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Exercise attenuates the association between household pesticide exposure and depressive symptoms: Evidence from NHANES, 2005–2014

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ABSTRACT

Background: The effect of household pesticide exposure on depressive symptoms in the general population is underexplored, and the role of exercise in the association between pesticide exposure and depressive symptoms is unclear.
Objective: The goals of this study are to examine whether the associations between household pesticide exposure and depressive symptoms exist in the general population, and whether exercise can attenuate these associations.
Methods: We used data from the 2005–2014 National Health and Nutrition Examination Surveys (NHANES), including a total of 14708 US adult participants who were 20 years or older. Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9). Exercise information on the recreational physical activity (RPA) and pesticide exposure were self-reported in an interview.
Results: Participants with exposure of household pesticide had a higher odds ratio ([OR]; OR = 1.32, 95% confidence intervals [CI]: 1.12–1.56) for depressive symptoms, compared to those who had not been unexposed. A significant interaction between exercise and pesticide exposure on depressive symptoms was observed (P = 0.038). Stratified analysis showed that household pesticide exposure was associated with a 50% higher risk of depressive symptoms (OR = 1.50, 95% CI: 1.20–1.86) in the population with light RPA. However, we did not find a significant association in the group with moderate + vigorous RPA (P = 0.305).
Conclusion: This study further confirms that household pesticide exposure is associated with an elevated risk of depressive symptoms in the general population. More importantly, we for the first time reports that moderate + vigorous RPA attenuates the positive association between household pesticide exposure and depressive symptoms.

1. Introduction

Pesticides are widely used in households to control insects. Household pesticide use and exposure have been very common in the United States of America and worldwide(Alavanja, 2009; Narayan et al., 2013). Previous findings have shown that occupational or residential pesticide exposure was associated with increased risks of many health problems, including asthma, diabetes, Parkinson's disease, birth and fetal defects, certain cancers, and psychiatric disorders(Freire and Koifman, 2013; Kim et al., 2017; Koh et al., 2017). Although the association between pesticide exposure and depressive symptoms was found in several studies, most studies are limited in their generalizability due to performing in occupational population, such as agricultural workers(Beard et al., 2013; Freire; Koifman, 2013; Onwuameze et al., 2013; Tarone et al., 1997). Also, the conflictive results exist. For example, a cross-sectional study by Solomon and colleagues reported that past use of pesticides was not associated with current anxiety or depressive symptoms(Solomon et al., 2007). Household pesticide exposure may differ greatly from occupational exposure in terms of the frequency, duration, intensity, and type of exposure. However, the data on the associations between household pesticides exposure and depressive symptoms in the general population are scarce.

A systematic review concluded that exercise could improve depressive symptoms in depressive patients, although highlighted that this finding should be interpreted with caution since analyses of

Abbreviations: BMI, body mass index; CI, Confidence intervals; PHQ, Patient Health Questionnaire; OR, Odds ratio; NHANES, National Health and Nutrition Examination Surveys

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methodologically robust trials showed a much smaller effect in favor of exercise(Rimer et al., 2012). Similarly, another recent systematic review also reported that physical activity can protect against depressive symptoms regardless of age and geographical region(Schuch et al., 2018). Although the underlying mechanisms are still poorly understood, previous studies suggest that exercise-induced cortisol, endorphin, or monoamine secretion, and neurotransmitter function promotion may play a role in the beneficial effect(Anderson and Shivakumar, 2013; Duclos et al., 2003; Hamer et al., 2012; Lucassen et al., 2010). Notable psychological benefits have also been reported. For example, a population study in Finland found that those who exercised at least twice a week reported higher levels of sense of coherence and a stronger feeling of social integration than their less frequently exercising counterparts(Hassmen et al., 2000). Also, previous studies have indicated that physical activity might detox harmful chemicals from the body and can alleviate depressive symptoms(Agudelo et al., 2014; Zaitseva et al., 2015). Therefore, the goals of this study are to examine whether the associations between household pesticide exposure and depressive symptoms exist in the general population, and whether exercise can attenuate these associations.

2. Methods

2.1. Study population

The National Health and Nutrition Examination Surveys (NHANES) is a series of large, multistage probability surveys designed to be representative of the US civilian, noninstitutionalized population that is conducted by the National Center for Health Statistics (NCHS) and Centers for Disease Control and Prevention. Detailed descriptions of the survey design and data collection procedures are available elsewhere. (National Center for Health Statistics, 2005–2016) The data are collected via an in-home interview and a visit to a mobile examination center. All participants provided written informed consent and the research ethics boards of the NCHS approved all protocols.

We used data from the 2005–2014 NHANES (including 5 cycles: 2005–2006, 2007–2008, 2009–2010, 2011–2012, and 2013–2014). The following selection criteria were used: 1) aged 20 years or older; 2) data available on age, sex, race, body mass index (BMI), recreational physical activity (RPA), education attainment, and poverty income ratio; 3) the participants responded to the questions on pesticide exposure and depressive symptoms. Finally, a total of 14,708 US adult participants were included in the study.

2.2. Measures

Although the assessment on self-reported physical activity have changed since 2007–2010 wave, the majority of the core questions on physical activity remained unchanged during 2005 and 2014. Exercise information on the (RPA was self-reported during an interview, In the 2005–2006 data, self-reported moderate/vigorous RPA was determined by the responses to the following questions: 'Over the past 30 days, did {you/study participant(SP)} do any vigorous activities for at least 10 min that caused heavy sweating, or large increases in breathing or heart rate? Some examples are running, lap swimming, aerobics classes or fast bicycling.', and 'Over the past 30 days, did {you/SP} do moderate activities for at least 10 min that cause only light sweating or a slight to moderate increase in breathing or heart rate? Some examples are brisk walking, bicycling for pleasure, golf, and dancing.' In the 2007–2014 data, the corresponding questions are: 'In a typical week {you/SP} do any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate like running or basketball for at least 10 min continuously?', and 'In a typical week {you/SP} do any moderate-intensity sports, fitness, or recreational activities that cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or volleyball for at least 10 min continuously?'. The participants answered 'Yes' to any questions above were defined as vigorous/moderate RPA, and others were defined as light RPA.

To account for the occupational/domestic physical activity and leisure-time sedentary behavior, we performed a sensitivity analysis using the 2005–2006 data, where physical activity and sedentary behavior were objectively assessed using the ActiGraph accelerometer (model 7164; ActiGraph LLC, Pensacola, FL). The threshold for moderate-intensity was 2020 counts and the threshold for vigorous-intensity was 5999 counts (Troiano et al., 2008). High physical activity was defined as having at least 10 min of moderate-intensity per day, and others were defined as with low physical activity. In this sub-analysis, we included accelerometer data from 2240 healthy individuals who met our minimum wear time criteria, recommended by NHANES Tutorials(National Cancer Institute, 2019).

Household pesticide exposure was defined as the responses to the question "In the past 7 days, were any chemical products used in {your/his/her}home to control fleas, roaches, ants, termites, or other insects?" Chlorophenols, carbamates, and organophosphorus metabolites (2,4,5-trichlorophenol, 2,4,6-trichlorophenol, 2,5-dichlorophenol, o-phenyl phenol, 2,4-dichlorophenol, 2,4,6-trichlorophenol, acephate, ethylenethio urea, methamidaphos, dimethoate, and propylenethio urea) were measured in spot urine. (National Center for Health Statistics, 2005–2016) A total of 2831 participants for chlorophenols metabolites, and 1851 participants for carbamates and organophosphorus metabolites were eligible for the analysis.

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9), which is a 9-item depressive symptoms screening instrument that asks participants to choose 1 of 4 responses about the frequency of depressive during the previous 2 weeks(Kroenke et al., 2001). Those scoring ≥ 10 were considered as having moderate, moderately severe, or severe depressive symptoms.

Antidepressant use was defined as taking at least one prescribed antidepressant medication in the past 30 days. We identified antidepressants using the Lexicon Plus® therapeutic classification (first-level category "Psychotherapeutic Agents", the second-level category "Antidepressants"), which included selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, phenylpiperazine, and miscellaneous antidepressants(Wang et al., 2016). For psychological counseling, we defined counseling and various types of therapy as treatment with a mental health professional, which was measured by the survey question, "During the past 12 months, have you seen or talked to a mental health professional such as a psychologist, psychiatrist, psychiatric nurse, or clinical social worker about your health?" We defined depressive symptoms as PHQ-9 total scores ≥ 10, or taking at least one prescribed antidepressant medication in the past 30 days, or receiving psychological counseling treatment.

Weight and height were measured by trained technicians who used standardized procedures. The race was categorized as non-Hispanic white, non-Hispanic black, Mexican-American, or other categories. The poverty income ratio is the ratio of a family's income to the US Census Bureau's poverty threshold, which is adjusted for family size and is updated annually for inflation. The poverty income ratio was used as the indicator of socioeconomic status in the analyses. Participants were categorized as never smokers (individuals who have smoked < 100 cigarettes in life), former smokers (having smoked > 100 cigarettes in life but do not currently smoke), and current smokers.

2.3. Statistical analysis

All analyses included sample weights to account for oversampling and nonresponse to provide nationally representative results, as recommended by NHANES.(National Center for Health Statistics, 2005–2016) Continuous variables were presented as mean and standard deviation (SD), whereas categorical variables were presented as cases (n) and percentage (%). Chi-squared tests and 2-tailed Student *t* tests were used to compare the characteristics of the pesticide exposed and unexposed group. Logistic regression was used to calculate the odds ratio (OR) for the associations of self-reported pesticide exposure and their metabolites with depressive symptoms. Univariate analyses were performed in Model 1. Model 2 was adjusted for age, sex, and race; Model 3 was adjusted for BMI, RPA, marital status, education attainment, and poverty income ratio in addition to Model 2. Also, the interactions between pesticide exposure and RPA on depressive symptoms were investigated. The NHANES does not provide details on antidepressant use and psychological counseling, but the individuals seeking psychological counseling might suffer from other mental illnesses rather than depression, and antidepressants were prescribed for reasons other than depression, so we performed a sensitivity analysis by excluding the participants with antidepressant medication or receiving psychological counseling treatment (1608 participants). In addition, we performed another sensitivity analysis using the PHQ-9 score as a continuous variable. All data analyses were performed using Stata software version 12.1 (STATA Corp., TX, US). A two-sided $P < 0.05$ was considered statistically significant.

3. Results

There were 14708 participants eligible for our final analysis, of them 1835 (12.5%) participants self-reported an exposure of household pesticide. The mean age of participants was 48.0 ± 17.7 years, 55.6% of the participants were female, and 22.1% participants with depressive symptoms. The characteristics of the pesticide exposed and unexposed groups were statistically significantly different except for sex (Table 1).

The prevalence of depressive symptoms in the pesticide exposed and unexposed groups were 28.9% and 21.1%. Table 2 showed the relationship between household pesticide exposure and risk of depressive symptoms, in which participants who exposed to household pesticide had a higher OR (OR = 1.46, 95% CI [confidence intervals]: 1.24–1.72, $P < 0.001$) for depressive symptoms, compared to those unexposed (model 1). Additionally, adjusted for age, sex, and race (model 2), the OR remains the same; and further adjusted for BMI, RPA, marital status, education attainment, and income ratio (model 3), the OR was 1.32 (95%CI: 1.12–1.56, $P = 0.001$) (Supplementary STable 1). Moreover, we further investigated the associations between pesticide metabolites and depressive symptoms, and found that O-Phenyl phenol was significantly associated with a higher risk of depressive symptoms (OR = 1.19, 95% CI: 1.02–1.39, $P = 0.028$) (Table 3).

A significant interaction between RPA and household pesticide exposure on depressive symptoms was observed ($P = 0.016$) (Fig. 1). Stratified analysis by RPA (moderate + vigorous vs. light) was performed. In the group with moderate + vigorous RPA, the prevalence of depressive symptoms in the pesticide exposed and unexposed groups were 21.0% and 17.2%. After adjusting for other covariates, the association between household pesticide exposure and depressive symptoms was not statistically significant (OR = 1.12, 95% CI: 0.90–1.41, $P = 0.305$). However, for light RPA group, the prevalence of depressive symptoms in the pesticide exposed and unexposed groups were 35.1% vs. 24.9% (Table 4). After adjusting for other covariates, household pesticide exposure was associated with a 50% higher risk of depressive symptoms (OR = 1.50, 95% CI: 1.20–1.86, $P < 0.001$) in the population with light RPA. Sensitivity analysis showed similar results, although the associations were not statistically significant using accelerometer data (Supplementary STable 2–6).

Table 1
Characteristics of the study sample.

Variable	Pesticide exposed (n = 1835)	Pesticide unexposed (n = 12873)	*P* value
Age (years)	49.9 ± 17.3	47.8 ± 17.8	< 0.001
Sex (Females, %)	1009(55.0)	7163(55.6)	0.596
Race (%)			
Non-Hispanic white	752(41.0)	6393(49.7)	< 0.001
Non-Hispanic black	514(28.0)	2487(19.3)	
Mexican-American	277(15.1)	1851(14.4)	
Other	292(15.9)	2142(16.6)	
Body mass index (kg/m^2)	29.8 ± 7.5	29.4 ± 7.2	0.008
Smoking status (%)			
Current smoker	869(47.4)	6769(52.6)	< 0.001
Former smoker	405(22.1)	2874(22.3)	
Never smoker	561(30.6)	3230(25.1)	
Marital status (%)	822(44.8)	6420(49.9)	< 0.001
Education attainment (%)			
< 9 years	201(11.0)	1116 (8.7)	< 0.001
9–11 years	341(18.6)	1982(15.4)	
12 years	450(24.5)	3021(23.5)	
> 12 years	843(45.9)	6757(52.5)	
Vigorous/Moderate RPA(%)	805(43.9)	6353(49.4)	< 0.001
Poverty income ratio	2.1 ± 1.5	2.5 ± 1.6	< 0.001
Depressive symptoms (%)	530(28.9)	2715(21.1)	< 0.001

PRA = recreational physical activity.
Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as cases (percentage).

Table 2
The associations between pesticide use in home and depressive symptoms.

	N(%)	OR	95%CI	*P* value
Model 1				
Pesticide unexposed	2715(21.1%)	Reference		
Pesticide exposed	530(28.9)	1.46	1.24–1.72	< 0.001
Model 2				
Pesticide unexposed	2715(21.1%)	Reference		
Pesticide exposed	530(28.9)	1.46	1.24–1.72	< 0.001
Model 3				
Pesticide unexposed	2715(21.1%)	Reference		
Pesticide exposed	530(28.9)	1.32	1.12–1.56	0.001

OR = odds ratio, CI = confidence intervals.
Model 1 unadjusted.
Model 2 adjusted for age, sex, and race.
Model 3 adjusted for age, sex, race, body mass index, recreational physical activity, marital status, education attainment, and poverty income ratio.

4. Discussion

Our study shows that household pesticide exposure is significantly associated with depressive symptoms in the general population. We for the first time report that there is an interaction between physical exercise and pesticide exposure on the risk of depressive symptoms,

Table 3
The associations between pesticide metabolites and depressive symptoms.

	OR	95%CI	*P* value
2,4,5-trichlorophenol (ug/L)	0.93	0.69–1.26	0.630
2,4,6-trichlorophenol (ug/L)	0.99	0.89–1.09	0.823
2,5-dichlorophenol (ug/L)	1.00	1.00–1.00	0.403
O-Phenyl phenol (ug/L)	1.19	1.02–1.39	0.028
2,4-dichlorophenol (ug/L)	1.00	1.00–1.00	0.274
2,4,6-trichlorophenol (ug/L)	0.93	0.69–1.26	0.630
Acephate (ug/L)	0.46	0.18–1.17	0.101
Ethylenethio urea (ug/L)	0.95	0.75–1.21	0.686
Methamidaphos (ug/L)	0.07	0.00–1256.2	0.486
Dimethoate (ug/L)	2.66	0.35–38.3	0.268
Propylenethio urea (ug/L)	0.50	0.35–204.1	0.179

OR = odds ratio, CI = confidence intervals.
Adjusted for age, sex, race, body mass index, recreational physical activity, marital status, education attainment, and poverty income ratio.

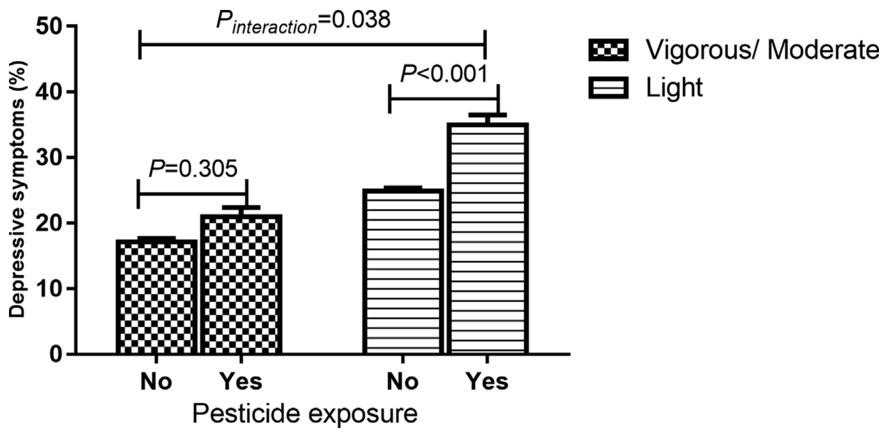

Fig. 1. The proportions of depressive symptoms in the pesticide-exposed and unexposed group by recreational physical activity.

Table 4
The associations between pesticide use in home and depressive symptoms by physical activity.

	N(%)	OR	95%CI	*P* value
Light RPA				
Pesticide unexposed	1621(24.9%)	Reference		
Pesticide exposed	361(35.1%)	1.50	1.20–1.86	< 0.001
Vigorous/Moderate RPA				
Pesticide unexposed	1094(17.2%)	Reference		
Pesticide exposed	169(21.0%)	1.12	0.90–1.41	0.305

OR = odds ratio, CI = confidence intervals, RPA = recreational physical activity.
Adjusted for age, sex, race, body mass index, marital status, education attainment, and poverty income ratio.

indicating that exercise might be able to attenuate the association of pesticide exposure with depressive symptoms.

Previous studies have reported that pesticide exposure was associated with depressive disorders in occupational settings(Beard et al., 2014; Beseler and Stallones, 2008; Suarez-Lopez et al., 2019). For example, Serrano-Medina et al. reported that chronic occupational exposure of pesticides, mainly including organophosphate pesticides, was associated with neuropsychological effects such as depression, suicidal risk, and major anxiety(Serrano-Medina et al., 2019). Suarez-Lopez et al. found that the enzyme acetylcholinesterase, a biomarker of organophosphates and carbamates pesticide exposure, was associated with the depression and anxiety symptoms among adolescents(Suarez-Lopez et al., 2019). The Agricultural Health Study showed that the use of pesticides was longitudinally associated with a high risk of depression among male private pesticide applicators(Beard et al., 2014). Another cohort study, the Colorado Farm Family Health and Hazard Surveillance (CFFHHS) project, also showed that a history of pesticide poisoning was associated with a high risk of depression(Beseler and Stallones, 2008). A systematic review study published in 2013 including 11 studies on pesticide exposure and depression found that depression or other psychiatric disorders have shown increased risks associated with previous pesticide poisoning in 5 studies, with statistically significant OR ranging from 2.08 to 5.95, indicating that scientific evidence of the association between pesticide exposure and depression is still very limited and inconclusive(Freire and Koifman, 2013). An ecological study by Parrón et al. demonstrated that the population living in areas with high pesticide use had an increased risk for Alzheimer's disease and suicide attempts and that males living in these areas had increased risks for polyneuropathies, affective disorders and suicide attempts at the level of the general population(Parron et al., 2011). This study supported and extended previous findings and reported that pesticide exposure was associated with depressive disorders in the general population. However, the underlying mechanisms of this relationship are still poorly understood. Previous studies have shown that many pesticides have neurotransmitter toxicity, including inhibition of cholinesterase activity, increasing excitatory amino acid, decreasing the level of Dopamine(Liu, 2012), which could be the possible mechanisms in the association between pesticide exposure and depressive disorders. Our findings showed that O-Phenyl phenol was significantly associated with elevated risk of depressive symptoms, and this result has to be further confirmed.

To date, numerous studies, including randomized controlled trials, prospective study, and meta-analysis, have demonstrated the benefits of physical activity on depression(Conn, 2010; Dunn et al., 2005; Schuch et al., 2018). In our study, an interaction between physical activity and pesticide exposure in terms of depression is observed, but still, the underlying mechanisms are unclear. One possible explanation is that physical activity may promote the clearance of harmful chemicals with neurotoxicity from the body. An animal study demonstrated that cardiovascular exercise training activates PGC-1α1:PPARα/δ:KAT, which controls plasma and brain kynurenine/kynurenic acid balance and has a protective effect on stress-induced depression in the mouse(Agudelo et al., 2014). This study suggests that cardiovascular exercise may detox harmful chemicals from the body and then can alleviate stress-induced depression. Another study including 133 students by Zaitseva et al. found that increased physical activity was associated with decreased hair copper, vanadium, bismuth, and mercury content in comparison to the low physical activity groups(Zaitseva et al., 2015). Other biochemicals are also likely to be responsible, including biological mechanisms through which exercise increases neurogenesis and reduces inflammatory and oxidant markers and activates the endocannabinoid system(Brellenthin et al., 2017; Schuch et al., 2016, 2018).

There is unclarity about the chemical types, intensity, and forms of exposure concerning the risk of depression(Koh et al., 2017). A study of 567 agricultural workers in France evaluated the effect of several pesticide families and reported positive associations of depression with the exposure to herbicides in general and dinitrophenol herbicides, but not associated with the exposure of the other 12 herbicide families, any pesticide, fungicides, or insecticides(Weisskopf et al., 2013). In the Agricultural Health Study, depression was positively associated with ever-use of two pesticide classes, fumigants, and organochlorine insecticides, as well as with ever-use of seven individual pesticides: the fumigants aluminum phosphide and ethylene dibromide; the phenoxy herbicide 2,4,5-T; the organochlorine insecticide dieldrin; and the OPs diazinon, malathion, and parathion(Beard et al., 2014). Therefore, more research is needed to identify the specific harmful components, toxicity, and dose of pesticides for depression.

4.1. Limitations and strengths

The strengths of our study include the large sample size and performed in the general population. Also, we for the first time reported the interaction between physical exercise and household pesticide exposure on the risk of depressive symptoms. There were also several limitations in our study. One limitation is that the cross-sectional nature of the present study precludes the inference of the cause-effect relationship. Another limitation is that the NHANES study did not collect detailed information on household pesticide, such as chemical types and intensity, which may have a varied effect on depression. Third, the information on pesticide use and exercise was self-reported and could be misclassified. Fourth, NHANES has geographical limitations and may not be sufficient to represent other geographic regions. Last, although the PHQ-9 has excellent reliability and validity in primary care, it is only for screening purposes for “current major depressive episode” as a result of its low positive predictive value(Inoue et al., 2012). Therefore, we performed a sensitivity analysis using the PHQ-9 score as a continuous variable, and found similar results.

5. Conclusion

In conclusion, this study adds further evidence that household pesticide exposure is associated with an elevated risk of depression in the general population. We for the first time reported that there was an interaction between exercise and household pesticide exposure on the depression indicating that moderate or vigorous RPA tends to attenuate the effect of household pesticide exposure on depressive symptoms. Our results highlight the importance of the cautious use of household pesticides because the chronic effects of poisoning may contribute to an elevated risk of depression. Further cohort studies will be necessary to confirm our results and to identify the specific harmful components, toxicity, and a dose of pesticide for depression and other neuropsychological disorders.

Ethics approval and consent to participate

All participants provided written informed consent and the research ethics boards of the National Center for Health Statistics approved all protocols.

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Availability of data and materials

The data of this study are available at https://www.cdc.gov/nchs/nhanes/index.htm.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Haiyan Chen: Formal analysis, Writing - original draft. **Li Chen:** Writing - review & editing. **Guang Hao:** Conceptualization, Writing - original draft, Writing - review & editing.

Declaration of competing interest

All authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.109760.

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