Second-hand smoking and depressive symptoms among in-school adolescents

Running title: SHS and depressive symptoms in adolescents

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Data sharing

The datasets supporting the conclusions of this article are available at www.cdc.gov.

Abstract

Introduction: Smoking has been linked with depressive symptoms in adolescents but data on second-hand smoking (SHS) and depressive symptoms in low- and middle-income countries (LMICs) are scarce. Thus, the aim of this study was to analyze the association between SHS and depressive symptoms among in-school adolescents from 22 LMICs.

Methods: Data from the Global School-based Student Health Survey (GSHS) 2003-2008 were analyzed in June 2019. Data on past-week exposure to second-hand smoke and past-year depressive symptoms were collected. The association between SHS and depressive symptoms was studied using multivariable logistic regressions and meta-analyses.

Results: The sample consisted of 37,505 adolescents aged 12-15 years who never smoked. The prevalence of depressive symptoms increased from 23.0% in adolescents with no SHS to 28.9% in those with SHS everyday in the past week. After adjusting for sex, age, food insecurity, and country, there was a dose-response relationship between SHS and depressive symptoms in the overall sample [0 day: reference; 1-2 days: OR=1.06 (95%CI=0.95-1.18); 3-6 days: OR=1.38 (95%CI=1.20-1.58); 7 days: OR=1.63 (95%CI=1.44-1.86)]. Finally, the country-wise analysis showed that SHS on at least 3 days (vs. <3 days) in the past week was associated with a 1.48-fold increase in the odds of depressive symptoms (95%CI=1.39-1.59), with a low level of between-country heterogeneity (I^2=4.2%).

Conclusions: There was a positive association between SHS and depressive symptoms among in-school adolescents from LMICs. Further research should investigate causality and assess whether prevention of exposure to second-hand smoke can have a positive effect on the mental well-being of adolescents.

Keywords: second-hand smoking; depressive symptoms; in-school adolescents; low- and middle-income countries

Introduction

Depression affects around 264 million people in the world.[1] In terms of years lived with disability (YLDs), depression is the third leading cause of disability worldwide.[1] Depressive disorders occur throughout the life course and are also prevalent in young age. For example, the prevalence of adolescent depression has been estimated to be around 12.5%.[2] Adolescent depression is associated with an increased risk of mental (e.g., alcohol use disorder,[3] suicidal behavior[4]) and physical morbidity (e.g., overweight,[5] type 2 diabetes,[6] high blood pressure[7]) later in life. It also confers an increased risk of continued or recurrent depression in adulthood. Indeed, the majority (75%) of adolescents with major depressive disorder will go on to experience any depression in adulthood.[8] Furthermore, adolescent depression can have particularly devastating consequences since adolescence is a period of life characterized by the development of knowledge and skills, learning of management of emotion and relationships, and the acquisition of attributes and abilities,[9] and experiencing depression during this transitional period may have a critical impact on the future socioeconomic status and familial and romantic relationships of the individual.[2] Therefore, the identification of potentially modifiable risk factors for depression among adolescents is a public health priority.

In recent years, there has been an increasing interest in the role of second-hand smoking (SHS) on depression onset. SHS, also known as passive smoking, is defined as the unintended inhalation of smoke by non-smokers.[10] SHS can increase risk for depression via stress, chronic adverse physical conditions, and the biological effects of nicotine.[11] Indeed, several studies conducted among adults have found that SHS increases the risk for depressive

symptom onset.[12–14] Furthermore, a recent meta-analysis of observational studies showed that SHS is associated with depressive symptoms in a dose-dependent manner.[15]

However, three key limitations of the existing literature necessitate further research. First, most of the previous studies on SHS and depression were conducted in adults, and thus, little is known about the SHS-depression relationship in adolescents.[15] Studies on adolescents are particularly important not only for the devastating consequences of adolescent depression but also because the developing brain in children is particularly susceptible to substances found in second-hand smoke (e.g., nicotine).[16] Second, data from low- and middle-income countries (LMICs) are scarce. This is an important omission as enforcement of tobacco control policy legislation is weaker in LMICs compared to high-income countries (HICs).[17] A high prevalence of depressive symptoms among adolescents has been further reported in this setting,[18] while mental health care is also limited.[19] Finally, there are no multi-country studies on this topic. The only two previous studies investigating the SHS-depressive symptom relationship in adolescents from LMICs were single-country studies conducted in Iran[20] and China,[21] and only one was nationally representative.[20] Multi-country studies are important as they can provide information on whether associations are country-specific and also illustrate a global picture of the association between SHS and depressive symptoms.

Thus, the aims of the present study were to analyze the association between SHS and depressive symptoms among 37,505 in-school adolescents aged 12-15 years who never smoked from 22 LMICs (five WHO regions), and to assess whether there are dose-dependent associations, and whether associations are consistent across countries. Given that there are important sex differences in nicotine metabolism[11] and depression susceptibility,[22] sex-differences in the SHS-depressive symptom relationship were also assessed.

Methods

The survey

Publicly available data from the Global School-based Student Health Survey (GSHS) 2003-2008 were analyzed. Details on this survey can be found at http://www.who.int/chp/gshs and http://www.cdc.gov/gshs. Briefly, the GSHS was jointly developed by the WHO and the US Centers for Disease Control and Prevention (CDC), and other UN allies. The survey draws content from the CDC Youth Risk Behavior Survey (YRBS) for which test-retest reliability has been established.[23] The survey used a standardized two-stage probability sampling design for the selection process within each participating country. For the first stage, schools were selected with probability proportional to size sampling. The second stage involved the random selection of classrooms that included students aged 13-15 years within each selected school. All students in the selected classrooms were eligible to participate in the survey regardless of age. Data collection was performed during one regular class period. The questionnaire was translated into the local language in each country and consisted of multiple-choice response options; students recorded their response on computer scannable sheets. All GSHS surveys were approved, in each country, by both a national government administration (most often the Ministry of Health or Education) and an institutional review board or ethics committee. Student privacy was protected through anonymous and voluntary participation, and informed consent was obtained as appropriate from the students, parents and/or school officials. Data were weighted for non-response and probability selection.

From all publicly available data, all datasets from LMICs that included the variables pertaining to this analysis were selected. If there were more than two datasets from the same country, the most recent dataset was chosen. Surveys conducted after 2008 were not

included, as depressive symptoms were not assessed. Thus, a total of 22 countries were included in the current study. The characteristics of each country or survey are provided in **Table 1**. Data were nationally representative for all countries except Tanzania (Dar Es Salaam), China (Beijng), Ecuador (Quito), and Chile (Metropolitan).

Second-hand smoking (exposure)

Exposure to second-hand smoke was ascertained by asking "During the past 7 days, on how many days have people smoked in your presence?" with answer options: 0 day, 1 or 2 days, 3 to 4 days, 5 to 6 days, and all 7 days. Adolescents who replied "0 day" were considered to have no second-hand smoke exposure, while those who were exposed to second-hand smoke in the past 7 days were grouped into the following categories: 1-2 days, 3-6 days, and 7 days.

Depressive symptoms (outcome)

Depressive symptoms were assessed by asking the following question: "During the past 12 months, did you ever feel so sad or hopeless almost every day for two weeks or more in a row that you stopped doing your usual activities?" with yes/no answer options.[24]

Control variables

Control variables included sex, age, food insecurity (as a proxy for socioeconomic status), and country. As in a previous GSHS study, food insecurity was used as a proxy for socioeconomic status as there were no variables on socioeconomic status in the GSHS.[25] Specifically, this was assessed by the question "During the past 30 days, how often did you go hungry because there was not enough food in your home?" Answer options were categorized as "never", "rarely/sometimes", and "most of the time/always".[26]

Statistical analysis

The data was analyzed in June 2019. The analysis was restricted to adolescents aged 12-15 years as information on the exact age outside of this age range was not available, and the majority of the students were within this age range. Data on 48,963 adolescents aged 12-15 years were available but the final sample consisted of 37,505 adolescents who had never smoked a cigarette to avoid the confounding effect of tobacco use. Multivariable logistic regression analysis was used to estimate the association between SHS (exposure) and depressive symptoms (outcome) using the overall, sex-wise and country-wise samples. The exposure variable was the four-category variable on SHS when the overall and sex-wise samples were used. However, for country-wise analyses, a dichotomized variable (≥3 days/week vs. <3 days/week) was used to obtain stable estimates, as the sample size in each country was small. Three days/week was used as the cut-off as the risk for depressive symptoms was particularly increased beyond this threshold based on the overall sample (see **Table 2**). In order to assess between-country heterogeneity in the association between SHS and depressive symptoms, the Higgins's I^2 was calculated. The Higgins's I^2 represents the degree of heterogeneity that is not explained by sampling error with a value of <40% often considered as negligible and 40-60% as moderate heterogeneity.[32] Additional analyses were conducted to assess whether there was a significant between-group heterogeneity for country income level and region. Finally, sex and food insecurity were tested as effect modifiers in the association between SHS and depressive symptoms by including product terms (i.e., SHS X sex, SHS X food insecurity) in the model using the overall sample.

All analyses were adjusted for sex, age, food insecurity, and country with the exception of the country-wise and sex-stratified analyses, which were not adjusted for country and sex, respectively. Multilevel models were not used as such analyses can produce biased estimates

when used with complex study designs.[27] Taylor linearization methods were used in all analyses to account for the sample weighting and complex study design. Results from the logistic regression analyses are presented as ORs with 95% confidence intervals (CIs). The level of statistical significance was set at $p < 0.05$. Statistical analyses were performed with Stata 14.1 (Stata Corp LP, College station, Texas).

Results

The final sample consisted of 37,505 adolescents aged 12-15 years who never smoked [56.3% girls; mean (SD) age 13.8 (0.9) years]. Overall, 53.6% of the sample was exposed to second-hand smoke on at least one day in the past week, and 24.5% of adolescents had depressive symptoms in the past year. The prevalence of SHS ranged from 34.4% in Thailand to 83.3% in Indonesia (**Table 1**). The prevalence of depressive symptoms increased from 23.0% in adolescents with no SHS to 28.9% in those with SHS everyday in the past week (**Figure 1**). The results of the multivariable regression models are shown in **Table 2**. After adjusting for sex, age, food insecurity, and country, there was a dose-response relationship between SHS and depressive symptoms in the overall sample [0 day: reference; 1-2 days: OR=1.06 (95% CI=0.95-1.18); 3-6 days: OR=1.38 (95%CI=1.20-1.58); 7 days: OR=1.63 (95%CI=1.44-1.86)]. Sex and food insecurity were not significant effect modifiers in the SHS-depressive symptom relationship. **Figure 2** illustrates the results of the country-wise analysis. Overall, SHS on at least three days in the past week was associated with a 1.48-fold increase in the odds for depressive symptoms (95%CI=1.39-1.59), while the level of between-country heterogeneity was low (I^2=4.2%). Finally, there was no significant between-group heterogeneity for country income level (**Figure S1**) and region (**Figure S2**).

Discussion

Main findings

Overall, more than half (54%) of the adolescents in the sample who had never smoked reported exposure to second-hand smoke. Moreover, there was a dose-response relationship between SHS and depressive symptoms. When compared with no SHS, SHS everyday in the past seven days was associated with a 1.63 times higher odds for depressive symptoms. Finally, the country-wise analysis showed that SHS on at least three days in the past week (vs. less than three days) was associated with a 1.48-fold increase in the odds for depressive symptoms, and this association was similar across all countries (I^2=4.2%). This is the first multi-country study as well as one of the very few studies from LMICs on this topic.

Interpretation of the findings

Findings from the present study support those of previous cross-sectional studies on SHS and depression or depressive symptoms among adolescents conducted in single HICs (i.e., United States,[11] Korea[33–36]) and LMICs (i.e., Iran,[20] China[21]), and add to the literature by demonstrating for the first time that this association exits in a variety of countries across multiple continents. There are several hypotheses to explain the association between SHS and depressive symptoms in adolescents. First, it has been shown that SHS may increase levels of perceived stress by factors such as physical discomfort (e.g., coughing, eye irritation),[35] and stress is a strong predictor of depressive symptoms in male and female adolescents.[37] Second, exposure to second-hand smoke is positively associated with several chronic physical conditions in childhood and adolescence (e.g., increased body mass index,[38] asthma,[39] sensorineural hearing loss[40]), and these conditions can in turn favor the occurrence of depressive symptoms or depression.[41–43] Third, nicotine may increase vulnerability to

depression via its influence on other neurotransmitters (e.g., acetylcholine, catecholamine, serotonin).[44] For example, it was observed in an animal study that chronic nicotine infusion leads to a significant decrease in the synthesis of serotonin transporter in the raphe nucleus of rats, and this reduction could precipitate depression after cessation of exposure to second-hand smoke.[45] SHS may also lead to lower levels of dopamine and γ-aminobutyric acid, and previous research has shown that this is positively associated with depressive symptoms.[46,47] Fourth, SHS is a risk factor for inflammation and the production of inflammatory cytokines, which can indirectly increase risk for depression and depressive symptoms.[48,49] Finally, although the regression models were adjusted for food insecurity (a proxy of socioeconomic status), it is possible that adolescents exposed to second-hand smoke are more likely to live in disadvantaged neighborhoods than those not exposed to second-hand smoke,[50] and this could also partly explain the findings.

Public health implications and directions for future research

If corroborated by further longitudinal studies, these findings suggest that reducing second-hand smoke exposure may be important not only for the prevention of physical diseases such as ischemic heart disease, lung cancer, and asthma[51] but also for adolescent depressive symptoms in LMICs. Since LMICs often suffer from a lack of smoke-free air policies,[17] better implementation of these policies in LMICs is needed, and these policies should target public places where children and adolescents are frequently present (e.g., schools, hospitals, outdoor playgrounds). Furthermore, apart from protection of adolescents from second-hand smoke exposure, a more fundamental solution to reduce SHS among adolescents is the reduction in the number of smokers in a population. Strategies to reduce smoking itself at a population level include monitoring of tobacco use, provision of affordable and accessible support for smokers to quit smoking, increasing awareness among the general population

about the dangers of smoking, enforcement of bans on tobacco advertising, and tax increase on tobacco.[52] Regarding SHS at home, parent education programs focusing on the deleterious effects of passive smoking on both physical and mental health are likely to be important. In terms of future research, longitudinal and intervention studies in adolescent samples are warranted to gain a better understanding on causality and the potential utility of SHS prevention in reducing depression risk.

Strengths and limitations

Strengths of this study are the large sample size and the use of predominantly nationally representative data of young adolescents attending school from multiple continents. Moreover, the restriction of the analysis to adolescents who never smoked precludes the possibility of confounding by smoking. However, the findings should be interpreted in the light of several limitations. There was a lack of detailed data on SHS (e.g., type of smoke, place, circumstances, intensity), and these data could have provided more insight into the association between SHS and depressive symptoms. In particular, future studies should take place of second-hand smoke exposure into account as a study including Korean adolescents showed that the SHS-depressive symptom relationship was significant when SHS exposure occurred at home but not at school.[34] Relatedly, the question on SHS was based on the number of days people smoked in the presence of the student. Given that the level of exposure within a day can vary widely between students, it may not accurately reflect the level of second-hand smoke exposure. Moreover, SHS and depression were assessed with a single question based on self-report for which validity and reliability have not been established. Although these measures have been used in numerous previous publications,[24,31,53,54] self-reported data are subject to biases (e.g., social desirability bias, recall bias) and misclassification is possible. It is also possible that these questions were

interpreted differently across various cultures and languages. The use of 3 days/week as the cut-off for second-hand smoke exposure in the country-wise analysis is likely to have improved specificity, while the question on depressive symptoms referred to core symptoms of depression but future studies with biochemical verification of SHS (e.g., salivary cotinine) and clinical assessments of depressive symptoms are warranted. Besides, although it is unlikely that exposure to second-hand smoke changes within a timeframe of a year, variables on SHS (past week) and depressive symptoms (past year) used different timeframes. Also, food insecurity may not completely capture differences in socioeconomic status playing a significant role in the SHS-depression relationship, and thus residual confounding by socioeconomic status remains possible. For example, since family structure has been reported to be associated with both second-hand smoke exposure[55] and depression in adolescents,[56] residual confounding due to this factor may exist. Data on chronic physical conditions (e.g., asthma) were also not available in the dataset. Thus, their mediating role in the association between second-hand smoke exposure and depression could not be assessed. In addition, since one in three children and adolescents is out of school in LMICs,[57] the present results may not be generalizable to adolescents not attending school. Furthermore, parental consent may have been more difficult to obtain for adolescents with a low socioeconomic status who were at a potentially increased risk for both SHS exposure and depressive symptoms. This may have led to an underestimation of the prevalence of SHS and depressive symptoms among adolescents from LMICs, as well as an underestimation of the association of the two variables. Finally, since this was a cross-sectional study, one cannot draw any conclusions regarding causality or temporality of the SHS-depressive symptom relationship. That being said, the mere fact that depressive symptoms are more common in adolescents who are more highly exposed to second-hand smoke is a concern given the devastating consequences of

adolescent depression and the higher risk for non-communicable diseases associated with second-hand smoke exposure.

Conclusion

This multi-country cross-sectional study found a positive association between SHS and depressive symptoms among approximately 37,500 in-school adolescents from 22 LMICs. Further research is warranted to investigate causality and to assess whether prevention of exposure to second-hand smoke can reduce the burden of adolescent depression.

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Figure 1 Prevalence of depressive symptoms by number of days exposed to second-hand smoke in the past seven days
Restricted to those who had never smoked.
Bars denote 95% confidence intervals.

Figure 2 Country-wise association between ≥3 days/week of second-hand smoking (vs. <3 days/week of second-hand smoking) and depressive symptoms estimated by multivariable logistic regression
Abbreviation: OR Odds ratio; CI Confidence interval.
Analysis is restricted to those who had never smoked.
Models are adjusted for age, sex, and socioeconomic status (food insecurity).
Overall estimate was obtained by meta-analysis with fixed effects.

Table 1 Survey characteristics by country

Country income[a]	Country	WHO Region	Year	Response rate (%)	N (Non-smokers)[b]	SHS (%)[c]
Low	Kenya	AFR	2003	84	2,085	47.3
	Myanmar	SEAR	2007	95	2,092	66.7
	Tanzania (Dar Es Salaam)	AFR	2006	87	1,538	57.0
	Uganda	AFR	2003	69	1,526	39.6
Lower middle	China (Beijing)	WPR	2003	99	1,678	54.2
	Djibouti	EMR	2007	83	840	48.6
	Ecuador (Quito)	AMR	2007	86	1,072	52.7
	Guyana	AMR	2004	80	730	58.8
	India	SEAR	2007	83	6,808	35.2
	Indonesia	SEAR	2007	93	2,398	83.3
	Jordan	EMR	2007	100	1,094	68.8
	Morocco	EMR	2006	84	1,770	51.0
	Philippines	WPR	2007	81	2,650	38.0
	Thailand	SEAR	2008	93	2,124	34.4
	Tunisia	EMR	2008	83	2,097	60.1
Upper middle	Argentina	AMR	2007	77	896	69.5
	Botswana	AFR	2005	95	1,060	40.0
	Chile (Metropolitan)	AMR	2004	85	823	72.8
	Grenada	AMR	2008	78	932	54.6
	Saint Lucia	AMR	2007	82	703	55.4
	Saint Vincent and the Grenadines	AMR	2007	84	768	58.9
	Uruguay	AMR	2006	71	1,821	68.7

Abbreviation: AFR African Region; AMR Region of the Americas; EMR Eastern Mediterranean Region; SEAR South-East Asia Region; SHS Second-hand smoking; WHO World Health Organization; WPR Western Pacific Region.

[a] Based on the World Bank classification at the time of the survey.

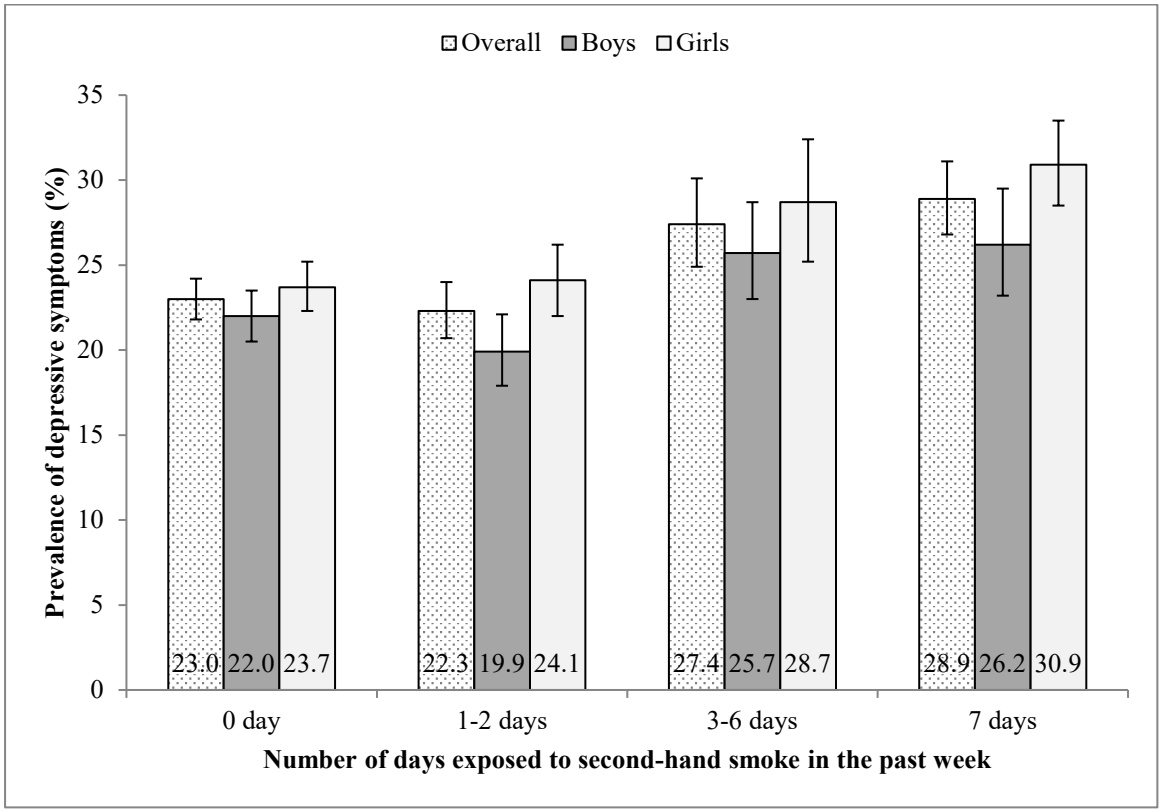
[b] N is based on those aged 12-15 years.

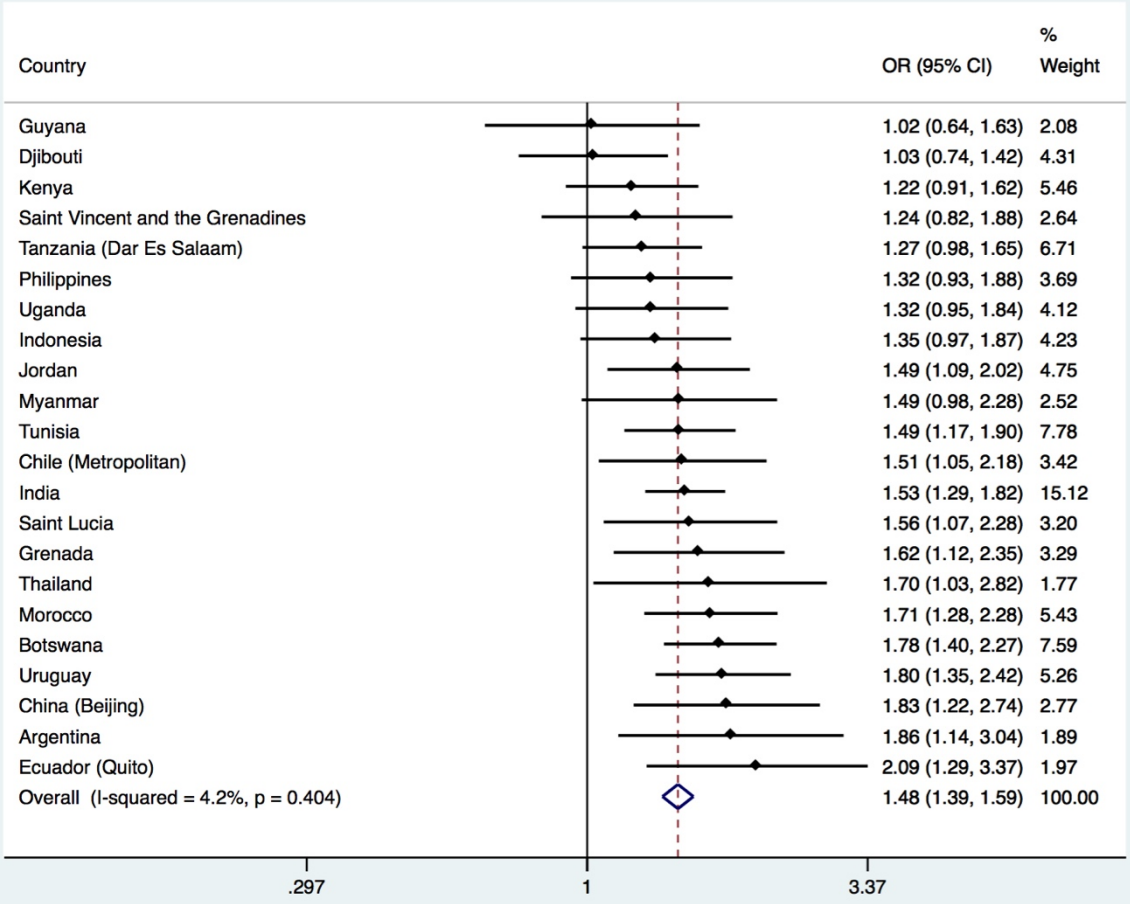
[c] Prevalence of exposure to second-hand smoke on at least one day in the past seven days among those who had never smoked.

Table 2 Association between second-hand smoking (exposure) and depressive symptoms (outcome) estimated by multivariable logistic regression

	Overall[a]		Boys[b]		Girls[b]	
Second-hand smoking	OR	95%CI	OR	95%CI	OR	95%CI
0 day	1.00		1.00		1.00	
1-2 days	1.06	[0.95,1.18]	0.99	[0.83,1.17]	1.12	[0.99,1.26]
3-6 days	**1.38**	**[1.20,1.58]**	**1.34**	**[1.12,1.61]**	**1.40**	**[1.16,1.68]**
7 days	**1.63**	**[1.44,1.86]**	**1.52**	**[1.25,1.86]**	**1.71**	**[1.45,2.01]**

Abbreviation: OR Odds ratio; CI Confidence interval.
Analysis is restricted to those who had never smoked.
[a] Adjusted for sex, age, food insecurity (proxy of socioeconomic status), and country.
[b] Adjusted for age, food insecurity (proxy of socioeconomic status), and country.
Note: Boldface indicates statistical significance ($p<0.05$).




Country
OR (95% CI)
% Weight
Guyana 1.02 (0.64, 1.63) 2.08
Djibouti 1.03 (0.74, 1.42) 4.31
Kenya 1.22 (0.91, 1.62) 5.46
Saint Vincent and the Grenadines 1.24 (0.82, 1.88) 2.64
Tanzania (Dar Es Salaam) 1.27 (0.98, 1.65) 6.71
Philippines 1.32 (0.93, 1.88) 3.69
Uganda 1.32 (0.95, 1.84) 4.12
Indonesia 1.35 (0.97, 1.87) 4.23
Jordan 1.49 (1.09, 2.02) 4.75
Myanmar 1.49 (0.98, 2.28) 2.52
Tunisia 1.49 (1.17, 1.90) 7.78
Chile (Metropolitan) 1.51 (1.05, 2.18) 3.42
India 1.53 (1.29, 1.82) 15.12
Saint Lucia 1.56 (1.07, 2.28) 3.20
Grenada 1.62 (1.12, 2.35) 3.29
Thailand 1.70 (1.03, 2.82) 1.77
Morocco 1.71 (1.28, 2.28) 5.43
Botswana 1.78 (1.40, 2.27) 7.59
Uruguay 1.80 (1.35, 2.42) 5.26
China (Beijing) 1.83 (1.22, 2.74) 2.77
Argentina 1.86 (1.14, 3.04) 1.89
Ecuador (Quito) 2.09 (1.29, 3.37) 1.97
Overall (I-squared = 4.2%, p = 0.404) 1.48 (1.39, 1.59) 100.00
.297
1
3.37

APPENDIX

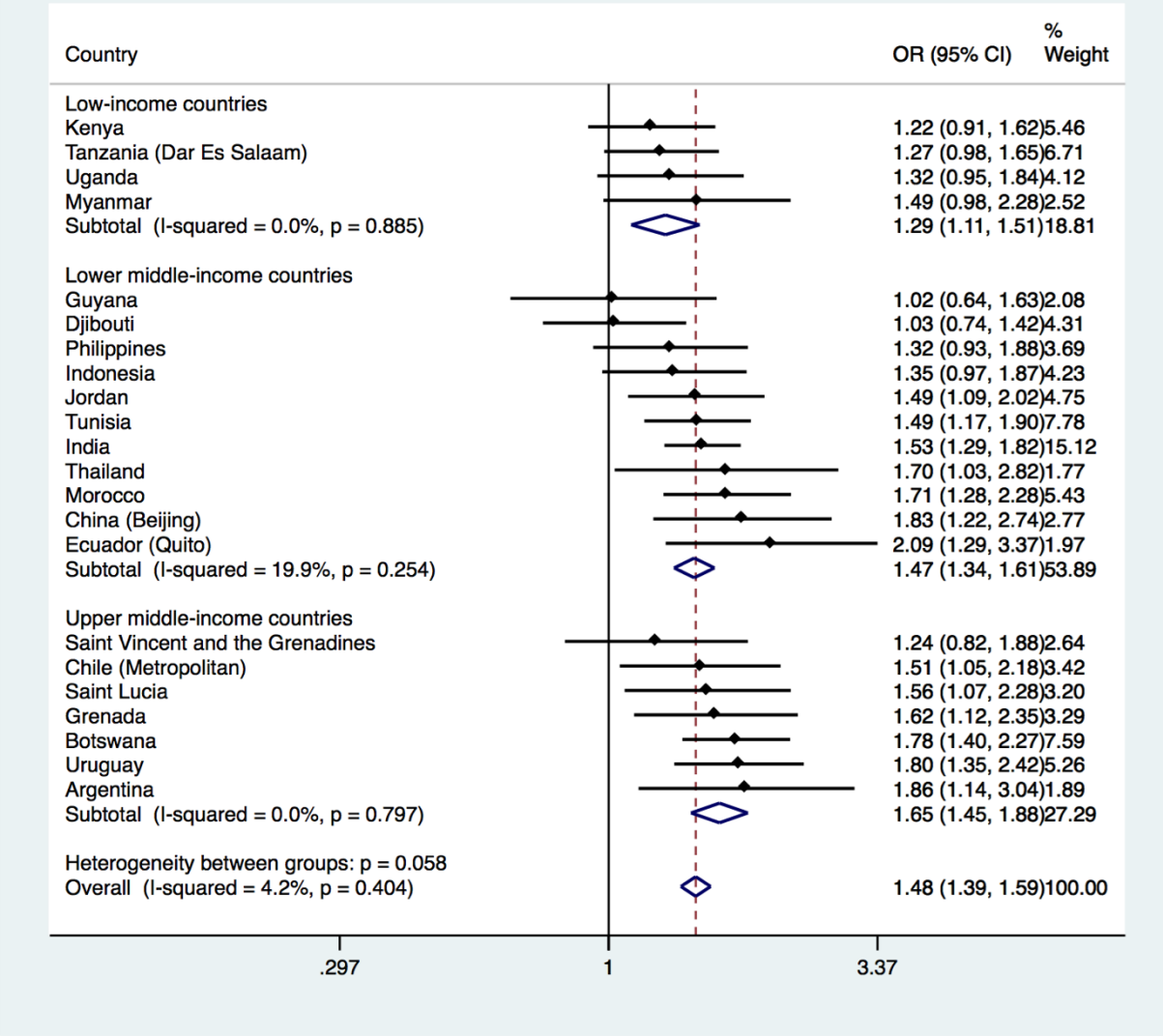


Figure S1. Country-wise association between ≥3 days/week of second-hand smoking (vs. <3 days/week of second-hand smoking) and depressive symptoms estimated by multivariable logistic regression (stratified by country income level).

Abbreviation: OR Odds ratio; CI Confidence interval.

Analysis is restricted to those who had never smoked.

Models are adjusted for age, sex, and socioeconomic status (food insecurity).

Subtotal and overall estimates were obtained by meta-analysis with fixed effects.

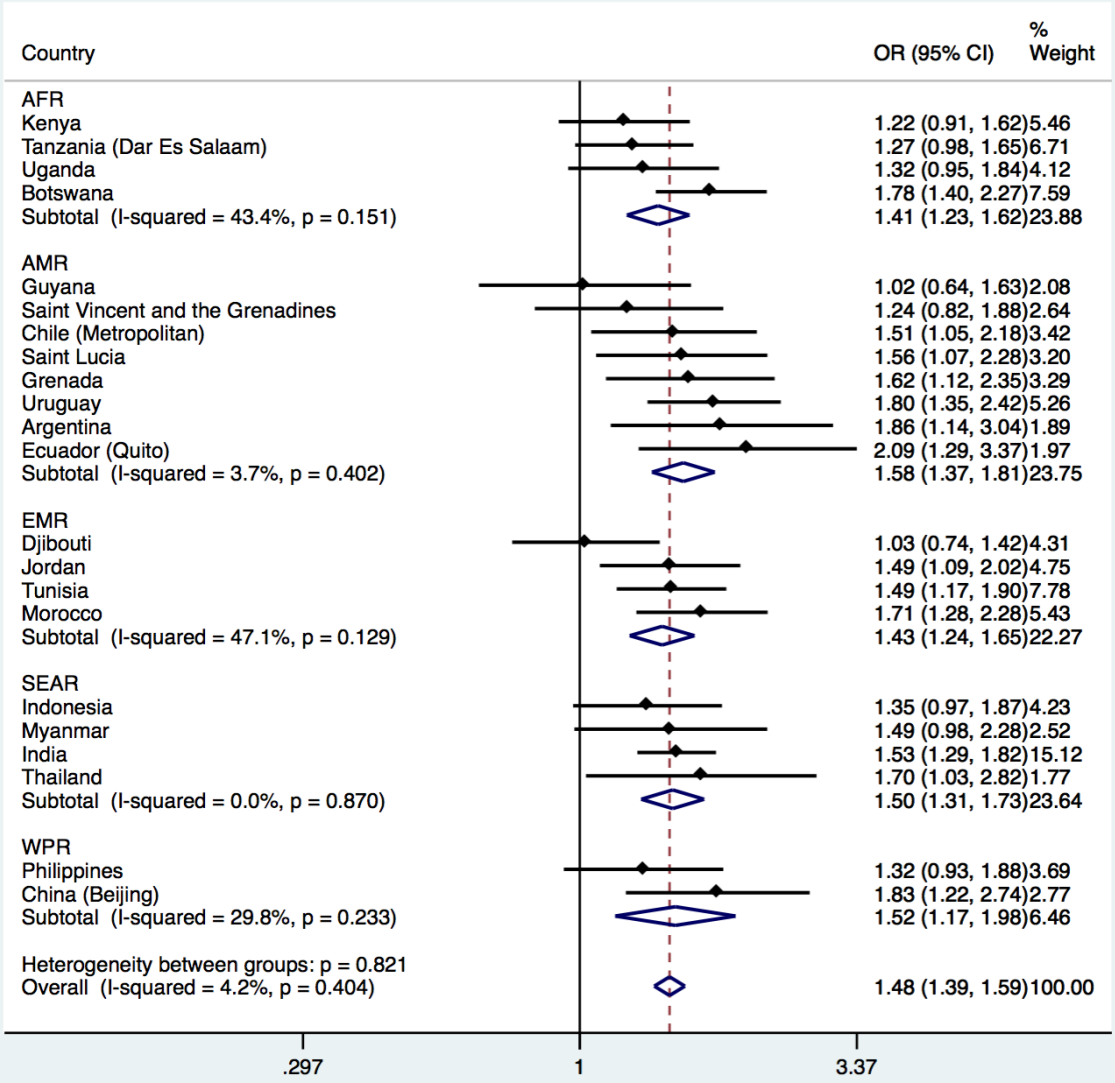


Figure S2. Country-wise association between ≥3 days/week of second-hand smoking (vs. <3 days/week of second-hand smoking) and depressive symptoms estimated by multivariable logistic regression (stratified by region).

Abbreviation: OR Odds ratio; CI Confidence interval; AFR African Region; AMR Region of the Americas; EMR Eastern Mediterranean Region; SEAR South-East Asia Region; WPR Western Pacific Region.

Analysis is restricted to those who had never smoked.

Models are adjusted for age, sex, and socioeconomic status (food insecurity).

Subtotal and overall estimates were obtained by meta-analysis with fixed effect