atmosphere

MDPI

Article

Effect of Prenatal Exposure to Household Air Pollution from Multiple Sources on Risk of Preterm Birth

Xin-Chen Liu [1], Esben Strodl [2], Li-Hua Huang [1], Bing-Jie Hu [3] and Wei-Qing Chen [1,4,*]

[1] Department of Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[2] School of Psychology and Counselling, Queensland University of Technology, Brisbane, QLD 4000, Australia
[3] School of Basic Medical Science, Guangzhou Medical University, Guangzhou 510080, China
[4] School of Health, Xinhua College of Guangzhou, Guangzhou 510080, China
* Correspondence: chenwq@mail.sysu.edu.cn

Abstract: Prenatal exposure to air pollution has been suggested as a major risk factor for preterm birth (PTB). This study aimed to explore the independent and joint effects of prenatal exposure to multiple household air pollution (HAP) sources on PTB. This study involved 63,038 mother–child pairs from the Longhua Child Cohort Study in 2017. A series of logistic regression analyses on associations of environmental tobacco smoke (ETS), cooking oil fumes (COFs), burning mosquito coils (BMCs), indoor burning incense (IBI) and household renovation (HR) with PTB were conducted to evaluate their independent and joint effects on PTB. Compared to mothers without exposure, prenatal exposure to each individual HAP source increased the PTB risk. Moreover, the PTB risk increased incrementally with the number of prenatal HAP exposure sources. Finally, we found a synergistic interaction effect from COFs and HR on risk of PTB. Our results suggest that prenatal exposure to five sources of HAP might increase the risk of PTB, with the risk increasing with the number of exposure sources and synergistic interaction effects between some pollution sources.

Keywords: household air pollution; prenatal exposure; preterm birth; joint effect

Citation: Liu, X.-C.; Strodl, E.; Huang, L.-H.; Hu, B.-J.; Chen, W.-Q. Effect of Prenatal Exposure to Household Air Pollution from Multiple Sources on Risk of Preterm Birth. *Atmosphere* **2022**, *13*, 2022. https://doi.org/10.3390/atmos13122022

Academic Editor: Kai Jen Chuang

Received: 10 November 2022
Accepted: 30 November 2022
Published: 1 December 2022

1. Introduction

Preterm birth (PTB) is defined as birth delivery that occurs at less than 37 weeks' gestational age, and the rate of PTBs has risen, rather than fallen, over time [1,2]. The World Health Organization (WHO) reported that PTBs accounted for over 10% of newborns worldwide, with about 15 million preterm births delivered each year [3]. In China, the nationwide incidence of PTBs is 7.3% of all births and 6.7% of live births [4]. In 2015, PTB-related complications were the leading and the second most common causes of mortality for children under 5 years of age worldwide and in China, respectively [5,6]. PTB is also associated with long-term adverse neurological effects and other health outcomes in children's later lives [7]. The economic burden of PTB relates not only to perinatal intensive care unit use but also to the use of medical, social and specialist educational services through individuals' entire lives [8].

There are plenty of validated risk factors for PTB, including smoking, psychological stress, multiple gestations, intraamniotic or intrauterine infections, use of assisted reproductive technologies and prior PTB history [9]. Recently, consistent evidence has been emerging that air pollution exposure might increase the risk of PTB [10–13]. These studies have mainly focused on ambient air pollution. However, pregnant women spend a larger portion of their daytime at home and are exposed to greater air pollution indoors than outdoors [14]. It is likely that similar effects on PTB may exist with household air pollution as for outdoor air pollution. Unfortunately, there is a paucity of evidence on the effects of indoor household air pollution on PTB [15].

Household air pollution (HAP) has become a global public health problem in the past few decades [16]. This is due to many individuals now spending 90% of their time indoors,

with indoor air being up to five times more polluted than outside air [14]. It has been reported by the WHO that 3.8 million people die prematurely from illnesses attributable to HAP exposure each year [17]. The State of the Global Air 2020 reported that nearly 500,000 infants died in the first month of life because of air pollution exposure, with nearly 64% of these deaths being related to HAP [18].

HAP consists mostly of anthropogenic pollutants, which mainly come from (1) indoor combustion process, such as cigarette smoking (environmental tobacco smoke (ETS)), cooking (burning fuels for cooking/heating/lighting and cooking oil fumes (COFs)), burning mosquito coils (BMCs) and indoor burning incense (IBI); and (2) household renovation/redecoration (HR) materials [19]. Recently, several studies reported that prenatal ETS exposure and solid/biomass fuel use were associated with PTB [20–25]. Moreover, other studies also indicated that household renovation exposure within one year before pregnancy or during pregnancy may be a risk factor for PTB [24,26,27]. Furthermore, some harmful substances commonly contained in household air pollutants, such as fine particular matter ($PM_{2.5}$), formaldehyde (FA) and polycyclic aromatic hydrocarbons (PAHs), have been reported to be associated with PTB and the length of gestation [28–30]. However, most studies regarding HAP have been conducted in Western countries. This is problematic given that the concentrations and combinations of household air pollutants in Eastern countries are different due to varying cultural factors and not well-recognized [31]. To the best of our knowledge, few studies have so far examined the hazardous effects of household air pollution from traditional Chinese cooking, mosquito coil burning and indoor incense burning on the risk of PTB [32]. In addition, most studies have only focused on individual indoor air pollutants or individual sources of HAP, but none have investigated the joint effects of different sources of HAP on PTB.

Since pregnant women are frequently exposed to multiple sources of HAP at the same time, it is critical to examine the effects of combinations of sources of HAP on the risk of PTB. Thus, the current study aimed to explore the joint effects of prenatal exposure to multiple sources of HAP (including ETS, COFs, BMCs, IBI and HR) on PTB. Our hypothesis was that there would be accumulative effects, as well as synergistic effects, from multiple HAP sources on PTB.

2. Methods

2.1. Study Population

This study was a sub-analysis of the data from the 2017 Longhua Child Cohort Study (LCCS), which was designed to explore the impact of early-life exposure (including mothers' prenatal exposure and children's preschool exposure). In autumn of 2017, 67,861 children aged around 3 to 5 years and their mothers were enrolled in this study at their first entrance into any of the 171 kindergartens in the Longhua District of Shenzhen, China. Mothers were asked to fill out an online, self-administered, structured questionnaire. After excluding mothers (1) who were active smokers before or during pregnancy; (2) who did not provide complete information on the five sources of HAP exposure and PTB outcomes; (3) whose children (children who were included in our study) were not singleton births; and (4) who had pregnancy complications, including pregnancy-induced hypertension (PIH), preeclampsia (PE) and gestational diabetes mellitus (GDM), the final sample involved 63,038 child–mother dyads. The study protocol was approved by the Ethics Committee of the School of Public Health of Sun Yat-sen University, and written informed consent was obtained from all participants.

2.2. Data Collection

The mothers of enrolled children were asked to complete a self-administered, structured questionnaire under the guidance of well-trained interviewers regarding the sociodemographic characteristics of the child's parents (including age at delivery, educational level, employment status, marital status and family income), the reproductive and medical history of the mother (including parity, pre-pregnancy body mass index (BMI), use of

assisted reproductive technology and the above-mentioned pregnancy complications), the sex of the child, maternal HAP exposure during pregnancy and preterm birth (questions in the questionnaire are presented in Table S1).

2.3. Measurement of HAP

In accordance with previous studies [31,33–35], as well as general knowledge about Chinese lifestyles and local customs, ETS, COFs, BMCs, IBI and HR were defined as the five main sources of HAP in this study. A set of questions were asked about prenatal HAP exposure. Table 1 presents the questions and options. If the answers to Q1, Q2, Q3, Q4 and Q5 were "Yes", then the mother was considered to have been subject to exposure to ETS, COFs, BMCs, IBI and HR, respectively. To analyze the association between accumulative prenatal HAP exposure and PTB risk, we calculated the accumulative HAP exposure index by counting the number of sources of HAP exposure (ranging from 0 to 5). For example, if a mother was exposed to all five sources of HAP, the accumulative HAP exposure index was counted as 5. Due to the low number of participants exposed to five sources of HAP, this category was collapsed with the category for four sources of HAP, so the HAP exposure index was categorized into 0, 1, 2, 3 and $\geq$4.

Table 1. Questions and options regarding prenatal HAP exposure.

No.	Questions	Options
Q1.	Were there any family members smoking at home during your pregnancy?	0 = "No" 1 = "Yes"
Q1.1	If "Yes", how many cigarettes did your family members smoked per day at home?	1 = "1–10 cigarettes per day" 2 = ">10 cigarettes per day"
Q2.	Did you cook for your family during pregnancy	0 = "No" 1 = "Yes"
Q2.1	If "Yes", how often did you expose to cooking oil fumes during pregnancy?	1 = "Sometimes (at least 1 time twice a week)" 2 = "Often (at least 1 time per week)" 3 = "Everyday (at least 1 time per day)"
Q3.	Did you burn mosquito coil during your pregnancy?	0 = "No" 1 = "Yes"
Q3.1	If "Yes", how often did you burn mosquito coil during your pregnancy?	1 = "Not everyday" 2 = "Everyday"
Q4.	Did your family have a habit of burning incense indoor during your pregnancy?	0 = "No" 1 = "Yes"
Q4.1	If "Yes", how often did your family burn incense indoor during your pregnancy?	1 = "Sometimes (at least 1 time twice a week)" 2 = "Often (at least 1 time per week)" 3 = "Everyday (at least 1 time per day)"
Q5.	Had your house been renovated during your pregnancy?	0 = "No" 1 = "Yes"

HAP: household air pollution.

2.4. PTB Assessment

In the questionnaire in the current study, the mothers were asked "Whether the child was diagnosed with PTB at birth by a doctor?". The response options were "Yes" vs. "No". If the answer was "Yes", the child was considered as a PTB.

2.5. Potential Confounders

Based on the previous published literature and in order to ensure data accessibility [20,23,24,26,32], a range of potential confounders were initially included: maternal age at delivery, paternal age at delivery, maternal educational level, paternal educational level, maternal employment status, family income, marital status, parity, whether this pregnancy was conceived through assisted reproductive technology and pre-pregnancy BMI. Then, we put all these potential confounders into a multiple logistic model with PTB as the dependent variable. If the p value of a certain variable was equal to or higher than 0.1 ($p \geq 0.1$), then this variable was excluded from the list of potential covariates. We re-

peated this process until the p values of all the potential confounders included in the model were lower than 0.1 ($p < 0.1$). Finally, the following variables were used as covariates in our analyses: child's sex (male or female), maternal age at delivery (continuous), maternal educational level (middle school or below, high school or college or above), family income (≤10,000 CNY/month, 10,001–20,000 CNY/month or >20,000 CNY/month), marital status (single or married), parity (nulliparous or multiparous) and maternal pre-pregnancy BMI (<18.5, 18.5~23.9 or >24).

2.6. Statistical Analysis

For descriptive analysis, frequencies and proportions were used to describe categorical variables, while means (standard deviation) and medians (quartile) were applied to continuous variables, depending on whether the distribution of the data was normal or skewed.

A series of logistic regression models were produced to evaluate both the independent and joint effects of prenatal exposure to five different HAP sources on the risk of PTB.

The independent effect of prenatal exposure to each source of HAP on the risk of PTB was assessed using binary logistic regression analyses, with each individual HAP source as the independent variable and PTB as the dependent variable and either not adjusting or adjusting for potential covariates.

In order to assess the joint effects of prenatal exposure to the five sources of HAP on PTB [36], we first assessed the association between the HAP exposure index and the risk of PTB to ensure that it reflected the accumulative effect of prenatal exposure to the five HAP sources. Second, we estimated two-way interactions for prenatal exposure to HAP sources and their effects on the risk of PTB. Since it has been suggested that reporting both additive and multiplicative interactions is essential, we estimated the interactions on both scales [37]. This was undertaken by calculating the risk of PTB in three different exposure combinations compared to the no-exposure combination; for example: (1) ETS and NO COFs (OR_{10}), (2) COFs and NO ETS (OR_{01}), (3) ETS and COFs (OR_{11}) and (4) NO ETS and NO COFs (OR_{00}: the reference group).

We estimated the interactions on the multiplicative scale by adding the product term into the two-pollution-source model [38]. In the results section, we present odds ratios (ORs) for the independent effects and the interactions of odds ratio (IORs) for the interaction effects. IOR measures the extent to which the effect of both exposures together exceeds the product of the effect of the two exposures considered separately, and it was calculated with the following equation:

$$IOR = OR_{11}/(OR_{10}OR_{01})$$

If the IOR was not equal to 1 and the 95% confidence interval (95% CI) of the IOR did not span 1, the multiplicative interaction was considered significant. Then, if the IOR was >1, the multiplicative interaction was understood to be positive (synergistic), and if the IOR was <1, the multiplicative interaction was understood to be negative (antagonistic).

We further estimated the interactions on the additive scale. Interactions on the additive scale are often not reported in logistic regression because they are not immediately available in standard statistical software output [37]. However, we further estimated the interactions on the additive scale because a general consensus has been reached in the epidemiological community that measuring interactions on the additive scale is the most appropriate method for assessing the public health significance of interactions [37,39–42]. The additive interactions were estimated using the relative excess risk due to interaction (RERI), the proportion attributable to interaction (AP). These terms were calculated based on excess odds ratios (EORs) with the following equations:

$$EOR_{10} = OR_{10} - OR_{00}\ EOR_{01} = OR_{01} - OR_{00}\ EOR_{11} = OR_{11} - OR_{00}$$

$$RERI = EOR_{11} - EOR_{10} - EOR_{01}$$

$$AP = RERI/EOR_{11}$$

If the RERI and AP did not equal 0 and their 95% CIs did not span 0, then the additive interaction was considered significant [43]. Then, if the RERI was >0 and the AP was >0, the additive interaction was understood to be positive (synergistic), and if the RERI was <0 and the AP was <0, the additive interaction was understood to be negative (antagonistic).

p-values were two-sided. Type *I* errors were set at 0.05. The statistical analysis was conducted with R statistical software (version 4.0.0, http://www.r-project.org (accessed on 6 May 2020)).

3. Results

3.1. Characteristics of the Participants

This study included 63,038 mother–infant dyads, and the summary description of the characteristics of the study population and a comparison between PTBs and FTBs are shown in Table 2. Among the total number of participants, the prevalence of PTB was 6.9%, and 27.3%, 77.7%, 44.6%, 47.6% and 6.6% mothers were exposed to ETS, COFs, BMCs, IBI and HR during pregnancy, respectively. There were slightly more boys than girls (54.2% vs. 45.8%). Participating mothers were 27.0 years old (SD = 4.1) on average at the child's delivery, and they tended to be married (97.4%) and well-educated (with 74.7% completing at least high school). Furthermore, significant differences in socio-demographic characteristics between PTBs and FTBs were found for child's sex, maternal age at delivery, maternal educational level, marital status, parity and maternal pre-pregnancy BMI but not family income. Compared with FTB mothers, PTB mothers were more likely to be exposed to ETS (31.3% vs. 27.0%), COFs (78.1% vs. 77.6%), BMCs (47.8% vs. 44.4%), IBI (50.2% vs. 47.4%) and HR (7.8% vs. 6.5%) during their pregnancy.

Table 2. Characteristics of the study population and comparison of PTB and FTB participants.

Characteristics	Total (N = 63,038)	FTB (*n* = 58,709)	PTB (*n* = 4329)	*p*
Child's sex, *n* (%)				<0.001
Male	34,144 (54.2)	31,581 (53.8)	2563 (59.2)	
Female	28,894 (45.8)	27,128 (46.2)	1766 (40.8)	
Maternal age at delivery, mean ± SD	27.0 ± 4.1	26.9 ± 4.1	27.2 (4.3)	0.001
Maternal educational level, *n* (%)				<0.001
Middle school or below	15,968 (25.3)	14,983 (25.5)	985 (22.8)	
High school	18,746 (29.7)	17,434 (29.7)	1312 (30.3)	
College or above	28,324 (44.9)	26,292 (44.8)	2032 (46.9)	
Family income (CNY/month)				0.945
≤10,000	26,537 (42.1)	24,724 (42.1)	1813 (41.9)	
10,001–20,000	21,147 (33.5)	19,693 (33.5)	1454 (33.6)	
>20,000	15,354 (24.4)	14,292 (24.4)	1062 (24.5)	
Marital status, *n* (%)				0.002
Single	1640 (2.6)	1496 (2.5)	144 (3.3)	
Married	61,398 (97.4)	57,213 (97.5)	4185 (96.7)	
Parity, *n* (%)				<0.001
Nulliparous	29,315 (46.5)	27,053 (46.1)	2262 (52.3)	
Multiparous	33,723 (53.5)	31,656 (53.9)	2067 (47.7)	
Pre-pregnancy BMI, kg/m^2, *n* (%)				0.001
Underweight (<18.5)	9184 (14.6)	8517 (14.5)	667 (15.4)	
Normal (18.5–23.9)	48,390 (76.8)	45,157 (76.9)	3233 (74.7)	
Overweight (>24)	5464 (8.7)	5035 (8.6)	429 (9.9)	
ETS, *n* (%)				<0.001
No	45,853 (72.7)	42,878 (73.0)	2975 (68.7)	
Yes	17,185 (27.3)	15,831 (27.0)	1354 (31.3)	
COFs, *n* (%)				0.480
No	14,084 (22.3)	13,136 (22.4)	948 (21.9)	
Yes	48,954 (77.7)	45,573 (77.6)	3381 (78.1)	
BMCs, *n* (%)				<0.001
No	34,909 (55.4)	32,648 (55.6)	2261 (52.2)	
Yes	28,129 (44.6)	26,061 (44.4)	2068 (47.8)	

Table 2. *Cont.*

Characteristics	Total (N = 63,038)	FTB (*n* = 58,709)	PTB (*n* = 4329)	*p*
IBI, n (%)				<0.001
No	33,048 (52.4)	30,892 (52.6)	2156 (49.8)	
Yes	29,990 (47.6)	27,817 (47.4)	2173 (50.2)	
HR, *n* (%)				<0.001
No	58,864 (93.4)	548,74 (93.5)	3990 (92.2)	
Yes	4174 (6.6)	3835 (6.5)	339 (7.8)	

PTB: preterm birth; FTB: full-term birth; BMI: body mass index; ETS: environmental tobacco smoke; COFs: cooking oil fumes; BMCs: burning mosquito coils; HR: home renovation.

The socio-demographic data for the overall population (*n* = 67,861) and the included population (*n* = 63,038) were compared (see Table S2). There were no significant differences between them, which means that the subjects included in the study were suitably representative of the whole population.

3.2. Independent Effects of Prenatal Exposure to Five Sources of HAP on PTB

Table 3 summarizes the independent effects of prenatal exposure to five sources of HAP on the risk of PTB. After adjusting for child's sex, maternal age at delivery, maternal educational level, family income, marital status, parity and maternal pre-pregnancy BMI, compared to mothers with no exposure, prenatal exposure to ETS increased the risk of PTB with an adjusted OR of 1.30 (95% CI: 1.22–1.40). The PTB risk increased with the average level of daily ETS exposure (Table S3). Prenatal exposure to COFs was associated with increased risk of PTB with marginal significance (OR = 1.07, 95% CI: 0.99~1.15). The risk increased incrementally with the frequency (never, sometimes, often or always) of COF exposure (Table S4). The other three sources of HAP, maternal exposure to BMCs, IBI and HR during pregnancy, were all significantly associated with increased risk of PTB, with their adjusted ORs being 1.15 (95% CI = 1.08~1.22), 1.12 (95% CI = 1.05~1.19) and 1.21 (95% CI = 1.07~1.35), respectively. As can be seen in Table S5, prenatal exposure to BMCs both every day and not every day showed significantly higher risk of PTB, and only those exposed to IBI every day had a significantly higher risk of PTB (Table S6).

Table 3. PTB risk attributable to prenatal exposure to individual HAP sources during pregnancy.

HAP Exposure Source	No. of Subjects	No. of PTBs	cOR (95% CI)	aOR (95% CI) [a]
ETS				
NO	45,853	2975	1.00	1.00
YES	17,185	1354	1.23 (1.15, 1.32) ***	1.30 (1.22, 1.40) ***
COFs				
NO	14,084	948	1.00	1.00
YES	48,954	3381	1.03 (0.95, 1.11)	1.07 (0.99, 1.15)
BMC				
NO	34,909	2261	1.00	1.00
YES	28,129	2068	1.15 (1.08, 1.22) ***	1.16 (1.09, 1.24) ***
IBI				
NO	33,048	2156	1.00	1.00
YES	29,990	2173	1.12 (1.05, 1.19) ***	1.13 (1.06, 1.20) ***
HR				
NO	58,864	3990	1.00	1.00
YES	4174	339	1.22 (1.08, 1.36) ***	1.21 (1.07, 1.35) ***

[a]: Adjusted for child's sex, maternal age at delivery, maternal educational level, family income, marital status, parity and pre-pregnancy BMI. ***: $p < 0.001$. HAP: household air pollution; PTB: preterm birth; ETS: environmental tobacco smoke; COFs: cooking oil fumes; BMCs: burning mosquito coils; IBI: indoor burning incense; HR: home renovation.

3.3. Joint Effects of Prenatal Exposure to Five Sources of HAP on PTB

As shown in Figure 1, compared with mothers who were never exposed to any sources of HAP, maternal exposure to two, three or four or more sources of HAP significantly

increased the risk of PTB, with adjusted ORs of 1.36 (95% CI = 1.19~1.57), 1.49 (95% CI = 1.30~1.72) and 1.97 (95% CI = 1.62~2.40), respectively; while exposure to one source of HAP alone was not significantly associated with an increased risk of PTB (with adjusted OR of 1.08 (95% CI = 0.94~1.26)). The risk of PTB increased incrementally with the number of HAP exposure sources (p for trend <0.001). The sample size and effect size for each HAP exposure index are listed in Table S7.

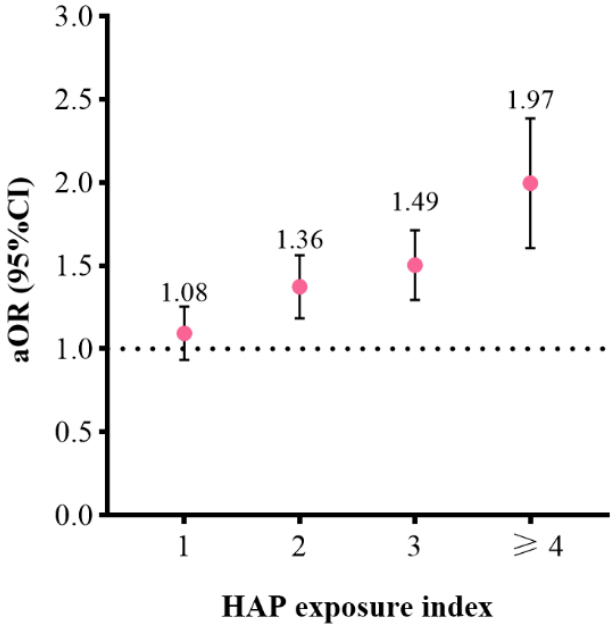

Figure 1. The accumulative effect of prenatal exposure to HAP on PTB. HAP exposure index: how many household air pollution sources the mother was exposed to during pregnancy; aOR: adjusted for child's sex, maternal age at delivery, maternal educational level, family income, marital status, parity and pre-pregnancy BMI.

Table 4 presents the interaction effects for prenatal exposure to the five sources of HAP on PTB. After adjusting for potential confounders, we only detected synergistic interactions that affected the risk of PTB in both the multiplicative and additive scales for COFs and HR, with an IOR of 1.42 (95% CI = 1.04~1.97), RERI of 0.39 (95% CI = 0.08~0.70) and AP of 0.29 (95% CI = 0.08~0.51). Specifically, on the multiplicative scale, synergistic interaction between COFs and HR contributed to a 42% greater risk of PTB than the product of their independent effects; on additive scale, synergistic interaction between COFs and HR contributed to a 39% greater risk of PTB, and 29% of PTBs were attributed to their interaction. More details are presented in Table 4.

Table 4. Interaction effects of prenatal exposure to five sources of HAP on PTB.

HAP Exposure		FTB (n = 58,709)	PTB (n = 4329)	OR (95% CI)	IOR (95% CI)	RERI (95% CI)	AP (95% CI)
ETS	COFs				0.91 (0.77, 1.07)	−0.10 (−0.33, 0.12)	−0.08 (−0.23, 0.08)
No	No	10,244	691	1.00			
Yes	No	2892	257	1.40 (1.21, 1.63) ***			
No	Yes	32,634	2284	1.09 (0.99, 1.19)			
Yes	Yes	12,939	1097	1.39 (1.25, 1.54) ***			
ETS	BMC				0.95 (0.82, 1.11)	0.06 (−0.19, 0.32)	0.03 (−0.10, 0.17)
No	No	19,811	1207	1.00			
Yes	No	12,837	1054	1.47 (1.34, 1.60) ***			
No	Yes	23,067	1768	1.32 (1.22, 1.43) ***			
Yes	Yes	2994	300	1.85 (1.61, 2.12) ***			
ETS	IBI				1.00 (0.80, 1.23)	−0.23 (−0.21, 0.66)	0.10 (−0.07, 0.28)
No	No	16,156	325	1.00			
Yes	No	14,736	1231	1.60 (1.46, 1.75) ***			

Table 4. *Cont.*

HAP Exposure		FTB (n = 58,709)	PTB (n = 4329)	OR (95% CI)	IOR (95% CI)	RERI (95% CI)	AP (95% CI)
No	Yes	26,722	2050	1.40 (1.29, 1.52) ***			
Yes	Yes	1095	123	2.23 (1.82, 2.71) ***			
ETS	HR				0.82 (0.64, 1.05)	−0.22(−0.54, 0.11)	−0.16 (−0.42, 0.11)
No	No	40,333	2751	1.00			
Yes	No	14,541	1239	1.32 (1.23, 1.42) ***			
No	Yes	2545	224	1.27 (1.10, 1.46) **			
Yes	Yes	1290	115	1.37 (1.12, 1.66) **			
COFs	BMC				1.01 (0.86, 1.18)	0.02 (−0.16, 0.19)	0.01 (−0.13, 0.16)
No	No	9009	622	1.00			
Yes	No	23,639	1639	1.04 (0.95, 1.15)			
No	Yes	4127	326	1.15 (1.00, 1.32) *			
Yes	Yes	21,934	1742	1.21 (1.10, 1.34) ***			
COFs	IBI				1.10 (0.95, 1.28)	0.11 (−0.05, 0.26)	0.09 (−0.04, 0.23)
No	No	8058	574	1.00			
Yes	No	22,834	1582	1.01 (0.92, 1.12)			
No	Yes	5078	374	1.04 (0.91, 1.19)			
Yes	Yes	22,739	1799	1.16 (1.05, 1.28) **			
COFs	HR				1.42 (1.04, 1.97) *	0.39 (0.08, 0.70)	0.29 (0.08, 0.51)
No	No	12,370	897	1.00			
Yes	No	42,504	3093	1.04 (0.96, 1.13)			
No	Yes	766	51	0.90 (0.67, 1.19)			
Yes	Yes	3069	288	1.33 (1.16, 1.53) ***			
BMC	IBI				1.01 (0.88, 1.17)	0.02 (−0.14, 0.18)	0.02 (−0.11, 0.15)
No	No	24,467	1670	1.00			
Yes	No	6425	486	1.12 (1.01, 1.25) *			
No	Yes	8181	591	1.05 (0.96, 1.16)			
Yes	Yes	19,636	1582	1.20 (1.12, 1.29) ***			
BMC	HR				1.18 (0.94, 1.50)	0.25 (−0.05, 0.54)	0.17 (−0.02, 0.35)
No	No	30,629	3108	1.00			
Yes	No	24,245	1882	1.15 (1.07, 1.22) ***			
No	Yes	2019	153	1.10 (0.92, 1.30)			
Yes	Yes	1816	186	1.49 (1.27, 1.74) ***			
IBI	HR				1.04 (0.83, 1.32)	0.08 (−0.21, 0.37)	0.06 (−0.15, 0.26)
No	No	28,979	2001	1.00			
Yes	No	25,895	1989	1.12 (1.05, 1.20) ***			
No	Yes	1913	155	1.17 (0.99, 1.39)			
Yes	Yes	1922	184	1.37 (1.17, 1.60) ***			

*: $p < 0.05$; **: $p < 0.01$, ***: $p < 0.001$. HAP: household air pollution; PTB: preterm birth; FTB: full-term birth; ETS: environmental tobacco smoke; COFs: cooking oil fumes; BMCs: burning mosquito coils; IBI: indoor burning incense; HR: home renovation; IOR: interaction of odds ratios; RERI: relative excess risk due to interaction; AP: proportion attributable to interaction.

4. Discussion

To the best of our knowledge, this was the first study to examine both the independent and joint effects of prenatal exposure to five different sources of HAP (ETS, COFs, BMCs, IBI and HR) on PTB. Compared to mothers without exposure, maternal exposure to HAP from the five sources during pregnancy demonstrated higher risks of PTB. Moreover, we found the PTB risk accumulated with the number of HAP sources. Finally, we also found a synergistic interaction effect for prenatal exposure to COFs and HR on the risk of PTB.

In the past few decades, scientists have generally focused on examining the association between outdoor air pollution and PTB. For example, a study found significant associations between traffic-related air pollution during pregnancy and preterm birth in populations from four counties in California [44]. Another study found that prenatal exposure to air pollution generated from dust episodes increased the risk of preterm birth [45]. However, in contrast, Smith and his colleagues found that, in London, ozone (O_3) and $PM_{2.5}$ exposure during pregnancy was associated with increased risk of PTB, but they did not find an association between particulate matter smaller than 10 μm in diameter (PM_{10}) and preterm birth [46]. Three other studies did not find prenatal nitrogen dioxide (NO_2) exposure to be related to the occurrence of PTB [47–49]. As a consequence, the source and type of air pollution may be important in terms of influence on the risk of PTB.

Based upon the previous research, in the present study, we examined the impact of five different sources of household air pollution on the risk of PTB. We found that maternal exposure to HAP from ETS, COFs, BMCs, IBI and HR during pregnancy respectively increased the risk of PTB, which indicates that prenatal exposure to each HAP source could independently affect the occurrence of PTB. In agreement with our findings, several previous studies also indicated that prenatal ETS exposure was a major risk factor for PTB [50–53]. However, only one prior study found a detrimental effect from prenatal exposure to cooking oil fumes on PTB [32], and two prior studies found that household renovation during pregnancy was associated with increased risk of PTB [24,26]. Although two recent studies found that prenatal exposure to ultrafine particles ($PM_{0.1}$) generated from burning mosquito coils indoors might increase the risk of low birthweight [54,55], and a birth cohort study in Taiwan indicated that prenatal exposure to incense smoke might be positively associated with lower birth weight for boys and smaller head circumference for both boys and girls [56], there is no existing evidence showing any correlation between prenatal BMC and IBI exposure with PTB. However, we found that 27.3% mothers were exposed to ETS during pregnancy, and prenatal ETS exposure led to a stronger risk of PTB than exposure to COFs, BMCs, IBI or HR. Pregnant women should be protected from ETS as much as possible.

Given that environmental exposure often involves exposure to a complex mixture of multiple sources of environmental pollution, it is possible that their joint effects might differ from their individual effects. Therefore, there has been increased interest in examining the joint effects of exposure to multiple sources of environmental pollution in the past few years [57–59]. A few studies have reported joint effects from different types of ambient air pollution or from ambient air pollution and other types of pollution on birth outcomes. For example, one study found that prenatal cadmium and phthalate co-exposure, as well as cadmium and arsenic co-exposure, were associated with reduced birth weight [60]. Siddika and his colleagues also discovered that exposure to individual air pollutants, such as $PM_{2.5}$ and O_3, across the entire course of pregnancy may be synergistic and potentiate the different pollutants' adverse effects on the risk of PTB [61]. Additionally, a prospective cohort study observed that the combined effects of PM_{10} and NO_2 in early pregnancy and of Pb and Hg in late pregnancy were associated with reduced birth weight [62]. Zhang and his colleagues found a positive joint effect from prenatal phenol and phthalate exposure on PTB [63]. Another study reported a potential synergistic interaction between Zn and Cu on PTB [64].

In the present study, we tried to assess whether there were joint effects among five different sources of HAP on the risk of PTB and obtained some interesting findings. Firstly, we found that the PTB risk increased incrementally with the number of prenatal HAP exposure sources (Figure 1). This indicated that mothers who were exposed to more sources of HAP had a higher risk of PTB than mothers who were exposed to a single source of HAP, which means that accumulative effects from prenatal exposure to five HAP sources on the risk of PTB might exist [36]. Therefore, if some sources of HAP exposure are unavoidable, the risk of PTB can be reduced by limiting exposure to other HAP sources. Moreover, we further found synergistic interaction effects for prenatal COFs and HR exposure on the risk of PTB. This indicates that simultaneous prenatal exposure to both COFs and HR might produce an additional hazardous impact on PTB greater than the sum or product of their independent effects.

The mechanisms that cause prenatal exposure to HAP and increase the risk of PTB are not well-documented. However, it is known that HAP has many common sources, such as ETS, cooking, burning mosquito coils, burning incense and home renovation, especially in developing countries. HAP from these five sources may contain many hazardous components. For example, ETS contains over 4000 chemical constituents and additives, among which nicotine, carbon monoxide (CO), PAHs and PM are proven to have roles in the causes of pregnancy-related disease [65]. Moreover, Chinese-style cooking can involve the volatilization of larger amounts of pollutants, including PM, PAHs, volatile organic

compounds (VOCs), CO, sulfur dioxide (SO_2), NO_2 and other gaseous compounds [66]. Additionally, it has been reported that both burning mosquito coils and burning incense indoors can produce larger amounts of PM than burning cigarettes [67,68] and a larger amount of PAHs [69–71], as well as CO, SO_2, NO_2 and other gaseous compounds [72]. Furthermore, home renovation may produce plenty of PM and volatilize large amounts of VOCs, including phthalate esters (PAEs), PAHs and bisphenol A (BPA), and, in addition to pollutants, it may also produce high amounts of noise [73,74]. First, some of these above-mentioned hazardous pollutants can move rapidly across the placenta barrier and gain access to fetal circulation, leading to abnormal placentation and placental dysfunction, which have been linked to impaired uteroplacental perfusion, chronic hypoxia and placental ischemia and result in many adverse birth outcomes, including PTB [75–78]. Moreover, some of these pollutants can induce oxidative stress and systemic inflammation, which collectively stimulate prostaglandin and matrix metalloproteinase production [72], leading to cervical ripening, membrane rupture and uterine contractions and resulting in PTB [79,80]. Finally, studies have indicated that noise pollution might result in psychosocial stress, which has been reported to be associated with adverse birth outcomes [26,81]. It has been proven that exposure to noise may activate the hypothalamus–pituitary–adrenal (HPA) axis and increase secretion of cortisol [82–85], which is involved in the biological pathway that leads to preterm labor [80].

Drawing on the literature [86–88], we can explain the mechanism underlying the joint effects of some sources of HAP on PTB as follows. First, before absorption into the body, pollutants might react with each other, producing novel toxic pollutants that have stronger detrimental effects than the sum of the original individual pollutants. Second, some pollutants might enhance or inhibit the absorption, distribution, metabolism and elimination (ADME) of one or more of the other components, which may cause their combined effect to deviate from the sum of the original individual pollutants. Third, some pollutants might alter the damage, repair, compensation and signaling processes of the human body to amplify or reduce the health effects caused by other pollutants. However, only one prior study discovered relevant evidence, showing that the lung epithelium barrier becomes more permeable following oxidant gas exposure (e.g., NO_2), which may then facilitate the absorption of particles directly into the circulatory system [89]. This finding might help to explain the interactive effect we found from COFs and HR on the risk of PTB. Given the paucity of research in this area, further studies are needed to determine the underlying biological mechanisms of the effects of different indoor air pollutants on PTB.

To the best of our knowledge, this is the first study with a very large sample size to focus on both the independent and joint effects of multiple sources of HAP on PTB within a Chinese population. However, when interpreting the results of our study, it is important to be cognizant of the limitations of the study, since it was a cross-sectional study that used the data provided by mothers completing a self-reported, structured questionnaire in the 2017 LCCS. The prenatal HAP exposure was retrospectively recalled by mothers, which may have resulted in information bias. However, there are results for mothers' retrospective recall of perinatal events that consistently support the validity and reliability of this measurement strategy [90–92]. Furthermore, in practical terms, biological monitoring and physician assessment or assessment of medical records are very expensive (especially in studies with large sample sizes); as such, there is great value in conducting preliminary large studies using self-report measures. Second, PTB was assessed using mothers' recall of the hospital diagnosis of PTB. However, it is common to apply self-report information to assess birth outcome in large-scale observational study; for example, the China, Children, Homes, Health (CCHH) study [24,26]. Moreover, the incidence of PTB in this study was similar to the nationwide incidence of PTB in China [2,4]. Third, we did not measure the specific ingredients contained in each HAP source (such as $PM_{2.5}$, PAHs, CO, etc.) or the exposure duration of each HAP source, which prevented us from investigating the association of the ingredients and the exposure duration for different HAP sources with PTB. Fourth, there were potentially residual or unmeasured covariates in our analysis. For

example, unfortunately, we had no information on mothers' previous history of PTBs and the condition of houses (such as home ventilation, number of floors, distance from main road, dampness), which might have influenced the veracity of the relationship between prenatal HAP exposure and PTB in our results. Fifth, all subjects recruited in this study were located in one district in Shenzhen, China. This might have introduced selection bias and limit the generalizability of our results in different areas of China. Sixth, although the recruited mothers were likely to have experienced similar ambient air pollution exposure because they were from the same district, we could not obviate the influence of ambient air pollution on indoor air pollution and the confounding effect on the association between HAP and PTB. We did not collect home addresses, so we were unable to consider mothers' exposure to ambient air pollution during their pregnancy.

5. Conclusions

To conclude, our study provides evidence of the hazardous effects of pregnant mothers' exposure to HAP from multiple sources on PTB. In particular, this is the first study to report the synergistic interaction effects from specific sources of HAP on the risk of PTB. In addition, we found that the PTB risk increased incrementally with the number of prenatal HAP exposure sources. Given the widespread exposure to HAP and the profound effect that PTB has upon children's future development, it is important to further test these identified associations through longitudinal studies. If replicated, then these findings highlight the importance of public health interventions aiming to minimize prenatal exposure to HAP from multiple sources in reducing the risk of PTB.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/atmos13122022/s1, Table S1. Questions and options in the questionnaire; Table S2. Comparison of socio-demographic characteristics among the overall population and the included population; Table S3. Association between the dose of prenatal ETS exposure and risk of PTB; Table S4. Association between the frequency of prenatal COFs exposure and risk of PTB; Table S5. Association between the frequency of prenatal BMCs exposure and risk of PTB; Table S6. Association between the frequency of prenatal IBI exposure and risk of PTB; Table S7. Association between HAP exposure index and risk of PTB.

Author Contributions: All authors contributed to the study conception and design. Conceptualization, X.-C.L. and W.-Q.C.; methodology, X.-C.L., E.S. and W.-Q.C.; software, X.-C.L.; visualization, X.-C.L.; formal analysis, X.-C.L.; investigation, L.-H.H. and X.-C.L.; resources, W.-Q.C.; data curation, L.-H.H. and X.-C.L.; writing—original draft preparation, X.-C.L.; writing—review and editing, X.-C.L., E.S. and W.-Q.C.; supervision, E.S. and W.-Q.C.; project administration, L.-H.H., B.-J.H. and W.-Q.C.; funding acquisition, W.-Q.C. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Natural Science Foundation of China (grant no. 81973143) and the Shenzhen Longhua District Government of China (Longhua STE Fund) (grant no. 2013142).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki 2.2 and approved by the Ethics Committee of the School of Public Health of Sun Yat-sen University in Guangzhou, China (project identification code: no. 2015–016).

Informed Consent Statement: All the participants were informed of the aims and process of the study and participated deliberately in the study. Informed consent was obtained from all participants involved.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Acknowledgments: This study was conducted as part of Longhua Child Cohort Study, which was supported by the Shenzhen Longhua District Government of China. The School of Public Health of Sun Yat-sen University undertook this study. The authors would like to thank the staff in Longhua Maternal and Child Health Care Center, who offered much help during the field investigation. We are also grateful to all families who took part in this study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. WHO. Preterm Birth: Fact sheet 2016. Available online: https://www.who.int/en/news-room/fact-sheets/detail/preterm-birth (accessed on 19 February 2018).
2. Deng, K.; Liang, J.; Mu, Y.; Liu, Z.; Wang, Y.; Li, M.; Li, X.; Dai, L.; Li, Q.; Chen, P.; et al. Preterm births in China between 2012 and 2018: An observational study of more than 9 million women. *Lancet Glob. Health* **2021**, *9*, e1226–e1241. [CrossRef] [PubMed]
3. World Health Organization. *Born Too Soon: The Global Action Report on Preterm Birth*; World Health Organization: Geneva, Switzerland, 2012.
4. Chen, C.; Zhang, J.W.; Xia, H.W.; Zhang, H.X.; Betran, A.P.; Zhang, L.; Hua, X.L.; Feng, L.P.; Chen, D.; Sun, K.; et al. Preterm Birth in China Between 2015 and 2016. *Am. J. Public Health* **2019**, *109*, 1597–1604. [CrossRef] [PubMed]
5. Liu, L.; Oza, S.; Hogan, D.; Chu, Y.; Perin, J.; Zhu, J.; Lawn, J.E.; Cousens, S.; Mathers, C.; Black, R.E. Global, regional, and national causes of under-5 mortality in 2000–2015: An updated systematic analysis with implications for the Sustainable Development Goals. *Lancet* **2016**, *388*, 3027–3035. [CrossRef] [PubMed]
6. He, C.; Liu, L.; Chu, Y.; Perin, J.; Dai, L.; Li, X.; Miao, L.; Kang, L.; Li, Q.; Scherpbier, R.; et al. National and subnational all-cause and cause-specific child mortality in China, 1996-2015: A systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob. Health* **2017**, *5*, e186–e197. [CrossRef]
7. Saigal, S.; Doyle, L.W. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet* **2008**, *371*, 261–269. [CrossRef]
8. Chernausek, S.D. Update: Consequences of abnormal fetal growth. *J. Clin. Endocrinol. Metab.* **2012**, *97*, 689–695. [CrossRef]
9. Goldenberg, R.L.; Culhane, J.F.; Iams, J.D.; Romero, R. Epidemiology and causes of preterm birth. *Lancet* **2008**, *371*, 75–84. [CrossRef]
10. Stieb, D.M.; Chen, L.; Eshoul, M.; Judek, S. Ambient air pollution, birth weight and preterm birth: A systematic review and meta-analysis. *Environ. Res.* **2012**, *117*, 100–111. [CrossRef]
11. Klepac, P.; Locatelli, I.; Korošec, S.; Künzli, N.; Kukec, A. Ambient air pollution and pregnancy outcomes: A comprehensive review and identification of environmental public health challenges. *Environ. Res.* **2018**, *167*, 144–159. [CrossRef] [PubMed]
12. Ju, L.; Li, C.; Yang, M.; Sun, S.; Zhang, Q.; Cao, J.; Ding, R. Maternal air pollution exposure increases the risk of preterm birth: Evidence from the meta-analysis of cohort studies. *Environ. Res.* **2021**, *202*, 111654. [CrossRef]
13. Ghosh, R.; Causey, K.; Burkart, K.; Wozniak, S.; Cohen, A.; Brauer, M. Ambient and household PM2.5 pollution and adverse perinatal outcomes: A meta-regression and analysis of attributable global burden for 204 countries and territories. *PLoS Med.* **2021**, *18*, e1003718. [CrossRef] [PubMed]
14. US EPA. *Report to Congress on Indoor Air Quality. Volume 2: Assessment and Control of Indoor air Pollution*; EP/400/1-89/001C; U.S. Environmental Protection Agency, Office of Air and Radiation: Washington, DC, USA, 1989.
15. Ouidir, M.; Giorgis-Allemand, L.; Lyon-Caen, S.; Morelli, X.; Cracowski, C.; Pontet, S.; Pin, I.; Lepeule, J.; Siroux, V.; Slama, R. Estimation of exposure to atmospheric pollutants during pregnancy integrating space-time activity and indoor air levels: Does it make a difference? *Environ. Int.* **2015**, *84*, 161–173. [CrossRef] [PubMed]
16. Bruce, N.; Perez-Padilla, R.; Albalak, R. Indoor air pollution in developing countries: A major environmental and public health challenge. *Bull World Health Organ.* **2000**, *78*, 1078–1092. [PubMed]
17. WHO. *Burden of Disease from Household Air Pollution for 2016*; World Health Organization: Geneva, Switzerland, 2018.
18. HEI. *State of Global Air 2020*; Health Effects Institute: Boston, MA, USA, 2020.
19. Hulin, M.; Simoni, M.; Viegi, G.; Annesi-Maesano, I. Respiratory health and indoor air pollutants based on quantitative exposure assessments. *Eur. Respir. J.* **2012**, *40*, 1033–1045. [CrossRef] [PubMed]
20. Jaakkola, J.J.K.; Jaakkola, N.; Zahlsen, K. Fetal growth and length of gestation in relation to prenatal exposure to environmental tobacco smoke assessed by hair nicotine concentration. *Environ. Health Perspect.* **2001**, *109*, 557–561. [CrossRef]
21. Salmasi, G.; Grady, R.; Jones, J.; McDonald, S.D.; Knowledge Synth, G. Environmental tobacco smoke exposure and perinatal outcomes: A systematic review and meta-analyses. *Acta Obstet. Gynecol. Scand.* **2010**, *89*, 423–441. [CrossRef]
22. Leonardi-Bee, J.; Smyth, A.; Britton, J.; Coleman, T. Environmental tobacco smoke and fetal health: Systematic review and meta-analysis. *Arch. Dis. Child Fetal. Neonatal. Ed.* **2008**, *93*, F351–F361. [CrossRef]
23. Wylie, B.J.; Coull, B.A.; Hamer, D.H.; Singh, M.P.; Jack, D.; Yeboah-Antwi, K.; Sabin, L.; Singh, N.; MacLeod, W.B. Impact of biomass fuels on pregnancy outcomes in central East India. *Environ. Health* **2014**, *13*, 1. [CrossRef]
24. Liu, W.; Huang, C.; Cai, J.; Wang, X.; Zou, Z.; Sun, C. Household environmental exposures during gestation and birth outcomes: A cross-sectional study in Shanghai, China. *Sci. Total Environ.* **2018**, *615*, 1110–1118. [CrossRef]

25. Younger, A.; Alkon, A.; Harknett, K.; Jean Louis, R.; Thompson, L.M. Adverse birth outcomes associated with household air pollution from unclean cooking fuels in low- and middle-income countries: A systematic review. *Environ. Res.* **2021**, *204*, 112274. [CrossRef]
26. Liu, W.; Huang, C.; Li, B.; Zhao, Z.; Yang, X.; Deng, Q.; Zhang, X.; Qian, H.; Sun, Y.; Qu, F.; et al. Household renovation before and during pregnancy in relation to preterm birth and low birthweight in China. *Indoor Air* **2019**, *29*, 202–214. [CrossRef]
27. Pan, D.; Liu, S.; Huang, D.; Zeng, X.; Zhang, Y.; Pang, Q.; Wu, H.; Tan, H.J.J.; Liang, J.; Sheng, Y.; et al. Effects of household environmental exposure and ventilation in association with adverse birth outcomes: A prospective cohort study in rural China. *Sci. Total Environ.* **2022**, *822*, 153519. [CrossRef]
28. Amiri, A.; Pryor, E.; Rice, M.; Owns, C.A.; Turner-Henson, A.; Fanucchi, M.V. Formaldehyde Exposure During Pregnancy. *Am. J. Matern. Child Nurs.* **2015**, *40*, 180–185. [CrossRef]
29. Agarwal, P.; Singh, L.; Anand, M.; Taneja, A. Association Between Placental Polycyclic Aromatic Hydrocarbons (PAHS), Oxidative Stress, and Preterm Delivery: A Case-Control Study. *Arch. Environ. Contam. Toxicol.* **2018**, *74*, 218–227. [CrossRef] [PubMed]
30. Shezi, B.; Jafta, N.; Asharam, K.; Tularam, H.; Jeena, P.; Naidoo, R.N. Maternal exposure to indoor PM(2.5) and associated adverse birth outcomes in low socio-economic households, Durban, South Africa. *Indoor Air* **2022**, *32*, e12934. [CrossRef] [PubMed]
31. Lin, T.-S.; Li, M. Indoor air pollution: Unusual sources. In *Encyclopedia of Environmental Health*; Nriagu, J.O., Ed.; Elsevier: Amsterdam, The Netherlands, 2011; pp. 201–207. [CrossRef]
32. Hu, P.; Wang, C.; Ding, P.; He, Y.H.; Xie, C.; Tian, F.Y.; Yuan, S.; Jia, D.; Chen, W.Q. Placental weight mediates association between prenatal exposure to cooking oil fumes and preterm birth. *J. Matern. Fetal. Neonatal. Med.* **2021**, *35*, 7248–7258. [CrossRef] [PubMed]
33. Zhang, Y.; Mo, J.; Weschler, C.J. Reducing health risks from indoor exposures in rapidly developing urban China. *Environ. Health Perspect.* **2013**, *121*, 751–755. [CrossRef]
34. Gordon, S.B.; Bruce, N.G.; Grigg, J.; Hibberd, P.L.; Kurmi, O.P.; Lam, K.-b.H.; Mortimer, K.; Asante, K.P.; Balakrishnan, K.; Balmes, J.; et al. Respiratory risks from household air pollution in low and middle income countries. *Lancet Respir. Med.* **2014**, *2*, 823–860. [CrossRef]
35. Schluger, N. Household air quality in high-income countries: Forgotten but not gone. *Lancet Respir. Med.* **2014**, *2*, 781–783. [CrossRef]
36. Ben-Shlomo, Y.; Mishra, G.; Kuh, D. Life Course Epidemiology. In *Handbook of Epidemiology*; Ahrens, W., Pigeot, I., Eds.; Springer: New York, NY, USA, 2014; pp. 1521–1549.
37. Knol, M.J.; VanderWeele, T.J. Recommendations for presenting analyses of effect modification and interaction. *Int. J. Epidemiol.* **2012**, *41*, 514–520. [CrossRef]
38. De Mutsert, R.; Jager, K.J.; Zoccali, C.; Dekker, F.W. The effect of joint exposures: Examining the presence of interaction. *Kidney Int.* **2009**, *75*, 677–681. [CrossRef] [PubMed]
39. Rothman, K.J.; Lash, T.L.; VanderWeele, T.J.; Haneuse, S. *Modern Epidemiology*, 4th ed.; Library of Congress Cataloging-in-Publication Data: Philadelphia, PA, USA, 2021; pp. 619–648.
40. Blot, W.J.; Day, N.E. Synergism and interaction: Are they equivalent? *Am. J. Epidemiol.* **1979**, *110*, 99–100. [CrossRef] [PubMed]
41. Rothman, K.J.; Greenland, S.; Walker, A.M. Concepts of interaction. *Am. J. Epidemiol.* **1980**, *112*, 467–470. [CrossRef] [PubMed]
42. Saracci, R. Interaction and synergism. *Am. J. Epidemiol.* **1980**, *112*, 465–466. [CrossRef]
43. Knol, M.J.; VanderWeele, T.J.; Groenwold, R.H.; Klungel, O.H.; Rovers, M.M.; Grobbee, D.E. Estimating measures of interaction on an additive scale for preventive exposures. *Eur. J. Epidemiol.* **2011**, *26*, 433–438. [CrossRef]
44. Padula, A.M.; Mortimer, K.M.; Tager, I.B.; Hammond, S.K.; Lurmann, F.W.; Yang, W.; Stevenson, D.K.; Shaw, G.M. Traffic-related air pollution and risk of preterm birth in the San Joaquin Valley of California. *Ann. Epidemiol.* **2014**, *24*, 888–895.e4. [CrossRef]
45. Viel, J.F.; Mallet, Y.; Raghoumandan, C.; Quenel, P.; Kadhel, P.; Rouget, F.; Multigner, L. Impact of Saharan dust episodes on preterm births in Guadeloupe (French West Indies). *Occup. Environ. Med.* **2019**, *76*, 336–340. [CrossRef]
46. Smith, R.B.; Beevers, S.D.; Gulliver, J.; Dajnak, D.; Fecht, D.; Blangiardo, M.; Douglass, M.; Hansell, A.L.; Anderson, H.R.; Kelly, F.J.; et al. Impacts of air pollution and noise on risk of preterm birth and stillbirth in London. *Environ. Int.* **2020**, *134*, 105290. [CrossRef]
47. Stieb, D.M.; Chen, L.; Hystad, P.; Beckerman, B.S.; Jerrett, M.; Tjepkema, M.; Crouse, D.L.; Omariba, D.W.; Peters, P.A.; van Donkelaar, A.; et al. A national study of the association between traffic-related air pollution and adverse pregnancy outcomes in Canada, 1999-2008. *Environ. Res.* **2016**, *148*, 513–526. [CrossRef]
48. Qian, Z.; Liang, S.; Yang, S.; Trevathan, E.; Huang, Z.; Yang, R.; Wang, J.; Hu, K.; Zhang, Y.; Vaughn, M.; et al. Ambient air pollution and preterm birth: A prospective birth cohort study in Wuhan, China. *Int. J. Hyg. Environ. Health* **2016**, *219*, 195–203. [CrossRef]
49. Liang, Z.; Yang, Y.; Li, J.; Zhu, X.; Ruan, Z.; Chen, S.; Huang, G.; Lin, H.; Zhou, J.Y.; Zhao, Q. Migrant population is more vulnerable to the effect of air pollution on preterm birth: Results from a birth cohort study in seven Chinese cities. *Int. J. Hyg. Environ. Health* **2019**, *222*, 1047–1053. [CrossRef] [PubMed]
50. Rang, N.N.; Hien, T.Q.; Chanh, T.Q.; Thuyen, T.K. Preterm birth and secondhand smoking during pregnancy: A case-control study from Vietnam. *PLoS ONE* **2020**, *15*, e0240289. [CrossRef] [PubMed]
51. Kharrazi, M.; DeLorenze, G.N.; Kaufman, F.L.; Eskenazi, B.; Bernert, J.T., Jr.; Graham, S.; Pearl, M.; Pirkle, J. Environmental tobacco smoke and pregnancy outcome. *Epidemiology* **2004**, *15*, 660–670. [CrossRef] [PubMed]

52. Ion, R.C.; Wills, A.K.; Bernal, A.L. Environmental Tobacco Smoke Exposure in Pregnancy is Associated With Earlier Delivery and Reduced Birth Weight. *Reprod. Sci.* **2015**, *22*, 1603–1611. [CrossRef]
53. Windham, G.C.; Hopkins, B.; Fenster, L.; Swan, S.H. Prenatal active or passive tobacco smoke exposure and the risk of preterm delivery or low birth weight. *Epidemiology* **2000**, *11*, 427–433. [CrossRef]
54. Nyarku, M.; Buonanno, G.; Ofosu, F.; Jayaratne, R.; Mazaheri, M.; Morawska, L. Schoolchildren's personal exposure to ultrafine particles in and near Accra, Ghana. *Environ. Int.* **2019**, *133*, 105223. [CrossRef]
55. Laurent, O.; Hu, J.; Li, L.; Cockburn, M.; Escobedo, L.; Kleeman, M.J.; Wu, J. Sources and contents of air pollution affecting term low birth weight in Los Angeles County, California, 2001–2008. *Environ. Res.* **2014**, *134*, 488–495. [CrossRef]
56. Chen, L.Y.; Ho, C. Incense Burning during Pregnancy and Birth Weight and Head Circumference among Term Births: The Taiwan Birth Cohort Study. *Environ. Health Perspect.* **2016**, *124*, 1487–1492. [CrossRef]
57. Barrera-Gomez, J.; Agier, L.; Portengen, L.; Chadeau-Hyam, M.; Giorgis-Allemand, L.; Siroux, V.; Robinson, O.; Vlaanderen, J.; Gonzalez, J.R.; Nieuwenhuijsen, M.; et al. A systematic comparison of statistical methods to detect interactions in exposome-health associations. *Environ. Health* **2017**, *16*, 74. [CrossRef]
58. Johns, D.O.; Stanek, L.W.; Walker, K.; Benromdhane, S.; Hubbell, B.; Ross, M.; Devlin, R.B.; Costa, D.L.; Greenbaum, D.S. Practical advancement of multipollutant scientific and risk assessment approaches for ambient air pollution. *Environ. Health Perspect.* **2012**, *120*, 1238–1242. [CrossRef]
59. Oakes, M.; Baxter, L.; Long, T.C. Evaluating the application of multipollutant exposure metrics in air pollution health studies. *Environ. Int.* **2014**, *69*, 90–99. [CrossRef]
60. Govarts, E.; Remy, S.; Bruckers, L.; Den Hond, E.; Sioen, I.; Nelen, V.; Baeyens, W.; Nawrot, T.S.; Loots, I.; Van Larebeke, N.; et al. Combined Effects of Prenatal Exposures to Environmental Chemicals on Birth Weight. *Int. J. Environ. Res. Public Health* **2016**, *13*, 495. [CrossRef]
61. Siddika, N.; Rantala, A.K.; Antikainen, H.; Balogun, H.; Amegah, A.K.; Ryti, N.R.I.; Kukkonen, J.; Sofiev, M.; Jaakkola, M.S.; Jaakkola, J.J.K. Synergistic effects of prenatal exposure to fine particulate matter (PM(2.5)) and ozone (O(3)) on the risk of preterm birth: A population-based cohort study. *Environ. Res.* **2019**, *176*, 108549. [CrossRef] [PubMed]
62. Lee, S.; Hong, Y.C.; Park, H.; Kim, Y.; Ha, M.; Ha, E. Combined effects of multiple prenatal exposure to pollutants on birth weight: The Mothers and Children's Environmental Health (MOCEH) study. *Environ. Res.* **2020**, *181*, 108832. [CrossRef]
63. Zhang, Y.; Mustieles, V.; Williams, P.L.; Wylie, B.J.; Souter, I.; Calafat, A.M.; Demokritou, M.; Lee, A.; Vagios, S.; Hauser, R.; et al. Parental preconception exposure to phenol and phthalate mixtures and the risk of preterm birth. *Environ. Int.* **2021**, *151*, 106440. [CrossRef] [PubMed]
64. Liu, J.; Ruan, F.; Cao, S.; Li, Y.; Xu, S.; Xia, W. Associations between prenatal multiple metal exposure and preterm birth: Comparison of four statistical models. *Chemosphere* **2022**, *289*, 133015. [CrossRef] [PubMed]
65. Rogers, J.M. Tobacco and pregnancy. *Reprod. Toxicol.* **2009**, *28*, 152–160. [CrossRef] [PubMed]
66. Wang, L.; Xiang, Z.; Stevanovic, S.; Ristovski, Z.; Salimi, F.; Gao, J.; Wang, H.; Li, L. Role of Chinese cooking emissions on ambient air quality and human health. *Sci. Total Environ.* **2017**, *589*, 173–181. [CrossRef] [PubMed]
67. Liu, W.; Zhang, J.; Hashim, J.H.; Jalaludin, J.; Hashim, Z.; Goldstein, B.D. Mosquito coil emissions and health implications. *Environ. Health Perspect.* **2003**, *111*, 1454–1460. [CrossRef]
68. Mannix, R.C.; Nguyen, K.P.; Tan, E.W.; Ho, E.E.; Phalen, R.F. Physical characterization of incense aerosols. *Sci. Total Environ.* **1996**, *193*, 149–158. [CrossRef] [PubMed]
69. Chiang, K.C.; Liao, C.M. Heavy incense burning in temples promotes exposure risk from airborne PMs and carcinogenic PAHs. *Sci. Total Environ.* **2006**, *372*, 64–75. [CrossRef]
70. Liao, C.M.; Chiang, K.C. Probabilistic risk assessment for personal exposure to carcinogenic polycyclic aromatic hydrocarbons in Taiwanese temples. *Chemosphere* **2006**, *63*, 1610–1619. [CrossRef] [PubMed]
71. Yang, T.T.; Lin, S.T.; Lin, T.S.; Chung, H.Y. Characterization of polycyclic aromatic hydrocarbon emissions in the particulate and gas phase from smoldering mosquito coils containing various atomic hydrogen/carbon ratios. *Sci. Total Environ.* **2015**, *506–507*, 391–400. [CrossRef]
72. Lee, C.W.; Vo, T.T.T.; Wee, Y.; Chiang, Y.C.; Chi, M.C.; Chen, M.L.; Hsu, L.F.; Fang, M.L.; Lee, K.H.; Guo, S.E.; et al. The Adverse Impact of Incense Smoke on Human Health: From Mechanisms to Implications. *J. Inflamm. Res.* **2021**, *14*, 5451–5472. [CrossRef]
73. Bornehag, C.G.; Lundgren, B.; Weschler, C.J.; Sigsgaard, T.; Hagerhed-Engman, L.; Sundell, J. Phthalates in indoor dust and their association with building characteristics. *Environ. Health Perspect.* **2005**, *113*, 1399–1404. [CrossRef]
74. Myridakis, A.; Chalkiadaki, G.; Fotou, M.; Kogevinas, M.; Chatzi, L.; Stephanou, E.G. Exposure of Preschool-Age Greek Children (RHEA Cohort) to Bisphenol A, Parabens, Phthalates, and Organophosphates. *Environ. Sci. Technol.* **2016**, *50*, 932–941. [CrossRef] [PubMed]
75. Lindblad, A.; Marsál, K.; Andersson, K.E. Effect of nicotine on human fetal blood flow. *Obstet. Gynecol.* **1988**, *72*, 371–382.
76. Liu, S.; Krewski, D.; Shi, Y.; Chen, Y.; Burnett, R.T. Association between gaseous ambient air pollutants and adverse pregnancy outcomes in Vancouver, Canada. *Environ. Health Perspect.* **2003**, *111*, 1773–1778. [CrossRef]
77. Rennie, M.Y.; Detmar, J.; Whiteley, K.J.; Yang, J.; Jurisicova, A.; Adamson, S.L.; Sled, J.G. Vessel tortuousity and reduced vascularization in the fetoplacental arterial tree after maternal exposure to polycyclic aromatic hydrocarbons. *Am. J. Physiol. Heart Circ. Physiol.* **2011**, *300*, H675–H684. [CrossRef] [PubMed]

78. Van den Hooven, E.H.; Pierik, F.H.; de Kluizenaar, Y.; Hofman, A.; van Ratingen, S.W.; Zandveld, P.Y.; Russcher, H.; Lindemans, J.; Miedema, H.M.; Steegers, E.A.; et al. Air pollution exposure and markers of placental growth and function: The generation R study. *Environ. Health Perspect.* **2012**, *120*, 1753–1759. [CrossRef] [PubMed]
79. Olson, D.M. The role of prostaglandins in the initiation of parturition. *Best Pract. Res. Clin. Obstet. Gynaecol.* **2003**, *17*, 717–730. [CrossRef]
80. Medicine, I.O. 6 Biological Pathways Leading to Preterm Birth. In *Preterm Birth: Causes, Consequences, and Prevention*; The National Academies Press: Washington, DC, USA, 2007.
81. Gehring, U.; Tamburic, L.; Sbihi, H.; Davies, H.W.; Brauer, M. Impact of noise and air pollution on pregnancy outcomes. *Epidemiology* **2014**, *25*, 351–358. [CrossRef]
82. Jafari, Z.; Mehla, J.; Kolb, B.E.; Mohajerani, M.H. Prenatal noise stress impairs HPA axis and cognitive performance in mice. *Sci. Rep.* **2017**, *7*, 10560. [CrossRef]
83. Schmidt, F.P.; Basner, M.; Kroger, G.; Weck, S.; Schnorbus, B.; Muttray, A.; Sariyar, M.; Binder, H.; Gori, T.; Warnholtz, A.; et al. Effect of nighttime aircraft noise exposure on endothelial function and stress hormone release in healthy adults. *Eur. Heart J.* **2013**, *34*, 3508–3514a. [CrossRef]
84. Babisch, W.; Fromme, H.; Beyer, A.; Ising, H. Increased catecholamine levels in urine in subjects exposed to road traffic noise: The role of stress hormones in noise research. *Environ. Int.* **2001**, *26*, 475–481. [CrossRef]
85. Selander, J.; Bluhm, G.; Theorell, T.; Pershagen, G.; Babisch, W.; Seiffert, I.; Houthuijs, D.; Breugelmans, O.; Vigna-Taglianti, F.; Antoniotti, M.C.; et al. Saliva cortisol and exposure to aircraft noise in six European countries. *Environ. Health Perspect.* **2009**, *117*, 1713–1717. [CrossRef]
86. Sexton, K.; Hattis, D. Assessing cumulative health risks from exposure to environmental mixtures—Three fundamental questions. *Environ. Health Perspect.* **2007**, *115*, 825–832. [CrossRef] [PubMed]
87. Callahan, M.A.; Sexton, K. If cumulative risk assessment is the answer, what is the question? *Environ. Health Perspect.* **2007**, *115*, 799–806. [CrossRef]
88. Pastuszka, J.S. *Synergic Influence of Gaseous, Particulate, and Biological Pollutants on Human Health*; CRC Press, Taylor & Francis Group: Boca Raton, FL, USA, 2016; pp. 245–264.
89. Ciencewicki, J.; Trivedi, S.; Kleeberger, S.R. Oxidants and the pathogenesis of lung diseases. *J. Allergy Clin. Immunol.* **2008**, *122*, 456–468, quiz 469–470. [CrossRef] [PubMed]
90. Pickett, K.E.; Kasza, K.; Biesecker, G.; Wright, R.J.; Wakschlag, L.S. Women who remember, women who do not: A methodological study of maternal recall of smoking in pregnancy. *Nicotine Tob. Res.* **2009**, *11*, 1166–1174. [CrossRef] [PubMed]
91. Reich, W.; Todd, R.D.; Joyner, C.A.; Neuman, R.J.; Heath, A.C. Reliability and stability of mothers' reports about their pregnancies with twins. *Twin Res.* **2003**, *6*, 85–88. [CrossRef] [PubMed]
92. Xie, C.; Wen, X.; Niu, Z.; Ding, P.; Liu, T.; He, Y.; Lin, J.; Yuan, S.; Guo, X.; Jia, D.; et al. Comparison of secondhand smoke exposure measures during pregnancy in the development of a clinical prediction model for small-for-gestational-age among non-smoking Chinese pregnant women. *Tob. Control.* **2015**, *24*, e179–e187. [CrossRef] [PubMed]