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Pattern and risk of developing alcohol use disorders, illegal substance use and psychiatric disorders after early onset of alcohol use: Results of the Thai National Mental Health Survey 2013



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ABSTRACT

Introduction: Although underage drinking is a global concern, little is known about the relationship between age at first drink and development of various psychiatric comorbidities.

Methods: A secondary data analysis was done among 2928 lifetime drinkers from the Thai National Mental Health Survey 2013. Age at first drink, and onset of related psychiatric outcomes were inquired. Survival analysis using Cox regression was performed to estimate the risk over time for psychiatric problems across age ranges at first drink.

Results: Two-thirds of male and one-third of female drinkers were considered underage at drinking onset. Substance use and abuse developed earlier (<5 years) than alcohol use disorders (AUDs) and other outcomes (mostly >10 years). Those who started drinking before age 15 years were more likely to develop use of cannabis (HR = 4.75; 95% CI 2.73, 8.24), club drugs (HR = 2.88; 95% CI 1.46, 5.71) and inhalants (HR = 6.46; 95% CI 1.64, 25.37), compared to those who were 20 years or older at drinking onset. Using age as an alternative time-scale, those aged <15 years at drinking onset were significantly more likely to experience AUDs, psychotic symptoms, intermittent explosive disorder and panic disorder. However, the early onset drinkers were less likely to develop depression compared to those who started at age 20 years and over.

Conclusion: Premature alcohol consumption tends to be a gateway to various serious consequences. Efforts of such drinking age policy and interventions are needed to address vulnerable young populations.

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1. Introduction

Underage drinking has been a steadily serious problem for many decades worldwide. In 2013, approximately one-fourth of US adolescents currently drank alcohol and 14% of these were defined as binge (i.e., ≥ 5 drinks on the same occasion) drinkers (Patrick and Schulenberg, 2014). A national survey in Thailand, which has the same legal drinking age as the United States, found that 25.5% of male and 14.5% of female students were past year drinkers (Assanangkornchai et al., 2009). The rates of counterparts in European countries might be even higher due to the lower legal age for drinking (Anderson et al., 2012). Although the age which is consid-

ered to be appropriate or acceptable to drink alcoholic beverages varies across nations, there is consistent agreement concerning the effect of alcohol on adolescents, both biologically and behaviorally. Exposure to alcoholic beverages before or during the early teenage years has been linked to increased heavier drinking habits (Eliassen et al., 2009; Strunin et al., 2007), development of more severe, recurrent and persisting alcohol use disorders (Hingson et al., 2006), traffic accidents (Gruber et al., 1996; Hingson et al., 2008) and involvement of alcohol related self-harms and harm to others (Hingson and Zha, 2009), all of which might persist in adulthood (McCarty et al., 2004). Pathological pathways responsible for these impacts have been well established. Adolescents who consume alcohol earlier have been observed with a reduced volume of hippocampus, prefrontal cortex as well as white matter, resulting in deleterious alterations of various cognitive abilities including memory, planning and spatial tasks (De Bellis et al., 2005, 2000).

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Alcohol use and psychiatric illnesses are commonly co-occurring disorders as well as being important predictors for each other, depending on whichever came first. A large 10-year follow-up cross-sectional study found that the odds of developing alcohol and drug use disorders were 2–5 times higher among persons with anxiety and depressive disorders (Swendsen et al., 2010). Conversely, the chance of developing depressive disorders had a dose-response relationship with alcohol use severity (Gilman and Abraham, 2001). Along with nicotine and cannabis, alcohol is also believed to be the starting drug according to the gateway drug theory in which the more harmful and addictive drugs are causally preceded by relatively milder ones. Although this gateway drug theory has been supported in some studies (Chen et al., 2002; Kirby and Barry, 2012), many have questioned the universal existence of this causal relationship and suggested the prevalence of the initial drug use in a specific time and setting to be confounder of the relationship (Degenhardt et al., 2010; Vanyukov et al., 2012). Given the fact that exposure to alcohol during adolescence introduces irreversible structural and functional changes to the brain, the chances of developing subsequent comorbidities could be plausibly increased. Studies among school-aged population revealed the associations between various psychiatric illnesses, including mood disorders and psychotic symptoms, and alcohol use even in a subdiagnostic pattern (Deas, 2006; Rohde et al., 1996; Shrier et al., 2003).

Unfortunately, studies regarding these issues have been largely concentrated in northern American and European regions, and relatively little is known about alcohol use in countries with different sociocultural and economic backgrounds. Knowledge about relationships between onset of alcohol use and co-occurring substance use is also limited to conventional so-called “gateway drugs,” resulting in an underestimation of the problem of more extensive illicit substances. Moreover, previous studies which explored relationships between alcohol use and mental health disorders have some limitation issues due to unclear chronology between age at first alcohol use and onset of the illnesses. Altogether, the results of these studies are difficult to compare, due to the different analytic approaches, study populations, as well as study time and setting. The main objective of this study is to determine the effect of age at first alcohol consumption on development of various psychiatric consequences including alcohol use disorders (AUDs), common illicit substance uses and abuses (IUDs) as well as DSM-IV alcohol related mental disorders. The secondary objectives are to describe the prevalence of underage drinking as well as the differences in prevalence and time sequence of developing each psychiatric consequence across ages of drinking onset. Our hypothesis is that younger persons exposed to alcohol are more likely to develop various related psychiatric problems.

2. Methods

2.1. Data source and study population

The study used data from Thai National Mental Health Survey 2013 (TNMHS2013) conducted in four districts of Bangkok and 16 provinces of Thailand. TNMHS2013 was aimed to estimate the current national prevalence and relevant information of mental health problems as well as mental wellbeing. The survey was carried out following the protocol of the World Mental Health Survey Initiative (“The World Mental Health Survey Initiative,” n.d.). In brief, a stratified four-stage cluster sampling strategy was used to select national representatives of aged 18 years and older, non-institutionalized who had been living in a private household for at least 3 months. Disproportional sampling technique was used to assure the equal sample sizes from five strata, which were comprised of one Bangkok

metropolitan area and all four regions of Thailand (i.e., north, northeast, central and south). Districts of Bangkok and provinces of each region (i.e., primary sampling units), enumeration areas, households and eligible members in each household served as sample frames for respective sampling stages. The detailed sampling methods for each sampling stage are described elsewhere (Kittirattanapaiboon et al., 2016). Of a total of 4727 respondents who completed the full survey, 2928 lifetime drinkers, defined by having ever consumed at least one drink (10g of alcohol) of any alcoholic beverages on one occasion, were included in the present study. The original national survey as well as the present study received ethical approval by Ethical Review Committee for Research in Human Subjects, Ministry of Public Health.

2.2. Measures

The WMH version of World Health Organization Composite International Diagnostic Interview (WHO-CIDI 3.0) (Kessler and Üstün, 2004) was the main instrument used in TNMHS2013. WHO-CIDI is a fully structured, face-to-face, DSM-IV and ICD-10 based diagnostic interview used in many mental health surveys worldwide (Kessler et al., 2009; Wang et al., 2007). Internal validity (area under the receiver operator curve) and reliability of overall psychiatric diagnosis of the instrument are generally acceptable (Haro et al., 2006; Kessler et al., 2004). In the Thai translated version, selected sections for a national survey included screening for depression, mania, panic disorder, agoraphobia, generalized anxiety disorder, intermittent explosive disorder, suicidality, alcohol use, illegal substance use, tobacco use, psychosis, gambling, post-traumatic stress disorder, service, chronic conditions and demographic data. Content validity of the questionnaire was made by agreement among a group of three psychiatrists, cognitive comprehension was tested on persons diagnosed with major psychiatric illness and a pilot study was carried out in selected areas to revise wordings of the questionnaire. Questionnaires were read and completed by trained personnel, who were mostly nurses, at the private area of the respondent's house to maintain confidentiality regarding sensitive issues.

2.3. Age at drinking onset and covariates

Age at first drink was categorized into three levels, with cut-offs differentiating early teenage years (<15 years), later teenage years (15–19 years old) and adult years (20 years old and over, the age at which drinking is legally permitted in Thailand). Sex, age at interview, region and area of residence, income, smoking status and family history of alcohol related problems were included in the analysis on the basis of their possible relationship with age at first drink. Current age was categorized into six groups (18–24 years; 25–34 years; 35–44 years; 45–54 years; 55–64 years and 65 years and over) corresponding to the original report of the national survey in order to be comparable with the main study (Kittirattanapaiboon et al., 2016). Monthly income (≤5000; 5001–15,000; 15,001–30,000 and more than 30,000 baht) was selected as it could indirectly reflect individual economic background. Smoking status was categorized into “never smoke” and “ever smoke” (currently or previously smoked). Family history of alcohol problems was derived from the item “How many of your close relatives – including your biological parents, brothers and sisters, and children – ever had problems with alcohol use?”. Respondents who reported one or more first degree relatives were classified as having a family history.

2.4. Outcomes

Alcohol related outcomes included in this study were lifetime alcohol abuse, lifetime alcohol dependence and current drinking patterns. Alcohol abuse and alcohol dependence herein were separate DSM-IV diagnoses, with dependency higher in the diagnostic hierarchy (i.e., respondents who met the criteria for both alcohol abuse and dependence were categorized as having dependence only). Age at first experience of abuse or dependence was inquired if the respondent reported information that met sufficient criteria for abuse or dependence. Illicit substance outcomes included experience of ever use and abuse of club drugs, cannabis, heroin, cocaine, inhalants, hallucinogens and non-medical sedatives. Respondents were asked whether they ever used each individual substance and then were asked about age at first use. Those who reported having ever used each substance were subsequently questioned about problems related to abuse or dependence as well as age at first experiencing sufficient criteria for each disorder.

Other psychiatric outcomes were those established in DSM-IV “Alcohol induced mental disorders” categories, including mood disorders (major depressive disorder, dysthymic disorder and bipolar disorders), anxiety disorders (generalized anxiety disorder and panic disorder), impulse control disorders (intermittent explosive disorder) and psychotic symptoms. Diagnoses were derived based on the DSM-IV algorithm except for psychosis, which was defined as having a history of any psychotic symptoms (hallucinations or delusions) rather than meeting the full criteria for psychotic disorders. Respondents who reported positively for screening questions of each mental disorder were subsequently asked about detailed questions including diagnostic criteria in each corresponding mental disorder section. Age at onset of each mental disorder was derived from a question regarding age at first experiencing operational criteria of that disorder in each individual section. Due to very low positive responses and unavailable age at onset data of some diagnostic categories, the outcomes remaining in the subsequent analyses were alcohol abuse and dependence, club drugs use and abuse, cannabis use and abuse, inhalants use, opioid use, depressive disorders, panic disorder, psychotic experiences and intermittent explosive disorder.

2.5. Statistical analysis

Descriptive statistics were used to present the prevalence, distributions and risks of psychiatric consequences according to age at first alcohol consumption. Frequency, weighted mean age of first drink and proportions of age group at onset, with estimated standard errors, were described according to demographic characteristics, drinking pattern and psychiatric outcomes. Chi squared tests were used to assess bivariate associations between age groups of drinking onset and each categorical variable with a *p*-value of less than 0.05 regarded as significant.

Survival analyses, in which time variables were controlled, were used to describe the effect of age at first drink on various outcomes. Given the age at first drink the starting point of observation for each subject, time to reach an outcome in years was derived by the interval between age at first drink and age at first use, abuse, dependence or meeting the diagnostic criteria. Persons who did not experience the outcome by the date of survey were treated as censored, giving the interval between age at first drink and age at survey the time for not experiencing that outcome. Those who reportedly developed a psychiatric outcome on the same or less than age at onset of alcohol use were excluded to ensure that initial drinking preceded the outcome, except for alcohol use disorders which always came after initial drinking onset. Kaplan-Meier curves (Rich et al., 2010) were constructed to graphically compare the cumulative proportion of events occurring over time for each subgroup.

Cox proportional hazards models were fit to estimate the hazard ratios over time of developing psychiatric outcomes between different onset age groups, using 20 years and older at onset as the reference group. Models for predicting AUDs and IUDs were controlled for current age (i.e., birth cohort), sex, area of residence, region, income, smoking status and family history of alcohol problems. Past year amount of alcohol use per drinking day (i.e., number of drinks consumed per drinking day) was also controlled as it has been suggested that having a binge drinking pattern increased the risk for negative health outcomes, regardless of when the person started drinking (Naimi et al., 2003). The model for predicting alcohol related mental health disorders were additionally adjusted for lifetime illicit substance use. Multicollinearity was checked by calculating a variance inflation factor (VIF) for each Cox model where all variables were included. We found that there was not likely to be any multicollinearity since all VIF values were less than 1.5. The choice of time scales for the model has been discussed by other studies, mostly based on choosing between time-on study and attained age. Previous survival analytic studies related to our topic mostly used time since first drink (i.e., time-on-study) as the time scale to determine the effect of age at first drink regardless of how long the exposure to alcohol (DeWit et al., 2000; Hingson et al., 2006). However, it has been argued that, for some diseases, the effect of age on an individual's hazard is usually greater than the effect of time on study. Moreover, age effects often fail the proportional hazards assumption and therefore choosing age as time-scale is more appropriate (Griffin et al., 2012; Korn et al., 1997). We decided to use both time since first drink and age as time-scales to see whether there is any difference between two types of models. Scaled Schoenfeld residuals distribution was then evaluated to test for proportional hazard assumption by two methods (Beyersmann, 2009). Pearson correlations of the residuals of age of onset and each covariate with elapsed time were tested individually and globally. To deal with violation of assumption, any covariate that yielded statistical significance of inconstant hazard over time was then stratified to omit its coefficient until all individual and global chi-square values became non-significant value.

Data were analyzed using R. Post-stratification weights for strata according to the 2010 Population and Housing Census and compensation for non-response rate were applied to adjust the estimates and standard errors.

3. Results

3.1. Age of drinking onset by demographic covariates

Table 1 compares the mean ages at drinking onset for various demographic characteristics. Underage drinking (age <20 years) was more prevalent among males compared to females (67.9% vs. 35.5%), younger people (91% of 18–24 years old vs. 32% of >60 years old), resident of southern and central regions (62% of southern, 59% of Bangkok and 57% of central region) and smokers (67% vs. 43% of never smoke). There were no differences between prevalence of underage drinking among persons who lived in urban and rural areas across regions and among persons with different economic backgrounds.

3.2. Current drinking patterns and psychiatric outcomes by age of drinking onset

As shown in Table 2, subjects who began drinking before age 15 had a significantly higher proportion of weekly binge drinkers (19% vs. 11%) and monthly intoxicated drinkers (17% vs. 6.5%) compared with those who started drinking at age 20 years or higher. The most common illegal substances used among lifetime alcohol

Table 1

Mean age and proportions of age group (2 levels) at onset of alcohol use by demographic characteristics.

										Mean age at first drink ^a	Age onset of drinking groups ^a				p-value				
										Total	Male	Female	Before 20 (n = 1318)			After 20 (n = 1610)			
													%	SE		%	SE		
n ^b																			
Sex																			
Males										1509	18.6	–	–	67.92	1.27	32.08	1.27		<0.001
Female										1409	24.5	–	–	35.47	1.70	64.53	1.70		
Region																			0.019
Bangkok										422	19.8	18.0	22.4	58.56	1.31	41.44	1.31		
Central										639	20.6	18.3	24.2	56.77	2.42	43.23	2.42		
North										719	21.0	18.8	24.2	53.23	2.32	46.77	2.32		
Northeast										670	22.0	19.1	25.9	51.33	2.87	48.67	2.87		
South										478	20.2	18.5	25.2	62.07	1.28	37.93	1.28		
Area																			0.215
Urban										1468	20.9	18.6	24.2	53.87	1.40	46.13	1.40		
Rural										1460	20.9	18.6	25.0	56.81	1.97	43.19	1.97		
Age (years)																			<0.001
18–24	25–35	35–44	45–54	55–59	60+					169	16.4	16.0	17.0	90.50	2.81	9.50	2.81		
										381	18.3	17.3	19.7	66.72	2.67	33.28	2.67		
										640	20.0	17.5	23.5	58.01	2.30	41.99	2.30		
										706	22.7	19.0	28.4	43.42	2.11	56.58	2.11		
										301	24.0	19.8	31.0	32.03	2.62	67.97	2.62		
										731	26.0	24.5	33.2	31.95	1.95	68.05	1.95		
Monthly income (baht)																			0.158
≤5000	5001–15,000	15,001–30,000	>30,000							1483	22.0	18.9	25.4	52.12	2.52	47.88	2.52		
										982	21.1	18.4	23.8	58.30	1.79	41.70	1.79		
										317	19.6	18.4	22.2	58.81	3.36	41.19	3.36		
										146	19.4	18.3	22.4	56.03	5.31	43.97	5.31		
Smoking status																			<0.001
Ever smoke										1395	18.8	18.5	23.0	66.95	1.31	33.05	1.31		
Never smoke										1533	23.1	19.0	24.7	42.76	1.97	57.24	1.97		
Family history of alcohol use																			<0.001
Yes										324	18.1	17.6	20.8	75.41	2.30	24.59	2.30		
No										2604	21.3	18.8	24.8	52.24	3.30	47.76	3.30		
Education																			<0.001
Primary or less										1664	23.3	19.9	28.7	43.91	1.58	56.09	1.58		
Junior high										313	18.9	17.6	21.1	66.91	3.48	33.09	3.48		
Senior high										541	19.2	17.6	21.8	61.65	2.78	33.35	2.78		
Tertiary or higher										410	18.7	17.5	20.4	66.52	1.86	33.48	1.86		

^a weighted results.^b non-weighted data.

Table 2
Recent drinking patterns and psychiatric outcomes by age onset of alcohol use (3 levels).

	Age onset groups ^a						p-value
	<15 (n=198)		15-19 (n=1120)		After 20 (n=1610)		
	%	SE	%	SE	%	SE	
Past 12 months ≥ 1 drink(s)							<0.001
Every day	7.70	1.76	6.27	0.92	3.25	0.42	
Nearly every day	6.67	2.05	6.71	1.00	3.68	0.66	
3 – 4 days per week	6.62	1.94	7.43	0.92	5.60	0.87	
1 – 2 days per week	7.22	1.50	12.37	1.41	7.67	0.78	
1 – 3 days per month	15.29	3.62	13.91	0.97	7.68	1.01	
Less than once a month	14.46	2.48	15.86	1.52	13.55	0.74	
Did not drink in past 12 months	42.04	4.10	37.45	1.68	58.57	1.25	
Past 12 months ≥ 5 drinks							<0.001
Every day	4.00	1.17	3.44	0.59	1.01	0.31	
Nearly every day	3.60	1.44	4.23	0.93	1.68	0.63	
3 – 4 days per week	6.63	2.08	5.22	0.75	3.34	0.62	
1 – 2 days per week	5.05	1.57	9.40	0.93	5.32	0.99	
1 – 3 days per month	12.51	3.03	8.84	0.98	6.07	1.38	
Less than once a month	16.35	3.29	15.65	1.84	12.20	0.62	
Neve	51.87	4.52	53.21	2.15	70.38	1.81	
Past 12 months intoxication							<0.001
Every day	1.36	0.85	0.68	0.29	0.24	0.13	
Nearly every day	0.88	0.80	1.00	0.38	0.23	0.08	
3 – 4 days per week	2.45	1.49	1.32	0.58	0.45	0.19	
1 – 2 days per week	3.05	1.11	4.35	0.82	1.84	0.44	
1 – 3 days per month	9.37	2.61	6.60	0.83	3.82	0.85	
Less than once a month	22.81	2.64	22.25	1.72	14.55	1.43	
Never	60.08	4.00	63.80	2.56	78.87	1.76	
Past 12 months drink(s) per drinking day							<0.001
never	43.09	4.07	38.41	1.66	59.06	1.22	
1–4 drinks	30.61	3.69	38.16	1.51	30.74	1.28	
5 drinks and more	26.30	4.19	23.43	1.17	10.20	1.52	
Psychiatric outcomes							
Alcohol abuse	28.73	4.47	25.12	1.68	12.22	1.20	<0.001
Alcohol dependence	13.28	3.17	6.28	0.87	4.03	0.86	<0.001
Cannabis use	33.94	3.93	17.97	0.84	4.33	0.64	<0.001
Cannabis abuse	2.90	1.31	1.06	0.32	0.42	0.31	.019
Club drug use	18.80	3.06	13.05	1.13	3.05	0.69	<0.001
Club drug abuse	9.24	2.76	3.55	0.83	0.55	0.23	<0.001
Opioids use	1.47	0.69	1.37	0.39	0.23	0.07	0.001
Inhalants use	9.13	3.27	2.03	0.48	0.37	0.20	<0.001
Psychosis	9.52	2.98	5.75	0.77	5.34	0.67	0.229
Depression	0.95	0.32	1.29	0.34	1.97	0.42	0.141
Intermittent explosive disorder	5.62	1.88	3.46	0.62	2.08	0.54	0.061
Panic disorder	10.36	4.10	3.35	0.60	4.00	0.63	0.003

^a weighted results.

users who began drinking before age 15 were cannabis (34%), club drugs (19%) and inhalant (9%), all of which were significantly more prevalent than those who started drinking at a later age. Generally, those who began drinking before age 15 had a slightly higher prevalence of other mental health problems, such as nonorganic psychotic symptoms (9.5%) and depression (0.95%). Only panic disorder was significantly higher among the youngest onset groups (10.5%), compared to the oldest onset group (4.0%).

Fig. 1 displays the time intervals between drinking onset and development of various outcomes among subjects whose drinking occurred first. Those who started drinking before age 15 years old took a relatively longer time (median = 10 years) to develop alcohol abuse than those who started at later years (median = 8 years). Times for development of alcohol dependence were not different across age at drinking onset groups. Among young beginners, the most commonly used drugs were also the earliest used drugs after drinking onset for around 2 years, 3 years and 5 years in inhalants, cannabis and club drugs, respectively. Subsequent cannabis abuse, though less common, developed earlier than club drugs abuse in all age of onset groups. Among those who were subsequently comorbid with lifetime mental illnesses, those whose onset of drinking

occurred before age 15 developed earlier psychotic symptoms and later onset of depressive episodes, compared to those whose drinking onset occurred at 20 years old and after.

3.3. Survival analysis of psychiatric outcomes by age of drinking onset

Fig. 2 shows Kaplan-Meier curves illustrating cumulative probability of developing common comorbidities over time since drinking onset. The probability of developing AUDs continued to increase over 50 years of drinking, especially in young beginners, whereas the probability of both club drugs use and abuse became stable in 30 years. Additionally, the chances of inhalants and cannabis use remained constant ten years after drinking onset.

After adjusting for potential confounders, Cox proportional hazards models (Table 3) did not reveal significant difference in hazard ratios among both younger onset groups compared with older group of developing alcohol abuse and dependence. However, using years since birth as the time variable revealed a significantly increased hazard rate (HR) of developing abuse among onset <15 year (HR = 1.50; 95% CI, 1.02 – 2.22) and onset 15–19 years

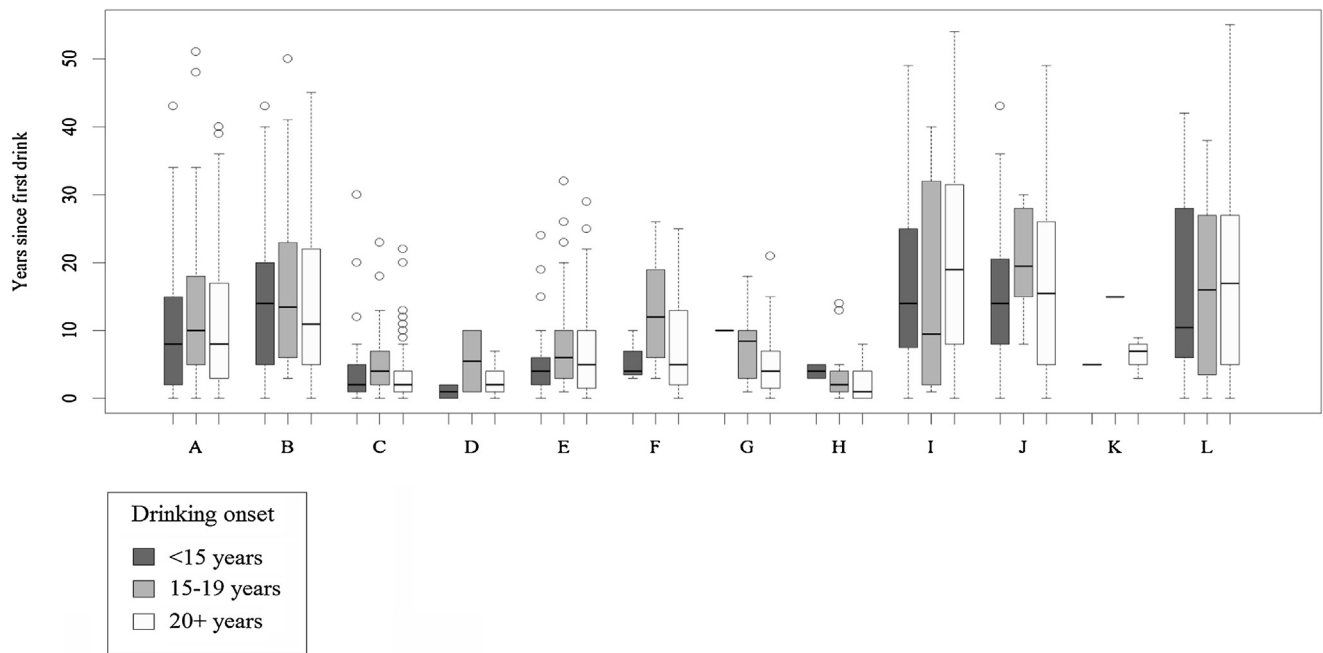


Fig. 1. Years since first drink to onset of each outcome according to age of drink onset. Both ends of the box represent interquartile range (between 1st and 3rd quartile) of each outcome. The band inside each box represents median of interval of developing each outcome. (A = alcohol abuse, B = alcohol dependence, C = cannabis use, D = cannabis abuse, E = club drugs use, F = club drugs abuse, G = opioid use, H = inhalant use, I = psychosis, J = depressive disorders, K = intermittent explosive disorder, L = panic disorder).

Table 3

Cox regression models showing the relationship between age at first drink and various psychiatric outcomes.

	Event/n. at risk	Age at first drink ^a	
		<15	15–19
Hazard ratios over years since first drink			
Alcohol use disorders ^a			
Alcohol abuse	398/2849	0.88 (0.59–1.31)	0.99 (0.79–1.23)
Alcohol dependence	134/2911	1.29 (0.64–2.60)	0.75 (0.42–1.35)
Illicit substance use ^a			
Club drug use	167/2892	2.88 (1.46–5.71)**	2.30(1.53–3.47)***
Club drug abuse	54/2922	5.04 (1.62–15.72)**	2.06 (0.80–5.29)
Cannabis use	187/2833	4.75 (2.73–8.24)***	2.16 (1.26–3.72)**
Cannabis abuse	18/2924	1.03 (0.22–4.83)	0.58 (0.11–3.04)
Opioids use	23/2921	40.22 (12.65–127.94) ***	36.95 (5.29–258.00) ***
Inhalant use	24/2916	6.46 (1.64–25.37)*	1.07 (0.18–6.40)
Sedatives use	117/2907	0.57 (0.24–1.33)	0.71 (0.45–1.12)
Mental disorders ^b			
Panic disorder	135/2859	1.30 (0.53–3.19)	0.64 (0.39–1.05)
Psychosis	128/2881	1.22 (0.53–2.82)	0.94 (0.56–1.57)
Intermittent explosive disorder	74/2921	0.11(0.03–0.49)**	0.21 (0.08–0.55)**
Depression	59/2913	0.26 (0.09–0.77)*	0.50 (0.26–0.95)*
Hazard ratios over years since birth			
Alcohol use disorders ^a			
Alcohol abuse	398/2849	1.50 (1.02–2.22)*	1.36 (1.08–1.72)**
Alcohol dependence	134/2911	2.23 (1.11–4.48)*	1.00 (0.57–1.76)
Illicit substance use ^a			
Club drug use	167/2892	4.02 (2.19–7.38)***	2.47 (1.73–3.54)***
Club drug abuse	54/2922	6.50 (2.19–19.24)***	2.41 (0.97–6.00)
Cannabis use	187/2833	5.69 (3.32–9.56) ***	2.82 (1.82–4.38)***
Cannabis abuse	18/2924	1.49 (0.31–7.10)	0.59 (0.12–2.95)
Opioids use	23/2921	41.33 (13.16–129.8)***	37.88 (5.49–261.5)***
Inhalant use	24/2916	8.14 (2.48–26.7)***	1.18 (0.24–5.66)
Sedatives use	117/2907	1.50 (0.82–2.73)	1.25 (0.82–1.91)
Mental disorders ^b			
Panic disorder	135/2859	2.86 (1.24–6.61)*	1.03 (0.61–1.73)
Psychosis	128/2881	2.49 (1.15–5.41)*	1.41 (0.71–2.83)
Intermittent explosive disorder	74/2921	2.82 (1.09–7.28)*	1.65 (0.60–4.53)
Depression	59/2913	0.71 (0.20–2.49)	0.98 (0.50–1.92)

+ Reference = 20 years and older, a: Adjusted for age, sex, income, region, area, smoking and family history; b: Adjusted for age, sex, income, region, area, past 12 months drink(s) per drinking day, family history of alcohol use and illegal substance use, p-value (Wald test) *** < 0.001; ** < 0.01; * < 0.05.

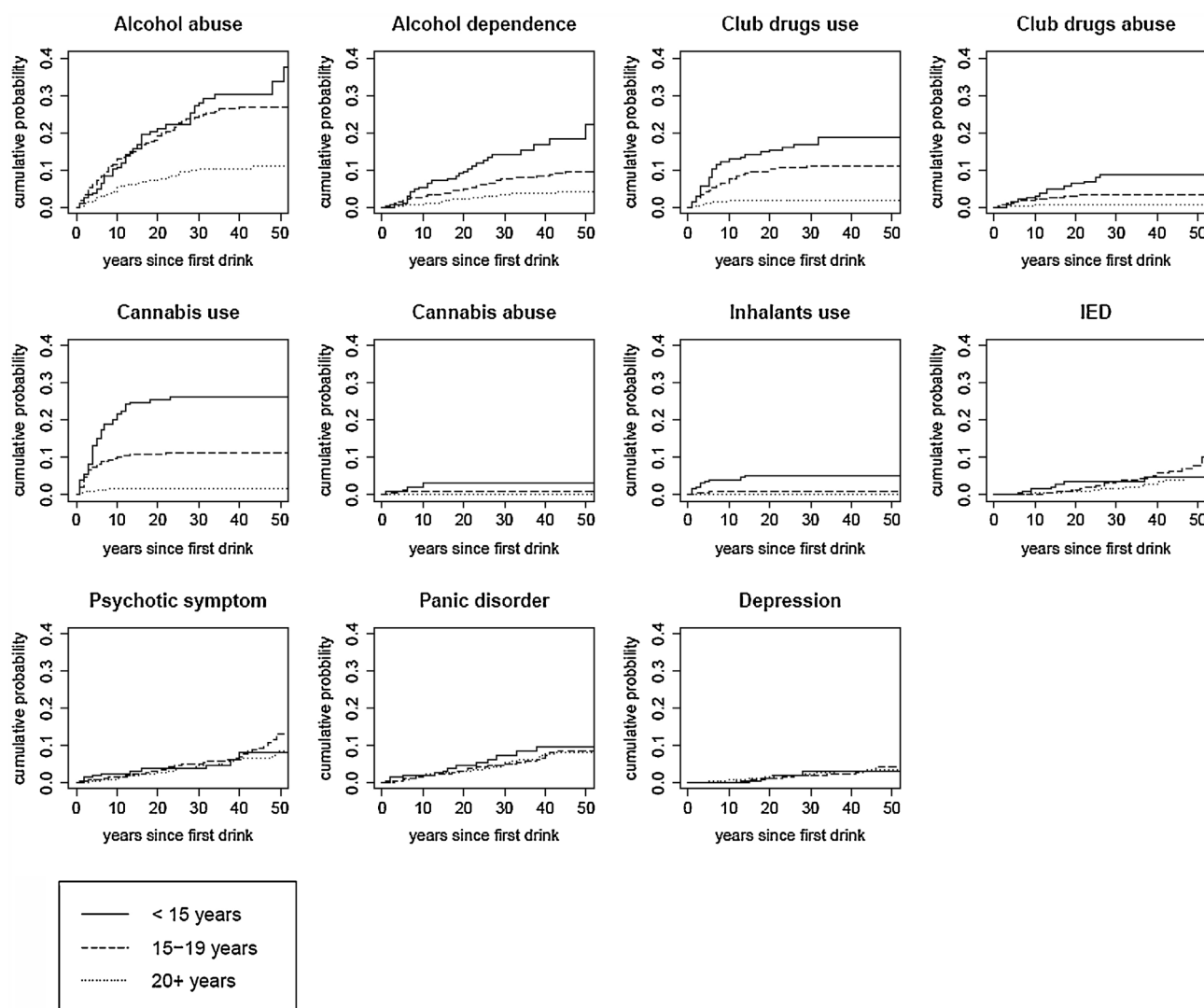


Fig. 2. Kaplan-Meier curves of psychiatric outcomes over years since first drink.

(HR=1.36; 95% CI, 1.08–1.72), compared to the onset ≥ 20 years group. Those who began drinking before age 15 were also more likely to develop dependence (HR=2.23; 95%CI, 1.11–4.48), compared to the oldest onset group.

In contrast to alcohol use outcomes, both <15 and 15–19 years at onset had increased hazards of using club drugs (HR=2.88; 95% CI, 1.46–5.71 and HR=2.30; 95% CI, 1.53–3.47, respectively), cannabis (HR=4.75; 95% CI, 2.73–8.24 and HR=2.16; 95% CI, 1.26–3.72) and opioids (HR=40.22; 95% CI, 12.65–127.9 and HR=36.95; 95% CI, 5.29–258.00) despite using years since first drink as the time variable. Those who drank before age 15 also had a higher hazard of inhalants use (HR=6.46; 95% CI, 1.64–25.37). The rate of subsequent abuse, however, was significantly increased only for club drugs among the youngest onset group (HR=5.04; 95% CI, 1.62–15.72).

Regarding mental health disorders, depression (HR=0.26; 95% CI, 0.09–0.77) and intermittent explosive disorder (HR=0.11; 95% CI, 0.03–0.49) were less likely to develop among those who initially drank before age 15 compared to those who started drinking on or after age 20. However, when using age as time scale, the hazards of developing psychotic symptoms, panic disorder and intermittent explosive disorder were increased among the youngest drinking onset group (HR=2.49; 95% CI, 1.15–5.41, HR=2.86; 95% CI,

1.24–6.61 and HR=2.82; 95% CI, 1.09–7.28, respectively), compared to those who started drinking on or after age 20.

4. Discussion

The findings emphasize two major issues regarding age of first alcohol use: the underage drinking onset and its consequences. The increasing percentage of underage drinking onset together with decreasing mean age of onset among both males and females in younger age groups indirectly imply the tendency of increasing magnitude of the problem among recent cohorts. Analysis of the overall 4727 subjects (not shown here) showed that the proportions of ever drinkers were similarly large among each age group (70%–76%), compared to the oldest group (60%). This indicates that even though some alcohol-naïve adults may start to drink later in their lives, the proportion of those who were underage at first drink may not be likely to remarkably change. The higher prevalence of lifetime alcohol use among young adults found in the current survey, compared to the previous national survey in 2007 in which lifetime alcohol use was found in 60% of Thai young male adults (Assanangkornchai et al., 2010), also signifies the increasing problem among youths.

Initially, the relationships between age of drinking onset and each AUD in the models using time since first drink were not

demonstrated. This result contrasts two previous survival analytic studies in which age at first drink was an independent predictor of AUDs by the time of first exposure (DeWit et al., 2000; Hingson et al., 2006). However, our alternative models using age as the time-scale showed that those who drank before age 15 years had significantly higher hazards of alcohol abuse and alcohol dependence. Together with results in Fig. 1, which showed that younger onset drinkers took a slightly longer time to develop AUDs than older onset drinkers, it seems that age at first drink has an effect on the risk of alcohol use disorders when the critical age of AUDs onset is reached. The difference between our finding and previous studies may be partly due to societal reasons. By considering the criteria of alcohol abuse, social problems tend to be endorsed when a person has responsibilities, such as a job, as they could see the effect of alcohol on their lives. Compared to Western counterparts, Thais generally start working at a later age, i.e., when they graduate from school or university. Therefore, they tend to meet the criteria at the same age regardless of when they start drinking.

On the other hand, those with early onset of alcohol use had increased hazards of using several illegal substances at any point after drinking onset. The tendency of the younger adolescents to rapidly use substances once they start drinking may highlight alternative pathways other than the direct impact of alcohol on subsequent drinking patterns. In Thailand, methamphetamines, marijuana and heroin are common among youths and are often used in the same situation and pattern as alcohol. These drugs are commonly shared among peer groups in which more experienced users may encourage beginners to try stronger drugs (Sherman et al., 2008). Thai drug users are also likely to combine different drugs with alcohol to enhance desired effects and to reduce the cost of more expensive drugs (Werb et al., 2009). The vulnerability of psychological and emotional changes during teenage years, with or without effects of alcohol on impulse control (Boes et al., 2008; Verdejo-García et al., 2008), may act in concert with external environmental factors, such as alcoholic peer pressure, on risk taking behaviors of young beginners more than their older peers (Rai et al., 2003; Steinberg et al., 1994). Inhalants are also likely to be used more during early teenage years. In Thailand, glues, lacquer and thinner are inhalants commonly used among early and middle adolescents because of their cheap price and wide availability (Kin, 1995; Poshychinda et al., 2005). Use and abuse of these inhalants remains a serious problem, especially in slum areas (Embleton et al., 2013). However, due to the availability, convenience of access and relatively more social and legal acceptance, alcoholic beverages tend to be nearly always used prior to any other substances. Accordingly, it is difficult to exclude the possibility of more genetically extreme subtypes who could readily use alcohol together with multiple substances at an early age (Galvan et al., 2007; Johnson et al., 2000).

Noteworthy are the trivial trends regarding the hazard over time of using and abusing some substances observed in this study which indicate that the very early years after first alcohol exposure is a critical period for developing further negative consequences. These findings underscore the importance of prompt, extensive and intensive screening for co-occurring substance use as soon as drinking behavior has been acknowledged. Also, further prospective studies examining the pathway mediating between initiation of alcohol use and development of substance use through these critical periods will provide more insight about targeted strategies to prevent or delay alcohol use and subsequent substance use among young drinkers.

After years since first drink, subjects with different starting ages seem not to differ in rates of developing non-organic psychotic symptoms and panic disorder. Also, those who started drinking before 15 were, surprisingly, less likely to develop IED sooner than those who started drinking after 20. However, as suggested from

the contradiction between Table 2 and Fig. 2, respondents with younger drinking onset were more likely to eventually develop these disorders than were older beginners but at a different rate from the older counterparts. Repeated Cox models which used years since birth concordantly revealed that those with younger drink onset were more likely to develop earlier panic disorder, non-organic psychotic symptoms and intermittent explosive disorder. This indicates that, as with alcohol use disorders, risks of these mental illnesses among those who started drinking before age 15 seem to increase with age, rather than time since first exposure. In the case of intermittent explosive disorder, impulse control deficit could result from altered neurocognitive functions after exposure to alcohol during adolescence (Li et al., 2009). However, there are a number of undetectable “in-between” confounders that might mediate the manifestation of intermittent explosive disorder such as parental nurturing, behavioral shaping from society, as well as continuation of successive drinking (Kuppens et al., 2013; Lee et al., 2014).

With respect to depressive disorders, there were reversal relationships against our hypothesis. A reasonable explanation for this may be understandable from previous observations that much more of those who had such comorbidity developed depression before using alcohol (Abraham and Fava, 1999; Kuo et al., 2006). These studies also found that the effect of depression on initiating alcohol use was substantial whereas the opposite direction of relationship was negligible. This agrees with our findings given that prior to onset of full blown depression, which commonly began in adult life, the affected adults might have suffered from longstanding distress of subclinical depressive symptoms (Allen et al., 2014; Angold et al., 1998; Hasin et al., 2005). Accordingly, more tend to start self-medicating with alcohol to relieve their suffering during late adult years. In this regard, older age at drinking onset might rather be an indicator than a predictor of undermining depression.

A number of cautious considerations are needed in interpreting the results. First and most important, an inherent weakness of a cross-sectional study is the lack of temporal evidence for causal relationships between covariates and outcomes and within covariates. Alcohol use of first degree relatives may be either a predisposing factor or a reaction to the drinking behavior of respondents. Also, recall biases may arise among persons who did not experience serious mental disorders and could not remember the year or even existence of the onset or, on the other hand, from persons who suffered from any consequences and could even remember all details of the onset (Sartor et al., 2011). This would yield either an over or underestimation of the strength of relationship and inevitably affect the reliability of the analysis. Another limitation arising from the nature of community-based studies is selection bias. By the exclusion of subjects who were hospitalized and/or incarcerated, subjects with heavier alcohol use and severe outcomes or serious physical and mental illnesses were not represented. Furthermore, these people tend to be involved in accidents or die prematurely (i.e., survival bias). Together with nonresponse bias, which could also occur due to legal or cultural prohibitions of alcohol and substance use, some associations could be underestimated. In addition, a number of potential confounders such as childhood negative experiences and childhood onset psychiatric comorbidities were not examined due to unavailability of data from the survey. However, contradicting results among studies that evaluated the effect of child abuse on alcohol related consequences suggested that history of child abuse may itself be confounded with history of parental alcohol problems (Shin et al., 2009; Widom et al., 2007).

Despite these limitations, this study has many advantages in terms of analytic strategies and generalizability. This nationwide community-based survey can elicit information from subjects with milder forms of mental health problems who never sought services,

thus, this population could be well represented. Weighted analyses were conducted to get better precision of estimates. The analysis has an advantage in controlling for time variables and contributes more detailed information. To our knowledge, this is the only study in which effects of underage drinking on the development of a variety of comorbidities were examined altogether on the same study sample so that prevalence, time sequence of onset and effect sizes could be directly compared. Lastly, the key results reported in the study, in spite of possible underestimation, provide considerable implications for clinical practice and suggestions to focus on issues for future research.

Age at first alcohol consumption is one of the strongest predictors of various psychiatric consequences including alcohol and illicit substance use disorders. These findings, together with the trend of increasing magnitude of underage drinking problems, warrant a comprehensive strategy from policymakers, providing the screening for clinical intervention to reduce and delay premature alcohol consumption and prevent young drinkers from developing further negative outcomes. Drinking initiation at rather older ages also calls for a thorough searching for undermining comorbidity, especially depression. Furthermore, the increased likelihood of many consequences during the early years after exposure to alcohol highlight the critical time frame for intervention and future research for understanding the interrelated pathway.

Conflict of interest

No conflict declared.

Author disclosures

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Contributors

Athip Tanaree developed conception and design of the work, performed data analysis and interpretation and wrote the manuscript. Sawitri Assanangkornchai supervised conception and design of the work and provided critical revision of the article. Phunnapa Kittirattanapaiboon was the Principal investigator of TNMHS2013, the source of data for this article, and provided critical revision of the article. All authors contributed approval of the final version of the manuscript.

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