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Frequency-risk relationships between second-hand smoke exposure and respiratory symptoms among adolescents in Guangzhou, China

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20 ABSTRACT

Objectives: Although previous studies have suggested an association between second-hand smoke
 (SHS) exposure and respiratory symptoms, current evidence is inconsistent. Additionally, it
 remains unclear whether there are frequency-risk relationships between SHS exposure and
 respiratory symptoms among adolescents.

Methods: A cross-sectional survey was conducted using a stratified cluster sampling method to
obtain representative students. The univariable and multivariable logistic regression models were
fitted to explore the potential frequency-risk relationships between SHS exposure and respiratory
symptoms.

Results: Among 3575 students, the prevalence of SHS exposure was 49.5% in indoor public places, 34.5% in homes, 22.7% in indoor campuses, and 29.2% in outdoor campuses. There were significantly increased risks of respiratory symptoms corresponding to SHS exposure in public places (odds ratio [OR]=1.60, 95% CI 1.30-1.95), in homes (OR=1.53, 95% CI 1.25-1.87), in indoor campuses (OR = 1.43, 95% CI 1.14-1.79) and in outdoor campuses (OR = 1.37, 95% CI 1.10-1.69) using no exposure as reference. Notably, we also observed monotonically frequency-risk relationships between setting-specific (e.g., homes, public places, and campuses) SHS exposure and respiratory symptoms.

37 Conclusion: Our findings suggest that setting-specific SHS exposure is associated with a
38 significant, dose-dependent increase in risk of respiratory symptoms.

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49 INTRODUCTION

It is well established that inhaling second-hand smoke (SHS) is harmful and that no scientific evidence establishes a risk-free level of exposure.^{1,2} To note, a retrospective analysis of data from 192 countries revealed that 40% of children (including 35% of female non-smokers and 33% of male non-smokers) were exposed to SHS, which results in an annual estimate of 603000 deaths attributable to SHS.³ Global youth tobacco surveillance also reported that nearly half the adolescents worldwide were exposed to SHS at home (42.5%) and in public places (55.1%), which constitutes a substantial public health threat and demands urgent intervention.⁴ In recent years, much attention has been focused on SHS exposure in public places and in homes, but there is limited information in published reports regarding SHS exposure in indoor and outdoor campuses among adolescents.

Increasing epidemiological studies of adolescents have demonstrated the relations between SHS exposure and respiratory symptoms (such as nose irritation, coughing, and sore throat),⁵⁻⁸ but current evidence is inconsistent. Some studies demonstrated significant positive associations in adolescents, ^{9,10} while the report from Malaysian adolescents revealed no association.¹¹ To note, it was unclear whether there are dose–response relationships between SHS exposure and respiratory symptoms. Furthermore, SHS exposure occurs in varying amounts in public places, homes, and other indoor spaces, but few studies have differentiated SHS exposure in indoor and outdoor to make the setting-specific relations between SHS exposure and respiratory symptoms clearer. Of particular concern is that little is known about the effects of

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SHS exposure from indoor and outdoor campuses on respiratory symptoms, although a significant body of literature has associated indoor SHS exposure with respiratory symptoms. This study builds on previous literature to explore setting-specific (e.g., public places, homes, and campuses) and frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents.

76

77 METHODS

78 Ethics statement

The study was approved by the Ethics Committee of Guangdong Pharmaceutical University, and it was performed in accordance with the approved guidelines. This survey was qualified as involving no risks to participants. All participants provided an informed consent regarding the goals of the study and the willingness to participate.

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84 Study design and data collection

85 This cross-sectional study was conducted in Guangzhou city, China, from March to April 2016. The target population was high school students in Guangzhou city. A 86 stratified cluster sampling process was used to obtain a representative sample. In the 87 88 first stage, all high schools were divided into two categories (prestigious or non-prestigious schools) according to level of education and the education quality. 89 Three high schools were randomly sampled from prestigious schools, and four high 90 91 schools were randomly sampled from non-prestigious schools, with the probability of selection proportional to the number of the schools. In the second stage, classes in the 92

selected schools were randomly sampled with proportional to school enrollment size, and all students in sampled classes were eligible to participate. All interviewers in each school were centrally trained to ensure that the survey was carried out according to the protocol and that operation procedures were identical across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in the study, and the effective response rate was 95.4% (3657/3833). To note, only non-smokers were included in the analyses and a total of 3575 non-smokers were included in this study. **Study variables** The main outcome variable was self-reported respiratory symptoms. The respiratory symptoms were defined as persistent coughed or sputum for 3 consecutive months in a row during the past 12 months, as had been used in previous studies.¹²⁻¹⁴ The main independent variable of respiratory symptoms was self-reported SHS exposure, which was defined as non-smokers' inhalation of the smoke exhaled from smokers on ≥ 1 day a week for at least the last six months.¹ SHS exposure was asked separately in indoor public places, in homes, in indoor campuses and in outdoor campuses. Frequency of SHS exposure was continuous data (days/week), and was also categorized into three groups: <1 day/week (no exposure), '1-4 days/week' and '5-7 days/week'. Smoking status was classified as non-smokers and smokers (defined as 'has smoked over 100 cigarettes in their lifetime').

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115 Covariates including potential mediators and confounders were chosen a priori 116 on the basis of literature review. Potential covariates in our study included age (year), 117 gender (male or female), grade (4-5 or 1-2), only-child (yes or no), monthly pocket 118 money (\leq 100, \leq 100-399, or $\geq \leq$ 400), prestigious school (yes or no), father's 119 education (primary school, middle school, or university and above), mother's 120 education (primary school, middle school, or university and above), and asthma 121 history (yes or no).

Data analysis

All data were entered in duplicate into EpiData version 3.1 database (The EpiData Association, Odense Denmark). The univariable and multivariable logistic regression models were fitted to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for evaluating the frequency-risk relationships between SHS exposure (including ordinal and continuous variables) and respiratory symptoms. Linear trends of SHS exposure were assessed by modeling exposure as continuous variables (arithmetic or logarithmic scale) or ordinal variables in multivariable models. Two-sided p-value of ≤ 0.05 was regarded as being of statistical significance. All statistical analyses were conducted using Stata version 14.0(StataCorp LP, College Station, Texas, USA).

RESULTS

136 Characteristics of the sample

Sample characteristics are given in Table 1. A total of 3575 non-smoking students were interviewed, of whom 477 (13.3%) were classified as having respiratory symptoms. Participants' mean age was 15.0 ± 1.8 years, and 50.9% were male students. About 62.2% of the students were the only child in their family and 63.4% from prestigious schools. The prevalence of SHS exposure in indoor public places, homes, indoor campuses, and outdoor campuses was 49.5%, 34.5%, 22.7% and 29.2%, respectively.

145 Relation between binary SHS exposure and respiratory symptoms

Table 2 shows the relations between binary SHS exposure and respiratory symptoms. The prevalence of respiratory symptoms was significantly higher in students with SHS exposure (OR=1.60, 95% CI 1.30-1.95, for SHS in indoor public places; OR=1.53, 95% CI 1.25-1.87, for SHS in homes; OR = 1.43, 95% CI 1.14-1.79, for SHS in indoor campuses) than in those with no exposure. Similar positive associations were observed among students with SHS exposure in indoor campuses from smoking teachers (OR =1.34, 95% CI 1.05-1.71) or from smoking classmates (OR = 1.54, 95% CI 1.15-2.06). To note, the effects of SHS exposure in outdoor campuses cannot be ignored. Students with SHS exposure in outdoor campuses had significantly higher rates of respiratory symptoms (OR = 1.37, 95% CI 1.10-1.69) as compared with unexposed students, and there were similar positive associations between respiratory symptoms and SHS exposure in outdoor campuses from smoking teachers (OR =1.38, 95% CI 1.09-1.75) or from smoking classmates (OR = 1.33, 95%

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159 CI 1.03-1.71).

161 Relation between ordinal SHS exposure and respiratory symptoms

162	Table 3 indicates the relations between ordinal frequency of SHS exposure and
163	respiratory symptoms. Compared with no SHS exposure, ordinal frequency of SHS
164	exposure was associated with respiratory symptoms in a increasing manner (SHS in
165	public places: OR=1 for no exposure, OR=1.50 for 1-4 days/week, OR=1.87 for 5-7
166	days/week, p for linear trend <0.001; SHS in indoor campuses: OR=1 for no exposure,
167	OR=1.24 for 1-4 days/week, OR=1.84 for 5-7 days/week, p for linear trend <0.001).
168	When examining the relations by source of exposure, significant increasing trends
169	were observed for SHS exposure in indoor campuses from smoking teachers (p for
170	linear trend =0.001) and from smoking classmates (p for linear trend =0.005).
171	Additionally, there was a significantly increasing relation between ordinal frequency
172	of SHS exposure in outdoor campuses and respiratory symptoms (OR=1 for no
173	exposure, OR=1.28 for 1-4 days/week, OR=1.56 for 5-7 days/week, p for linear trend
174	=0.007), and similar increasing trends were observed for SHS exposure in outdoor
175	campuses from smoking teachers (p for linear trend =0.004) and from smoking
176	classmates (p for linear trend =0.006). However, no increasing trend was observed for
177	SHS exposure in homes.

179 Relation between continuous SHS exposure and respiratory symptoms

180 Table 4 presents the relations between continuous frequency of SHS exposure and

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181	respiratory symptoms. There are significant frequency-risk relationships between
182	indoor SHS exposure and respiratory symptoms (OR = 2.30 , 95% CI: $1.67-3.16$, for
183	SHS in indoor public places; $OR = 1.64$, 95% CI: 1.23-2.20, for SHS in homes; $OR =$
184	2.09, 95% CI: 1.42-3.07, for SHS in indoor campuses; OR = 1.70, 95% CI: 1.18-2.47,
185	for SHS in outdoor campuses). When examining the relations by source of exposure,
186	there were similar frequency-risk relationships for SHS exposure in indoor or outdoor
187	campuses from smoking teachers or from smoking classmates. Additionally, we
188	observed a monotonically increasing frequency-risk trend for SHS exposure in indoor
189	public places (Figure 1A), in homes (Figure 1B), in indoor campuses (Figure 2A) or
190	in outdoor campuses (Figure 2B). When examining these trends by source of
191	exposure, there were similar increasing frequency-risk trends for SHS exposure from
192	smoking teachers (Figure 3A for indoor SHS and Figure 3B for outdoor SHS) and
193	from smoking classmates (Figure 4A for indoor SHS and Figure 4B for outdoor SHS).
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195 **DISCUSSION**

This observational study showed that non-smoking students with setting-specific (public places, homes, or campuses) SHS exposure experienced significantly higher risks of respiratory symptoms than those with no exposure. The most striking findings from this study were that there were monotonically increasing frequency-risk relationships between setting-specific SHS exposure and respiratory symptoms. When examining these relations by source of exposure, there were similar monotonically increasing frequency-risk relationships for SHS exposure from smoking teachers and

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It is well known that there is no risk-free level of exposure to SHS. According to 204 205 the partial smoke-free legislation implemented in Guangzhou on 1 September 2010, 206 full smoke-free ban covered indoor campuses, outdoor campuses and most indoor public places, but did not cover homes. It is disappointing that SHS exposure or 207 smoking behaviors in schools were not eliminated, and were still at a high level 208 209 (22.7% for SHS exposure in indoor campuses; 29.2% for SHS exposure in outdoor 210 campuses). This observation may be due to poor compliance with the full smoke-free ban in campuses, since we observed that SHS exposure among students was mainly 211 from smoking teachers (indoor SHS: 17.8%; outdoor SHS: 18.4%) and smoking 212 classmates (indoor SHS: 11.9%; outdoor SHS:19.6%) in both indoor and outdoor 213 214 campuses. Similarly, a recent population-based study in Tehran showed that 29.3% and 29.2% non-smoker students have been exposed to SHS from smoking teachers in 215 indoor and outdoor campuses, respectively, and another survey of Chinese college 216 students reported that 37% of non-smokers had SHS exposure from smoking teachers. 217 ^{15,16} More disappointing was that SHS exposure in indoor public places among 218 students was remarkably high in 49.5% in this study, which is similar to the latest 219 220 study on adult SHS exposure in Guangzhou (50.3%) and the Global Youth Tobacco Survey (47.8%).^{17,18} However, very few respondents (1-2%) reported smoking in 221 enclosed public places in England after the implementation of comprehensive 222 smoke-free legislation covering all enclosed public places and workplaces.¹⁹ These 223 findings point out the urgent need for a comprehensive smoke-free legislation 224

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covering all public places in Guangzhou to protect the public from SHS hazards.

A few published studies have indicated that SHS exposure may be a risk factor of 226 227 respiratory symptoms, but the potential relation for setting-specific exposure was still unclear.²⁰⁻²³ Recent studies of Chinese adolescents indicated that there was a positive 228 relation between household SHS exposure and respiratory symptoms, but the relation 229 for SHS exposure in workplaces or in schools was unknown.^{20,21} In addition, the 230 231 surveys of London casino workers and Shanghai workers revealed that there was an association between SHS exposure at work and respiratory symptoms, but the 232 association for SHS exposure in homes or in schools was unknown.^{22,23} To note, the 233 influence of SHS exposure from indoor campuses on respiratory symptoms is still 234 unclear, and the potential dose-response association between frequency of SHS 235 236 exposure and respiratory symptoms is also uncertain. Our study builds on previous 237 literature by exploring the potential dose-response relationships and differentiating SHS exposure in homes, public places, and campuses to make exposure and potential 238 relations clearer. We found that there were positive relations and frequency-risk 239 relationships between setting-specific (public places, homes, or campuses) SHS 240 exposure and respiratory symptoms. When examining the relations by source of 241 242 exposure, there was still evidence of similar dose-response relationships for SHS 243 exposure in indoor campuses from smoking teachers and smoking classmates. These findings provided new evidence of dose-response relationships between 244 245 setting-specific SHS exposure and respiratory symptoms among adolescents, and further research is needed to establish the causal relationship and its biological 246

mechanisms.

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248	Globally, outdoor smoking restrictions are uncommon, though the
249	outdoor-campus smoking bans implemented in Guangzhou City on 1 September 2010.
250	A few published studies have indicated that smoking increases PM _{2.5} concentrations in
251	outdoor areas to levels that are potentially hazardous to health, ^{24,25} but research
252	linking SHS exposures from outdoor environments to health effects is still limit.
253	Notably, the potential relation between outdoor SHS exposure and respiratory
254	symptoms is still unclear. To our knowledge, this is the first study to reveal the
255	relation between SHS exposure in outdoor campuses and respiratory symptoms
256	among adolescents, and found that outdoor SHS exposure was positively associated
257	with respiratory symptoms in a monotonically increasing trend. When examining the
258	relations by source of exposure, there were still similar frequency-risk relationships
259	for SHS exposure in outdoor campuses from smoking teachers and smoking
260	classmates. These findings provide more evidence for the adverse effects of outdoor
261	SHS exposure on human respiratory symptoms, and also support growing concern
262	about SHS exposure in outdoor campuses.

The most meaningful advantage of this study is that we contributes additionally to the literature by exploring the potential frequency-risk relationships and differentiating SHS exposure in specific settings (e.g., indoor or outdoor; public places, homes, or campuses) and specific sources (e.g., from smoking teachers or from smoking classmates) to make exposure and potential relations clearer. There are also some potential limitations in this study. First, all data were self-reported,

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269	including SHS exposure and respiratory symptoms. For SHS exposure, although
270	biochemical measures can give objective measurements, the biomarkers cannot
271	distinguish the sources of exposure, the key factors in this study. Previous survey has
272	found that school children are capable of reporting their health conditions reliably, ²⁶
273	and the presence of frequent cough and phlegm was quite obvious to the students and
274	explicit in the question to avoid measurement error. Second, causal association
275	between SHS exposure and respiratory symptoms could not be ascertained due to the
276	cross-sectional design. However, the notion of reverse causation that students with
277	respiratory symptoms deliberately increased their exposure to noxious SHS seems
278	improbable. The strong association observed in other studies also supported our data
279	validity and provided support for the deduction of causation. ^{20,27,28} Finally, few people
280	would be completely unexposed to SHS in densely populated Guangzhou even now,
281	when smoking was still allowed in public places such as amusement parks, restaurants,
282	workplaces, and so on. Therefore, the control groups who reported no SHS exposure
283	have probably underestimated their exposure, and the risk for respiratory symptoms in
284	these groups would also be underestimated.
285	In conclusion, SHS exposure in indoor and outdoor campuses is still at a high

level, which suggests poor compliance with the full smoke-free ban in schools and supports growing concern about SHS exposure in campuses. Additionally, this study contributes to the literature by finding monotonically increasing frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents in addition to differentiating SHS exposure in specific settings and specific sources to

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4	291	make these relationships clearer. Future longitudinal studies are needed to establish
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10	204	Contribution
11	294	Contributors
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13	295	CZ, LG, LS, JT, XB, CJ and YX were involved in the design of the study, data
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16	296	analysis and writing of the draft of the manuscript. All the authors read and approved
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23	299	Competing interests None
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376	Figure Legends
377	Figure 1. Predicted prevalence of respiratory symptoms based on second-hand smoke
378	exposure (A: exposure in indoor public places; B: exposure in homes).
379	
380	Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke
381	exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor
382	campuses).
383	
384	Figure 3. Predicted prevalence of respiratory symptoms based on second-hand smoke
385	exposure from smoking teachers (A: exposure in indoor campuses; B: exposure in
386	outdoor campuses).
387	
388	Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke
389	exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in
390	outdoor campuses).
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Page 19 of 28				BMJ Ope	n		
1							
2 3	392	Table 1. Demographic c	haracteristics of	the study pa	rticipants		
4		Characteristics	п	%	Characteristics	п	%
5		Respiratory symptoms			Grade		
7		No	3098	86.7	1-2	2329	65.2
8		Yes	477	13.3	4-5	1246	34.8
9		SHS exposure in indoor	public places		Only-child		
10		No	1806	50.5	No	1353	37.8
12		Yes	1769	49.5	Yes	2222	62.2
3		SHS exposure in homes			Prestigious school		
4		No	2342	65.5	No	1307	36.6
15		Yes	1233	34.5	Yes	2268	63.4
6 7		SHS exposure in indoor	campuses		Pocket money monthly(¥)	
8		No	2763	77.3	<100	2039	57.0
9		Yes	812	22.7	100-399	1125	31.5
20		SHS exposure in outdoo	r campuses		>400	411	11.5
21		No	2532	70.8	Father's education		
22		Yes	1043	29.2	Primary school	838	23.4
24		Gender		_>	Middle school	1215	34.0
25		Mala	1010	50.0	University and above	1522	12.6
26		Formale	1010	30.9 40.1	Mother's advection	1322	42.0
27		Female	1/5/	49.1	Driveers askes	079	27.4
28		Astrima history	2514	0.0.2		9/8	27.4
30		NO	3514	98.3		1165	32.6
31		Yes	01	1./	University and above	1432	40.1
32	393	<i>n</i> , number of participant	s; %, the proport	ion of partic	ipants.		
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SHS exposure	п	Respiratory	Unadjusted	Adjusted
_		symptoms (%)	OR(95%CI)	OR(95%CI) *
SHS exposure in inc	loor public place	es		
No	1806	200(11.1)	1.00	1.00
Yes	1769	277(15.7)	1.49(1.23-1.81)	1.60(1.30-1.95)
SHS exposure in ho	mes			
No	2342	275(11.7)	1.00	1.00
Yes	1233	202(16.4)	1.47(1.21-1.79)	1.53(1.25-1.87
SHS exposure in ind	loor campuses			
No	2763	338(12.2)	1.00	1.00
Yes	812	139(17.1)	1.48(1.19-1.84)	1.43(1.14-1.79
SHS exposure in ind	loor campuses fi	com smoking teachers		
No	2940	369(12.6)	1.00	1.00
Yes	635	108(17.0)	1.43(1.13-1.80)	1.34(1.05-1.71
SHS exposure in ind	loor campuses fi	om smoking classmate	es	
No	3149	399(12.7)	1.00	1.00
Yes	426	78(18.3)	1.54(1.18-2.02)	1.54(1.15-2.06
SHS exposure in ou	tdoor campuses			
No	2532	309(12.2)	1.00	1.00
Yes	1043	168(16.1)	1.38(1.13-1.69)	1.37(1.10-1.69
SHS exposure in ou	tdoor campuses	from smoking teachers		
No	2917	362(12.4)	1.00	1.00
Yes	658	115(17.5)	1.49(1.19-1.88)	1.38(1.09-1.75
SHS exposure in ou	tdoor campuses	from smoking classma	tes	
No	2873	366(12.7)	1.00	1.00
Yes	702	111(15.8)	1.29(1.02-1.62)	1.33(1.03-1.71

396	Table 2	. Relation	between	binary	SHS (exposure	and	res	piratory	v svi	nptoms
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^a: adjusted for gender (male vs female), grade (4-5 vs 1-2), only-child (yes vs no) and asthma

history (yes vs no).

Page 21 of 28				BMJ Open		
1						
2 3	401	Table 3. Relation betwe	een ordinal frequ	ency of SHS exposure	e and respiratory sy	mptoms
4	401	Frequency of	<i>n</i>	Respiratory	Unadjusted	Adjusted
5		SHS exposure	n	symptoms (%)	OR(95%CI)	OR(95%CI) ^a
6		SHS exposure in indoor	r public places			
/		No exposure	1806	200(11.1)	1.00	1.00
0 9		1-4 days/week	1242	184(14.8)	1.40(1.13-1.73)	1.50(1.20-1.86)
10		5-7 days/week	527	93(17.7)	1.72(1.32-2.25)	1.87(1.41-2.46)
11		p for linear trend			< 0.001	< 0.001
12		SHS exposure in homes	5			
13		No exposure	2342	275(11.7)	1.00	1.00
14		1-4 days/week	570	97(17.0)	1.54(1.20-1.98)	1.62(1.25-2.09)
15		5-7 days/week	663	105(15.8)	1.41(1.11-1.80)	1.45(1.13-1.87)
16		p for linear trend			_b	_ b
1/		SHS exposure in indoor	r campuses			
10		No exposure	2763	338(12.2)	1.00	1.00
20		1-4 days/week	539	81(15.0)	1.27(0.98-1.65)	1.24(0.95-1.63)
21		5-7 days/week	273	58(21.3)	1.94(1.42-2.64)	1.84(1.32-2.56)
22		p for linear trend			< 0.001	< 0.001
23		SHS exposure in indoor	r campuses from	smoking teachers		
24		No exposure	2940	369(12.6)	1.00	1.00
25		1-4 days/week	412	59(14.3)	1.16(0.87-1.57)	1.13(0.84-1.53)
26		5-7 days/week	223	49(22.0)	1.96(1.40-2.74)	1.78(1.25-2.53)
27		p for linear trend			< 0.001	0.001
28		SHS exposure in indoor	r campuses from	smoking classmates		
29		No exposure	3149	399(12.7)	1.00	1.00
31		1-4 days/week	271	45(16.6)	1.37(0.98-1.92)	1.38(0.97-1.97)
32		5-7 days/week	155	33(21.3)	1.86(1.25-2.78)	1.84(1.20-2.82)
33		p for linear trend			< 0.001	0.005
34		SHS exposure in outdo	or campuses			
35		No exposure	2532	309(12.2)	1.00	1.00
36		1-4 days/week	704	105(14.9)	1.26(0.99-1.60)	1.28(1.01-1.64)
37		5-7 days/week	339	63(18.6)	1.64(1.22-2.21)	1.56(1.13-2.15)
38		p for linear trend			< 0.001	0.007
39		SHS exposure in outdo	or campuses fron	n smoking teachers		
40 41		No exposure	2917	362(12.4)	1.00	1.00
42		1-4 days/week	456	71(15.6)	1.30(0.99-1.72)	1.24(0.94-1.64)
43		5-7 davs/week	202	44(21.8)	1.97(1.38-2.79)	1.74(1.20-2.50)
44		p for linear trend		()	<0.001	0.004
45		SHS exposure in outdo	or campuses from	n smoking classmates		
46		No exposure	2873	366(12.7)	1.00	1.00
47		1-4 days/week	451	62(13.8)	1.00	1 16(0 86-1 57)
48		5-7 days/week	251	49(19.5)	1.66(1.19-2.31)	1.66(1.16-2.39)
49		n for linear trend		17(17.0)	<0.001	0.006
5U 51	100	n number of participan	te SHS second	hand smoke OP add	le ratio: CL confida	nce interval
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53	403	aujusted for gender	(male vs female	e), grade (4-5 vs 1-2)	, only-child (yes v	(s no) and astnma
54	404	history (yes vs no).				
55	405	": No estimate of p valu	e for linear trend	is provide since no li	near trend was obs	erved.
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	(days/week, logarithmic scale)	β	SE	Ζ	p-value	OR(95% CI)
	SHS exposure in indoor public place	s				
	Univariable regression	0.73	0.16	4.68	< 0.001	2.06(1.52-2.80)
	Multivariable regression ^a	0.83	0.16	5.11	< 0.001	2.30(1.67-3.16)
	SHS exposure in homes					
	Univariable regression	0.45	0.14	3.14	0.002	1.56(1.18-2.07)
	Multivariable regression ^a	0.49	0.15	3.32	0.001	1.64(1.23-2.20)
	SHS exposure in indoor campuses					
	Univariable regression	0.78	0.18	4.30	< 0.001	2.19(1.53-3.12)
	Multivariable regression ^a	0.74	0.20	3.77	< 0.001	2.09(1.42-3.07)
	SHS exposure in indoor campuses from	om smokii	ng teachers			
	Univariable regression	0.82	0.20	4.16	< 0.001	2.27(1.54-3.33)
	Multivariable regression ^a	0.72	0.21	3.47	0.001	2.06(1.37-3.09)
	SHS exposure in indoor campuses fr	om smokii	ng classmate	es		
	Univariable regression	0.71	0.23	3.11	0.002	2.04(1.30-3.20)
	Multivariable regression ^a	0.69	0.25	2.77	0.006	2.00(1.22-3.26)
	SHS exposure in outdoor campuses					
	Univariable regression	0.58	0.17	3.32	0.001	1.79(1.27-2.51)
	Multivariable regression ^a	0.53	0.19	2.82	0.005	1.70(1.18-2.47)
	SHS exposure in outdoor campuses f	r̀om smok	ing teachers	5		
	Univariable regression	0.93	0.20	4.65	< 0.001	2.53(1.71-3.74)
	Multivariable regression ^a	0.78	0.21	3.72	< 0.001	2.20(1.45-3.33)
	SHS exposure in outdoor campuses f	rom smok	ing classma	ites		
	Univariable regression	0.44	0.20	2.22	0.027	1.55(1.05-2.30)
	Multivariable regression ^a	0.45	0.22	2.08	0.037	1.58(1.03-2.42)

^a: adjusted for gender (male vs female), grade (4-5 vs 1-2), only-child (yes vs no) and asthma
history (yes vs no).







Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor campuses).

125x64mm (300 x 300 DPI)









Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in outdoor campuses).

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	ltem #	Recommendation	Reported on page #				
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2				
	(b) Provide in the abstract an informative and balanced summary of what was done and what was found						
Introduction							
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5				
Objectives	3	State specific objectives, including any prespecified hypotheses	5				
Methods	Methods						
Study design	4	Present key elements of study design early in the paper	5				
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5				
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5				
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7				
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	6-7				
measurement		comparability of assessment methods if there is more than one group					
Bias	9	Describe any efforts to address potential sources of bias	6-7				
Study size	10	Explain how the study size was arrived at	5-6				
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7				
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7				
		(b) Describe any methods used to examine subgroups and interactions	7				
		(c) Explain how missing data were addressed	No missing data				
		(d) If applicable, describe analytical methods taking account of sampling strategy	No applicable				
		(e) Describe any sensitivity analyses	7				
Results							

Page	28 o	of 28
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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	8
·		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	No applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	8
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	8-10
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	8-10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	No applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	No applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	No funding
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Frequency-risk relationships between second-hand smoke exposure and respiratory symptoms among adolescents: a cross-sectional study in South China

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Manuscript ID	bmjopen-2017-019875.R1
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Complete List of Authors:	Chen, Zhiyao; Guangdong Pharmaceutical University Liu, Guocong; Guangzhou Yuexiu Center for Disease Control and Prevention Li, Shunming; Guangdong Pharmaceutical University Jiang, Ting; Guangzhou Yuexiu Center for Disease Control and Prevention Xu, Bin; Guangzhou Yuexiu Center for Disease Control and Prevention Chen, Jianying; Guangzhou Yuexiu District for Community Health Service Center of Baiyun Street Ye, Xiaohua; Guangdong Pharmaceutical University
Primary Subject Heading :	Smoking and tobacco
Secondary Subject Heading:	Epidemiology, Public health, Respiratory medicine, Smoking and tobacco
Keywords:	second-hand smoke exposure, respiratory symptoms, adolescents

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3	1	Frequency-risk relationships between second-hand smoke exposure and
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б	2	respiratory symptoms among adolescents: a cross-sectional study in South China
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9 10		
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30	13	These authors contributed equally to this work.
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20	ABSTRACT

Objectives: Although previous studies have suggested an association between second-hand smoke
 (SHS) exposure and respiratory symptoms, current evidence is inconsistent. Additionally, it
 remains unclear whether there are frequency-risk relationships between SHS exposure and
 respiratory symptoms among adolescents.

Methods: A cross-sectional survey was conducted using a stratified cluster sampling method to obtain a representative sample of high school students in Guangzhou, China. The respiratory symptoms were defined as persistent cough or sputum for 3 consecutive months during the past 12 months. Self-reported SHS exposure was defined as non-smokers' inhalation of the smoke exhaled from smokers on ≥1 day a week in the past 7 days. The univariable and multivariable logistic regression models were fitted to explore the potential frequency-risk relationships between SHS exposure and respiratory symptoms.

Results: Among 3575 students, the overall prevalence of SHS exposure was 69.2%, including 49.5% in public places, 34.5% in homes, 22.7% in indoor campuses, and 29.2% in outdoor campuses. There were significantly increased risks of having respiratory symptoms corresponding to SHS exposure in public places (odds ratio [OR]=1.60, 95% CI 1.30-1.95), in homes (OR=1.53, 95% CI 1.25-1.87), in indoor campuses (OR = 1.43, 95% CI 1.14-1.79) and in outdoor campuses (OR = 1.37, 95% CI 1.10-1.69) using no exposure as reference. Notably, we observed monotonically frequency-risk relationships between setting-specific (e.g., homes, public places, and campuses) SHS exposure and respiratory symptoms.

- 40 Conclusion: Our findings suggest that setting-specific SHS exposure is associated with a
- 41 significant, dose-dependent increase in risk of respiratory symptoms.

 Strengths and limitations of this study This study contributes additionally to the literature by exploring the potential frequency-risk relationship between SHS exposure and respiratory symptoms. This study differentiates SHS exposure in specific settings and specific sources to make exposure and potential relations clearer. SHS exposure and respiratory symptoms were self reported, which is a limitation. Our findings highlight the need for further longitudinal studies to establish the causal relationship and its biological mechanisms. 	1	
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53 INTRODUCTION

54	It is well established that inhaling second-hand smoke (SHS) is harmful and that no
55	scientific evidence establishes a risk-free level of exposure. ^{1,2} Notably, a retrospective
56	analysis of data from 192 countries revealed that 40% of children (including 35% of
57	non-smoking women and 33% of non-smoking men) were exposed to SHS, and this
58	exposure is estimated to result in an annual estimate of 603000 deaths attributable to
59	SHS. ³ Global youth tobacco surveillance also reported that nearly half the adolescents
60	worldwide were exposed to SHS at home (42.5%) and in public places (55.1%),
61	which constitutes a substantial public health threat and demands urgent intervention. ⁴
62	China is the world's largest producer and consumer of tobacco. The 2010 Global
63	Adult Tobacco Survey reported and 2014 Chinese adolescents Tobacco Survey
64	reported that 72.4% adult and 72.9% adolescents in China were exposed to SHS,
65	suggesting that the tremendous burden from tobacco-induced diseases makes tobacco
66	prevention an essential health priority in China. ^{5,6} In recent years, much attention has
67	been focused on SHS exposure in public places and in homes, but there is limited
68	reports on SHS exposure in indoor and outdoor campuses among adolescents.

Epidemiological studies of adolescents have explored the relations between SHS exposure and respiratory symptoms (such as nose irritation, coughing, and sore throat) or infection,⁷⁻¹¹ but current evidence is inconsistent. Some studies demonstrated significantly positive associations, ^{12,13} while the report from Malaysia revealed no association.¹⁴ Recent Chinese studies indicated that there was a positive relation between household SHS exposure and respiratory symptoms in adolescents, but the

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relation for SHS exposure in public places or in schools was unknown.^{15,16} SHS exposure occurs in varying amounts in public places, homes, and other indoor spaces, but few studies have differentiated SHS exposure in indoor and outdoor to make the setting-specific relations between SHS exposure and respiratory symptoms clearer. Of particular concern is that little is known about the effects of campus SHS exposure on respiratory symptoms. Furthermore, it was unclear whether there are dose-response relationships between SHS exposure and respiratory symptoms. This study builds on previous literature to explore setting-specific (e.g., public places, homes, and campuses) and frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents. telle

METHODS

Ethics statement

The study was approved by the Ethics Committee of Guangdong Pharmaceutical University, and it was performed in accordance with the approved guidelines. The goals of the study were given to study participants and they should express their willingness to participate. Before participating, written informed consents were obtained from their parents or guardians.

Study design and data collection

This cross-sectional study was conducted in Guangzhou, China, from March to April

2016. The target population was high school students. A stratified cluster sampling
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97	process was used to obtain a representative sample. Notably, middle schools in most
98	part of China are generally rated by the Bureau of Education as key schools (or
99	prestigious schools) and ordinary schools (or non-prestigious schools) according to
100	level of education and the education quality. In the first stage, all high schools were
101	divided into two categories (prestigious or non-prestigious schools). Three high
102	schools were randomly sampled from prestigious schools, and four high schools were
103	randomly sampled from non-prestigious schools, with the probability of selection
104	proportional to the number of the schools. In the second stage, classes in the selected
105	schools were randomly sampled with proportional to school enrollment size, and all
106	students in sampled classes were eligible to participate.
107	All interviewers in each school were centrally trained to ensure that the survey
108	was carried out according to the protocol and operation procedures were identical
109	across all areas. After obtaining informed consent, eligible students were asked to
110	complete a face-to-face survey by trained interviewers. A total of 3833 participants
111	were enrolled in the study, and the effective response rate was 95.4% (3657/3833).
112	Only non-smokers were included in the analyses and a total of 3575 non-smokers
113	were included in this study.
114	
115	Study variables

The main outcome variable was self-reported respiratory symptoms. The respiratory symptoms were defined as persistent cough or sputum for 3 consecutive months during the past 12 months.¹⁷⁻¹⁹ The main independent variable of respiratory

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119	symptoms was self-reported SHS exposure, which was defined as non-smokers'
120	inhalation of the smoke exhaled from smokers on ≥ 1 day a week in the past 7 days for
121	at least 6 months (first question: "In the past 7 days, how many days did you breathe
122	in SHS in homes (or indoor public places, indoor campuses, outdoor campuses)";
123	second question for those having SHS exposure: "Did you breathe in SHS in this
124	venue for at least 6 months?"). In order to recall SHS exposure for at least 6 months,
125	we use both curriculum schedules and calendars as an assistive device to facilitate
126	recall the time. Frequency of SHS exposure was continuous data (days/week), and
127	was also categorized into three groups: <1 day/week (no exposure), '1-4 days/week'
128	and '5-7 days/week'. Smoking status was classified as non-smokers and smokers
129	(defined as 'has smoked over 100 cigarettes in their lifetime').
130	Covariates including potential mediators and confounders were chosen a priori
131	on the basis of literature review. Potential covariates in our study included age (year),
132	gender (male or female), grade (4-5 or 1-2), only-child (yes or no), monthly pocket
133	money (< $\$100$, $\$100-399$, or \ge $\$400$), prestigious school (yes or no), father's
134	education (primary school, middle school, or university and above), mother's

education (primary school, middle school, or university and above), and asthmahistory (yes or no).

137

138 Data analysis

All data were entered in duplicate into EpiData version 3.1 database (The EpiData
Association, Odense Denmark). The univariable and multivariable logistic regression

models were fitted to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for evaluating the frequency-risk relationships between SHS exposure (including ordinal and continuous variables) and respiratory symptoms. Linear trends of SHS exposure were assessed by modeling exposure as continuous variables (arithmetic or logarithmic scale) or ordinal variables in multivariable models. Two-sided p-value of <0.05 was regarded as being of statistical significance. All statistical analyses were conducted using Stata version 14.0(StataCorp LP, College Station, Texas, USA). RESULTS Characteristics of the sample A total of 3575 non-smoking students were interviewed, of whom 477 (13.3%) were classified as having respiratory symptoms. Participants' mean age was 15.0 ± 1.8 years, and 50.9% were male students. About 62.2% of the students were the only child in their family and 63.4% from prestigious schools. The overall prevalence of SHS exposure was 69.2%, including 49.5% in indoor public places, 34.5% in homes, 22.7% in indoor campuses, and 29.2% in outdoor campuses (Table 1). **Relation between binary SHS exposure and respiratory symptoms** The prevalence of respiratory symptoms was significantly higher in students with

- 161 SHS exposure (OR=1.72, 95% CI 1.35-2.17, for SHS in general; OR=1.60, 95% CI
- 162 1.30-1.95, for SHS in indoor public places; OR=1.53, 95% CI 1.25-1.87, for SHS in

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163	homes; $OR = 1.43$, 95% CI 1.14-1.79, for SHS in indoor campuses) than in those with
164	no exposure (Table 2). Similar positive associations were observed in students with
165	SHS exposure in indoor campuses from smoking teachers (OR =1.34, 95% Cl
166	1.05-1.71) or from smoking classmates (OR = 1.54 , 95% CI 1.15-2.06). Notably, the
167	effects of SHS exposure in outdoor campuses cannot be ignored. Students with SHS
168	exposure in outdoor campuses had significantly higher rates of respiratory symptoms
169	(OR = $1.37, 95\%$ CI 1.10-1.69) as compared with unexposed students, and there were
170	similar positive associations between respiratory symptoms and SHS exposure in
171	outdoor campuses from smoking teachers (OR =1.38, 95% CI 1.09-1.75) or from
172	smoking classmates (OR = 1.33, 95% CI 1.03-1.71).

173

174 Relation between ordinal SHS exposure and respiratory symptoms

175 Compared with no SHS exposure, ordinal frequency of SHS exposure was associated with respiratory symptoms in an increasing manner (SHS in public places: OR=1 for 176 no exposure, OR=1.50 for 1-4 days/week, OR=1.87 for 5-7 days/week, p for linear 177 178 trend <0.001; SHS in indoor campuses: OR=1 for no exposure, OR=1.24 for 1-4 days/week, OR=1.84 for 5-7 days/week, p for linear trend <0.001; Table 3). When 179 180 examining these relations by source of exposure, significant increasing trends were 181 observed for SHS exposure in indoor campuses from smoking teachers (p for linear trend =0.001) and from smoking classmates (p for linear trend =0.005). Additionally, 182 183 there was a significantly increasing relation between ordinal frequency of SHS exposure in outdoor campuses and respiratory symptoms (OR=1 for no exposure, 184

OR=1.28 for 1-4 days/week, OR=1.56 for 5-7 days/week, p for linear trend =0.007; Table 3), and similar increasing trends were observed for SHS exposure in outdoor campuses from smoking teachers (p for linear trend =0.004) and from smoking classmates (p for linear trend =0.006). However, no increasing trend was observed for SHS exposure in homes.

191 Relation between continuous SHS exposure and respiratory symptoms

As to continuous SHS exposure, there were significant frequency-risk relationships between indoor SHS exposure and respiratory symptoms (OR = 2.30, 95% CI: 1.67-3.16, for SHS in indoor public places; OR = 1.64, 95% CI: 1.23-2.20, for SHS in homes; OR = 2.09, 95% CI: 1.42-3.07, for SHS in indoor campuses; OR = 1.70, 95%CI: 1.18-2.47, for SHS in outdoor campuses; Table 3). When examining these relations by source of exposure, there were similar frequency-risk relationships for SHS exposure in indoor or outdoor campuses (Table 3). Additionally, we observed a monotonically increasing frequency-risk trend for SHS exposure in indoor public places (Figure 1A), in homes (Figure 1B), in indoor campuses (Figure 2A) or in outdoor campuses (Figure 2B). When examining these trends by source of exposure, there were similar increasing frequency-risk trends for SHS exposure from smoking teachers (Figure 3A for indoor SHS and Figure 3B for outdoor SHS) and from smoking classmates (Figure 4A for indoor SHS and Figure 4B for outdoor SHS).

DISCUSSION

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207	This observational study showed that non-smoking students with setting-specific
208	SHS exposure experienced significantly higher risks of respiratory symptoms than
209	those with no exposure. The most striking findings from this study were that there
210	were monotonically increasing frequency-risk relationships between setting-specific
211	SHS exposure and respiratory symptoms. When examining these relations by source
212	of exposure, there were similar monotonically increasing frequency-risk relationships
213	for SHS exposure from smoking teachers and from smoking classmates.
214	It is well known that there is no risk-free level of exposure to SHS. Although

previous studies have focused on SHS exposure among Chinese adolescents, ^{15,16,20} 215 there is limited reports regarding SHS exposure in specific settings and specific 216 sources to make exposure clearer. According to the partial smoke-free legislation 217 218 implemented in Guangzhou on 1 September 2010, full smoke-free ban covered indoor campuses, outdoor campuses and most indoor public places, but did not cover homes. 219 It is disappointing that SHS exposure in schools was not eliminated, and was still at a 220 high level (22.7% for SHS exposure in indoor campuses; 29.2% for SHS exposure in 221 outdoor campuses). This observation may be due to poor compliance with the full 222 smoke-free ban in campuses, since we observed that SHS exposure among students 223 224 was mainly from smoking teachers and smoking classmates in both indoor and 225 outdoor campuses. Similarly, a recent population-based study in Tehran showed that about 30% non-smoking students have been exposed to SHS from smoking teachers 226 in indoor or outdoor campuses, ²¹ and another survey of Chinese college students 227 reported that 37% of non-smokers had SHS exposure from smoking teachers. ²⁰ More 228

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229	disappointing was that SHS exposure in indoor public places among students was
230	remarkably high in 49.5% in this study, which is similar to the latest study on adult
231	SHS exposure in Guangzhou (50.3%) and the Global Youth Tobacco Survey
232	(47.8%). ^{22,23} After the implementation of a smoke-free legislation, very few
233	respondents (1-2%) reported smoking in public places in England, ²⁴ but smoking
234	behaviors still remained high in public places in Guangzhou because of unwillingness
235	of the policymakers to implement tougher smoke-free policies and poor compliance
236	with the smoke-free law among smokers. ²³ These findings reveal that a partial
237	smoke-free legislation has a weak impact on smoking cessation, but a comprehensive
238	smoke-free legislation can substantially attenuate smoking behaviors, which point out
239	the urgent need for a comprehensive smoke-free legislation covering all public places
240	in Guangzhou to protect the public from SHS hazards.
241	A few published studies have indicated that SHS exposure may be a risk factor of
242	respiratory symptoms, but the potential relation for setting-specific exposure was still
243	unclear. ^{15,16,25,26} Recent studies of Chinese adolescents indicated that there was a
244	positive relation between household SHS exposure and respiratory symptoms, but the

respiratory symptoms, but the potential relation for setting-specific exposure was still unclear.^{15,16,25,26} Recent studies of Chinese adolescents indicated that there was a positive relation between household SHS exposure and respiratory symptoms, but the relation for SHS exposure in public places or in schools was unknown.^{15,16} In addition, the surveys of London casino workers and Shanghai workers revealed that there was an association between SHS exposure at work and respiratory symptoms, but the association for SHS exposure in homes or in public places was unknown.^{25,26} It is noteworthy that the influence of SHS exposure from indoor campuses on respiratory symptoms is still unclear, and the potential dose-response association between Page 13 of 28

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frequency of SHS exposure and respiratory symptoms is also uncertain. Our study builds on previous literature by exploring the potential dose-response relationships and differentiating SHS exposure in homes, public places, and campuses to make exposure and potential relations clearer. We found that there were positive relations and frequency-risk relationships between setting-specific SHS exposure and respiratory symptoms. When examining the relations by source of exposure, there was still evidence of similar dose-response relationships for SHS exposure in indoor campuses from smoking teachers and smoking classmates. These findings provided new evidence of dose-response relationships between SHS exposure and respiratory symptoms among adolescents, and support that the future studies should focus more on differentiating these associations in setting-specific and source-specific exposure. Additionally, further research is needed to establish the causal relationship and potential biological mechanisms, and confirm that elimination of SHS exposure (or stricter smoke-free legislation in Guangzhou) will lead to a reduction in respiratory symptoms among adolescents.

Globally, outdoor smoking restrictions are uncommon, though the outdoor-campus smoking bans implemented in Guangzhou City on 1 September 2010. A few published studies have indicated that smoking increases $PM_{2.5}$ concentrations in outdoor areas to levels that are potentially hazardous to health,^{27,28} but research linking SHS exposures from outdoor environments to health effects is still rare. Notably, the potential relation between outdoor SHS exposure and respiratory symptoms is still unclear. To our knowledge, this is the first study to reveal the

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273 relation between SHS exposure in outdoor campuses and respiratory symptoms 274 among adolescents, and found that outdoor SHS exposure was positively associated 275 with respiratory symptoms in a monotonically increasing trend. When examining the 276 relations by source of exposure, there were still similar frequency-risk relationships for SHS exposure in outdoor campuses from smoking teachers and smoking 277 278 classmates. Although outdoor SHS is more transient than indoor SHS, evidence from 279 review of the research literature on SHS levels in outdoor hospitality venues suggested that tobacco-generated PM_{2.5} in outdoor setting may occasionally be 280 281 equivalent to or higher than levels observed in indoor setting when smoking is permitted at close proximity.²⁷ These findings provide more evidence for the adverse 282 effects of outdoor SHS exposure on human respiratory symptoms, and also support 283 284 growing concern about SHS exposure in outdoor campuses. Future studies on school SHS exposure in adolescents and protective measures against SHS should take 285 outdoor campuses SHS into consideration. 286

287 The most meaningful advantage of this study is that we contributes additionally to the literature by exploring the potential frequency-risk relationships and 288 differentiating SHS exposure in specific settings and specific sources to make 289 290 exposure and potential relations clearer. There are also some potential limitations in 291 this study. First, all data was self-reported, including SHS exposure and respiratory symptoms. For SHS exposure, biochemical measures can give objective 292 293 measurements, but cannot distinguish the sources of exposure, the key factors in this 294 study. Previous survey has found that school children are capable of reporting their Page 15 of 28

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health conditions reliably,²⁹ and the presence of frequent cough and phlegm was quite 295 296 obvious to avoid measurement error. Second, causal association between SHS 297 exposure and respiratory symptoms could not be ascertained due to the cross-sectional 298 design. However, the notion of reverse causation that students with respiratory 299 symptoms deliberately increased their exposure to noxious SHS seems improbable. 300 The strong association observed in other studies also supported our data validity and provided support for the deduction of causation.^{15,30,31} Finally, few people would be 301 302 completely unexposed to SHS in densely populated Guangzhou even now, when 303 smoking was still allowed in public places (e.g., cafes, bars, night clubs, amusement parks, restaurants, and workplaces). Therefore, the control groups who reported no 304 SHS exposure have probably underestimated their exposure, and the risk for 305 306 respiratory symptoms in these groups would also be underestimated. 307 In conclusion, SHS exposure in indoor and outdoor campuses is still at a high

level, which suggests poor compliance with the full smoke-free ban in schools and supports growing concern about SHS exposure in campuses. Additionally, this study contributes to the literature by finding monotonically increasing frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents in addition to differentiating SHS exposure in specific settings and specific sources to make these relationships clearer. Future longitudinal studies are needed to establish the causal relationship and its biological mechanisms.

315

316 Contributors

317	CZ, LG, LS, JT, XB, CJ and YX were involved in the design of the study, data
318	analysis and writing of the draft of the manuscript. All the authors read and approved
319	the final version of the manuscript.
320	
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322	The authors bore their own costs for conducting this study and hence no specific
323	funding line for this study.
324	
325	Competing interests None.
326	
327	Ethics approval
328	The Ethics Committee of Guangdong Pharmaceutical University.
329	
330	Data sharing statement
331	No additional data are available.
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414	Figure Legends
415	Figure 1. Predicted prevalence of respiratory symptoms based on second-hand smoke
416	exposure (A: exposure in indoor public places; B: exposure in homes).
417	
418	Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke
419	exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor
420	campuses).
421	
422	Figure 3. Predicted prevalence of respiratory symptoms based on second-hand smoke
423	exposure from smoking teachers (A: exposure in indoor campuses; B: exposure in
424	outdoor campuses).
425	
426	Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke
427	exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in
428	outdoor campuses).
429	

430	Table 1. Demographi	c characteristics	of the study par	ticipants		
	Characteristics	n	%	Characteristics	n	%
	Respiratory symptom	IS		Grade		
	No	3098	86.7	1-2	2329	65.
	Yes	477	13.3	4-5	1246	34.
	SHS exposure in gen	eral		Only-child		
	No	1101	30.8	No	1353	37.
	Yes	2474	69.2	Yes	2222	62.
	SHS exposure in inde	oor public places		Gender		
	No	1806	50.5	Male	1818	50.
	Yes	1769	49.5	Female	1757	49.
	SHS exposure in hon	nes		Pocket money monthly(¥	e)	
	No	2342	65.5	<100	2039	57.
	Yes	1233	34.5	100-399	1125	31.
	SHS exposure in inde	oor campuses	77.0	≥400	411	11.
	No	2763	77.3	Father's education	020	22
	res	812	22.1	Primary school	838 1215	23.
	SHS exposure in out	loor campuses		Middle school	1213	34.
	No	2532	70.8	University and above	1522	42.
	Yes	1043	29.2	Mother's education		
	Asthma history	2514		Primary school	978	27.
	No	3514	98.3	Middle school	1165	32.
	Yes	61	1.7	University and above	1432	40
431 //22	<i>n</i> , number of particip	ants; %, the prop	ortion of partici	pants.		
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SHS exposure	п	Respiratory	Unadjusted OB(95%CI)	Adjusted			
SHS exposure in ge	neral	Symptoms (70)	01())/001)	01(())/001)			
No	1101	106(9.6)	1.00	1.00			
Yes	2474	371(15.0)	1.66(1.32-2.08)	1.72(1.35-2.17)			
SHS exposure in inc	loor public place	es					
No	1806	200(11.1)	1.00	1.00			
Yes	1769	277(15.7)	1.49(1.23-1.81)	1.60(1.30-1.95)			
SHS exposure in ho	mes						
No	2342	275(11.7)	1.00	1.00			
Yes	1233	202(16.4)	1.47(1.21-1.79)	1.53(1.25-1.87)			
SHS exposure in inc	loor campuses						
No	2763	338(12.2)	1.00	1.00			
Yes	812	139(17.1)	1.48(1.19-1.84)	1.43(1.14-1.79)			
SHS exposure in indoor campuses from smoking teachers							
No	2940	369(12.6)	1.00	1.00			
Yes	635	108(17.0)	1.43(1.13-1.80)	1.34(1.05-1.71)			
SHS exposure in indoor campuses from smoking classmates							
No	3149	399(12.7)	1.00	1.00			
Yes	426	78(18.3)	1.54(1.18-2.02)	1.54(1.15-2.06)			
SHS exposure in ou	tdoor campuses						
No	2532	309(12.2)	1.00	1.00			
Yes	1043	168(16.1)	1.38(1.13-1.69)	1.37(1.10-1.69)			
SHS exposure in ou	tdoor campuses	from smoking teachers					
No	2917	362(12.4)	1.00	1.00			
Yes	658	115(17.5)	1.49(1.19-1.88)	1.38(1.09-1.75)			
SHS exposure in outdoor campuses from smoking classmates							
No	2873	366(12.7)	1.00	1.00			
Yes	702	111(15.8)	1.29(1.02-1.62)	1.33(1.03-1.71)			

437 history (yes vs no).

$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	1.20-1.86 1.41-2.46 1.67-3.16 1.25-2.09 1.13-1.87 1.23-2.20 0.95-1.63 1.32-2.56 1.42-3.07
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Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor campuses).

125x64mm (300 x 300 DPI)









Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in outdoor campuses).

124x63mm (300 x 300 DPI)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	6-7
measurement		comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	No missing data
		(d) If applicable, describe analytical methods taking account of sampling strategy	No applicable
		(e) Describe any sensitivity analyses	7
Results			

Page	28 o	of 28	
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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	8
·		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	No applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	8
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	8-10
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	8-10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	No applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	No applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	No funding
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Frequency-risk relationships between second-hand smoke exposure and respiratory symptoms among adolescents: a cross-sectional study in South China

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Primary Subject Heading :	Smoking and tobacco
Secondary Subject Heading:	Epidemiology, Public health, Respiratory medicine, Smoking and tobacco
Keywords:	second-hand smoke exposure, respiratory symptoms, adolescents

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6	2	respiratory symptoms among adolescents: a cross-sectional study in South China
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8	3	Zhiyao Chen MPH ^{1,#} , Guocong Liu MPH ^{2,#} , Jianying Chen BS ^{3, #} , Shunming Li MPH ¹ ,
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10		T' T' $DO^2 D' X MDH^2 X' + X DID^{1*}$
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20	ABSTRACT

Objectives: Although previous studies have suggested an association between second-hand smoke (SHS) exposure and respiratory symptoms, current evidence is inconsistent. Additionally, it remains unclear whether there are frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents.

Methods: A cross-sectional survey was conducted using a stratified cluster sampling method to
obtain a representative sample of high school students in Guangzhou, China. The respiratory
symptoms were defined as persistent cough or sputum for 3 consecutive months during the past 12
months. Self-reported SHS exposure was defined as non-smokers' inhalation of the smoke exhaled
from smokers on ≥1 day a week in the past 7 days. The univariable and multivariable logistic
regression models were fitted to explore the potential frequency-risk relationships between SHS
exposure and respiratory symptoms.

Results: Among 3575 students, the overall prevalence of SHS exposure was 69.2%, including 49.5% for SHS in public places, 34.5% in homes, 22.7% in indoor campuses, and 29.2% in outdoor campuses. There were significantly increased risks of having respiratory symptoms corresponding to SHS exposure in public places (odds ratio [OR]=1.60, 95% CI 1.30-1.95), in homes (OR=1.53, 95% CI 1.25-1.87), in indoor campuses (OR = 1.43, 95% CI 1.14-1.79) and in outdoor campuses (OR = 1.37, 95% CI 1.10-1.69) using no exposure as reference. Notably, we observed monotonically frequency-risk relationships between setting-specific (e.g., homes, public places, and campuses) SHS exposure and respiratory symptoms.

- 40 Conclusion: Our findings suggest that setting-specific SHS exposure is associated with a
 41 significant, dose-dependent increase in risk of respiratory symptoms.

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3	40	Strongths and limitations of this study
4	45	Strengths and minitations of this study
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6	44	This study aims to explore the potential frequency-risk relationship between SHS exposure
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8	45	and respiratory symptoms and adds to the literature by focusing on Chinese tobacco control
9	15	and respiratory symptoms, and adds to the netware by recasing on enness tookees control
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11	46	and Chinese youth along with its global context.
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13	47	■ This study differentiates SHS exposure in specific settings and specific sources to make
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15	10	avanceurs and notantial accognitions alcorer
16	40	exposure and potential associations clearer.
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18	49	SHS exposure and respiratory symptoms were self-reported, which is a limitation.
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20	50	Cross-sectional studies do not establish causal relationships but only depict associations. Our
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25	51	findings highlight the need for further longitudinal studies to establish the causal relationship
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25	52	and the biological mechanisms for the impact of SHS.
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54 INTRODUCTION

It is well established that inhaling second-hand smoke (SHS) is harmful and that no scientific evidence establishes a risk-free level of exposure.^{1,2} Notably, a retrospective analysis of data from 192 countries revealed that 40% of children (including 35% of non-smoking women and 33% of non-smoking men) were exposed to SHS, and this exposure is estimated to result in an annual estimate of 603000 deaths attributable to SHS.³ Global youth tobacco surveillance also reported that nearly half the adolescents worldwide were exposed to SHS at home (42.5%) and in public places (55.1%), which constitutes a substantial public health threat and demands urgent intervention.⁴ China is the world's largest producer and consumer of tobacco. The 2010 Global Adult Tobacco Survey revealed that 72.4% adults in China were exposed to SHS, and the 2014 Chinese adolescents Tobacco Survey also reported that 72.9% adolescents in China had SHS exposure, suggesting that the tremendous burden from tobacco-induced diseases makes tobacco prevention an essential health priority in China.^{5,6} In recent years, much attention has been focused on SHS exposure in public places and in homes, but there is limited reports on SHS exposure in indoor and outdoor campuses among adolescents.

Epidemiological studies of adolescents have explored the associations between SHS exposure and respiratory symptoms (such as nose irritation, coughing, and sore throat) or infection,⁷⁻¹¹ but current evidence is inconsistent. Some studies demonstrated significantly positive associations, ^{12,13} while the report from Malaysia revealed no association.¹⁴ Recent Chinese studies indicated that there were positive

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associations between household SHS exposure and respiratory symptoms in adolescents, but the association for SHS exposure in public places or in schools was unknown.^{15,16} SHS exposure occurs in varying amounts in public places, homes, and other indoor spaces, but few studies have differentiated SHS exposure in indoor and outdoor to make the setting-specific relationships between SHS exposure and respiratory symptoms clearer. Of particular concern is that little is known about the effects of campus SHS exposure on respiratory symptoms. Furthermore, it was unclear whether there are dose-response relationships between SHS exposure and respiratory symptoms. This study builds on previous literature to explore setting-specific (e.g., public places, homes, and campuses) and frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents.

88 METHODS

Ethics statement

The study was approved by the Ethics Committee of Guangdong Pharmaceutical University, and it was performed in accordance with the approved guidelines. The goals of the study were given to study participants and they should express their willingness to participate. Before participating, written informed consents were obtained from their parents or guardians.

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96 Study design and data collection

97 This cross-sectional study was conducted in Guangzhou, China, from March to April

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3	00	2016 The terrest nonvolation was high asked students. A stratified aluster compliant
4	98	2016. The target population was high school students. A stratified cluster sampling
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6	99	process was used to obtain a representative sample. Notably, middle schools in most
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8	100	next of China are generally rated by the Dyracy of Education on law schools (or
9	100	part of China are generally rated by the Bureau of Education as key schools (of
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11	101	prestigious schools) and ordinary schools (or non-prestigious schools) according to
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13	102	level of education and the education quality. In the first stage, all high schools were
14	102	level of education and the education quanty. In the first stage, all high schools were
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16	103	divided into two categories (prestigious or non-prestigious schools). Three high
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18	104	schools were randomly sampled from prestigious schools, and four high schools were
19	104	schools were randomly sampled nom prestigious schools, and rour high schools were
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21	105	randomly sampled from non-prestigious schools, with the probability of selection
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23	106	proportional to the number of the schools. In the second stage classes in the selected
24	100	proportional to the number of the sendols. In the second stage, classes in the selected
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26	107	schools were randomly sampled with proportional to school enrollment size, and all
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28	108	students in sampled classes were eligible to participate
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31	109	All interviewers in each school were centrally trained to ensure that the survey
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33	110	was carried out according to the protocol and operation procedures were identical
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35	111	corress all areas. After obtaining informed concert aligible students were asked to
35 36	111	across all areas. After obtaining informed consent, eligible students were asked to
35 36 37	111	across all areas. After obtaining informed consent, eligible students were asked to
35 36 37 38	111 112	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants
35 36 37 38 39	111 112	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants
35 36 37 38 39 40	111 112 112	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833)
35 36 37 38 39 40 41	111 112 113	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833).
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35 36 37 38 39 40 41 42 43	111 112 113 114	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833). Only non-smokers were included in the analyses and a total of 3575 non-smokers
35 36 37 38 39 40 41 42 43 44	111 112 113 114	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833). Only non-smokers were included in the analyses and a total of 3575 non-smokers
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35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	111 112 113 114 115 116	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833). Only non-smokers were included in the analyses and a total of 3575 non-smokers were included in this study.
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	111 112 113 114 115 116 117	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833). Only non-smokers were included in the analyses and a total of 3575 non-smokers were included in this study.
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35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52	111 112 113 114 115 116 117	across all areas. After obtaining informed consent, eligible students were asked to complete a face-to-face survey by trained interviewers. A total of 3833 participants were enrolled in this study, and the effective response rate was 95.4% (3657/3833). Only non-smokers were included in the analyses and a total of 3575 non-smokers were included in this study. Study variables
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120	during the past 12 months. ¹⁷⁻¹⁹ The main independent variable of respiratory
121	symptoms was self-reported SHS exposure, which was defined as non-smokers'
122	inhalation of the smoke exhaled from smokers on ≥ 1 day a week in the past 7 days for
123	at least 6 months (first question: "In the past 7 days, how many days did you breathe
124	in SHS in homes (or indoor public places, indoor campuses, outdoor campuses)";
125	second question for those having SHS exposure: "Did you breathe in SHS in this
126	venue for at least 6 months?"). In order to recall SHS exposure for at least 6 months,
127	we use both curriculum schedules and calendars as an assistive device to facilitate
128	recall the time. Frequency of SHS exposure was continuous data (days/week), and
129	was also categorized into three groups: <1 day/week (no exposure), '1-4 days/week'
130	and '5-7 days/week'. Smoking status was classified as non-smokers and smokers
131	(defined as 'has smoked over 100 cigarettes in their lifetime').
132	Covariates including potential mediators and confounders were chosen a priori
133	on the basis of literature review. Potential covariates in our study included age (year),
134	gender (male or female), grade (4-5 or 1-2), only-child (yes or no), monthly pocket
135	money (<¥100, ¥100-399, or \geq ¥400), prestigious school (yes or no), father's
136	education (primary school, middle school, or university and above), mother's
137	education (primary school, middle school, or university and above), and asthma
138	history (yes or no).

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140 Data analysis

141 All data were entered in duplicate into EpiData version 3.1 database (The EpiData

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142 Association, Odense Denmark). The univariable and multivariable logistic regression 143 models were fitted to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for evaluating the frequency-risk relationships between SHS exposure 144 145 (including ordinal and continuous variables) and respiratory symptoms. Linear trends of SHS exposure were assessed by modeling exposure as continuous variables 146 147 (arithmetic or logarithmic scale) or ordinal variables in multivariable models. 148 Two-sided p-value of <0.05 was regarded as being of statistical significance. All 149 statistical analyses were conducted using Stata version 14.0 (StataCorp LP, College 150 Station, Texas, USA). e e 151 152 RESULTS

153 **Characteristics of the sample**

A total of 3575 non-smoking students were interviewed, of whom 477 (13.3%) were 154 classified as having respiratory symptoms. Participants' mean age was 15.0 ± 1.8 155 156 years, and 50.9% were male students. About 62.2% of the students were the only child 157 in their family and 63.4% from prestigious schools. The overall prevalence of SHS 158 exposure was 69.2%, including 49.5% for SHS in indoor public places, 34.5% in 159 homes, 22.7% in indoor campuses, and 29.2% in outdoor campuses (Table 1).

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161 **Relationship between binary SHS exposure and respiratory symptoms**

- 162 The prevalence of respiratory symptoms was significantly higher in students with
- SHS exposure (OR=1.72, 95% CI 1.35-2.17, for SHS in general; OR=1.60, 95% CI 163

164	1.30-1.95, for SHS in indoor public places; OR=1.53, 95% CI 1.25-1.87, for SHS in
165	homes; $OR = 1.43$, 95% CI 1.14-1.79, for SHS in indoor campuses) than in those with
166	no exposure (Table 2). Similar positive associations were observed in students with
167	SHS exposure in indoor campuses from smoking teachers (OR =1.34, 95% CI
168	1.05-1.71) or from smoking classmates (OR = 1.54 , 95% CI 1.15-2.06). Notably, the
169	effects of SHS exposure in outdoor campuses cannot be ignored. Students with SHS
170	exposure in outdoor campuses had significantly higher rates of respiratory symptoms
171	(OR = 1.37, 95% CI 1.10-1.69) as compared with unexposed students, and there were
172	similar positive associations between respiratory symptoms and SHS exposure in
173	outdoor campuses from smoking teachers (OR =1.38, 95% CI 1.09-1.75) or from
174	smoking classmates (OR = 1.33, 95% CI 1.03-1.71).

176 Relationship between ordinal SHS exposure and respiratory symptoms

Compared with no SHS exposure, ordinal frequency of SHS exposure was associated with respiratory symptoms in an increasing manner (SHS in public places: OR=1 for no exposure, OR=1.50 for 1-4 days/week, OR=1.87 for 5-7 days/week, p for linear trend <0.001; SHS in indoor campuses: OR=1 for no exposure, OR=1.24 for 1-4 days/week, OR=1.84 for 5-7 days/week, p for linear trend <0.001; Table 3). When examining these associations by source of exposure, significant increasing trends were observed for SHS exposure in indoor campuses from smoking teachers (p for linear trend =0.001) and from smoking classmates (p for linear trend =0.005). Additionally, there was a significantly increasing relationship between ordinal

frequency of SHS exposure in outdoor campuses and respiratory symptoms (OR=1 for no exposure, OR=1.28 for 1-4 days/week, OR=1.56 for 5-7 days/week, p for linear trend =0.007; Table 3), and similar increasing trends were observed for SHS exposure in outdoor campuses from smoking teachers (p for linear trend =0.004) and from smoking classmates (p for linear trend =0.006). However, no increasing trend was observed for SHS exposure in homes.

193 Relationship between continuous SHS exposure and respiratory symptoms

As to continuous SHS exposure, there were significant frequency-risk relationships between indoor SHS exposure and respiratory symptoms (OR = 2.30, 95% CI: 1.67-3.16, for SHS in indoor public places; OR = 1.64, 95% CI: 1.23-2.20, for SHS in homes; OR = 2.09, 95% CI: 1.42-3.07, for SHS in indoor campuses; OR = 1.70, 95%CI: 1.18-2.47, for SHS in outdoor campuses; Table 3). When examining these associations by source of exposure, there were similar frequency-risk relationships for SHS exposure in indoor or outdoor campuses (Table 3). Additionally, we observed a monotonically increasing frequency-risk trend for SHS exposure in indoor public places (Figure 1A), in homes (Figure 1B), in indoor campuses (Figure 2A) or in outdoor campuses (Figure 2B). When examining these trends by source of exposure, there were similar increasing frequency-risk trends for SHS exposure from smoking teachers (Figure 3A for indoor SHS and Figure 3B for outdoor SHS) and from smoking classmates (Figure 4A for indoor SHS and Figure 4B for outdoor SHS).

208 DISCUSSIO	Ν
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This observational study showed that non-smoking students with setting-specific SHS exposure experienced significantly higher risks of respiratory symptoms than those with no exposure. The most striking findings from this study were that there were monotonically increasing frequency-risk relationships between setting-specific SHS exposure and respiratory symptoms. When examining these associations by source of exposure, there were similar monotonically increasing frequency-risk relationships for SHS exposure from smoking teachers and from smoking classmates. It is well known that there is no risk-free level of exposure to SHS. Although previous studies have focused on SHS exposure among Chinese adolescents, ^{15,16,20} there is limited reports regarding SHS exposure in specific settings and specific sources. According to the partial smoke-free legislation implemented in Guangzhou on 1 September 2010, full smoke-free ban covered indoor campuses, outdoor campuses and most indoor public places, but did not cover homes. It is disappointing that SHS exposure in schools was not eliminated, and was still at a high level (22.7% for SHS exposure in indoor campuses; 29.2% for SHS exposure in outdoor campuses). This observation may be due to poor compliance with the full smoke-free ban in campuses, since we observed that SHS exposure among students was mainly from smoking teachers and smoking classmates in both indoor and outdoor campuses. Similarly, a recent population-based study in Tehran showed that about 30% non-smoking students have been exposed to SHS from smoking teachers in indoor or outdoor campuses, ²¹ and another survey of Chinese college students reported that

230	37% of non-smokers had SHS exposure from smoking teachers. ²⁰ More disappointing
231	was that SHS exposure in indoor public places was remarkably high in 49.5% in this
232	study, which is similar to results from the latest study on Guangzhou adults (50.3%)
233	and the Global Youth Tobacco Survey (47.8%). ^{22,23} After the implementation of a
234	smoke-free legislation, very few respondents (1-2%) reported smoking in public
235	places in England, ²⁴ but smoking behaviors still remained high in public places in
236	Guangzhou because of unwillingness of the policymakers to implement tougher
237	smoke-free policies and poor compliance with the smoke-free law among smokers. ²³
238	These findings reveal that a partial smoke-free legislation has a weak impact on
239	smoking cessation, but a comprehensive smoke-free legislation can substantially
240	attenuate smoking behaviors, which point out the urgent need for a comprehensive
241	smoke-free legislation covering all public places in Guangzhou to protect the public
242	from SHS hazards.
243	A few published studies have indicated that SHS exposure may be a risk factor of
244	respiratory symptoms, but the potential relationship for setting-specific exposure was
245	still unclear. ^{15,16,25,26} Recent studies of Chinese adolescents indicated that there were
246	positive associations between household SHS exposure and respiratory symptoms, but
247	the association for SHS exposure in public places or in schools was unknown. ^{15,16} In
248	addition, the surveys of London casino workers and Shanghai workers revealed that
249	there was an significant association between SHS exposure at work and respiratory
250	
	symptoms, but the association for SHS exposure in nomes or in public places was
251	unknown. ^{25,26} It is noteworthy that the influence of SHS exposure from indoor
campuses on respiratory symptoms is still unclear, and the potential dose-response relationship between frequency of SHS exposure and respiratory symptoms is also uncertain. We found that there were positive and frequency-risk relationships between setting-specific SHS exposure and respiratory symptoms. When examining the associations by source of exposure, there was still evidence of similar dose-response relationships for SHS exposure in indoor campuses from smoking teachers and smoking classmates. These findings provide new evidence of dose-response relationships between SHS exposure and respiratory symptoms among adolescents. Further research is needed to establish the causal relationship, and confirm that elimination of SHS exposure (or stricter smoke-free legislation in Guangzhou) will lead to a reduction in respiratory symptoms among adolescents. Although the 2010 report of the Surgeon General explained beyond a shadow of a doubt how tobacco smoke causes disease,²⁷ additional research should establish the potential biological mechanisms for the impact of SHS.

Globally, outdoor smoking restrictions are uncommon, though the outdoor-campus smoking bans implemented in Guangzhou City on 1 September 2010. A few published studies have indicated that smoking increases $PM_{2.5}$ concentrations in outdoor areas to levels that are potentially hazardous to health,^{28,29} but research linking SHS exposures from outdoor environments to health effects is still rare. Notably, the potential relationship between outdoor SHS exposure and respiratory symptoms is still unclear. To our knowledge, this is the first study to reveal the relationship between SHS exposure in outdoor campuses and respiratory symptoms

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274 among adolescents, and found that outdoor SHS exposure was positively associated 275 with respiratory symptoms in a monotonically increasing trend. When examining the 276 associations by source of exposure, there were still similar frequency-risk 277 relationships for SHS exposure in outdoor campuses from smoking teachers and smoking classmates. Although outdoor SHS is more transient than indoor SHS, 278 279 evidence from review of the research literature on SHS levels in outdoor hospitality 280 venues suggested that tobacco-generated PM_{2.5} in outdoor setting may occasionally be 281 equivalent to or higher than levels observed in indoor setting when smoking is permitted at close proximity.²⁸ These findings provide more evidence for the adverse 282 effects of outdoor SHS exposure on human respiratory symptoms, and also support 283 growing concern about SHS exposure in outdoor campuses. Future studies on school 284 285 SHS exposure in adolescents and protective measures against SHS should take outdoor campuses SHS into consideration. 286

This study adds to the literature by focusing on Chinese tobacco control and 287 Chinese youth along with its global context. Additionally, we contribute additionally 288 to the literature by exploring the potential frequency-risk relationships and 289 differentiating SHS exposure in specific settings and specific sources to make 290 291 exposure and potential relationships clearer. There are also some potential limitations 292 in this study. First, all data was self-reported, including SHS exposure and respiratory symptoms. For SHS exposure, biochemical measures can give objective 293 294 measurements, but cannot distinguish the sources of exposure, the key factors in this 295 study. A previous survey has found that school children are capable of reporting their Page 15 of 28

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health conditions reliably, ^{30} and the presence of frequent cough and phlegm was quite
297 obvious to avoid measurement error. Second, causal association between SHS
exposure and respiratory symptoms could not be ascertained due to the cross-sectional
299 design. However, the notion of reverse causation that students with respiratory
300 symptoms deliberately increased their exposure to noxious SHS seems improbable.
301 The strong associations observed in other studies also supported our data validity and
provided support for the deduction of causation. ^{$15,31,32$} Finally, few people would be
303 completely unexposed to SHS in densely populated Guangzhou even now, when
304 smoking was still allowed in public places (e.g., cafes, bars, night clubs, amusement
305 parks, restaurants, and workplaces). Therefore, the control groups who reported no
306 SHS exposure have probably underestimated their exposure, and the risk for
respiratory symptoms in these groups would also be underestimated.
308 In conclusion, SHS exposure in indoor and outdoor campuses is still at a high
309 level, which suggests poor compliance with the full smoke-free ban in schools and

level, which suggests poor compliance with the full smoke-free ban in schools and supports growing concern about SHS exposure in campuses. Additionally, this study contributes to the literature by finding monotonically increasing frequency-risk relationships between SHS exposure and respiratory symptoms among adolescents in addition to differentiating SHS exposure in specific settings and specific sources to make these relationships clearer. Future longitudinal studies are needed to establish the causal relationship and the biological mechanisms for the impact of SHS.

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317 Contributors

318	CZ, LG, LS, JT, XB, CJ and YX were involved in the design of the study, data
319	analysis and writing of the draft of the manuscript. All the authors read and approved
320	the final version of the manuscript.
321	
322	Funding
323	The authors bore their own costs for conducting this study and hence no specific
324	funding line for this study.
325	
326	Competing interests None.
327	
328	Ethics approval
329	The Ethics Committee of Guangdong Pharmaceutical University.
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331	Data sharing statement
332	No additional data are available.
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413	Figure Legends
414	Figure 1. Predicted prevalence of respiratory symptoms based on second-hand smoke
415	exposure (A: exposure in indoor public places; B: exposure in homes).
416	
417	Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke
418	exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor
419	campuses).
420	
421	Figure 3. Predicted prevalence of respiratory symptoms based on second-hand smoke
422	exposure from smoking teachers (A: exposure in indoor campuses; B: exposure in
423	outdoor campuses).
424	
425	Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke
426	exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in
427	outdoor campuses).
428	

	n	%	Characteristics	n	%
Respiratory symp	otoms		Grade		
No	3098	86.7	1-2	2329	65
Yes	477	13.3	4-5	1246	34
SHS exposure in	general		Only-child		
No	1101	30.8	No	1353	37
Yes	2474	69.2	Yes	2222	62
SHS exposure in	indoor public places		Gender		
No	1806	50.5	Male	1818	50
Yes	1769	49.5	Female	1757	49
SHS exposure in	homes		Pocket money monthly(¥)	
No	2342	65.5	<100	2039	57
Yes	1233	34.5	100-399	1125	31
SHS exposure in	indoor campuses		$\geq \!\! 400$	411	11
No	2763	77.3	Father's education		
Yes	812	22.7	Primary school	838	23
SHS exposure in	outdoor campuses		Middle school	1215	34
No	2532	70.8	University and above	1522	42
Yes	1043	29.2	Mother's education		
Asthma history			Primary school	978	27
No	3514	98.3	Middle school	1165	32
Yes	61	1.7	University and above	1432	40

nhia ahar f the study participants Table 1 Da



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20	J

SHS exposure in ge No Yes SHS exposure in ind No Yes	neral 1101 2474 door public place	106(9.6) 371(15.0)	1.00	1.00
No Yes SHS exposure in ind No Yes	1101 2474 door public place	106(9.6) 371(15.0)	1.00	1.00
Yes SHS exposure in ind No Yes	2474 door public place	371(15.0)	1.66(1.32.2.08)	1.00
SHS exposure in ind No Yes	loor public place	571(15.0)		1 72(1 35-2
No Yes		25	1.00(1.52 2.00)	1.72(1.55 2.
Yes	1806	200(11.1)	1.00	1.00
100	1769	277(157)	1 49(1 23-1 81)	1 60(1 30-1
SHS exposure in ho	mes	2//(10.7)	1.19(1.25 1.01)	1.00(1.50 1
No	2342	275(117)	1.00	1.00
Yes	1233	202(16.4)	1 47(1 21-1 79)	1.53(1.25-1
SHS exposure in inc	loor campuses	202(10.1)	,(1.00(1.20 1.
No	2763	338(12.2)	1.00	1.00
Yes	812	139(17.1)	1.48(1.19-1.84)	1.43(1.14-1.
SHS exposure in ind	loor campuses fi	rom smoking teachers		
No	2940	369(12.6)	1.00	1.00
Yes	635	108(17.0)	1.43(1.13-1.80)	1.34(1.05-1
SHS exposure in ind	loor campuses fi	rom smoking classmate	es	× ×
No	3149	399(12.7)	1.00	1.00
Yes	426	78(18.3)	1.54(1.18-2.02)	1.54(1.15-2
SHS exposure in ou	tdoor campuses		, , ,	Ň
No	2532	309(12.2)	1.00	1.00
Yes	1043	168(16.1)	1.38(1.13-1.69)	1.37(1.10-1.
SHS exposure in ou	tdoor campuses	from smoking teachers		×
No	2917	362(12.4)	1.00	1.00
Yes	658	115(17.5)	1.49(1.19-1.88)	1.38(1.09-1
SHS exposure in ou	tdoor campuses	from smoking classma	tes	
No	2873	366(12.7)	1.00	1.00
Yes	702	111(15.8)	1.29(1.02-1.62)	1.33(1.03-1.
No Yes n, number of partici ^a : adjusted for gen history (yes vs no).	2873 702 pants; SHS, seco der (male vs fer	366(12.7) 111(15.8) ond-hand smoke; OR, c male), grade (4-5 vs 1	1.00 1.29(1.02-1.62) odds ratio; CI, confid -2), only-child (yes	1.00 1.33 lence i vs nc
	SHS exposure in ind No Yes SHS exposure in ind No Yes SHS exposure in ou No Yes SHS exposure in ou No Yes	SHS exposure in indoor campusesNo2763Yes812SHS exposure in indoor campuses from No2940Yes635SHS exposure in indoor campuses from No3149Yes426SHS exposure in outdoor campusesNoNo2532Yes1043SHS exposure in outdoor campusesNoNo2917Yes658SHS exposure in outdoor campusesNo2917Yes658SHS exposure in outdoor campusesNo2873Yes702 <i>n</i> , number of participants; SHS, seccorea : adjusted for gender (male vs fer history (yes vs no).	SHS exposure in indoor campusesNo2763 $338(12.2)$ Yes812 $139(17.1)$ SHS exposure in indoor campuses from smoking teachersNo 2940 Yes 635 $108(17.0)$ SHS exposure in indoor campuses from smoking classmateNo 3149 No 3149 $399(12.7)$ Yes 426 $78(18.3)$ SHS exposure in outdoor campusesNo 2532 No 2532 $309(12.2)$ Yes 1043 $168(16.1)$ SHS exposure in outdoor campuses from smoking teachersNoNo 2917 $362(12.4)$ Yes 658 $115(17.5)$ SHS exposure in outdoor campuses from smoking classmateNo 2873 $366(12.7)$ Yes 702 $111(15.8)$ <i>n</i> , number of participants; SHS, second-hand smoke; OR, ora': adjusted for gender (male vs female), grade (4-5 vs 1history (yes vs no).	SHS exposure in indoor campuses No 2763 338(12.2) 1.00 Yes 812 139(17.1) 1.48(1.19-1.84) SHS exposure in indoor campuses from smoking teachers No 2940 369(12.6) 1.00 Yes 635 108(17.0) 1.43(1.13-1.80) SHS exposure in indoor campuses from smoking classmates No 3149 399(12.7) 1.00 Yes 426 78(18.3) 1.54(1.18-2.02) SHS exposure in outdoor campuses No 2532 309(12.2) 1.00 Yes 1043 168(16.1) 1.38(1.13-1.69) SHS exposure in outdoor campuses from smoking teachers No 2917 362(12.4) 1.00 Yes 658 115(17.5) 1.49(1.19-1.88) SHS exposure in outdoor campuses from smoking classmates No 2917 362(12.4) 1.00 Yes 658 115(17.5) 1.49(1.19-1.88) SHS exposure in outdoor campuses from smoking classmates No 2873 366(12.7) 1.00 Yes 702 111(15.8) 1.29(1.02-1.62) Image: Shift or gender (male vs female), grade (4-5 vs 1-2), only-child (yes history (yes vs no). atad

Frequency of SHS exposure	n	Respiratory symptoms (%)	Unadjusted OR(95%CI)	Adjusted OR(95%CI)
SHS exposure in indoor	public places			
No exposure	1806	200(11.1)	1.00	1.00
1-4 days/week	1242	184(14.8)	1.40(1.13-1.73)	1.50(1.20-1
5-7 days/week	527	93(17.7)	1.72(1.32-2.25)	1.87(1.41-2
Continuous SHS in indo	or public places	b	2.06(1.52-2.80)	2.30(1.67-3
SHS exposure in homes			. ,	x
No exposure	2342	275(11.7)	1.00	1.00
1-4 days/week	570	97(17.0)	1.54(1.20-1.98)	1.62(1.25-2
5-7 days/week	663	105(15.8)	1.41(1.11-1.80)	1.45(1.13-1
Continuous SHS in hom	es ^b		1.56(1.18-2.07)	1.64(1.23-2
SHS exposure in indoor	campuses			
No exposure	2763	338(12.2)	1.00	1.00
1-4 days/week	539	81(15.0)	1.27(0.98-1.65)	1.24(0.95-1
5-7 days/week	273	58(21.3)	1.94(1.42-2.64)	1.84(1.32-2
Continuous SHS in indo	or campuses ^b		2.19(1.53-3.12)	2.09(1.42-3
SHS exposure in indoor	campuses from	smoking teachers		[×]
No exposure	2940	369(12.6)	1.00	1.00
1-4 days/week	412	59(14.3)	1.16(0.87-1.57)	1.13(0.84-1
5-7 days/week	223	49(22.0)	1.96(1.40-2.74)	1.78(1.25-2
Continuous SHS in indo	or campuses fro	m smoking teachers b	2.27(1.54-3.33)	2.06(1.37-3
SHS exposure in indoor	campuses from	smoking classmates		,
No exposure	3149	399(12.7)	1.00	1.00
1-4 days/week	271	45(16.6)	1.37(0.98-1.92)	1.38(0.97-1
5-7 days/week	155	33(21.3)	1.86(1.25-2.78)	1.84(1.20-2
Continuous SHS in indo	or campuses fro	m smoking classmates	^b 2.04(1.30-3.20)	2.00(1.22-3
SHS exposure in outdoor	r campuses	-		
No exposure	2532	309(12.2)	1.00	1.00
1-4 days/week	704	105(14.9)	1.26(0.99-1.60)	1.28(1.01-1
5-7 days/week	339	63(18.6)	1.64(1.22-2.21)	1.56(1.13-2
Continuous SHS exposu	re in outdoor ca	mpuses ^b	1.79(1.27-2.51)	1.70(1.18-2
SHS exposure in outdoor	r campuses fron	n smoking teachers		
No exposure	2917	362(12.4)	1.00	1.00
1-4 days/week	456	71(15.6)	1.30(0.99-1.72)	1.24(0.94-1
5-7 days/week	202	44(21.8)	1.97(1.38-2.79)	1.74(1.20-2
Continuous SHS in outd	oor campuses fr	om smoking teachers ^b	2.53(1.71-3.74)	2.20(1.45-3
SHS exposure in outdoor	r campuses fron	n smoking classmates		
No exposure	2873	366(12.7)	1.00	1.00
1-4 days/week	451	62(13.8)	1.09(0.82-1.46)	1.16(0.86-1
5-7 days/week	251	49(19.5)	1.66(1.19-2.31)	1.66(1.16-2
Continuous SHS in outd	oor campuses fr	om smoking classmate	s ^b 1.55(1.05-2.30)	1.58(1.03-2
<i>n</i> , number of participant	ts; SHS, second	-hand smoke; OR, odds	ratio; CI, confiden	ce interval.
^a : adjusted for gender	(male vs femal	e), grade (4-5 vs 1-2),	only-child (yes vs	s no) and as
				,
history (yes vs no).				

Table 3. Relationship between frequency of SHS exposure and respiratory symptoms







Figure 2. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure in campuses (A: exposure in indoor campuses; B: exposure in outdoor campuses).

125x64mm (300 x 300 DPI)









Figure 4. Predicted prevalence of respiratory symptoms based on second-hand smoke exposure from smoking classmates (A: exposure in indoor campuses; B: exposure in outdoor campuses).

124x63mm (300 x 300 DPI)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	6-7
measurement		comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	No missing data
		(d) If applicable, describe analytical methods taking account of sampling strategy	No applicable
		(e) Describe any sensitivity analyses	7
Results			

Page	28 o	of 28	
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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	8
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	No applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	8
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	8-10
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	8-10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	No applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	No applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	No funding
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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