## ARTICLE IN PRESS

## American Journal of Preventive Medicine

## **RESEARCH ARTICLE**

# Secondhand Smoking and Depressive Symptoms Among In-School Adolescents

Louis Jacob, PhD,<sup>1,2</sup> Lee Smith, PhD,<sup>3</sup> Sarah E. Jackson, PhD,<sup>4</sup> Josep Maria Haro, MD, PhD,<sup>2</sup> Jae II Shin, MD, PhD,<sup>5</sup> Ai Koyanagi, MD, PhD<sup>2,6</sup>

Introduction: Smoking has been linked with depressive symptoms in adolescents, but data on secondhand smoking and depressive symptoms in low- and middle-income countries are scarce. Thus, this study analyzes the association between secondhand smoking and depressive symptoms among in-school adolescents from 22 low- and middle-income countries.

Methods: Data from the 2003-2008 Global School-Based Student Health Survey were analyzed in June 2019. Data on past-week exposure to secondhand smoke and past-year depressive symptoms were collected. The association between secondhand smoke 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 secondhand smoking to 28.9% in those with secondhand smoking every day in the past week. After adjusting for sex, age, food insecurity, and country, there was a dose-response relationship between secondhand smoking and depressive symptoms in the overall sample (0 days: 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). The country-wise analysis showed that secondhand smoking on at least 3 days (versus <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 secondhand smoking and depressive symptoms among in-school adolescents from low- and middle-income countries. Further research should investigate causality and assess whether prevention of exposure to secondhand smoke can have a positive effect on the mental well-being of adolescents.

Am J Prev Med 2020;000(000):1–9. © 2020 American Journal of Preventive Medicine. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

## INTRODUCTION

epression affects around 264 million people in the world. In terms of years lived with disability, depression is the third leading cause of disability worldwide. 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<sup>3</sup> and suicidal behavior<sup>4</sup>) and physical morbidity (e.g., overweight,<sup>5</sup> type 2 diabetes,<sup>6</sup> and high blood pressure<sup>7</sup>) later in life. It also confers an increased risk of continued or From the <sup>1</sup>Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, Montigny-le-Bretonneux, France; <sup>2</sup>Research and Development Unit, Parc Sanitari Sant Joan de Déu, CIBERSAM, Sant Boi de Llobregat, Barcelona, Spain; <sup>3</sup>Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University, Cambridge, United Kingdom; <sup>4</sup>Department of Behavioural Science and Health, University College London, London, United Kingdom; 5Department of Pediatrics, Yonsei University College of Medicine, Seoul, Republic of Korea; and <sup>6</sup>ICREA, Barcelona, Spain

Address correspondence to: Louis Jacob, PhD, Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, 2 avenue de la Source de la Bièvre, Montigny-Le-Bretonneux 78180, France.

E-mail: louis.jacob.contacts@gmail.com.

0749-3797/\$36.00

https://doi.org/10.1016/j.amepre.2019.12.008

recurrent depression in adulthood. Indeed, most (75%) adolescents with major depressive disorder will go on to experience any depression in adulthood. Furthermore, adolescent depression can have particularly devastating consequences because 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, and experiencing depression during this transitional period may have a critical impact on the future SES and familial and romantic relationships of the individual. 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 secondhand smoking (SHS) on depression onset. SHS, also known as passive smoking, is defined as the unintended inhalation of smoke by nonsmokers. SHS can increase risk for depression via stress, chronic adverse physical conditions, and the biological effects of nicotine. Indeed, several studies conducted among adults have found that SHS increases the risk for depressive symptom onset. In Furthermore, a recent meta-analysis of observational studies showed that SHS is associated with depressive symptoms in a dose-dependent manner.

However, 3 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.<sup>15</sup> 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 SHS (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 with high-income countries.<sup>17</sup> A high prevalence of depressive symptoms among adolescents has been further reported in this setting, 18 and mental health care is also limited. Finally, there are no multi-country studies on this topic. The only 2 previous studies investigating the SHS-depressive symptom relationship in adolescents from LMICs were single-country studies conducted in Iran20 and China,21 and only 1 was nationally representative.<sup>20</sup> 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 this study are 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 (5 WHO regions), assess whether there are dose-dependent associations, and examine whether associations are consistent across countries. Given that there are important sex differences in nicotine metabolism<sup>11</sup> and depression susceptibility,<sup>22</sup> sex differences in the SHS—depressive symptom relationship are also assessed.

## **METHODS**

#### Study Sample

Publicly available data from the 2003-2008 Global School-Based Student Health Survey (GSHS) were analyzed. Details on this survey can be found at www.who.int/chp/gshs and www.cdc.gov/ gshs. Briefly, the GSHS was jointly developed by WHO and the U. S. Centers for Disease Control and Prevention (CDC) and other UN allies. The survey draws content from the CDC Youth Risk Behavior Survey, for which test-retest reliability has been established.<sup>23</sup> The survey used a standardized 2-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 IRB or ethics committee. Student privacy was protected through anonymous and voluntary participation, and informed consent was obtained as appropriate from the students, parents, or school officials. Data were weighted for nonresponse and probability selection.

From all publicly available data, all data sets from LMICs that included the variables pertaining to this analysis were selected. If there were more than 2 data sets from the same country, the most recent data set was chosen. Surveys conducted after 2008 were not included, as depressive symptoms were not assessed. Thus, a total of 22 countries were included in this 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).

#### Measures

Exposure to SHS was ascertained by asking: During the past 7 days, on how many days have people smoked in your presence? Answer options were: 0 days, 1 or 2 days, 3–4 days, 5–6 days, and all 7 days. Adolescents who replied 0 days were considered to have no SHS exposure, whereas those who were exposed to SHS in the past 7 days were grouped into the following categories: 1–2 days, 3–6 days, and 7 days.

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 2 weeks or more in a row that you

#### Jacob et al / Am J Prev Med 2020;000(000):1-9

Table 1. Survey Characteristics by Country

Country income <sup>a</sup>	WHO region	Year	Response rate (%)	N (nonsmokers) <sup>b</sup>	SHS (%)°
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

<sup>&</sup>lt;sup>a</sup>Based on the World Bank classification at the time of the survey.

AFR, African Region; AMR, Region of the Americas; EMR, Eastern Mediterranean Region; SEAR, South-East Asia Region; SHS, secondhand smoking; WPR, Western Pacific Region.

stopped doing your usual activities? Response options were yes and no.<sup>24</sup>

Control variables included sex, age, food insecurity (as a proxy for SES), and country. As in a previous GSHS study, food insecurity was used as a proxy for SES as there were no variables on SES in the GSHS.<sup>25</sup> 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.<sup>26</sup>

#### Statistical Analysis

Data were 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 most 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 4-category variable on SHS when the overall and sex-

wise samples were used. However, for country-wise analyses, a dichotomized variable (≥3 days/week versus <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 (Table 2). To assess between-country heterogeneity in the association between SHS and depressive symptoms, Higgins's  $I^2$  was calculated. Higgins's *I*<sup>2</sup> represents the degree of heterogeneity that is not explained by sampling error, with a value of <40% often considered negligible and 40%-60% considered moderate heterogeneity.<sup>27</sup> 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 and 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.<sup>28</sup> Taylor linearization methods were used in all analyses

<sup>&</sup>lt;sup>b</sup>N is based on those aged 12–15 years.

<sup>&</sup>lt;sup>c</sup>Prevalence of exposure to secondhand smoke on at least 1 day in the past 7 days among those who had never smoked.

**Table 2.** Association Between Secondhand Smoking (Exposure) and Depressive Symptoms (Outcome) Estimated by Multivariable Logistic Regression

Secondhand smoking	Overall <sup>a</sup> OR (95% CI)	Boys <sup>b</sup> OR (95% CI)	Girls <sup>b</sup> OR (95% CI)
0 days	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)

Note: Analysis is restricted to those who had never smoked. Boldface indicates statistical significance (p<0.05).

to account for the sample weighting and complex study design. Results from the logistic regression analyses are presented as ORs with 95% CIs. The level of statistical significance was set at p<0.05. Statistical analyses were performed with Stata, version 14.1.

## **RESULTS**

The final sample consisted of 37,505 adolescents aged 12-15 years who never smoked (56.3% girls; mean age=13.8 [SD=0.9] years). Overall, 53.6% of the sample was exposed to SHS on at least 1 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 every day 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 days: 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 countrywise analysis. Overall, SHS on at least 3 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), and the level of between-country heterogeneity was low  $(I^2=4.2\%)$ . Finally, there was no significant betweengroup heterogeneity for country income level (Appendix Figure 1, available online) and region (Appendix Figure 2, available online).

## DISCUSSION

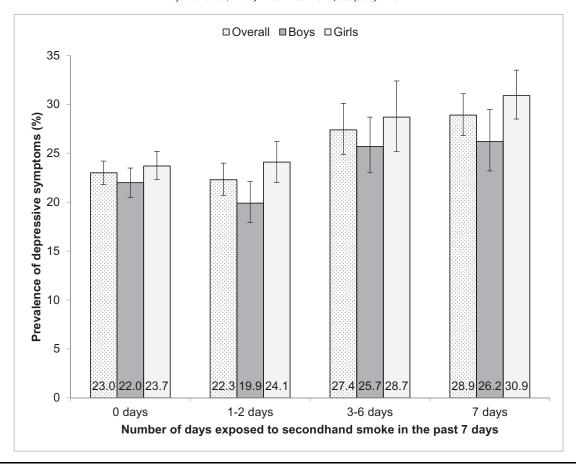
Overall, more than half (54%) of the adolescents in the sample who had never smoked reported SHS exposure. Moreover, there was a dose—response relationship between SHS and depressive symptoms. When

compared with no SHS, everyday exposure in the past 7 days was associated with a 1.63-times higher odds for depressive symptoms. Finally, the country-wise analysis showed that SHS on at least 3 days in the past week (versus fewer than 3 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.

Findings from this study support those of previous cross-sectional studies on SHS and depression or depressive symptoms among adolescents conducted in single high-income countries (i.e., U.S.<sup>11</sup> and Korea<sup>29-32</sup>) and LMICs (i.e., Iran<sup>20</sup> and China<sup>21</sup>) 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 and eye irritation),<sup>31</sup> and stress is a strong predictor of depressive symptoms in male and female adolescents.<sup>33</sup> Second, SHS exposure is positively associated with several chronic physical conditions in childhood and adolescence (e.g., increased BMI,<sup>34</sup> asthma,<sup>35</sup> and sensorineural hearing loss<sup>36</sup>), and these conditions can favor the occurrence of depressive symptoms or depression.<sup>37–39</sup> Third, nicotine may increase vulnerability to depression via its influence on other neurotransmitters (e. g., acetylcholine, catecholamine, and serotonin).<sup>40</sup> 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 SHS exposure. 41 SHS may also lead to lower levels of dopamine and  $\gamma$ -aminobutyric acid, and previous research has shown that this is positively associated with depressive symptoms. 42,43 Fourth, SHS is a risk factor for inflammation and the production of inflammatory cytokines, which can indirectly increase risk for

<sup>&</sup>lt;sup>a</sup>Adjusted for sex, age, food insecurity (proxy of SES), and country.

<sup>&</sup>lt;sup>b</sup>Adjusted for age, food insecurity (proxy of SES), and country.



**Figure 1.** Prevalence of depressive symptoms by number of days exposed to secondhand smoke in the past 7 days. Restricted to those who had never smoked. Bars denote 95% Cls.

depression and depressive symptoms. 44,45 Finally, although the regression models were adjusted for food insecurity (a proxy of SES), it is possible that adolescents exposed to SHS are more likely to live in disadvantaged neighborhoods than those not exposed to SHS, 46 and this could also partly explain the findings.

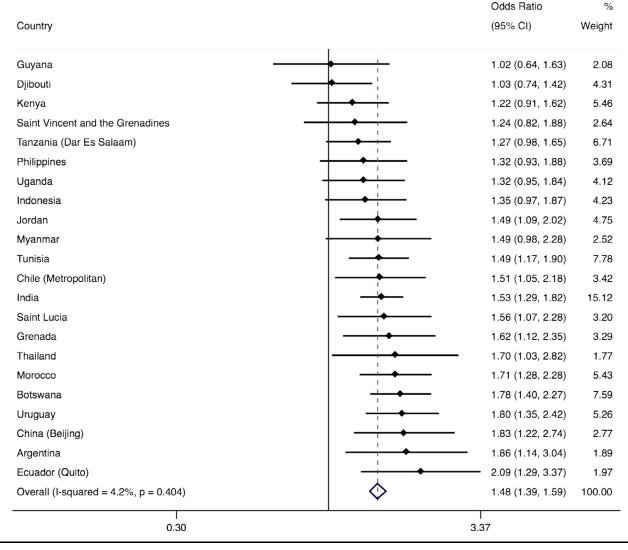
If corroborated by further longitudinal studies, these findings suggest that reducing SHS exposure may be important not only for the prevention of physical diseases such as ischemic heart disease, lung cancer, and asthma,<sup>47</sup> but also for adolescent depressive symptoms in LMICs. As LMICs often suffer from a lack of smoke-free air policies, <sup>17</sup> 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, and outdoor playgrounds). Furthermore, apart from protection of adolescents from SHS 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. 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 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.

#### Limitations

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, and intensity),

#### Jacob et al / Am J Prev Med 2020;000(000):1-9



**Figure 2.** Country-wise association between ≥3 days/week of secondhand smoking (vs <3 days/week of secondhand smoking) and depressive symptoms estimated by multivariable logistic regression. Analysis is restricted to those who had never smoked. Models are adjusted for sex, age, and SES (food insecurity). Overall estimate was obtained by meta-analysis with fixed effects.

and these data could have provided more insight into the association between SHS and depressive symptoms. In particular, future studies should take place of SHS 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.<sup>30</sup> 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 SHS 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, 24,49-51 self-reported data are subject to biases (e.g., social desirability bias and 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 SHS exposure in the country-wise analysis is likely to have improved specificity; 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. Although it is unlikely that exposure to SHS 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 SES playing a significant role in the SHS-depression relationship, and thus residual confounding by SES

remains possible. For example, as family structure has been reported to be associated with both SHS exposure<sup>52</sup> and depression in adolescents,<sup>53</sup> residual confounding because of this factor may exist. Data on chronic physical conditions (e.g., asthma) were also not available in the data set. Thus, their mediating role in the association between SHS exposure and depression could not be assessed. In addition, given that 1 in 3 children and adolescents is out of school in LMICs,<sup>54</sup> these 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 SES 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 2 variables. Finally, as this was a cross-sectional study, one cannot draw any conclusions regarding causality or temporality of the SHS-depressive symptom relationship. However, the mere fact that depressive symptoms are more common in adolescents who are more highly exposed to SHS is a concern given the devastating consequences of adolescent depression and the higher risk for noncommunicable diseases associated with SHS exposure.

## CONCLUSIONS

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 assess whether prevention of SHS exposure can reduce the burden of adolescent depression.

## **ACKNOWLEDGMENTS**

This research was based on data from the Global School-Based Student Health Survey, which was made available for use by the Chronic Diseases and Health Promotion Department of the WHO and the U.S. Centers for Disease Control and Prevention.

Ai Koyanagi's work is supported by the PI15/00862 project, integrated into the National R+D+I and funded by the ISCIII - General Branch Evaluation and Promotion of Health Research - and the European Regional Development Fund (ERDF-FEDER).

LJ contributed to the design of the study, undertook the statistical analysis, managed the literature searches, wrote the first draft of the manuscript, and contributed to the correction of the manuscript. LS, SEJ, JMH, and JIS contributed to the design of the study and the correction of the manuscript. AK contributed to the design of the study, undertook the statistical analysis, and contributed to the correction of the manuscript. All authors contributed to and have approved the final manuscript.

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

No financial disclosures were reported by the authors of this paper.

#### SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at <a href="https://doi.org/10.1016/j.amepre.2019.12.008">https://doi.org/10.1016/j.amepre.2019.12.008</a>.

## **REFERENCES**

- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1789–1858. https://doi.org/10.1016/S0140-6736(18)32279-7.
- Clayborne ZM, Varin M, Colman I. Systematic review and meta-analysis: adolescent depression and long-term psychosocial outcomes. *J Am Acad Child Adolesc Psychiatry*. 2019;58(1):72–79. https://doi.org/10.1016/j.jaac.2018.07.896.
- 3. McKenzie M, Jorm AF, Romaniuk H, Olsson CA, Patton GC. Association of adolescent symptoms of depression and anxiety with alcohol use disorders in young adulthood: findings from the Victorian Adolescent Health Cohort Study. *Med J Aust.* 2011;195(suppl 3):S27–S30. https://doi.org/10.5694/j.1326-5377.2011.tb03262.x.
- Fergusson DM, Horwood LJ, Ridder EM, Beautrais AL. Subthreshold depression in adolescence and mental health outcomes in adulthood. *Arch Gen Psychiatry*. 2005;62(1):66–72. https://doi.org/10.1001/arch-psyc.62.1.66.
- Liem ET, Sauer PJJ, Oldehinkel AJ, Stolk RP. Association between depressive symptoms in childhood and adolescence and overweight in later life: review of the recent literature. Arch Pediatr Adolesc Med. 2008;162(10):981–988. https://doi.org/10.1001/ archpedi.162.10.981.
- Suglia SF, Demmer RT, Wahi R, Keyes KM, Koenen KC. Depressive symptoms during adolescence and young adulthood and the development of type 2 diabetes mellitus. *Am J Epidemiol*. 2016;183(4):269– 276. https://doi.org/10.1093/aje/kwv149.
- Srinivas S, Rajendran S, Anand K, Chockalingam A. Self-reported depressive symptoms in adolescence increase the risk for obesity and high BP in adulthood. *Int J Cardiol.* 2018;269:339–342. https://doi. org/10.1016/j.ijcard.2018.07.089.
- 8. Fombonne E, Wostear G, Cooper V, Harrington R, Rutter M. The Maudsley long-term follow-up of child and adolescent depression: I. Psychiatric outcomes in adulthood. *Br J Psychiatry*. 2001;179(3):210–217. https://doi.org/10.1192/bjp.179.3.210.
- WHO. Maternal, newborn, child and adolescent health. www.who. int/maternal\_child\_adolescent/topics/adolescence/development/en/. Published 2019. Accessed December 18, 2019.
- Kim S, Kang SH, Han D, et al. Relation between secondhand smoke exposure and cardiovascular risk factors in never smokers. *J Hypertens*. 2017;35(10):1976–1982. https://doi.org/10.1097/HJH.0000000000001426.
- Bandiera FC, Richardson AK, Lee DJ, He JP, Merikangas KR. Secondhand smoke exposure and mental health among children and adolescents. *Arch Pediatr Adolesc Med.* 2011;165(4):332–338. https://doi. org/10.1001/archpediatrics.2011.30.
- Nakata A, Takahashi M, Ikeda T, Hojou M, Nigam JA, Swanson NG. Active and passive smoking and depression among Japanese workers. *Prev Med.* 2008;46(5):451–456. https://doi.org/10.1016/j. ypmed.2008.01.024.

- Bandiera FC, Arheart KL, Caban-Martinez AJ, et al. Secondhand smoke exposure and depressive symptoms. *Psychosom Med.* 2010;72 (1):68–72. https://doi.org/10.1097/PSY.0b013e3181c6c8b5.
- 14. Kawasaki Y, Miyake Y, Tanaka K, Furukawa S, Arakawa M. Smoking and secondhand smoke exposure and prevalence of depressive symptoms during pregnancy in Japan: baseline data from the Kyushu Okinawa Maternal and Child Health Study. *Tob Induc Dis.* 2017;15:34. https://doi.org/10.1186/s12971-017-0139-6.
- Han C, Liu Y, Gong X, Ye X, Zhou J. Relationship between secondhand smoke exposure and depressive symptoms: a systematic review and dose—response meta-analysis. *Int J Environ Res Public Health*. 2019;16(8):1356. https://doi.org/10.3390/ijerph16081356.
- Yuan M, Cross SJ, Loughlin SE, Leslie FM. Nicotine and the adolescent brain. J Physiol. 2015;593(16):3397–3412. https://doi.org/10.1113/IP270492.
- Stone E, Peters M. Young low and middle-income country (LMIC) smokers—implications for global tobacco control. *Transl Lung Cancer Res.* 2017;6(suppl 1):S44–S46. https://doi.org/10.21037/tlcr.2017.10.11.
- 18. Yatham S, Sivathasan S, Yoon R, da Silva TL, Ravindran AV. Depression, anxiety, and post-traumatic stress disorder among youth in low and middle income countries: a review of prevalence and treatment interventions. *Asian J Psychiatry*. 2018;38:78–91. https://doi.org/10.1016/j.ajp.2017.10.029.
- Morris J, Belfer M, Daniels A, et al. Treated prevalence of and mental health services received by children and adolescents in 42 low-and-middle-income countries. *J Child Psychol Psychiatry*. 2011;52(12):1239–1246. https://doi.org/10.1111/j.1469-7610.2011.02409.x.
- Kelishadi R, Babaki AES, Qorbani M, et al. Joint association of active and passive smoking with psychiatric distress and violence behaviors in a representative sample of Iranian children and adolescents: the CASPIAN-IV Study. *Int J Behav Med.* 2015;22(5):652–661. https:// doi.org/10.1007/s12529-015-9462-6.
- Huang J, Xu B, Guo D, et al. Dose—response relationships between second-hand smoke exposure and depressive symptoms among adolescents in Guangzhou, China. Int J Environ Res Public Health. 2018;15(5):985. https://doi.org/10.3390/ijerph15050985.
- Lewis AJ, Kremer P, Douglas K, et al. Gender differences in adolescent depression: differential female susceptibility to stressors affecting family functioning. *Aust J Psychol.* 2015;67(3):131–139. https://doi.org/ 10.1111/ajpy.12086.
- Brener ND, Collins JL, Kann L, Warren CW, Williams BI. Reliability of the Youth Risk Behavior Survey questionnaire. Am J Epidemiol. 1995;141(6):575–580. https://doi.org/10.1093/oxfordjournals.aje. a117473.
- Vancampfort D, Stubbs B, Firth J, Van Damme T, Koyanagi A. Sedentary behavior and depressive symptoms among 67,077 adolescents aged 12–15 years from 30 low- and middle-income countries. *Int J Behav Nutr Phys Act.* 2018;15(1):73. https://doi.org/10.1186/s12966-018-0708-y.
- Carvalho AF, Stubbs B, Vancampfort D, et al. Cannabis use and suicide attempts among 86,254 adolescents aged 12–15 years from 21 low- and middle-income countries. *Eur Psychiatry*. 2019;56:8–13. https://doi.org/10.1016/j.eurpsy.2018.10.006.
- McKinnon B, Gariépy G, Sentenac M, Elgar FJ. Adolescent suicidal behaviours in 32 low- and middle-income countries. *Bull World Health Organ*. 2016;94(5):340–350F. https://doi.org/10.2471/BLT.15.163295.
- Higgins JPT, Thompson SG. Quantifying heterogeneity in a metaanalysis. Stat Med. 2002;21(11):1539–1558. https://doi.org/10.1002/ sim.1186.
- 28. Rabe-Hesketh S, Skrondal A. Multilevel modelling of complex survey data. *J R Stat Soc A*. 2006;169(4):805–827. https://doi.org/10.1111/j.1467-985X.2006.00426.x.
- Lee KJ. Current smoking and secondhand smoke exposure and depression among Korean adolescents: analysis of a national cross-

- sectional survey. BMJ Open. 2014;4(2):e003734. https://doi.org/10.1136/bmjopen-2013-003734.
- Kim NH, Park JH, Choi DP, Lee JY, Kim HC. Secondhand smoke exposure and depressive symptoms among Korean adolescents: JS High School Study. *PLoS One*. 2016;11(12):e0168754. https://doi.org/ 10.1371/journal.pone.0168754.
- Bang I, Jeong YJ, Park YY, Moon NY, Lee J, Jeon TH. Secondhand smoking is associated with poor mental health in Korean adolescents. *Tohoku J Exp Med.* 2017;242(4):317–326. https://doi.org/10.1620/ tjem.242.317.
- Park S. Associations between household secondhand smoke exposure and health problems among non-smoking adolescents in the Republic of Korea. J Prim Prev. 2017;38(4):385–402. https://doi.org/10.1007/ s10935-017-0467-6.
- Moksnes UK, Bradley Eilertsen M-EB, Lazarewicz M. The association between stress, self-esteem and depressive symptoms in adolescents. Scand J Psychol. 2016;57(1):22–29. https://doi.org/10.1111/sjop.12269.
- 34. Kwok MK, Schooling CM, Lam TH, Leung GM. Paternal smoking and childhood overweight: evidence from the Hong Kong "Children of 1997". *Pediatrics.* 2010;126(1):e46–e56. https://doi.org/10.1542/peds.2009-2642.
- Gonzalez-Barcala FJ, Pertega S, Sampedro M, et al. Impact of parental smoking on childhood asthma. *J Pediatr (Rio J)*. 2013;89(3):294–299. https://doi.org/10.1016/j.jped.2012.11.001.
- Lalwani AK, Liu YH, Weitzman M. Secondhand smoke and sensorineural hearing loss in adolescents. Arch Otolaryngol Head Neck Surg. 2011;137(7):655–662. https://doi.org/10.1001/archoto.2011.109.
- Fellinger J, Holzinger D, Sattel H, Laucht M, Goldberg D. Correlates of mental health disorders among children with hearing impairments. *Dev Med Child Neurol.* 2009;51(8):635–641. https://doi.org/10.1111/ j.1469-8749.2008.03218.x.
- Lu Y, Mak KK, Bever HPS van, Ng TP, Mak A, Ho RC-M. Prevalence of anxiety and depressive symptoms in adolescents with asthma: a meta-analysis and meta-regression. *Pediatr Allergy Immunol.* 2012;23 (8):707–715. https://doi.org/10.1111/pai.12000.
- Eidsdottir ST, Kristjansson AL, Sigfusdottir ID, Garber CE, Allegrante JP. Association between higher BMI and depressive symptoms in Icelandic adolescents: the mediational function of body image. Eur J Public Health. 2014;24(6):888–892. https://doi.org/10.1093/eurpub/ckt180.
- Flensborg-Madsen T, von Scholten MB, Flachs EM, Mortensen EL, Prescott E, Tolstrup JS. Tobacco smoking as a risk factor for depression. A 26-year population-based follow-up study. *J Psychiatr Res.* 2011;45(2):143–149. https://doi.org/10.1016/j.jpsychires.2010.06.006.
- Semba J, Wakuta M. Chronic effect of nicotine on serotonin transporter mRNA in the raphe nucleus of rats: reversal by co-administration of bupropion. *Psychiatry Clin Neurosci.* 2008;62(4):435–441. https://doi.org/10.1111/j.1440-1819.2008.01822.x.
- Petty F, Kramer GL, Fulton M, Moeller FG, Rush AJ. Low plasma GABA is a trait-like marker for bipolar illness. *Neuropsychopharma-cology*. 1993;9(2):125–132. https://doi.org/10.1038/npp.1993.51.
- Petty F. GABA and mood disorders: a brief review and hypothesis.
  J. Affect Disord. 1995;34(4):275–281. https://doi.org/10.1016/0165-0327(95)00025-i.
- Dowlati Y, Herrmann N, Swardfager W, et al. A meta-analysis of cytokines in major depression. *Biol Psychiatry*. 2010;67(5):446–457. https://doi.org/10.1016/j.biopsych.2009.09.033.
- Jefferis BJ, Lowe GDO, Welsh P, et al. Secondhand smoke (SHS) exposure is associated with circulating markers of inflammation and endothelial function in adult men and women. *Atherosclerosis*. 2010;208 (2):550–556. https://doi.org/10.1016/j.atherosclerosis.2009.07.044.
- Park S, Lim S, Kim J, Lee H, June KJ. Socioeconomic disparities in household secondhand smoke exposure among non-smoking adolescents in the Republic of Korea. *Glob Public Health*. 2017;12 (9):1104–1121. https://doi.org/10.1080/17441692.2015.1117119.

- 47. Oberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. *Lancet*. 2011;377 (9760):139–146. https://doi.org/10.1016/S0140-6736(10)61388-8.
- WHO. Tobacco free initiative (TFI). www.who.int/tobacco/mpower/ en/. Published 2017. Accessed December 18, 2019.
- Ranasinghe S, Ramesh S, Jacobsen KH. Hygiene and mental health among middle school students in India and 11 other countries. *J Infect Public Health*. 2016;9(4):429–435. https://doi.org/10.1016/j.jiph.2015.11.007.
- 50. Xi B, Liang Y, Liu Y, et al. Tobacco use and second-hand smoke exposure in young adolescents aged 12–15 years: data from 68 low-income and middle-income countries. *Lancet Glob Health*. 2016;4(11):e795–e805. https://doi.org/10.1016/S2214-109X(16)30187-5.
- 51. Lange S, Koyanagi A, Rehm J, Roerecke M, Carvalho AF. Association of tobacco use and exposure to second-hand smoke with suicide

- attempts among adolescents—findings from 33 countries. Nicotine Tob Res. In press. Online September 5, 2019. https://doi.org/10.1093/ntr/ntz172.
- Bird Y, Staines-Orozco H, Moraros J. Adolescents' smoking experiences, family structure, parental smoking and socio-economic status in Ciudad Juárez, Mexico. *Int J Equity Health*. 2016;15:29. https://doi.org/10.1186/s12939-016-0323-y.
- Culpin I, Heron J, Araya R, Melotti R, Joinson C. Father absence and depressive symptoms in adolescence: findings from a UK cohort. *Psychol Med.* 2013;43(12):2615–2626. https://doi.org/ 10.1017/S0033291713000603.
- 54. Sustainable Development Goals. New Education Data for SDG4: Focus on Out-Of-School Children. www.sdg4education2030.org/new-education-data-sdg4-focus-out-school-children-27-september-2018. Published 2018. Accessed December 18, 2019.