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Psychosocial Problems Syndemically Increase Adolescent Substance Use

Findings From a Cross-sectional Survey of 82,812 Chinese Adolescents

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Abstract: A growing body of studies have indicated the associations between substance use and psychosocial problems in adolescents. However, few of them have examined whether these psychosocial problems form a syndemic, which means the co-occurrence of psychosocial problems accompanied by additional effects on substance use.

We conducted a cross-sectional survey with 82,812 Chinese adolescents who were selected using a multistage random procedure. Bivariate associations were estimated between selected syndemic indicators and adolescent substance use. Multivariate logistic regression was used to estimate the association between the syndemic indicator count score (the count of syndemic indicators) and adolescent substance use. In addition, cluster analysis was used to partition participants reporting at least one of syndemic indicators to assess associations between resolved cluster memberships and adolescent substance use.

All selected syndemic indicators were associated with each other and with adolescent substance use. As the number of syndemic indicators increases, stronger associations with substance use were found in our analysis: the range of adjusted OR was from 1.57 (95% CI: 1.38–1.79) for 1 syndemic indicator to 9.45 (95% CI: 7.60–11.76) for 5 or 6 syndemic indicators. There was no effect modification of gender on these additive associations. The multivariate logistic regression indicated that the cluster membership of nonlow SES academic failures has the highest odds of using substance (OR = 2.26, 95% CI: 2.12–2.41), compared to students reporting none syndemic indicators.

Our findings support the syndemic hypothesis that adolescents bearing multiple psychosocial problems experience additive risks of

using substance. Our findings support that a comprehensive approach to substance use prevention in adolescents would necessitate the involvement of a variety of providers.

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Abbreviations: CES-DC = the Center for Epidemiology Studies Depression Scale for Children, CI = confidence interval, OR = odds ratio, PBT = problem behavior theory, SD = standard deviations, SES = socioeconomic status.

INTRODUCTION

Adolescent substance use is a public health epidemic worldwide. A large body of studies has indicated the associations between adolescent substance use and psychosocial problems, including depression,^{1,2} peer bully,^{3,4} school violence,^{4,5} school absence⁶ or dropout,^{7,8} academic failure,⁹ family structure,¹⁰ and family socioeconomic status (SES).¹¹ Studies also suggested that these psychosocial problems tend to cluster and interconnect with each other.^{12,13} Although researchers have been aware of the interdependence of substance-use-related psychosocial problems in adolescents for a long time, few of them have examined whether these problems form a syndemic association with substance use, which means the co-occurrence of psychosocial problems accompanied by additional effects on substance use.

The term “syndemic” was initially used in medical anthropology to explain the co-occurrence of health conditions and social disparities exacerbating one another to produce an overall health effect more negative than any individual condition.¹⁴ Unlike the term “comorbidity” that describes 1 or more additional disorders (or diseases) co-occurring with a primary disease or disorder in medicine, the syndemic approach focuses on communities experiencing co-occurring epidemics that additively increase negative health consequences. Furthermore, instead of treating social determinants as confounders, syndemic theory acknowledges social determinants as important components in disease etiology and may provide environment for other health conditions or problems to interact and then produce an excess harm on overall wellbeing.¹⁵ In the past decades, syndemic theory has been widely used in public health research, especially in the marginalized populations.^{16–19} However, few studies have extended this theory to the general population except for 1 recent study, which investigated the syndemic of psychosocial problems on suicide attempts in men with different sexual orientations, including heterosexual men.²⁰ This study is significant because it demonstrates that syndemic is not unique to the marginalized population, but also exists in the general population.

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To our limited knowledge, syndemic theory has not been applied to study substance use in the general adolescents. We hypothesized 6 psychosocial problems, including depression, bully, academic failure, school absence, coming from non-nuclear family, and low family SES will operate syndemically to affect the extent to which adolescents engage in substance use. Understanding the syndemic of psychosocial problems on adolescent substance use is of significance for many reasons. First, it helps us to understand whether or not adolescents reporting multiple psychosocial problems suffer an excess burden of substance use, which has not been addressed in the prior literature. Second, the recognition of this syndemic can help to guide screening approaches for the co-occurrence of psychosocial problems that may exacerbate substance use in adolescents. Finally, comprehensive interventions guided by syndemic orientation can be developed, which may increase the cost-effectiveness of our efforts to eliminate substance use epidemic in adolescents.

We conducted a study to understand the syndemic of psychosocial problems on adolescent substance use. Our primary aim was to test the hypothesis that the syndemic of depression, bully, academic failure, school absence, coming from non-nuclear family, and low family SES have an additive association with substance use, including current smoking, current alcohol use, and lifetime illicit drug use in adolescents. As men may disproportionately suffer from substance use, the effect modification of gender in the association between syndemic of psychosocial problems and substance use was also investigated. In addition, to understand the relative importance of the different clusters of psychosocial problems, our secondary aim was to reveal how multiple psychosocial problems are clustered and associated with substance use by using cluster analytic methods.

METHODS

Participants

We conducted a cross-sectional study with school-based Chinese adolescents. Participants were consisted of all eligible students attending a random sample of classes in schools serving grades 7 to 12 in Guangdong province, China. Our samples were selected using a multistage random sampling of public and private junior high schools (grades 7–9), senior high schools (grades 10–12), and vocational schools (grades 10–12). In the first stage, we included all of the 21 administrative regions in Guangdong province, China. In the second stage, all schools serving students in grades 7 to 12 in each administrative region were stratified by type of school (junior high school, high school, and vocational school) and academic performance (superior school and regular school), and then grades 7 to 12 schools were randomly selected from the created stratas in each region. A total of 291 schools were finally selected in our study. In each elected school, we randomly selected 2 classes in each grade. The original data were collected from $N = 83,276$ students with a mean age of 16.01 years, between September 2011 and January 2012.

The study protocol was reviewed and approved by the ethics committees of Sun Yat-sen University. The principals of the schools attended by the participants also reviewed and approved the study procedure. Oral informed consent was obtained from each participant.

MEASURES

Syndemic Indicators and Count Score

As aforementioned, we specifically elected 6 psychosocial problems as syndemic indicators, including depression, bully, family structure, low family SES, academic failure, and school absence. We dichotomized all psychosocial problems to create a count score of the numbers of syndemic indicators to represent the co-occurring of psychosocial problems. The range of syndemic indicator count score is from 0 to 5 and above.

We used the *Center for Epidemiology Studies Depression Scale for Children (CES-DC)* to assess the depressive symptoms in adolescents,²¹ which is a modified version of the adult *Center for Epidemiological Studies Depression Scale (CES-D)*.²² The CES-DC has been widely used in many countries including China. The internal consistency of the Chinese version of the CES-DC is reliable ($\alpha = 0.82$).²³ We adopted the cutoff of a score >28 , indicating severe depressed mood consistent with major depression,²⁴ to define depression in our study.

Involvement in the bullying either as a bully or as the person being bullied or both was ascertained using standard wording adopted from previous bully studies.^{25,26} The respondents were asked to indicate (a) how frequently they had been bullied during the current school term and (b) how frequently they had bullied others during the current school term. The response categories were “not at all,” “once or twice,” “sometimes,” “about once a week,” and “several times a week.” Those who bullied others or were bullied at least once in the current school term were classified as engaged in bullying.

The family structure was ascertained by posing the question “Do your parents live in the same household as you in most or all the time?”, which was adopted from WHO Health Behaviour in School-aged Children (HBSC) study.²⁷ Respondents who live with single parent or none parents were classified as coming from non-nuclear family.

Participants were asked to rank the SES of their family on a 5-point Likert scale with the following question: “Imagine society as being like a ladder; 1 = at the bottom are those with the lowest standing/position, and 5 = at the top are those with highest standing/position. If you think about how your own family is compared with the rest of society, where would you place your family on this scale?” This measure was also adopted from the previous adolescent study;²⁸ however we changed the original 7-point Likert scale to 5-point Likert scale in order to be in accordance with other response items in our survey. Students who chose 1 out of 5 were regarded as coming from low SES family.

We measured academic performance of students with the question that “how do you evaluate your academic performance in the last school term?” The response item is a 5-point Likert scale; from 1 = “better than 20% of my classmates” to 5 = “better than 80% of my classmates.” Students who selected 1 out of 5 would be coded as academic failures. In terms of school absence, we asked the adolescents that how many days have they been absent from school without permission in the past 30 days, as usually used in the previous study.²⁹ Students who reported at least 1 day of school absence was coded as positive for school absence.

Substance Use

In our study, we assessed 3 types of substance use including current smoking, current alcohol use, and lifetime illicit drug use. Current smoking was defined as smoking at least 1

cigarette per day in the last 30 days (The question was that how frequently have you smoked cigarettes during the last 30 days? with response items: not at all, <1 cigarette per week, <1 per day, 1 to 5 per day, 6 to 10 per day, 11 to 20 per day, >20 per day). Current alcohol use was defined as drinking alcohol at least 10 times in the last 30 days, obtained by the responses to question about the consumption of any beer, wine, and spirits with possible responses: not at all, once or twice, 3 to 5 times, 6 to 9 times, 10 to 19, 20 to 39, and 40 times or more. Any lifetime use of illicit drugs was established from responses to the question that asked how many times the respondent had ever used a list of marijuana, amphetamines, hallucinogenics, cocaine, heroin, or ecstasy. Participants indicating used any kind of illicit drug in lifetime was coded as illicit drug users.

Covariates

We also collected a set of covariates including age, gender (male, female), parental education (categorized as at least 1 of them had a college degree and none of them had a college degree), and parental tobacco (at least 1 of them use tobacco, none of them use tobacco) and alcohol use (at least 1 of them use alcohol, none of them use alcohol).

Statistical Analysis

Subjects' demographic-characteristics, syndemic indicators, and substance use are summarized with means and standard deviations (SDs) for continuous variables, and with frequencies and proportions for categorical variables. Gender stratified analysis was used to compare the differences between women and men. Chi-square analyses, Fisher's exact tests, or *t* tests, whenever applicable, were used to test for the differences between 2 groups.

We followed the syndemic analytic framework in previous studies. In the first place, we estimated the prevalence of 6 syndemic indicators. Second, we calculated bivariate odds ratios (ORs) for each pair of syndemic indicators as well as their associations with substance use to determine whether the 6 psychosocial problems interconnect with each other. Finally, we calculated syndemic indicator count score based on the number of syndemic indicators reported, yielding scores ranging from 0 to 5 or more. Multivariate logistic regression was used to estimate the association between syndemic indicator count score and adolescent substance use.

Another objective of our study is to investigate the cluster of syndemic indicators to evaluate whether they contribute equally to adolescent substance use. The *k*-medians cluster analysis was used to group respondents who reported at least 1 syndemic indicator into homogeneous profiles. The *k*-medians partition method aims to minimize the distance between observed median scores and the cluster medioids and is therefore more robust to outliers.³⁰ We were aware of the limitation of cluster analysis; therefore both internal and external evaluations of cluster solution were carried out. We used the Calinski-Harabasz index to measure internal validity,³⁰ with higher values suggesting more distinct clusters. External validation of the cluster solution examined whether there were significant and meaningful differences between clusters on frequency of syndemic indicators. Once the cluster membership of each participants was determined, we created a new categorical variable to represent the cluster membership of each participant, those students reporting none syndemic indicator were coded as 0 or the reference group, the other students were coded according to resolved cluster solution.

Multivariate logistic regression was used to estimate the association between categories of cluster membership and substance use, using the cluster membership of students reporting none syndemic indicators as the reference.

Because of the multistage sampling procedure, all odds ratios (ORs) and 95% confidence intervals (95% CIs) were weighted by the probability of selection, and all frequencies were weighted with Taylor series linearization to adjust for variations in sample selection probability.³¹ For this part of the analysis, svy: table, svy:mean, and svy: logistic of STATA, version 12.1, software (StataCorp LP, College Station, TX) were used. All statistical tests were 2-tailed, and probability values <0.05 were considered statistically significant.

RESULTS

After excluding missing data on substance use, a total of 82,812 adolescents were finally included in our analysis. Table 1 presents the characteristics of our sample. The mean age of all respondents was 15.9 ranging from 12 to 18 years old. Female students accounted for 55.6% of our total participants. About 54% of respondents were high school or vocational school students (grades 10–12). The majority of participants (88.3%) reported that neither of their parents have a college degree. Approximately half of students (50.9%) reported that at least one of their parents use tobacco and 22.9% use alcohol.

Table 1 also presents the prevalence of syndemic indicators and substance use. The most prevalent syndemic indicator is academic failure (28.6%), followed by coming from non-nuclear family (18.6%), low family SES (13.5%), bully (13%), school absence (11.1%), and depression (8.9%). Generally, men were more likely to report syndemic indicators than women except for depression. The overall prevalence of any substance use in our sample was 9.1%. The most common substance used in our study was alcohol (5.7%), followed by tobacco (3.5%), and illicit drug (0.9%). Male participants tend to report higher prevalence of substance use than females, especially for tobacco.

Table 2 presents the bivariate associations between syndemic indicators and substance use, stratified by gender. In women, all 6 indicators were associated with each other except for the pair of low family SES and school absence. In addition, among those 6 syndemic indicators, only low family SES was not associated with substance use; the other 5 indicators were all associated with substance use, and the strongest association was found between school absence and substance use with OR = 2.57, 95% CI: 2.19 to 3.01. The associations of syndemic indicators and substance use in men were even more striking. All listed syndemic indicators were intertwined with each other and associated with substance use. Similar to females, school absence has the strongest association with substance use (OR = 2.46, 95% CI: 2.29–2.65).

Results of multivariate regression are summarized in Table 3. As the number of syndemic indicators increases, stronger associations with substance use were found in our analysis. For example, the adjusted OR was 1.57 (95%CI: 1.38–1.79) for participants reporting 1 syndemic indicator, compared to adolescents reporting none syndemic indicator, whereas respondents indicating 2 syndemic indicators had an OR = 2.27 (95%CI: 1.87–2.76), compared to adolescents reporting none syndemic indicator. This trend continues to students reporting 5–6 syndemic indicators had an OR = 9.45 (95%CI: 7.60–11.76). These additive associations hold for all 3 types of substance use in our study. The likelihood

TABLE 1. Demographic Characteristics, Syndemic Indicators, and Substance Use in Chinese Adolescents (N = 82,812)

Characteristic	Total No. (Weighted %)	Female No. (Weighted %)	Male No. (Weighted %)	P Value
Age, mean, years (SD)	15.9 (1.69)	16.1 (1.69)	15.9 (1.68)	$P < 0.01$
Grade				$P < 0.01$
Elementary school*	38,698 (46.5)	19,959 (43.7)	18,739 (49.9)	
High school* & Vocational school†	44,114 (53.5)	25,093 (56.3)	19,021 (50.1)	
Parental education				$P < 0.01$
None of them have college degree	73,429 (88.3)	40,451 (89.5)	32,978 (86.8)	
At least one of them have college degree	9383 (11.7)	4601 (10.5)	4783 (13.2)	
Parental tobacco use				$P < 0.01$
None of them use tobacco	39,408 (49.1)	20,920 (48.0)	18,488 (50.6)	
At least one of them use tobacco	43,404 (50.9)	24,132 (52.0)	19,272 (59.4)	
Parental alcohol use				$P < 0.01$
None of them use alcohol	63,419 (77.1)	34,843 (77.8)	28,576 (76.2)	
At least one of them use alcohol	19,393 (22.9)	10,209 (22.2)	9184 (23.8)	
Syndemic indicators				
Depression	7376 (8.9)	4354 (9.6)	3022 (8.0)	$P < 0.01$
Bullying	10,688 (13.0)	4807 (10.9)	5881 (15.6)	$P < 0.01$
Non-nuclear family	15,777 (18.6)	8170 (17.7)	7607 (19.7)	$P < 0.01$
Low family SES	11,352 (13.5)	5731 (12.5)	5621 (14.6)	$P < 0.01$
Academic failure	23,781 (28.6)	10,765 (23.7)	13,016 (34.5)	$P < 0.01$
School absence	9414 (11.1)	4781 (10.3)	4633 (12.1)	$P < 0.01$
Any substance use	7651 (9.1)	2557 (5.7)	5096 (13.2)	
Current tobacco use	3039 (3.5)	436 (0.95)	2603 (6.6)	$P < 0.01$
Current alcohol use	4764 (5.7)	2054 (4.6)	2710 (7.1)	$P < 0.01$
Lifetime illicit drug use	752 (0.9)	231 (0.53)	521 (1.4)	$P < 0.01$

SD = standard deviation; SES = socioeconomic status.

* Grades 7–9

† Grades 10–12.

ratio test rejected that the gender may modify the associations between syndemic indicator count score and adolescent substance use (chi-square:0.43, $P = 0.513$); therefore, we did not present gender-specific associations in Table 3.

A 3-cluster solution using k-medians was identified as the most appropriate and reliable representation of the study population, which had the highest Calinski–Harabasz index (Calinski–Harabasz index = 32208.85) and relatively clear boundary of clusters, compared with other cluster solutions. We identified relatively clear 3-cluster memberships: multiple indicators carriers, nonlow SES academic failures, and family structure victims. Table 4 presents the results of cluster membership differences in level of 6 syndemic indicators. The labels given to each cluster were based on high or low proportion for each of the 6 syndemic indicators relative to the other clusters. The cluster membership of multiple indicators carriers was characterized by small to large proportion for all 6 syndemic indicators. The cluster membership of nonlow SES academic failures was characterized by null proportion for low family SES and 100% for academic failure. The cluster membership of family structure victims was characterized by 100% for non-nuclear family. The associations between cluster membership and substance use are summarized in Table 5. The multivariate logistic regression indicated that the cluster membership of non-low SES academic failures had the highest odds of using substance (OR = 2.26, 95% CI: 2.12–2.41), compared to students reporting nonsyndemic indicators, followed by multiple

indicators carriers (OR = 2.12, 95% CI: 1.99–2.26), and family structure victims (OR = 1.69, 95% CI: 1.54–1.85).

DISCUSSION

Our study supports that adolescents experience substantial psychosocial problems, and these problems tend to co-occur and act to raise risk for adolescent substance use. In addition, we found a syndemic: the experience of more psychosocial problems was significantly associated with higher odds of using substance including tobacco, alcohol, and illicit drug use. These additive associations were found to be true for both women and men, and no significant effect modification of gender was identified, which suggests that syndemic of psychosocial problems on adolescent substance use is not specific to men who disproportionately report substance use.

Our study confirms that psychosocial problems tend to cluster and interconnect with each other in adolescents. Researchers have noticed that behavioral problems tend to cluster in adolescents for a long time. For example, Jessor and Jessor³² proposed a model to account for the strong intercorrelations between multiple youth problem behaviors, including drug use, heavy alcohol use, early sexual intercourse, general deviance (eg, aggression and delinquency), low academic motivation, and achievement—which has come to be known as Problem Behavior Theory (PBT). In the past several decades, numerous studies have confirmed PBT;^{12,33,34} however

TABLE 2. Bivariate Associations for Syndemic Indicators and Substance Use in Chinese Adolescents (N = 82,812)

	Bully		Family Structure		Low SES		Academic Failure		School Absence		Substance Use	
	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)
Overall												
Depression	2205	3.38 (2.99–3.81)	1815	1.45 (1.39–1.52)	1829	2.27 (1.96–2.62)	3111	1.93 (1.81–2.07)	1348	1.95 (1.63–2.33)	1176	2.08 (1.73–2.49)
Bully			2420	1.29 (1.17–1.42)	1997	1.54 (1.46–1.63)	3899	1.52 (1.48–1.57)	1658	1.52 (1.39–1.66)	1671	2.05 (1.93–2.17)
Non-nuclear family					3186	1.78 (1.60–1.99)	5214	1.31 (1.21–1.42)	2149	1.29 (1.19–1.40)	1838	1.37 (1.24–1.51)
Low family SES							4049	1.45 (1.19–1.77)	1517	1.26 (1.08–1.47)	1509	1.63 (1.54–1.73)
Academic failure									3810	1.77 (1.57–2.01)	3244	1.96 (1.87–2.05)
School absence											1721	2.55 (2.40–2.70)
Female												
Depression	1113	3.35 (2.76–4.06)	1069	1.53 (1.43–1.66)	955	2.10 (1.60–2.75)	1659	2.15 (2.05–2.26)	756	2.00 (1.76–2.28)	478	2.40 (1.78–3.24)
Bully			1067	1.35 (1.20–1.52)	811	1.40 (1.17–1.68)	1454	1.44 (1.29–1.61)	708	1.52 (1.31–1.77)	500	2.12 (1.83–2.46)
Non-nuclear family					1611	1.91 (1.68–2.18)	2284	1.33 (1.17–1.52)	1020	1.27 (1.14–1.42)	608	1.38 (1.08–1.72)
Low family SES*							1691	1.38 (1.07–1.77)	661	1.10 (0.83–1.45)	405	1.25 (0.92–1.70)
Academic failure									1593	1.67 (1.55–1.80)	826	1.56 (1.43–1.70)
School absence											565	2.57 (2.19–3.01)
Male												
Depression	1092	3.65 (3.00–4.42)	746	1.30 (1.12–1.50)	1186	2.55 (2.41–2.70)	2930	1.84 (1.68–2.01)	856	1.92 (1.45–2.54)	698	2.07 (1.89–2.27)
Bully			1353	1.21 (1.10–1.34)	847	1.56 (1.46–1.68)	1452	1.46 (1.29–1.66)	592	1.47 (1.30–1.68)	1176	1.77 (1.65–1.90)
Non-nuclear family					1575	1.68 (1.58–1.80)	2445	1.25 (1.18–1.34)	950	1.30 (1.14–1.49)	1230	1.31 (1.23–1.39)
Low family SES							2358	1.47 (1.34–1.62)	1129	1.40 (1.19–1.64)	1104	1.72 (1.46–2.04)
Academic failure									2217	1.90 (1.78–2.02)	2418	2.44 (2.21–2.70)
School absence											1156	2.46 (2.29–2.65)

CI = confidence interval, OR = odds ratio, SES = socioeconomic status.
 * Not statistically associated with school absence and substance use.

TABLE 3. Logistic Regression of Syndemic Score on Substance Use in Chinese Adolescents (N = 82,812)

No. of Syndemic Indicators	Substance Use							
	Any Substance Use		Tobacco Use		Alcohol Use		Illicit Drug Use	
	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)
0 (Ref)	1833	1.00	440	1.00	1334	1.00	136	1.00
1	2565	1.57 (1.38–1.79)	918	2.27 (2.00–2.57)	1628	2.18 (1.94–2.45)	204	1.85 (1.41–2.43)
2	1852	2.27 (1.87–2.76)	871	4.00 (3.22–4.98)	1046	4.02 (3.57–4.53)	172	2.77 (2.23–3.45)
3	939	3.58 (3.06–4.20)	496	6.81 (5.67–8.17)	497	6.58 (5.74–7.54)	110	5.68 (3.62–8.92)
4	335	5.23 (3.86–7.08)	222	11.39 (8.76–14.84)	180	11.46 (9.55–13.75)	75	12.48 (7.56–20.60)
5–6	127	9.45 (7.60–11.76)	92	26.92 (19.71–36.77)	79	25.53 (19.18–33.99)	55	40.79 (24.76–67.20)

All models were adjusted for age, gender, parental education, parental alcohol and tobacco use. Likelihood ratio test of gender effect modification: chi-square = 0.43, P = 0.513. CI = confidence interval, OR = odds ratio, Ref = reference group.

few of them have dedicated to evaluate whether the multiple behavioral problems may cause additive consequences on health.³⁵ In addition, PBT does not take into account social determinants that are increasingly recognized as crucial in disease etiology. Our study contributes to existing literature by showing multiple psychosocial problems cluster and interact in the context of disadvantaged social and family status, and form an additive association with substance use. Specifically, our data highlight the need to approach substance use in adolescents within the context of overlapping psychosocial problems.

Another finding is that both women and men seem to be subject to syndemic association with substance use. This finding is surprising because a large body of evidence, including ours, suggest that men are at disproportionately higher risk of using substance.^{36,37} Our results suggest that even though women may be at lower risk of using substance, they are still subject to the additive associations between syndemic indicators and substance use, which underscores that the syndemic of psychosocial problems on substance use is independent of the epidemic of substance use. This finding may support that further psychosocial intervention should encompass women even though they are at lower risk of using substance, and the benefits could be the same as intervening men.

One of interesting finding is that in cluster analysis, the cluster membership of nonlow SES academic failures had the highest odds of using substance. In our bivariate analysis both low family SES and academic failure were related to substance

use; however, the combination of nonlow SES and academic failure forms the strongest association with substance use, which is a little counter-intuitive. This finding suggests complex mechanism of syndemic associations. For example, in our study, students reporting academic failures were at higher risk of using substances, which already suggested by many studies. For students reporting academic failures who also came from nonlow SES family were at the highest risk, which indicates that family SES aggregates the association between academic performance and substance use. This finding is also in accordance with syndemic theory that social conditions may elevate personal risk forming an additive effect on adverse health conditions.¹⁵

STRENGTHS AND LIMITATIONS

To our limited knowledge, our study is the first study to investigate substance use in adolescents using a syndemic approach. Although a large amount of studies have investigated the cluster of adolescent behavior problems, few of them have evaluated the consequences of the clusters on substance use, especially using a syndemic approach taking social determinants into account. Our results indicate that there is an additive association between syndemic indicators and substance use. Beyond that, we further disentangled the components of syndemic to demonstrate that students who were from nonlow SES family and reported academic failure are at the highest risk of

TABLE 4. Distribution of Syndemic Indicators of Cluster Membership in Resulting Cluster Solution (N = 49,226)

Cluster	Depression		Bullying		Non-Nuclear Family		Low Family SES		Academic Failure		School Absence	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	Multiple indicators carriers	4,428	21.2	6577	31.5	3186	15.2	11,352	54.3	4049	19.4	5397
Non-low SES academic failures	2,235	11.3	2987	15.1	4009	20.3	0	0	19,732	100	3060	15.5
Family structure victims	713	8.3	1124	13.1	8582	100	0	0	0	0	957	11.1

SES = socioeconomic status.

TABLE 5. Associations Between Cluster Membership and Substance Use in Chinese Adolescents (N = 82,812)

Cluster Membership	Substance Use							
	Any Substance Use		Tobacco Use		Alcohol Use		Illicit Drug Use	
	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)
None syndemic indicator carriers (Ref)	1823	1.00	440	1.00	1334	1.00	136	1.00
Multiple indicator carriers	2542	2.12 (1.99–2.26)	1134	3.53 (3.15–3.96)	1541	1.77 (1.64–1.91)	343	3.64 (2.98–4.45)
Non-low SES academic failures	2530	2.26 (2.12–2.41)	1205	3.94 (3.52–4.41)	1396	1.72 (1.59–1.85)	139	2.16 (1.73–2.70)
Family structure victims	756	1.69 (1.54–1.85)	260	2.31 (1.98–2.71)	493	1.48 (1.33–1.65)	80	2.28 (1.72–3.01)

All models were adjusted for age, gender, parental education, parental alcohol, and tobacco use.
CI = confidence interval, OR = odds ratio, Ref = reference group.

using substance. These findings shed light on the complex associations between multiple behavioral problems, socioeconomic disparities, and substance use, suggesting a more nuanced understanding of risk factors of substance use in adolescents. Furthermore, the large sample selected with representative procedure may underscore the possible generalizability to broader adolescent populations.

One of the major limitations is that we only assessed cross-sectional associations, which suffer from reverse causality. Further longitudinal studies that investigate the precise sequence of psychosocial problems, and their joint associations with substance use are warranted. Another limitation should be noted in our study is that we used self-reported data. Although we used a series of standard measure adopted from previous adolescent studies, the information bias is highly possible especially in school institutions. In addition, although we carefully selected potential covariates to adjust for based on published studies, the estimated associations could still be confounded by unmeasured confounders especially those childhood experience and physical or mental abuse history. Given those unmeasured confounders are positively associated with both psychosocial problems and substance use, the direction of those confounding could be positive, which indicates that our estimated associations are more conservative.

Public Health Implications

In addition to adopt novel theory to study substance use in adolescents, our study also has significant public health implications. Our findings support the syndemic hypothesis that adolescents bearing multiple psychosocial problems experience additive risks of using substance. Substance use in adolescents is a major public health problem worldwide, with high social and economic costs. Individual-based interventions on substance use suggest disappointing results. Our findings support that a comprehensive approach to substance use prevention in adolescents would necessitate the involvement of a variety of providers, such as clinicians offering therapy or pharmacological treatments for adolescents with depression, social workers leading group-based approaches to address socioeconomic or family maladies for adolescents, and teachers focusing on provide helps to students who have academic difficulties or violence problems in school. In addition, significant efforts need to be invested to screen adolescents who experience multiple psychosocial problems, and therefore may be at elevated risk of using substance use. Targeting more

specific population is cost-effective, especially in developing settings where resource is generally limited.

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REFERENCES

- Gage SH, Hickman M, Heron J, et al. Associations of cannabis and cigarette use with depression and anxiety at age 18: findings from the avon longitudinal study of parents and children. *PLoS One*. 2015;10:e0122896.
- Pang RD, Farrahi L, Glazier S, et al. Depressive symptoms, negative urgency and substance use initiation in adolescents. *Drug Alcohol Depend*. 2014;144:225–230.
- Fleming LC, Jacobsen KH. Bullying among middle-school students in low and middle income countries. *Health Promot Int*. 2010;25:73–84.
- Kelly EV, Newton NC, Stapinski LA, et al. Suicidality, internalizing problems and externalizing problems among adolescent bullies, victims and bully-victims. *Prev Med*. 2015;73:100–105.
- Salom CL, Williams GM, Najman JM, et al. Substance use and mental health disorders are linked to different forms of intimate partner violence victimisation. *Drug Alcohol Depend*. 2015;151:121–127.
- van Gastel WA, Tempelaar W, Bun C, et al. Cannabis use as an indicator of risk for mental health problems in adolescents: a population-based study at secondary schools. *Psychol Med*. 2013;43:1849–1856.
- Orpinas P, Lacy B, Nahapetyan L, et al. Cigarette smoking trajectories from sixth to twelfth grade: associated substance use and high school dropout. *Nicotine Tob Res*. 2015[Epub ahead of print].
- Kelly AB, Evans-Whipp TJ, Smith R, et al. A longitudinal study of the association of adolescent polydrug use, alcohol use and high school non-completion. *Addiction (Abingdon, England)*. 2015;110:627–635.
- Andrade FH. Co-occurrences between adolescent substance use and academic performance: school context influences a multilevel-longitudinal perspective. *J Adolesc*. 2014;37:953–963.
- Small E, Suzuki R, Maleku A. The impact of family and parental education on adolescents' substance use: a study of U.S. high school seniors. *Soc Work Public Health*. 2014;29:594–605.
- Hanson MD, Chen E. Socioeconomic status and substance use behaviors in adolescents: the role of family resources versus family social status. *J Health Psychol*. 2007;12:32–35.

12. de Looze M, Ter Bogt TF, Raaijmakers QA, et al. Cross-national evidence for the clustering and psychosocial correlates of adolescent risk behaviours in 27 countries. *Eur J Public Health*. 2015;25:50–56.
13. DuRant RH, Smith JA, Kreiter SR, et al. The relationship between early age of onset of initial substance use and engaging in multiple health risk behaviors among young adolescents. *Arch Pediatr Adolesc Med*. 1999;153:286–291.
14. Singer M. AIDS and the health crisis of the U.S. urban poor; the perspective of critical medical anthropology. *Soc Sci Med (1982)*. 1994;39:931–948.
15. Singer M, Clair S. Syndemics and public health: reconceptualizing disease in bio-social context. *Med Anthropol Q*. 2003;17:423–441.
16. Jie W, Ciyong L, Xueqing D, et al. A syndemic of psychosocial problems places the MSM (men who have sex with men) population at greater risk of HIV infection. *PLoS One*. 2012;7:e32312doi: 10.1371/journal.pone.0032312.
17. Brennan J, Kuhns LM, Johnson AK, et al. Syndemic theory and HIV-related risk among young transgender women: the role of multiple, co-occurring health problems and social marginalization. *Am J Public Health*. 2012;102:1751–1757.
18. Stall R, Mills TC, Williams J, et al. Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. *Am J Public Health*. 2003;93:939–942.
19. Blashill AJ, Bedoya CA, Mayer KH, et al. Psychosocial syndemics are additively associated with worse ART adherence in HIV-infected individuals. *AIDS Behav*. 2015;19:981–986.
20. Mustanski B, Andrews R, Herrick A, et al. A syndemic of psychosocial health disparities and associations with risk for attempting suicide among young sexual minority men. *Am J Public Health*. 2014;104:287–294.
21. Faulstich ME, Carey MP, Ruggiero L, et al. Assessment of depression in childhood and adolescence: an evaluation of the Center for Epidemiological Studies Depression Scale for Children (CES-DC). *Am J Psychiatry*. 1986;143:1024–1027.
22. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Appl Psychol Meas*. 1977;1:385–401.
23. Li HC, Chung OK, Ho KY. Center for Epidemiologic Studies Depression Scale for Children: psychometric testing of the Chinese version. *J Adv Nurs*. 2010;66:2582–2591.
24. Radloff LS. The use of the Center for Epidemiologic Studies Depression Scale in adolescents and young adults. *J Youth Adolesc*. 1991;20:149–166.
25. Kaltiala-Heino R, Rimpela M, Marttunen M, et al. Bullying, depression, and suicidal ideation in Finnish adolescents: school survey. *BMJ (Clinical Research ed)*. 1999;319: 348–351.
26. King A, World B, Tudor-Smith C, Harel Y. The health of youth: a cross national survey. WHO Regional Publications, European Series No 69; 1996.
27. Moor I, Rathmann K, Lenzi M, et al. Socioeconomic inequalities in adolescent smoking across 35 countries: a multilevel analysis of the role of family, school and peers. *Eur J Public Health*. 2015;25: 457–463.
28. Aslund C, Leppert J, Starrin B, et al. Subjective social status and shaming experiences in relation to adolescent depression. *Arch Pediatr Adolesc Med*. 2009;163:55–60.
29. Eaton DK, Brener N, Kann LK. Associations of health risk behaviors with school absenteeism. Does having permission for the absence make a difference? *J School Health*. 2008;78: 223–229.
30. Everitt BS, Landau S, Leese M, Stahl D. Cluster Analysis, 5th Edition. Wiley; 2011.
31. Lee ES, Forthofer RN. Analyzing Complex Survey Data. Newbury Park, CA: Sage Publication, Inc; 2005.
32. Jessor R, Jessor SL. Problem Behavior and Psychosocial Development: A Longitudinal Study of Youth New York: Academic Press; 1977.
33. Yu M, Nebbitt VE, Lombe M, et al. Understanding tobacco use among urban African American adolescents living in public housing communities: a test of problem behavior theory. *Addict Behav*. 2012;37:978–981.
34. Cai Y, Li R, Zhu J, et al. Personality, perceived environment, and behavior systems related to future smoking intentions among youths: an application of problem-behavior theory in Shanghai, China. *PLoS One*. 2015;10:e0122276.
35. Racz SJ, McMahon RJ, Luthar SS. Risky behavior in affluent youth: examining the co-occurrence and consequences of multiple problem behaviors. *J Child Family Studies*. 2011;20: 120–128.
36. Evans-Polce RJ, Vasilenko SA, Lanza ST. Changes in gender and racial/ethnic disparities in rates of cigarette use, regular heavy episodic drinking, and marijuana use: ages 14 to 32. *Addict Behav*. 2015;41:218–222.
37. Chen P, Jacobson KC. Developmental trajectories of substance use from early adolescence to young adulthood: gender and racial/ethnic differences. *J Adolesc Health*. 2012;50:154–163.