2011;214:17–31. <https://doi.org/10.1007/s00213-010-1916-6>.
35. Teicher MH, Samson JA. Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. *J Child Psychol Psychiatry*. 2016;57:241–66. <https://doi.org/10.1111/jcpp.12507>.
36. Jiang H, Room R, Hao W. Alcohol and related health issues in China: action needed. *Lancet Global Health*. 2015;3:e190–1. [https://doi.org/10.1016/S2214-109X\(15\)70017-3](https://doi.org/10.1016/S2214-109X(15)70017-3).
37. Rich ZC, Xiao S. Tobacco as a social currency: cigarette gifting and sharing in China. *Nicotine Tob Res*. 2012;14:258–63. <https://doi.org/10.1093/ntr/ntr156>.
38. Redonnet B, Chollet A, Fombonne E, Bowes L, Melchior M. Tobacco, alcohol, cannabis and other illegal drug use among young adults: the socioeconomic context. *Drug Alcohol Depend*. 2012;121:231–9. <https://doi.org/10.1016/j.drugalcdep.2011.09.002>.
39. Gerra G, Benedetti E, Resce G, Potente R, Cutilli A, Molinaro S. Socioeconomic status, parental education, school connectedness and individual socio-cultural resources in vulnerability for drug use among students. *Int J Environ Res Public Health*. 2020;17:1306. <https://doi.org/10.3390/ijerph17041306>.
40. U.S. Centers for Disease Control and Prevention. People with low socioeconomic status encounter barriers to quitting successfully. Tobacco Health Equity. 2024. <https://www.cdc.gov/tobacco-health-equity/collection/low-ses-quitting-tobacco.html>. Accessed 10 June 2026.
41. Walsh D, McCartney G, Smith M, Armour G. Relationship between childhood socioeconomic position and adverse childhood experiences (ACEs): a systematic review. *J Epidemiol Community Health*. 2019;73:1087–93. <https://doi.org/10.1136/jech-2019-212738>.

42. Dube SR, Williamson DF, Thompson T, Felitti VJ, Anda RF. Assessing the reliability of retrospective reports of adverse childhood experiences among adult HMO members attending a primary care clinic. *Child Abuse Negl.* 2004;28:729–37. <https://doi.org/10.1016/j.chiabu.2003.08.009>.

Figures

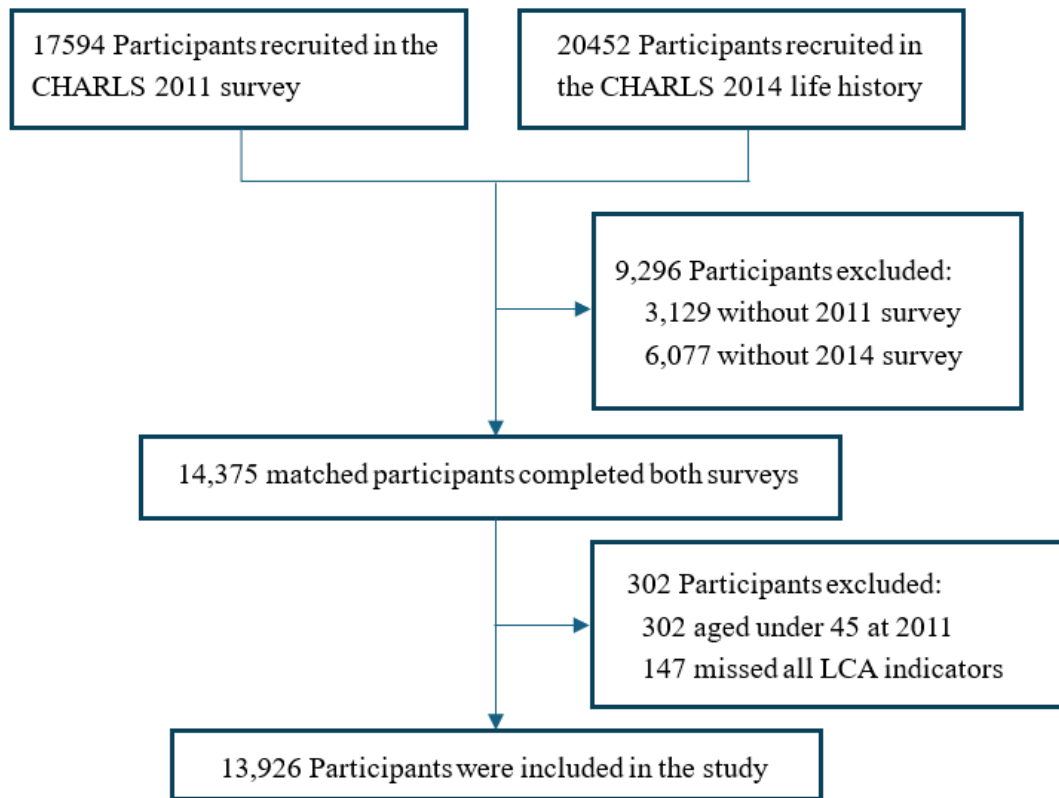


Figure 1

Flowchart of study participant selection

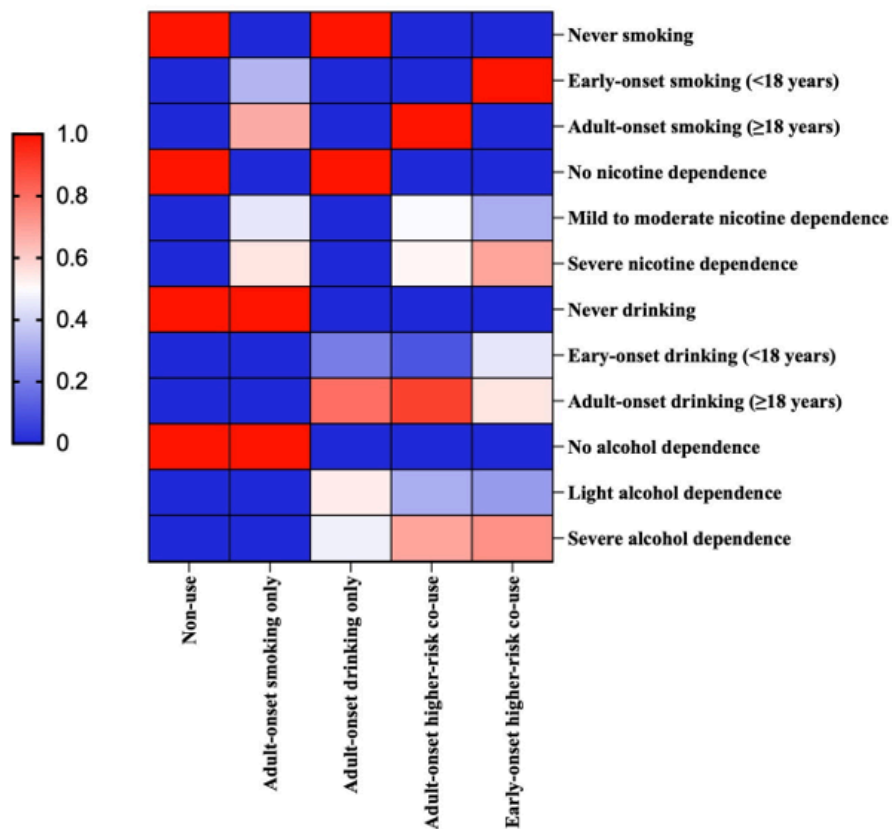


Figure 2

Visualization of predicted probability distribution

Supplementary Files

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