Journal of Affective Disorders 195 (2016) 136–143

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Prospective relationship of depressive symptoms, drinking, and tobacco smoking among middle-aged and elderly community-dwelling adults: Results from the China Health and Retirement Longitudinal Study (CHARLS)

Hui G. Cheng [a,b,*], Shengnan Chen [a], Orla McBride [c], Michael R. Phillips [a,d]

[a] Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[b] Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI, USA
[c] School of Psychology, University of Ulster, Londonderry, Northern Ireland
[d] Departments of Psychiatry and Global Health, Emory University, Atlanta, GA, USA

ARTICLE INFO

Article history:
Received 26 September 2015
Received in revised form
24 January 2016
Accepted 6 February 2016
Available online 11 February 2016

Keywords:
Depressive symptoms
Alcohol drinking
Smoking
Middle-aged and elderly adults
China

ABSTRACT

Background: Previous studies in Western countries have consistently documented positive associations of smoking and heavy drinking with depressive symptoms but a prospective analysis of these relationships among middle-aged and elderly community members in China have not previously been reported.

Methods: Using data from the China Health and Retirement Longitudinal Study, a two-wave nationally representative survey conducted in 15,628 adults 45 years of age and older, we estimated the prospective association between depressive symptoms and an array of smoking and drinking behaviors. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) short form.

Results: Inverse associations were the dominant pattern of association. For the population as a whole, individuals with baseline depressive symptoms were less likely to start drinking (OR=0.7, 95% CI=0.5, 0.9) or smoking (OR=0.6, 95% CI=0.4, 0.8). Similarly, baseline drinkers and smokers were less likely to develop depressive symptoms ($OR_{drinkers}$=0.6, 95% CI=0.5, 0.7; $OR_{smokers}$=0.7, 95% CJ=0.6, 0.9). No evidence was found for an increased incidence or persistence of depressive symptoms among high-frequency drinkers or heavy smokers or vice versa. Males who had never smoked prior to the onset of depressive symptoms tended to have more rapid onset of tobacco dependence compared to those without such symptoms. Males and females had different association patterns.

Limitations: The study is observational in nature and provides limited evidence for causality.

Discussion: The results are inconsistent with previous findings in Western countries, throwing into question the presumed universality of the association between alcohol drinking or tobacco use and depression among middle-aged and elderly adults.

1. Introduction

Positive associations between depression and smoking have been widely documented (Chaiton et al., 2009; Fergusson et al., 1996). Evidence obtained from studies conducted with adolescents and young adults suggests the existence of reciprocal relationships between the occurrence of depression and smoking (Chaiton et al., 2009; Munafo et al., 2008). Studies of adults have also found that depressive symptoms predict the persistence of smoking and the failure of attempts to quit smoking (Weinberger et al., 2012); conversely, other studies report that smoking predicts depressive symptoms (Korhonen et al., 2007; An and Xiang, 2015). Similarly, a high comorbidity between depression and heavy drinking and alcohol use disorder (AUD) has been well established in both retrospective studies (Chou et al., 2012; Hasin et al., 2007; Paljarvi et al., 2009) and prospective studies (Boden and Fergusson, 2011; Kuo et al., 2006; Fergusson et al., 2009).

Several mechanisms have been proposed to explain these observed associations. Tobacco and alcohol are psychoactive substances which can change neural activity after intake and provide a boost to mood. Based on this, the 'self-medication theory'

* Corresponding author at: Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, No. 3210 Humin Rd., Shanghai 201108, China.
E-mail address: chengyaojin@yahoo.com (H.G. Cheng).

http://dx.doi.org/10.1016/j.jad.2016.02.023

postulates that individuals with depressive symptoms smoke or drink to alleviate their symptoms (Bolton et al., 2009; McCarty et al., 2012). An alternative hypothesis for the association between depressive symptoms and alcohol or tobacco use is that changes in neurotransmitter activity induced by alcohol and tobacco increase the liability to depression (Johnson, 2004; Miguel-Hidalgo et al., 2002; Picciotto et al., 2002). Despite a myriad of studies on the relationship between AUD and depression, the prospective relationship between depression and drinking status (regardless of the presence of an AUD), which is an important approach to test the self-medication theory, remains largely unexplored in the general population. If the theory holds true, one would expect to observe that depression is predictive of drinking onset and persistence within a relatively short time frame.

Smoking and drinking are products of both cultural and genetic factors; it is therefore reasonable to assume that cultural and genetic factors would affect the association between depression and alcohol or tobacco use. China has a distinct smoking and drinking culture which produces very different demographic profiles of drinkers and smokers than reported in Western high-income countries, including a much larger male-to-female ratio and a much later age of onset than in Western countries (Cheng et al., 2010, 2015; Degenhardt et al., 2007). Additionally, the unpleasant 'flushing effect' that commonly occurs in Han Chinese after alcohol intake is the result of slow metabolism of ethanol due to race-based differences in the distribution of genetic polymorphisms (Goedde et al., 1992). These differences suggest that evidence from the Chinese population would be useful for understanding how cultural factors lead to differential presentations and correlates of health conditions. To date, the relationship of drinking, smoking, and depression has not been studied in the general Chinese population prospectively.

The majority of previous studies investigating the link between depression and smoking initiation were conducted during adolescence (Audrain-McGovern et al., 2009), with studies among middle-aged and elderly adults being rare (An and Xiang, 2015). Several factors indicate the importance of improving our understanding of these relationships in older adults: a) the Global Burden of Disease Project estimates indicate that depression is a leading cause of the disease burden and alcohol use and tobacco smoking are amongst the most important risk factors of ill health among middle-aged and elderly population groups (University of Washington Institute of Health Metrics and Evaluation, 2013); b) the presentation and trajectory of drinking, smoking, and depressive symptoms are different in older adults compared to adolescents (Ajdacic-Gross et al., 2009; Brunborg and Osthus, 2015); and c) the world is aging rapidly (in China persons 45 or older will increase from 32% to 51% of the total population from 2010 to 2040) (United Nation, 2012).

Last but not the least, the underlying mechanisms, patterns, and courses of smoking and drinking behaviors vary widely between males and females (Wells et al., 2011; WHO, 2005). In order to produce the most pertinent evidence to guide prevention and intervention efforts, it is important to generate sex-specific estimates. Furthermore, an individual's general health is arguably one of the most important modifiers of drinking and smoking behaviors (especially among older population cohorts), and it also interacts with depressive symptoms (Geerlings et al., 2000). It is therefore an important confounder to control for while studying the relationship between drinking, smoking and depression. To the best of our knowledge, there have been no prospective studies in community-dwelling middle-aged and elderly adults that considered drinking, smoking, and general health status simultaneously.

Against this background, the current study seeks to provide the first estimates for the prospective association between depressive symptoms and a range of drinking- and smoking-related variables among males and females using data from a large prospective survey of community-dwelling individuals 45 years of age or older in China.

2. Methods

2.1. Participants

Data come from the China Health and Retirement Longitudinal Study (CHARLS), a two-wave survey of non-institutionalized adults aged 45 years or older living in mainland China (including 28 provinces, municipal cities, and autonomous regions). A multi-stage stratified sampling design was used to ensure the representativeness of the sample. Details of the sampling procedure are available elsewhere (Zhao et al., 2009). Briefly, all county-level units in the 28 provinces were first stratified by region, urbanity, and economic development. Within each stratum, a systematic sampling method was used to select 150 counties. A probability proportionate to size method was used to select three rural villages or urban communities (primary sampling units, PSUs) within each selected county. Simple random sampling was used to select 80 households from each PSU. All age-eligible persons (i.e. 45 years or older) from the selected household were asked to participate. Face-to-face computer-assisted personal interviews were conducted with 17,708 individuals (80.5% response at the household level) at the first wave (W1) in 2011–2012. The second wave (W2) successfully re-interviewed 15,628 of these individuals in 2013–2014 (Zhao et al., 2014).

2.2. Assessments of depression

The 10-item Center for Epidemiologic Studies Depression Scale (CES-D) short form was used to measure depressive symptoms. The time frame for the CES-D questions refers to the week prior to the interview. Each item was rated on a 4-point Likert scale with answers varying from 'rarely or none of the time (<1 day)' to 'most or all of the time (5–7 days)'. CES-D has shown good validity and reliability in the Chinese population (Boey, 1999; Cheng and Chan, 2005). A previous validation study in elderly Chinese found a cutoff point of 12 provides the optimal threshold to identify clinically significant depression(Cheng and Chan, 2005), so a cutoff point of 12 was used in this study to generate the binary depressive symptom variable (1=yes, 0=no).

2.3. Assessments of drinking- and smoking-related variables

Current drinkers were identified based on a 'yes' response to the question "Did you drink any alcoholic beverages, such as beer, wine, or liquor in the past year? (If 'yes') How often?" Those who indicated they drank more than monthly in the last year were identified as 'current drinkers'. For all current drinkers, follow-up questions were asked about their drinking frequency of hard liquor, beer, and wine; those who reported drinking any type of alcoholic beverage twice a day or more than twice a day were classified as 'high frequency'. A 'yes' response to the question "in the last year, have you ever taken a drink first thing in the morning to steady your nerves or get rid of a hangover?" qualified the respondent to be classified as 'alcohol withdrawal' during the past year. Non-current drinkers were further divided based on their answers to the question "Did you ever drink alcoholic beverages in the past?". Those who indicated that they had never drank alcoholic beverages or had never drank more than once a month were classified as 'never drinkers' and those who had drank more than once a month were classified as 'former drinkers'.

Current smokers were identified using two questions. The first question asked if the respondent had "ever chewed tobacco, smoked

a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars"; the second question asked the respondent if he/she "still has the habit or has totally quit". Those who indicated that they still used tobacco were classified as 'current tobacco users' and those who had quit were classified as 'former tobacco users'. Because these tobacco products are bundled in one question, it was not possible for us to exclude smokeless tobacco users from the analysis. Nonetheless, the number of non-cigarette smokeless tobacco users is negligible in Chinese tobacco users ($<0.1\%$ in all tobacco users) and the vast majority of tobacco users are smokers ($>98\%$; GATSs Collaborative Group, 2015). Therefore, tobacco users in this study can be viewed as tobacco smokers. An average daily consumption of at least 20 cigarettes was considered an indicator of 'heavy smoking'. An item from the Fagerstrom Test of Nicotine Dependence (FTND, (Fagerstrom, 1978)) about how soon the participant needed to smoke a cigarette, cigar or pipe after waking up in the morning was used as a measure of tobacco dependence: a response of 'less than 30 min' was coded as 'tobacco dependence'. A recent study found good sensitivity and reliability using this item and this cut-off point (Schnoll et al., 2013).

The questionnaires can be found at the CHARLS website (http://charls.ccer.edu.cn/en).

2.4. Assessment of covariates

Covariates considered included sex (male or female), age (in years), and self-rated general health status (five Likert scale categories ranging from excellent to poor). Additionally, a binary variable was created to represent changes in marital status which were presumed to have negative impact on mood (i.e., becoming divorced, separated, or widowed was coded as '1'; unchanged marital status and other types of changes were coded as '0'). All information was based on self-report.

2.5. Statistical analysis

Unlike other modules of the interview in which proxy interviewees can provide information when the participant is not able to complete the interview, the CES-D must to be completed by the participants themselves. As a result, there were 1965 missing baseline CES-D scores and 2888 missing follow-up CES-D scores among individuals who participated in both interviews. The final analytic sample for depression consists of 13,663 individuals in W1 and 12,740 individuals in W2. Additional missing values in other variables are nominal (less than 20). Due to a skipping error in the computer-administered assessment at W2, individuals who indicated a positive history of tobacco use at W1 (including current and former users) skipped the entire tobacco section at W2, so it was not possible to generate estimates for the prospective association between baseline depression and persistent or recurrent tobacco use at W2. Descriptive statistics (i.e., frequencies and percentages) and bivariate associations were estimated between W1 depressive symptoms and W2 drinking- and tobacco-use-related variables. Similar analyses were conducted for W1 drinking- and tobacco-use -related variables and W2 depressive symptoms for those with (persistent) and without (incident) depressive symptoms at W1. In order to produce sex-specific estimates and to account for potential confounding or moderation of sex, stratified analyses were conducted adjusting for age and general health status at W1. Our main model (M1) adjusted for age and baseline drinking or smoking status. The adjustment of general health status and change in marital status served as a post-estimation exploration step to assess the degree of change in point estimates. Potential tobacco-use-by-drinking moderation was explored by including the product term in the regression models. Separate analyses were conducted comparing current tobacco users and drinkers with never or former tobacco users and drinkers to accommodate differences between never and former tobacco users and drinkers. Generalized linear regression with a logit link was used to produce estimates. The strength and precision of associations were gauged using odds ratios (OR) and their 95% confidence intervals (CI). Weights were used to take into account selection probability, non-response patterns, and post-stratification factors to bring the sample into balance with the source population. Taylor series linearization method was used to take into account potential clustering as a result of the sampling strategy. Statistical analysis was conducted using Stata 13.0 (College Station, TX, USA, 2013).

3. Results

Table 1 provides a description of the CHARLS data. In this table, the W1 sample was weighted using the W1 cross-sectional weight in order to compare the distribution of variables between the two waves. The last column shows comparisons of unweighted proportions of loss to follow-up. Individuals who drank more than daily were more likely to be followed up at W2 than those who did not drink more than daily; similarly, those who were current tobacco users were more likely to be followed up than those who were not, and those who had nicotine dependence were more likely to be followed up than those who did not. Individuals who were lost to follow-up were older (mean = 59.3 [s.d. = 10.5] vs. mean = 57.7 [s.d. = 10.1]; $t = 6.155$, $p < 0.001$) and more likely to report good health (12.0% loss of follow-up among those with good health vs. 8.3–9.5% among individuals with excellent, fair, poor or very poor health). Nonetheless, the weighted distributions of relevant variables were similar between the two waves (Table 1). Sex, current drinking, alcohol withdrawal, heavy smoking, and the presence of depressive symptoms were not associated with loss to follow-up.

3.1. Prospective association between Wave 1 depressive symptoms and Wave 2 drinking and smoking

Table 2 provides the bivariate associations between W1 depressive symptoms and an array of drinking- and tobacco-use-related behaviors at W2. For the population under study as a whole, the dominant pattern was an inverse association. That is, individuals with depression at W1 were less likely to start or maintain drinking or using tobacco. Statistically significant differences were observed for incident drinking, persistent drinking, persistent high frequency drinking, incident tobacco use, and incident heavy smoking. Persistence of tobacco use was not assessed due to the error in the skip pattern for questions in the W2 assessment.

Results of stratified analyses are presented in Supplementary Table S1. In general, controlling for age, baseline drinking or tobacco use, baseline self-rated health, and changes in marital status did not result in significant changes to the estimates. Male-female differences were found in the association between depressive symptoms and tobacco dependence. Among males who had never used tobacco, those with baseline depressive symptoms tended to be more likely to develop tobacco dependence at follow-up (OR = 1.8, $p = 0.035$). In contrast, females who had never used tobacco with depressive symptoms at baseline were less likely to develop tobacco dependence (OR = 0.3, $p = 0.049$).

3.2. Prospective association between Wave 1 drinking and smoking with Wave 2 depression

Table 3 presents the bivariate associations between W1 drinking and tobacco use with W2 depressive symptoms. Again, the point

Table 1
Description of the CHARLS sample.

		Wave 1 sample (n=17,708)		Wave 2 sample (n=15,628)		Differences in loss to follow-up		
		n	%[a]	n	%[a]	% Loss to follow-up	χ^2	p[b]
Sex	Male	8474	47.6	7449	47.6	9.3	<0.01	0.984
	Female	9226	52.4	8175	52.4	9.8		
	missing	8	<0.1	4	<0.1			
W1 current drinking	No	13,225	75.3	11,707	75.7	9.8	3.54	0.060
	Yes	4383	23.7	3890	24.0	8.8		
	missing	100	1.0	31	0.3			
W1 more than daily drinking	No	16,797	95.0	14,846	95.5	9.7	**14.49**	**<0.001**
	Yes	783	3.9	727	4.1	5.6		
	missing	128	1.2	55	0.4			
W1 withdrawal	No	16,503	92.8	14,662	93.7	9.4	1.77	0.183
	Yes	171	0.8	156	0.9	6.4		
	missing	1034	6.3	810	5.5			
W1 current tobacco use	No	12,045	69.3	10,671	69.9	9.8	**7.94**	**0.005**
	Yes	4862	25.5	4364	26.1	8.4		
	missing	801	5.2	593	4.0			
W1 daily cigarettes ≥20	No	12,451	71.2	11,006	71.7	9.9	2.02	0.155
	Yes	2828	15.5	2524	16.0	9.0		
	missing	2429	13.2	2098	12.2			
W1 nicotine dependence	No	14,328	81.5	12,715	82.3	9.6	**5.33**	**0.021**
	Yes	2550	13.1	2295	13.5	8.2		
	missing	830	5.4	618	4.2			
W1 depressive symptoms	No	10,986	61.8	9795	62.9	9.3	3.25	0.071
	Yes	4287	21.9	3868	22.4	8.4		
	missing	2435	16.3	1965	14.8			
W1 self-rated health status							**25.92**	**<0.001**
	Excellent	883	5.4	777	5.6	8.3		
	Good	2804	16.9	2421	16.5	8.9		
	Fair	7789	42.8	6905	43.5	9.4		
	Poor	4713	26.0	4204	26.2	12.1		
	Very poor	1354	7.5	1224	7.4	9.5		
	missing	165	1.3	97	0.8			

[a] n, unweighted frequency; %, weighted percentage (Wave 1 [W1] sample was weighted using W1 weight and Wave 2 [W2] sample was weighted using W2 weight; the sum may not be exactly 100% due to rounding.
[b] Unweighted comparisons; bold font indicates statistical significance at 0.05 level.

Table 2
Description of the CHARLS sample and bivariate prospective association between baseline depression and Wave 2 drinking- or smoking-related variables among individuals aged 45 and above[a].

	W1 depression n of cases (%)[a]	W1 no depression n of cases (%)[a]	Bivariate OR (95% CI)
***Among W1 never drinkers* (*n*=9446)**			
W2 incident drinking	175 (6.7)	593 (9.7)	**0.7 (0.5, 0.9)**
W2 incident more than daily drinking	19 (0.7)	33 (0.5)	1.4 (0.8, 2.2)
W2 incident alcohol withdrawal	5 (0.1)	9 (0.2)	0.9 (0.2, 3.0)
***Among W1 current drinkers* (*n*=3382)**			
W2 persistent drinking	474 (65.4)	1968 (75.8)	**0.6 (0.5, 0.8)**
W2 incident more than daily drinking	88 (15.6)	332 (15.6)	1.0 (0.7, 1.4)
W2 persistent more than daily drinking	61 (44.1)	310 (59.8)	**0.5 (0.3, 0.8)**
W2 incident alcohol withdrawal	20 (3.3)	73 (3.0)	1.1 (0.6, 1.9)
W2 persistent alcohol withdrawal	14 (23.6)	24 (26.2)	0.9 (0.4, 2.2)
***Among W1 prior drinkers* (*n*=833)**			
W2 resuming of drinking	52 (19.2)	130 (24.3)	0.7 (0.5, 1.1)
W2 occurrence of more than daily drinking	12 (3.7)	23 (4.5)	0.8 (0.4, 1.8)
W2 occurrence of alcohol withdrawal	3 (0.7)	4 (0.7)	1.0 (0.2, 4.8)
***Among W1 never tobacco users* (*n*=8299)**			
W2 incident tobacco use	59 (1.9)	188 (3.1)	**0.6 (0.4, 0.8)**
W2 incident heavy smoking (≥20 cigarettes/day)	39 (1.6)	172 (3.6)	**0.4 (0.2, 0.8)**
W2 incident tobacco dependence	24 (0.7)	51 (0.8)	0.9 (0.5, 1.5)

[a] n, unweighted frequency; %, weighted (using W2 weight) row percentage of incidence or persistence of W2 drinking- or tobacco-use-related variables among individuals with and without W1 depression; bold font indicates statistical significance at 0.05 level.

estimates indicate a dominant pattern of inverse association. Robust associations were found for W1 current drinking (vs. never drinking) with both incident depression and persistent depression at W2. Similarly, W1 current tobacco use (vs. never use) was inversely associated with incident depression and persistent depression (OR=0.8, 95% CI=0.6, 0.9). One exception is that W1 current tobacco users were more likely to develop depressive symptoms at W2 compared to former tobacco users (OR=1.6, 95% CI=1.1, 2.3;

Table 3
Bivariate prospective association between baseline drinking- or tobacco-use-related variables and Wave 2 depression among individuals aged 45 and above[a].

W1 predictors		Incidence of depression at W2		Persistence of depression at W2	
		n of cases (%)[a]	OR (95% CI)	n of cases (%)[a]	OR (95% CI)
Drinking status	Never	860 (14.1)		1145 (48.8)	
	Past	53 (11.3)	0.8 (0.5, 1.1)	95 (44.2)	0.8 (0.6, 1.2)
	Current	231 (8.8)	**0.6 (0.5, 0.7)**	238 (37.8)	**0.6 (0.5, 0.8)**
Tobacco use status	Never	758 (14.1)		1025 (48.3)	
	Past	66 (7.8)	**0.5 (0.4, 0.7)**	107 (45.7)	0.9 (0.6, 1.3)
	Current	320 (10.9)	**0.7 (0.6, 0.9)**	346 (41.6)	**0.8 (0.6, 0.9)**
		Among W1 current drinkers (n=2295)		**Among W1 current drinkers (n=629)**	
More than daily drinking	No	179 (8.5)		199 (39.1)	
	Yes	49 (9.9)	1.2 (0.8, 1.7)	39 (33.4)	0.8 (0.5, 1.3)
Alcohol withdrawal	No	202 (9.3)		189 (37.5)	
	Yes	8 (8.5)	0.9 (0.4, 2.0)	17 (57.3)	2.2 (0.9, 5.5)
		Among W1 current tobacco users (n=2686)		**Among W1 current tobacco users (n=822)**	
Daily cigarettes ≥ 20	No	93 (11.2)		88 (40.9)	
	Yes	131 (8.9)	0.8 (0.6, 1.1)	142 (40.8)	1.0 (0.6, 1.5)
Nicotine dependence	No	155 (11.0)		140 (39.2)	
	Yes	163 (10.8)	1.0 (0.7, 1.3)	206 (43.7)	1.2 (0.9, 1.7)

[a] n, unweighted frequency; %, weighted column percentage of incidence or persistence of depression among individuals with or without baseline drinking- or tobacco-use-related behaviors; bold font indicates statistical significance at 0.05 level.

not shown in table). And W1 drinkers with alcohol withdrawal tended (at trend level only) to have persistent depressive symptoms (OR=2.2, 95% CI=0.9, 5.5).

Stratified analyses found different patterns of associations in males and females (see Supplementary Table S2). Depressive symptoms were less likely to occur (OR=0.7, p=0.006) or persist (OR=0.7, p=0.051) among male current drinkers than among males who had never used alcohol even after controlling for age, baseline tobacco use status, baseline self-rated health status, and changes in marital status. W1 male drinkers with alcohol withdrawal were more likely than males who had never used alcohol to have persistent depressive symptoms. Current male tobacco users were more likely to develop incident depressive symptoms than former smokers (OR=1.8, p=0.001). Detailed analysis identified a moderating effect of drinking status on the relationship of current tobacco use and persistent depressive symptoms: current tobacco users who had never drank alcohol at W1 tended to be more likely to have persistent depressive symptoms (OR=1.7, p=0.057), but this relationship did not exist in current tobacco users who were current drinkers at W1 (OR=0.5, p=0.104) or former drinkers at W1 (OR=0.8, p=0.404). No other moderation effect were found ($p > 0.20$).

Among females, none of the associations were statistically robust, possibly due to the small number of female drinkers and tobacco users. Nonetheless, exploration of the potential moderating effects of alcohol use on the relationship of tobacco use status and depression identified some interesting findings. Compared to females who never drank and never used tobacco at W1, females who were concurrent drinkers and tobacco users at W1 tended to be less likely to have incident depressive symptoms (OR=0.2, p=0.068) or persistent depressive symptoms (OR=0.1, p=0.072) at W2.

4. Discussion

4.1. Strengths and limitations

The current study has several important strengths, including the analysis of survey data obtained from a large, representative sample of middle-aged and elderly adults in China. More than 90% of individuals with depression in China do not seek professional help (Chou et al., 2012; Kessler et al., 2005; Phillips et al., 2009), so community-based studies have superior external validity compared to clinical studies which are prone to selection biases (Almeida and Pfaff, 2005). The survey response rate (~80%) was very good, which strengthens confidence in the generalizability of the results. Moreover, the prospective design of the study makes it feasible to directly assess the temporal relationships of key variables – one of the most important prerequisites for causal inference – thus avoiding the recall bias that undermines the quality of cross-sectional and retrospective studies (Coughlin, 1990; Vrijheid et al., 2006).

Our findings should be interpreted in light of the following limitations. First, although we controlled for general health status and the loss of spouse, which are two potentially important confounders of the relationship between the use of tobacco or alcohol and depression, other confounders (e.g., other stressful life events, socioeconomic status, and genetic variants that increase susceptibility to both drinking and depression) were not considered. Future studies with more sophisticated statistical tools will be needed to disentangle the complex network of these potential confounders (i.e., unobserved heterogeneities). Nonetheless, to fully control for confounding effects, randomized controlled trials will be needed to infer causality. This study provides basic estimates needed for the planning of such studies. Second, a common concern about prospective studies is attrition. As shown in Table 1, there was no significant difference in the loss to follow-up between those with and without depression at W1, and the weighted distribution of all key variable were quite similar in W1 and W2, so we do not consider our estimates seriously biased due to attrition. Third, despite the popularity of the CES-D, it is not based on any specific diagnostic system. A previous meta-analysis on the relationship between smoking and depression found that estimates tend to be biased towards the null when assessment was based on depressive symptomology instead of on the formal diagnosis of depression (Chaiton et al., 2009), so our analysis may under-estimate the true strength of the associations between depression and tobacco use or drinking. Fourth, due to the lack of information about lifetime history of depression, we are not able to adjust for past history of depressive symptoms. Therefore, the 'incidence of depression' in this study includes both newly incident depression and recurrent depression which was not active at W1. Previous studies have found reciprocal relationships between drinking or

smoking and depression (Fergusson et al., 1996); future studies that are able to control for the history of depression are needed to address this issue in the Chinese population. Also, by dichotomizing the CES-D score, we did not explore potential J- or U-shaped relationships between depressive symptomatology and the use of tobacco or alcohol. Future studies that investigate the full spectrum of CES-D score may be able to shed some new light on this issue. Fifth, due to the small numbers of cases in some of the stratified analyses, the statistical power is low for some of the analyses among females and for rare outcomes (e.g., alcohol withdrawal). Future studies with larger sample sizes should resolve this problem. Sixth, the current study did not assess 'clinically significant' alcohol use disorder or tobacco dependence using validated assessments, so we were not able to provide evidence about the association of these conditions with the severity of depressive symptoms. Sixth, we are encouraged to discuss potential influences of illegally produced alcohol. The prevalence of drinking in Table 1 may have been under-estimated if some individuals consumed illegally produced alcohol only and were unwilling to disclose it. We do not consider this causes substantial under-estimation because the survey questions did not differentiate the consumption of legally and illegally produced alcohol. It is possible that the drinking-depression relationship varies among individuals who consume legally produced alcohol from those who consume illegally produced alcohol. For example, individuals from poorer areas may be more likely to consume illegally produced alcohol compared to those from wealthier areas. Again, we do not consider this has induced significant bias because the survey questions only asked about general consumption of alcohol regardless of the method of production.

4.2. Depression and drinking

This analysis did not find supporting evidence about self-medication of depressive symptoms with alcohol in middle-aged and elderly Chinese. To the contrary, we found that compared to individuals without depressive symptoms at baseline, individuals with depressive symptoms were less likely to start drinking, more likely to stop drinking, and less likely to maintain high-frequency drinking at the 2-year follow-up. These findings stand in stark contrast with previous findings in high-income western countries (Gea et al., 2013; Kirchner et al., 2007).

There are several possible factors that could result in the opposite relationship of alcohol use and depressive symptoms in China versus that seen in high-income western countries. Firstly, it has been well-documented that the Han Chinese population has high frequencies of genetic polymorphisms encoding alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) which produce an instantaneous unpleasant flushing effect after alcohol intake (Goedde et al., 1992). A substantial proportion of Chinese may not experience improved mood with alcohol use and, thus, be less inclined to use drinking as a means to 'treat' depressive symptoms. Secondly, the most prevailing drinking pattern in Chinese males is heavy episodic drinking at social occasions where mutual intoxication is used to establish or reinforce social and business relationships (Cheng et al., 2015; Wang et al., 2010). Thus the primary motive for drinking in China is to meet social expectations within a group, not for personal enjoyment, relaxation, or self-reward. Depressive symptoms typically result in self-imposed social isolation at which time the need to meet the social demand for collective drinking will be reduced. In support of this hypothesis, we also found that male current drinkers were less likely to develop or maintain depressive symptoms compared to never drinkers or former drinkers. Future studies with more direct measurement of drinking motives and genetic markers will provide direct evidence about the mechanisms underlying these observed inverse associations.

In the current study, there were insufficient numbers of females drinking behaviors to identify statistically significant associations; however, there was a statistical trend suggesting that current female drinkers at baseline were less likely to develop subsequent depressive symptoms than females who had never used alcohol at baseline.

Another interesting observation is that symptoms of alcohol withdrawal at baseline predicted persistent but not incident depressive symptoms at follow-up. This suggests that there may be one pathway between problematic drinking and the onset of depressive symptoms and another pathway between problematic drinking and the perpetuation (or resolution) of depressive symptoms.

4.3. Depression and tobacco use

We found an overall inverse association between baseline depressive symptoms and incident tobacco use or heavy smoking at follow-up for the population as a whole. These findings are inconsistent with previous findings among middle-aged and older adults in the United States where robust positive associations have been documented (An and Xiang, 2015). Possible explanations for this difference include cultural differences between western countries and China. Similar to drinking, cigarette toasting and cigarette gifting (preferably of expensive foreign brands) with business associates is a popular vehicle to maintain important relationships among middle-aged males in contemporary China, so it is, to a somewhat lesser extent than alcohol, a 'social' behavior and less of an individually focused behavior. To the extent that this is true, depressed individuals would have less social contacts and, thus, have less need to start or continue smoking (Harakeh and Vollebergh, 2012). Future research focusing on the relative importance of different motivations for smoking in both men and women and in individuals in different age groups may help to explain our unexpected findings about the relationship of depressive symptoms to smoking behavior.

The picture for the relationship between depression and tobacco dependence is more complicated. As was true for alcohol use, we found substantial differences between men and women in the relationship between tobacco dependence and depressive symptoms. Although males who had never used tobacco with depressive symptoms at baseline were just as likely to start tobacco use at follow-up as male never tobacco users without depressive symptoms, they were about two times more likely to develop tobacco dependence at the two-year follow-up assessment. This suggests that depressive symptoms predict a rapid transition from tobacco initiation to tobacco dependence, a finding that is in line with findings from previous studies in Canada (Khaled et al., 2011) and the United States (Dierker et al., 2015).

Some studies report that common genetic variants contribute to the vulnerability for both alcohol and tobacco dependence (Palmer et al., 2015). In this context, it is possible that the unpleasant 'flushing effect' following alcohol intake induces Chinese males to turn to tobacco, an easily accessible psychoactive drug, for short-term mood regulation (i.e., supporting the self-medication theory). In contrast, females with depressive symptoms at baseline were three times less likely to develop tobacco dependence at follow-up than females without depressive symptoms at baseline, suggesting that smoking (like drinking) has a different etiology, course, and covariates in Chinese women than in Chinese men. In the Chinese context, high levels of stigma towards female smoking may prevent females from considering smoking as a method for mood regulation. Alternatively, it is also possible that some particular characteristics related to female smoking (i.e., high social support among female smokers) decreases the risk of

subsequent depression. Future studies specifically focusing on the relatively small number of mainland Chinese females who smoke are needed to answer these questions.

In contrast to findings among middle-aged and older adults in high-income countries (An and Xiang, 2015), the current study found little evidence of a positive association between baseline smoking and subsequent depressive symptoms at follow-up for the population of elderly adults as a whole. We believe the aforementioned sociocultural factors play an important role in this difference between China and high-income countries. Due to the lack of information about lifetime history of depression, we were not able to adjust for a past history of depressive symptoms. Nonetheless, our findings are inconsistent with the large body of literature documenting positive reciprocal relationships between smoking and depression (Fergusson et al., 1996). However, this population-wide result did not hold true for all subgroups: current male tobacco users at baseline were about two times more likely to develop depressive symptoms at follow-up compared to men who were former tobacco users at baseline. This finding parallels the finding reported in high-income countries of a more rapid transition from tobacco use to tobacco dependence among males who had never used tobacco with depressive symptoms compared to males who have never used tobacco without depressive symptoms (Tjora et al., 2014). As was true with alcohol use, the relationships among females are different than those in males, a finding that has also been reported in a previous clinical sample of middle-aged Chinese women (Yang et al., 2014).

4.4. Implications and future directions

In contrast to multiple reports from Western countries, using data from a prospective survey of a large, representative sample of middle-aged and elderly residents of mainland China, we found robust inverse associations between depressive symptoms and subsequent alcohol consumption. The overall association between depressive symptoms and subsequent smoking was also inverse-to-null, especially among females. These findings highlight the importance of social context – particularly the local 'drinking culture' and 'smoking culture'—when assessing the relationship of depressive symptoms to different types of addictive behaviors. The findings also reaffirm the need to be very cautious when applying research findings about affect and behavior in high-income Western countries to China or other low- and middle-income countries. We also found robust differences between males and females in the association of drinking, smoking, and depressive symptoms, which clarifies the importance of stratifying the results of future studies (both in China and elsewhere) by sex. However, our study was a population-based study that did not distinguish different subgroups of depressed individuals, so there may be a positive relationship between specific subtypes of depression and subsequent patterns of substance abuse. Further subgroup-specific studies will be needed to clarify this issue. Our results are limited to middle-aged and elder adults so it is unknown whether or not these inverse associations observed are also present in adolescents and young adults in China.

Contributors

Author HGC designed the study, managed the literature review, conducted the analysis, and wrote the first draft. Author SC managed the literature searches. Authors OM and MRP revised the manuscript. All authors contributed to and have approved the final manuscript.

Funding

This analysis is funded by the Chinese Medical Board of New York (13-165). The funding agency has no role in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Acknowledgment

We are grateful for the CHARLS team to make the data publicly available. Authors wish to thank Dr. Chris Green for editorial assistance.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2016.02.023.

References

Ajdacic-Gross, V., Landolt, K., Angst, J., Gamma, A., Merikangas, K.R., Gutzwiller, F., Rossler, W., 2009. Adult versus adolescent onset of smoking: how are mood disorders and other risk factors involved? Addiction 104, 1411–1419.
Almeida, O.P., Pfaff, J.J., 2005. Depression and smoking amongst older general practice patients. J. Affect. Disord. 86, 317–321.
An, R., Xiang, X., 2015. Smoking, heavy drinking, and depression among U.S. middle-aged and older adults. Prev. Med. 81, 295–302.
Audrain-McGovern, J., Rodriguez, D., Kassel, J.D., 2009. Adolescent smoking and depression: evidence for self-medication and peer smoking mediation. Addiction 104, 1743–1756.
Boden, J.M., Fergusson, D.M., 2011. Alcohol and depression. Addiction 106, 906–914.
Bolton, J.M., Robinson, J., Sareen, J., 2009. Self-medication of mood disorders with alcohol and drugs in the National Epidemiologic Survey on Alcohol and Related Conditions. J. Affect. Disord. 115, 367–375.
Boey, K.W., 1999. Cross-validation of a short form of the CES-D in Chinese elderly. Int. J. Geriatr. Psychiatry 14, 608–617.
Brunborg, G.S., Osthus, S., 2015. Alcohol in the second half of life: do usual quantity and frequency of drinking to intoxication increase with increased drinking frequency? Addiction 110, 308–314.
Chaiton, M.O., Cohen, J.E., O'Loughlin, J., Rehm, J., 2009. A systematic review of longitudinal studies on the association between depression and smoking in adolescents. BMC Public Health 9, 356.
Cheng, H., Lee, S., Tsang, A., Huang, Y., Liu, Z., Anthony, J.C., Kessler, R.C., 2010. The epidemiological profile of alcohol and other drug use in metropolitan China. Int. J. Public Health 55, 645–653.
Cheng, H.G., Deng, F., Xiong, W., Phillips, M.R., 2015. Prevalence of alcohol use disorders in mainland China: a systematic review. Addiction 110 (5), 761–774.
Cheng, S.T., Chan, A.C., 2005. The Center for Epidemiologic Studies Depression Scale in Older Chinese: thresholds for long and short forms. Int. J. of Geriatr. Psychiatry 20, 465–470.
Chou, S.P., Lee, H.K., Cho, M.J., Park, J.I., Dawson, D.A., Grant, B.F., 2012. Alcohol use disorders, nicotine dependence, and co-occurring mood and anxiety disorders in the United States and South Korea – a cross-national comparison. Alcohol. Clin. Exp. Res. 36, 654–662.
Coughlin, S.S., 1990. Recall bias in epidemiologic studies. J. Clin. Epidemiol. 43, 87–91.
Degenhardt, L., Chiu, W.T., Sampson, N., Kessler, R.C., Anthony, J.C., 2007. Epidemiological patterns of extra-medical drug use in the United States: evidence from the National Comorbidity Survey Replication, 2001–2003. Drug Alcohol Depend. 90, 210–223.
Dierker, L., Rose, J., Selya, A., Piasecki, T.M., Hedeker, D., Mermelstein, R., 2015. Depression and nicotine dependence from adolescence to young adulthood. Addict. Behav. 41, 124–128.
Fagerstrom, K.O., 1978. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict. Behav. 3, 235–241.
Fergusson, D.M., Boden, J.M., Horwood, L.J., 2009. Tests of causal links between alcohol abuse or dependence and major depression. Arch. Gen. Psychiatry 66, 260–266.
Fergusson, D.M., Lynskey, M.T., Horwood, L.J., 1996. Comorbidity between depressive disorders and nicotine dependence in a cohort of 16-year-olds. Arch. Gen. Psychiatry 53, 1043–1047.
GATSs Collaborative Group, 2015. The GATS Atlas Global Adult Tobacco Survey. CDC Foundation. Myriad Editions. UK. ⟨http://gatsatlas.org/⟩. (accessed 19.11.15).
Gea, A., Beunza, J.J., Estruch, R., Sanchez-Villegas, A., Salas-Salvado, J., Buil-Cosiales, P., Gomez-Gracia, E., Covas, M.I., Corella, D., Fiol, M., Aros, F., Lapetra, J., Lamuela-Raventos, R.M., Warnberg, J., Pinto, X., Serra-Majem, L., Martinez-Gonzalez, M.A., Predimed, G., 2013. Alcohol intake, wine consumption and the development of depression: the PREDIMED study. BMC Med. 11, 192.

Geerlings, S.W., Beekman, A.T., Deeg, D.J., Van Tilburg, W., 2000. Physical health and the onset and persistence of depression in older adults: an eight-wave prospective community-based study. Psychol. Med. 30, 369–380.
Goedde, H.W., Agarwal, D.P., Fritze, G., Meier-Tackmann, D., Singh, S., Beckmann, G., Bhatia, K., Chen, L.Z., Fang, B., Lisker, R., et al., 1992. Distribution of ADH2 and ALDH2 genotypes in different populations. Hum. Genet. 88, 344–346.
Harakeh, Z., Vollebergh, W.A., 2012. The impact of active and passive peer influence on young adult smoking: an experimental study. Drug Alcohol Depend. 121, 220–223.
Hasin, D.S., Stinson, F.S., Ogburn, E., Grant, B.F., 2007. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch. Gen. Psychiatry 64, 830–842.
Johnson, B.A., 2004. Role of the serotonergic system in the neurobiology of alcoholism: implications for treatment. CNS Drugs 18, 1105–1118.
Kessler, R.C., Chiu, W.T., Demler, O., Merikangas, K.R., Walters, E.E., 2005. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch. Gen. Psychiatry 62, 617–627.
Khaled, S.M., Bulloch, A.G., Williams, J.V., Lavorato, D.H., Patten, S.B., 2011. Major depression IS a risk factor for shorter time to first cigarette irrespective of the number of cigarettes smoked per day: evidence from a National Population Health Survey. Nicotine Tob. Res. Off. J. Soc. Res. Nicotine Tob. 13, 1059–1067.
Kirchner, J.E., Zubritsky, C., Cody, M., Coakley, E., Chen, H., Ware, J.H., Oslin, D.W., Sanchez, H.A., Durai, U.N., Miles, K.M., Llorente, M.D., Costantino, G., Levkoff, S., 2007. Alcohol consumption among older adults in primary care. J. Gen. Intern. Med. 22, 92–97.
Korhonen, T., Broms, U., Varjonen, J., Romanov, K., Koskenvuo, M., Kinnunen, T., Kaprio, J., 2007. Smoking behaviour as a predictor of depression among Finnish men and women: a prospective cohort study of adult twins. Psychol. Med. 37, 705–715.
Kuo, P.H., Gardner, C.O., Kendler, K.S., Prescott, C.A., 2006. The temporal relationship of the onsets of alcohol dependence and major depression: using a genetically informative study design. Psychol. Med. 36, 1153–1162.
McCarty, C.A., Wymbs, B.T., King, K.M., Mason, W.A., Vander Stoep, A., McCauley, E., Baer, J., 2012. Developmental consistency in associations between depressive symptoms and alcohol use in early adolescence. J. Stud. Alcohol Drugs 73, 444–453.
Miguel-Hidalgo, J.J., Wei, J., Andrew, M., Overholser, J.C., Jurjus, G., Stockmeier, C.A., Rajkowska, G., 2002. Glia pathology in the prefrontal cortex in alcohol dependence with and without depressive symptoms. Biol. Psychiatry 52, 1121–1133.
Munafo, M.R., Hitsman, B., Rende, R., Metcalfe, C., Niaura, R., 2008. Effects of progression to cigarette smoking on depressed mood in adolescents: evidence from the national longitudinal study of adolescent health. Addiction 103, 162–171.
Paljarvi, T., Koskenvuo, M., Poikolainen, K., Kauhanen, J., Sillanmaki, L., Makela, P., 2009. Binge drinking and depressive symptoms: a 5-year population-based cohort study. Addiction 104, 1168–1178.
Palmer, R.H., Brick, L., Nugent, N.R., Bidwell, L.C., McGeary, J.E., Knopik, V.S., Keller, M.C., 2015. Examining the role of common genetic variants on alcohol, tobacco, cannabis and illicit drug dependence: genetics of vulnerability to drug dependence. Addiction 110, 530–537.
Phillips, M.R., Zhang, J., Shi, Q., Song, Z., Ding, Z., Pang, S., Li, X., Zhang, Y., Wang, Z., 2009. Prevalence, treatment, and associated disability of mental disorders in four provinces in China during 2001–05: an epidemiological survey. Lancet 373, 2041–2053.
Picciotto, M.R., Brunzell, D.H., Caldarone, B.J., 2002. Effect of nicotine and nicotinic receptors on anxiety and depression. Neuroreport 13, 1097–1106.
Schnoll, R.A., Goren, A., Annunziata, K., Suaya, J.A., 2013. The prevalence, predictors and associated health outcomes of High nicotine dependence using three measures among US smokers. Addiction 108, 1989–2000.
Tjora, T., Hetland, J., Aaro, L.E., Wold, B., Wiium, N., Overland, S., 2014. The association between smoking and depression from adolescence to adulthood. Addiction 109, 1022–1030.
United Nation, Department of Economic and Social Affairs, Population Division, 2012. World Population Prospects: The 2012 Revision, Volume II: Demographic Profiles.
University of Washington Institute of Health Metrics and Evaluation, 2013. Global Burden of Disease.
Vrijheid, M., Deltour, I., Krewski, D., Sanchez, M., Cardis, E., 2006. The effects of recall errors and of selection bias in epidemiologic studies of mobile phone use and cancer risk. J. Expo. Sci. Environ. Epidemiol. 16, 371–384.
Wang, M., Liu, S., Zhan, Y., Shi, J., 2010. Daily work-family conflict and alcohol use: testing the cross-level moderation effects of peer drinking norms and social support. J. Appl. Psychol. 95, 377–386.
Weinberger, A.H., Pilver, C.E., Desai, R.A., Mazure, C.M., McKee, S.A., 2012. The relationship of major depressive disorder and gender to Changes in smoking for current and former smokers: longitudinal evaluation in the US population. Addiction 107, 1847–1856.
Wells, J.E., Haro, J.M., Karam, E., Lee, S., Lepine, J.P., Medina-Mora, M.E., Nakane, H., Posada, J., Anthony, J.C., Cheng, H., Degenhardt, L., Angermeyer, M., Bruffaerts, R., de Girolamo, G., de Graaf, R., Glantz, M., Gureje, O., 2011. Cross-national comparisons of sex differences in opportunities to use alcohol or drugs, and the transitions to use. Subst. Use Misuse 46, 1169–1178.
WHO, 2005. Alcohol, Gender and Drinking Problems: Perspectives from Low and Middle Income Countries. WHO, Geneva.
Yang, F., Zhao, H., Wang, Z., Tao, D., Xiao, X., Niu, Q., Wang, Q., Li, Y., Guo, L., Li, J., Li, K., Xia, J., Wang, L., Shang, X., Sang, W., Shao, C., Gan, Z., He, K., Zhao, X., Tian, T., Xu, D., Gu, D., Weng, X., Li, H., Tian, J., Yang, L., Li, Q., Yang, Q., Wang, H., Dang, Y., Dai, L., Cui, Y., Ye, D., Cao, J., Kang, Z., Liu, J., Chen, B., Zhang, J., Yang, D., Jiao, B., Yu, F., Geng, F., Li, L., Yang, H., Dai, H., Liu, C., Liu, H., Peng, L., Wang, X., Wei, S., Liu, X., Li, C., Liu, Z., Zhang, Q., Di, D., Flint, J., Shi, S., Kendler, K.S., 2014. Age at onset of recurrent major depression in Han Chinese women – a replication study. J. Affect. Disord. 157, 72–79.
Zhao, Y., Hu, Y., Smith, J.P., Strauss, J., Yang, G., 2014. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). Int. J. Epidemiol. 43, 61–68.
Zhao, Y., Strauss, J., Park, A., Shen, Y., Sun, Y., 2009. China Health and Retirement Longitudinal Study – Pilot Users' Guide.