Environmental Pollution 334 (2023) 122170

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Stillbirths attributable to open fires and their geographic disparities in non-Western countries☆

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ARTICLE INFO

Keywords:
Stillbirths
Fire-sourced $PM_{2.5}$
Geographic disparity
Low- and middle-income countries
Gini index

ABSTRACT

Due to global warming, an increased number of open fires is becoming a major contributor to $PM_{2.5}$ pollution and thus a threat to public health. However, the burden of stillbirths attributable to fire-sourced $PM_{2.5}$ is unknown. In low- and middle-income countries (LMICs), there is a co-occurrence of high baseline stillbirth rates and frequent firestorms, which may lead to a geographic disparity. Across 54 LMICs, we conducted a self-matched case-control study, making stillbirths comparable to the corresponding livebirths in terms of time-invariant characteristics (*e.g.*, genetics) and duration of gestational exposure. We established a joint-exposure-response function (JERF) by simultaneously associating stillbirth with fire- and non-fire-sourced $PM_{2.5}$ concentrations, which were estimated by fusing multi-source data, such as chemical transport model simulations and satellite observations. During 2000–2014, 35,590 pregnancies were selected from multiple Demographic and Health Surveys. In each mother, a case of stillbirth was compared to her livebirth(s) based on gestational exposure to fire-sourced $PM_{2.5}$. We further applied the JERF to assess stillbirths attributable to fire-sourced $PM_{2.5}$ in 136 non-Western countries. The disparity was evaluated using the Gini index. The risk of stillbirth increased by 17.4% (95% confidence interval [CI]: 1.6–35.7%) per 10 $\mu g/m^3$ increase in fire-sourced $PM_{2.5}$. In 2014, referring to a minimum-risk exposure level of 10 $\mu g/m^3$, total and fire-sourced $PM_{2.5}$ contributed to 922,860 (95% CI: 578,451–1,183,720) and 49,951 (95% CI: 3,634–92,629) stillbirths, of which 10% were clustered within the 6.4% and 0.6% highest-exposure pregnancies, respectively. The Gini index of stillbirths attributable to fire-sourced $PM_{2.5}$ was 0.65, much higher than for total $PM_{2.5}$ (0.28). Protecting pregnant women against $PM_{2.5}$ exposure during wildfires is critical to avoid stillbirths, as the burden of fire-associated stillbirths leads to a geographic disparity in maternal health.

☆ This paper has been recommended for acceptance by Payam Dadvand.

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https://doi.org/10.1016/j.envpol.2023.122170
Received 7 January 2023; Received in revised form 6 July 2023; Accepted 8 July 2023
Available online 12 July 2023
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1. Introduction

Recent studies have demonstrated an epidemiological association between exposure to ambient fine particles ($PM_{2.5}$) and pregnancy loss, including stillbirth and miscarriage (Li et al., 2021a; Xie et al., 2021; Xue et al., 2021c; Xue et al., 2022; Xue et al., 2019a). However, the health effects for different components of the $PM_{2.5}$ mixture are not uniform. In the 2021 Global Air Quality Guidelines (AQGs), the World Health Organization (WHO) identified the distinguishable health effects corresponding to three $PM_{2.5}$ subtypes: black carbon, ultrafine particles, and particles originating from dust storms (World Health Organization, 2021). The effects of these $PM_{2.5}$ components on stillbirth remain unknown. In low- and middle-income countries (LMICs), air pollution originates not only from anthropogenic emissions but also from unique natural sources, such as Amazon rainforest wildfires, which makes the $PM_{2.5}$ rich in specific subtypes (Requia et al., 2021). Furthermore, climate change can increase the emission levels from natural $PM_{2.5}$ sources, such as open fires (Abatzoglou and Williams, 2016) and dust storms (Wu et al., 2021). In LMICs, the health effects of natural $PM_{2.5}$, which are different from anthropogenic $PM_{2.5}$ in terms of toxin composition, are unclear. To assess the risk of air pollution accurately, a joint-exposure-response function (JERF) is required to characterize the toxicities of different $PM_{2.5}$ components.

A key natural source of $PM_{2.5}$ in LMICs is open fire burning (*e.g.* wildfires and biomass burning). $PM_{2.5}$ produced by open fires (fire-sourced $PM_{2.5}$) is very rich in organic particles, such as black carbon, a component known to enhance $PM_{2.5}$ toxicity per-unit concentration (Liu and Peng, 2019). Our previous study showed that gestational exposure to fire-sourced $PM_{2.5}$ was significantly related to stillbirth in south Asia (Xue et al., 2021a). The results require further validation in hotspot regions of open fires, such as Sub-Saharan Africa (SSA) and Latin America. Other adverse outcomes, including low birthweight (Li et al., 2021a), preterm birth (Requia et al., 2022), infant mortality (Xue et al., 2021b) and acute respiratory infection in children (Li et al., 2023) have also been linked to open fire smoke or fire-sourced $PM_{2.5}$.

The stillbirth rate is unevenly distributed across the world. Countries with high stillbirth rates are clustered in SSA. For instance, the United Nations Inter-agency Group for Child Mortality Estimation (UN IGME) found that there were 2.0 million stillbirths globally in 2019 (Hug et al., 2021b). Among them, 0.86 million or 43% were in SSA. The regions with the highest stillbirth rate were West and Central Africa, followed by Eastern and Southern Africa. The high stillbirth rate may be related to low socioeconomic status (SES) and, consequently, reduced access to prenatal care. SSA happens to be a double hotspot, where pregnant women are simultaneously suffering from both SES-related risk factors and exposure to fire-sourced $PM_{2.5}$ (Madhi et al., 2019). Therefore, the burden of stillbirths attributable to fire-sourced $PM_{2.5}$ is a public health problem with a high degree of geographic disparity and, thus, contributes to global maternal health inequality.

We developed a self-matched case-control method to evaluate the health impact of fire-sourced $PM_{2.5}$ on stillbirths in South Asia (Li et al., 2021a). The method was recommended as a cost-effective approach to an exposure-response function, to link stillbirth or miscarriage with total $PM_{2.5}$ concentration (Ha and Mendola, 2019), and had been applied to estimate the burden of stillbirths attributable to $PM_{2.5}$ (Xue et al., 2022). In this study, we modified the approach by modeling the effect of $PM_{2.5}$ mixture in a two-dimensional spline function, and used it to develop a JERF for fire- and non-fire-sourced components. Combining the JERF derived from 54 LMICs, with state-of-the-art estimates in the population at risk, $PM_{2.5}$ concentration, and baseline risk, we estimated the number of stillbirths attributable to fire-sourced $PM_{2.5}$ exposure within a study domain of 136 non-Western countries (Fig. 1). For the first time, we evaluated the geographic disparity by calculating the Gini index based on the distribution of attributable stillbirths.

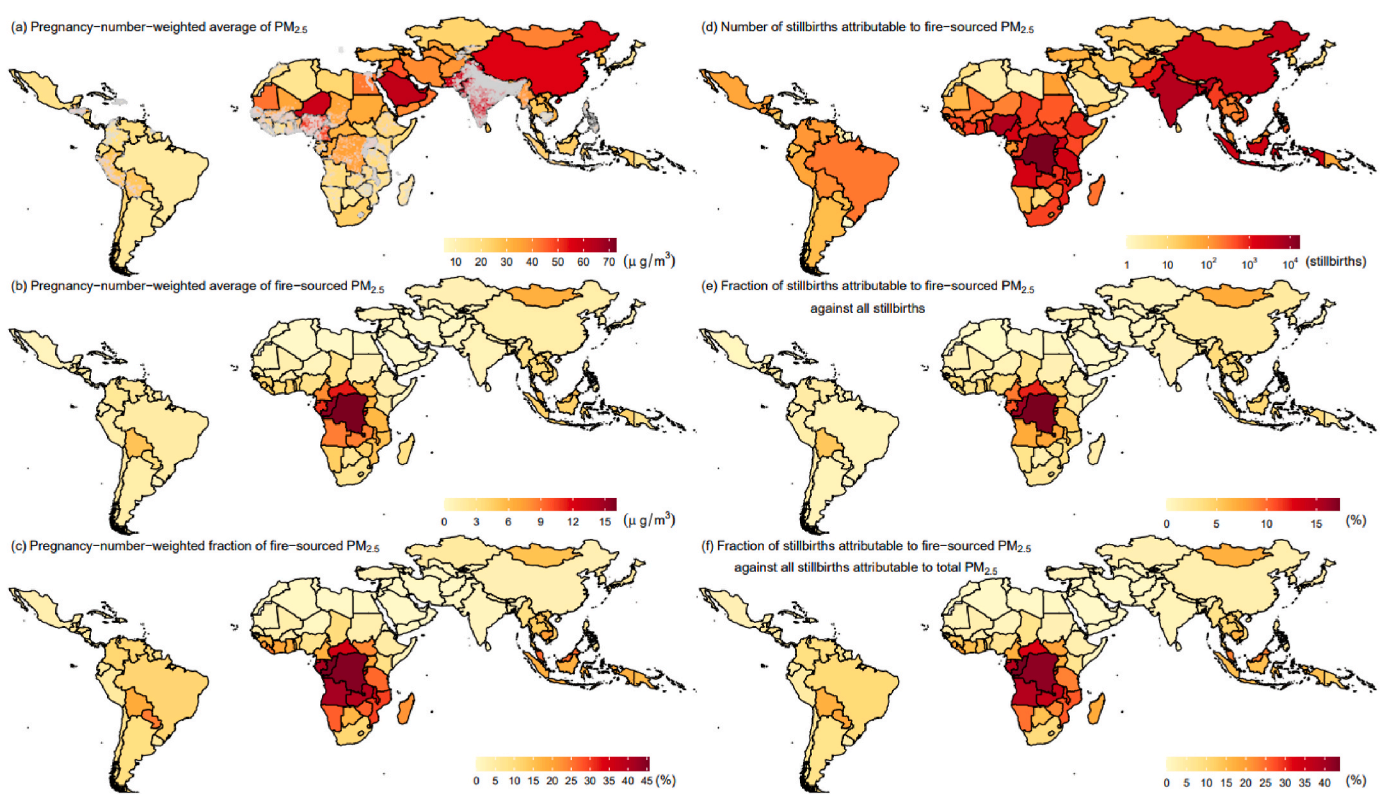

Fig. 1. Spatial distributions of exposures to $PM_{2.5}$ produced by open fires, and the estimated stillbirths attributable to the fire-sourced $PM_{2.5}$. In panel (a), the grey dots show the living clusters of analyzed samples.

2. Methods

2.1. Study population

To develop a JERF that links $PM_{2.5}$ with stillbirth and to distinguish the toxicity of fire-sourced components from the remaining components, we applied a well-developed epidemiological approach to individual pregnancy data obtained from the Demographic and Health Surveys (DHS) program between 2000 and 2014. The dataset was described in detail and utilized in our previous study to examine the association between fire-sourced $PM_{2.5}$ and pregnancy loss in South Asia (Xue et al., 2021a; Xue et al., 2022). Detailed information about the sampling procedure, survey questionnaire, and variable definitions are provided on the DHS website (https://www.dhsprogram.com/). The DHS dataset can be linked to environmental variables because, in recent surveys, the fieldworkers used Global positioning system (GPS) devices to collect geospatial information for each primary sampling unit (*e.g.* urban wards and rural villages). In this study, we collected 111 geocoded surveys of 54 LMICs (Table S1).

2.2. Assessment of $PM_{2.5}$ exposure from fire and non-fire sources

We assessed ambient exposure to fire-sourced $PM_{2.5}$ by calibrating chemical transport model (CTM) simulations with a gold-standard estimator of total $PM_{2.5}$ concentrations. A similar approach has previously been documented (Li et al., 2021a; Xue et al., 2021a; Xue et al., 2022; Xue et al., 2019a). In this study, we applied the same model to an up-to-date product of global monthly $PM_{2.5}$ concentrations (van Donkelaar et al., 2021). The approach is documented in the supplemental information (SI Text 1), and generated gridded concentrations for fire-sourced ($PM_{2.5}^{Fire}$) and non-fire-sourced $PM_{2.5}$ ($PM_{2.5}^{Non\text{-}fire}$) with a spatial resolution of 1 × 1 km.

Monthly temperature with a spatial resolution of approximately 50 km was obtained from the Modern-Era Retrospective analysis for Research and Applications (MERRA-2) between 2000 and 2014. The satellite nightlight during the study period was used as an indicator for economic growth, and was obtained from a harmonized product with a spatial resolution of 1 × 1 km by combining multiple raw products from different satellites (Li et al., 2020). For each DHS sample, environmental variables were assigned by selecting the pixel, which covered the centroid of sampling cluster.

2.3. Health outcome and epidemiological design

The primary health outcome of this study is stillbirth, defined as a baby born with no sign of life at ≥ 7 months of gestation, according to the WHO definition (https://www.who.int/health-topics/stillbirth). We analyzed the pregnancy data using a self-matched case-control design, which was developed and detailed in our previous studies on the association between pregnancy loss and $PM_{2.5}$ (Xue et al., 2021c; Xue et al., 2019a). The epidemiological design is also detailed documented in the supplemental materials (SI Text 2). Briefly, we extracted pregnancy-related variables for 11,402 mothers who had reported at least one livebirth and one stillbirth. For each eligible mother, the most recent stillbirth and all livebirths were analyzed. Conditional logit regression was utilized to associate the risk of stillbirth with exposure to $PM_{2.5}$ mixtures. For sensitivity analysis, we collected data for mothers who reported similar outcomes, including early stillbirth (at 5–6 months of gestation; n = 8207) and miscarriage (<5 months of gestation; n = 69, 707). We also examined robustness of our estimates, given different adjusted covariates, exposure time-windows or stratifications.

2.4. Joint exposure-response function estimation

To derive the JERF, the following statistical model was used:

$$\mathrm{Logit}(p_{i,j}) = f\left(\mathrm{PM}_{2.5,i,j}^{Non-fire}, \mathrm{PM}_{2.5,i,j}^{Fire}\right) + z_{i,j}\,\boldsymbol{\gamma} + \theta_i \tag{1}$$

where the subscripts i and j denote the mother ID and time index for the specific gestation, respectively, $p_{i,j}$ denotes the probability of stillbirth, $\boldsymbol{z}_{i,j}\,\boldsymbol{\gamma}$ controls for the longitudinal confounders, and θ_i is a nuisance parameter to control for the fixed effect. The covariates ($\boldsymbol{z}_{i,j}$) focus on longitudinal effects, including the nonlinear effect of maternal age, which is modeled as a spline with three degrees of freedom (DF), parity, the nonlinear effect of temperature as modeled by a 3-DF spline, seasonality as a 4-DF spline of month, and satellite nightlight. Considering heterogeneity between samples from different countries, we further adjusted for two types of random slopes: one for the $PM_{2.5}$ concentrations and the other for the temporal trend. *f()* denotes a two-dimensional thin-plate spline function to model the joint nonlinear effect of exposure to fire- and non-fire-sourced $PM_{2.5}$ during gestation. As described previously (Guan et al., 2019; Li et al., 2021a; Xue et al., 2021c) exposure to $PM_{2.5}$ components was assessed using a gestation-length-matched approach (SI Text 2). To illustrate that the JERF can reveal the complexities embedded in the health effect of $PM_{2.5}$ mixture, we further evaluated the interaction between $PM_{2.5,\,j}^{Non\text{-}fire}$ and $PM_{2.5,\,j}^{Fire}$ in either additive or multiplicative scale (SI Text 3).

2.5. Assessment of health impacts and their geographic disparities

First, we calculated the fraction or number of stillbirths attributable to $PM_{2.5}$ in 136 countries by 1 km × 1 km pixel (s) and year (y), using the following equation:

$$\mathrm{RR}_{s,y} = \mathrm{Max}\left\{\exp\left[f\left(\mathrm{PM}_{2.5,s,y}^{Non-fire}, \mathrm{PM}_{2.5,s,y}^{Fire}\right) - f\,(\mathrm{A},\mathrm{B})\right], 1\right\}, \mathrm{A}+\mathrm{B} = \mathrm{TMREL};$$

$$\mathrm{AF}_{s,y} = 1 - 1 \Big/ \mathrm{RR}_{s,y};\ \mathrm{AN}_{s,y} = \mathrm{AF}_{s,y} \times \mathrm{N}_{s,y}, \mathrm{N}_{s,y} = \left(\mathrm{P}_s \Big/ \sum_{s\in R} \mathrm{P}_s\right) \times \mathrm{N}_{R,y};$$

$$\mathrm{AN}_{R,y} = \sum_{s\in R} \mathrm{AN}_{s,y};\ \mathrm{AF}_{R,y} = \mathrm{AN}_{R,y} \Big/ \mathrm{N}_{R,y} \tag{2}$$

where the subscripts *s, R,* and *y* denote indexes for pixels, country ($s \in R$ represents a pixel for the R^{th} country), and calendar year; TMREL denotes the theoretical minimum risk exposure level for concentration of total $PM_{2.5}$; RR denotes the relative risk for a joint exposure to fire-sourced $PM_{2.5}$ ($PM_{2.5,\,s,\,y}^{Fire}$) and non-fire-sourced $PM_{2.5}$ ($PM_{2.5,\,s,\,y}^{Non\text{-}fire}$); AF and AN denote the attributable fraction and number of stillbirths attributable to $PM_{2.5}$ mixture, respectively; $N_{R,y}$ denotes the total number of stillbirths by country and year; and P_s denotes the total number of pregnancies by pixels. $N_{R,y}$ was obtained from a global country-level product estimated by UN IGME during 2000–2019, and P_s was obtained from a WorldPop product on gridded estimates of total pregnancies with a spatial resolution of 1 km × 1 km in 2015 for 161 countries or regions (James et al., 2018), covering Africa, Latin America, and the Caribbean, which have high stillbirth rates. Compared to our previous assessment on total $PM_{2.5}$ in 137 countries, this study excluded an island country, Maldives, where the spatial resolution of GEOS-Chem simulations was too rough to capture the fire-sourced $PM_{2.5}$ there. We finally performed the risk assessment on open fires for 136 countries (Fig. 1), which covered almost all non-Western countries.

TMREL was generally selected from air quality standards, such as the air quality guideline (AQG) or interim targets (IT) for long-term $PM_{2.5}$ concentration, launched by the WHO in 2021 (World Health Organization, 2021). However, these standards only make recommendations on total $PM_{2.5}$ concentration. To set the counterfactual scenario of safety, we utilized two approaches to set the references for non-fire-sourced $PM_{2.5}$ (A) and fire-sourced $PM_{2.5}$ (B). In the main approach, we fixed the ratio of the two references, and made it equal to the observed value by pixel and year ($A/B = PM_{2.5,\ s,\ y}^{Non\text{-}fire}/PM_{2.5,\ s,\ y}^{Fire}$). In the alternative approach, we set the references for fire- and non-fire-sourced $PM_{2.5}$ as zero and TMREL, respectively. Considering the new AQG on long-term $PM_{2.5}$ (5 μg/m^3) was mainly based on evidence from Western countries, such as Canada and United States, we selected IT-4 (10 μg/m^3) as the TMREL in our main analysis. Additionally, we utilized a Monte Carlo approach to obtain the empirical confidence intervals (CIs) for AF and AN. To further quantify the stillbirths specifically attributable to fire-sourced or non-fire-sourced $PM_{2.5}$, we replaced the $RR_{s,y}$ in equation (2) as follows:

$$RR_{s,y}^{Fire} = \mathrm{Max}\left\{\exp\left[f\left(PM_{2.5,s,y}^{Non-fire}, PM_{2.5,s,y}^{Fire}\right) - f\left(PM_{2.5,s,y}^{Non-fire}, B\right)\right], 1\right\},$$

or

$$RR_{s,y}^{Non-fire} = \mathrm{Max}\left\{\exp\left[f\left(PM_{2.5,s,y}^{Non-fire}, PM_{2.5,s,y}^{Fire}\right) - f\left(A, PM_{2.5,s,y}^{Fire}\right)\right], 1\right\} \quad (3)$$

We also assessed the inequalities in stillbirths attributable to $PM_{2.5}$ mixtures by calculating the Gini index. The inequality evaluated how the attributable stillbirths were distributed among the population at risk. The Gini index ranges from 0 to 1. A Gini index of 0 indicates that the attributable stillbirths are evenly distributed, while a larger Gini index suggests that a larger proportion of attributable stillbirths occurs within a small proportion of pregnancies. We calculated the Gini index for the 136 countries study domain, the subregions, or countries by year. For details on the calculation of Gini index, please refer to supplemental materials (SI Text 4).

All analyses were performed using the R software (The R foundation, Vienna, Austria). Statistical inference for the regression models was performed using the R package *survival*, and the two-dimensional nonlinear function was parameterized by thin-plate-splines using the R package *mgcv*.

Table 1
Population characteristics for the dataset used to establish the joint-exposure–response function between $PM_{2.5}$ mixture and stillbirth or other similar outcomes.

Variable	Group	Stillbirth	Early stillbirth	Miscarriage	Pregnancy loss
Categorical variables		Number (percentage)			
Total		35,590 (100%)	25,665 (100%)	214,170 (100%)	275,425 (100%)
Pregnancy loss	Control	24,188 (68.0%)	17,458 (68.0%)	144,463 (67.5%)	186,109 (67.6%)
	Case	11,402 (32.0%)	8,207 (32.0%)	69,707 (32.5%)	89,316 (32.4%)
Number of matched controls	1	9,462 (26.6%)	6,476 (25.2%)	55,952 (26.1%)	71,890 (26.1%)
	2	9,570 (26.9%)	7,380 (28.8%)	66,216 (30.9%)	83,166 (30.2%)
	3	7,360 (20.7%)	5,632 (21.9%)	44,324 (20.7%)	57,316 (20.8%)
	4	4,825 (13.6%)	3,245 (12.6%)	26,435 (12.3%)	34,505 (12.5%)
	5+	4,373 (12.3%)	2,932 (11.4%)	21,243 (9.9%)	28,548 (10.4%)
Maternal age	<20	7,375 (20.7%)	5,479 (21.3%)	39,096 (18.3%)	51,950 (18.9%)
	20–29	19,651 (55.2%)	13,724 (53.5%)	119,858 (56.0%)	153,233 (55.6%)
	30–34	5,183 (14.6%)	3,698 (14.4%)	32,333 (15.1%)	41,214 (15.0%)
	>34	3,381 (9.5%)	2,764 (10.8%)	22,883 (10.7%)	29,028 (10.5%)
Level of nightlight (NTL, Digit-Number)	Low (NTL ≤1.4)	22,489 (63.2%)	14,777 (57.6%)	99,165 (46.3%)	136,431 (49.5%)
	Middle (1.4 < NTL ≤16)	8,023 (22.5%)	5,988 (23.3%)	56,097 (26.2%)	70,108 (25.5%)
	High (NTL >16)	5,078 (14.3%)	4,900 (19.1%)	58,908 (27.5%)	68,886 (25.0%)
Parity	Nulliparous	10,112 (28.4%)	6,710 (26.1%)	57,438 (26.8%)	74,260 (27.0%)
	Multiparous	25,478 (71.6%)	18,955 (73.9%)	156,732 (73.2%)	201,165 (73.0%)
Continuous variable		Mean (Standard deviation, interquartile range)			
Maternal age (years)	Total	25.53 (6.39, 20.67–29.67)	25.66 (6.66, 20.58–30.00)	25.99 (6.46, 21.08–30.17)	25.90 (6.47, 21.00–30.08)
	Control	25.09 (6.06, 20.50–29.00)	25.07 (6.31, 20.25–29.25)	25.21 (6.09, 20.58–29.17)	25.18 (6.10, 20.50–29.08)
	Case	26.47 (6.96, 21.00–31.33)	26.92 (7.19, 21.42–31.83)	27.62 (6.89, 22.33–32.25)	27.41 (6.94, 22.08–32.08)
Temperature (°C)	Total	23.76 (4.65, 21.58–26.81)	23.75 (4.95, 21.34–26.90)	23.30 (6.16, 20.33–27.18)	23.40 (5.88, 20.64–27.09)
	Control	23.85 (4.67, 21.67–26.89)	23.82 (4.96, 21.41–26.94)	23.34 (6.13, 20.42–27.16)	23.45 (5.86, 20.74–27.09)
	Case	23.57 (4.62, 21.39–26.62)	23.59 (4.93, 21.23–26.83)	23.22 (6.21, 20.12–27.22)	23.30 (5.92, 20.44–27.08)
Nightlight (Digit-Number)	Total	7.50 (15.38, 0.00–6.70)	9.85 (17.62, 0.00–9.33)	14.05 (20.37, 0.00–21.00)	12.81 (19.69, 0.00–16.20)
	Control	7.18 (15.06, 0.00–6.00)	9.32 (17.17, 0.00–9.00)	13.37 (19.99, 0.00–18.00)	12.19 (19.30, 0.00–15.00)
	Case	8.17 (16.02, 0.00–7.00)	10.97 (18.49, 0.00–12.00)	15.47 (21.07, 0.00–25.33)	14.12 (20.43, 0.00–21.00)
Fire-sourced $PM_{2.5}$ (μg/m^3)	Total	4.45 (5.52, 0.70–6.09)	4.39 (5.97, 0.47–5.83)	3.60 (6.39, 0.26–4.16)	3.79 (6.26, 0.30–4.60)
	Control	4.50 (5.57, 0.69–6.16)	4.48 (6.11, 0.47–6.00)	3.65 (6.47, 0.26–4.18)	3.84 (6.33, 0.30–4.64)
	Case	4.36 (5.39, 0.70–5.92)	4.18 (5.64, 0.47–5.44)	3.50 (6.23, 0.27–4.11)	3.67 (6.09, 0.31–4.50)
Non-fire-sourced $PM_{2.5}$ (μg/m^3)	Total	36.65 (23.90, 18.83–47.66)	34.41 (25.54, 16.85–43.81)	36.00 (29.00, 17.59–44.42)	35.94 (28.08, 17.63–44.80)
	Control	36.52 (23.66, 18.88–47.32)	34.16 (25.09, 16.89–43.76)	35.78 (28.88, 17.55–44.20)	35.72 (27.92, 17.61–44.61)
	Case	36.93 (24.41, 18.74–48.35)	34.93 (26.45, 16.82–43.91)	36.46 (29.24, 17.67–44.90)	36.38 (28.42, 17.68–45.26)
$PM_{2.5}$ (μg/m^3)	Total	41.11 (22.42, 25.24–49.36)	38.80 (24.51, 22.57–46.37)	39.60 (28.62, 21.53–47.33)	39.72 (27.53, 22.07–47.50)
	Control	41.02 (22.13, 25.36–49.05)	38.65 (23.98, 22.80–46.28)	39.43 (28.43, 21.58–47.10)	39.56 (27.30, 22.16–47.27)
	Case	41.30 (23.02, 24.92–49.99)	39.12 (25.61, 22.08–46.61)	39.96 (29.01, 21.43–47.90)	40.05 (28.01, 21.91–48.02)

3. Results

3.1. Summary statistics

Our study included 35,590 pregnancies in 11,402 mothers between 2000 and 2014. On average, the control group (mean maternal age = 25.09 years, standard deviation [SD] = 6.06 years) was younger than the stillbirth group (mean 26.47 years; SD 6.96 years). The nightlight of controls (mean = 7.18 ; SD = 15.06 Digit-Number) was lower than for cases (mean = 8.17; SD = 16.02), suggesting a higher stillbirth rate in areas with greater development. Compared to the controls, the stillbirths were exposed to a higher concentration of total $PM_{2.5}$ (cases vs. controls: 41.30 vs. 41.02 μg/m^3), and the between-group difference was dominated by non-fire sources (36.93 vs. 36.52 μg/m^3). Only a small fraction of total $PM_{2.5}$ was produced by fires and, thus, the between-group difference in fire-sourced $PM_{2.5}$ was not apparent (4.36 vs. 4.50 μg/m^3).

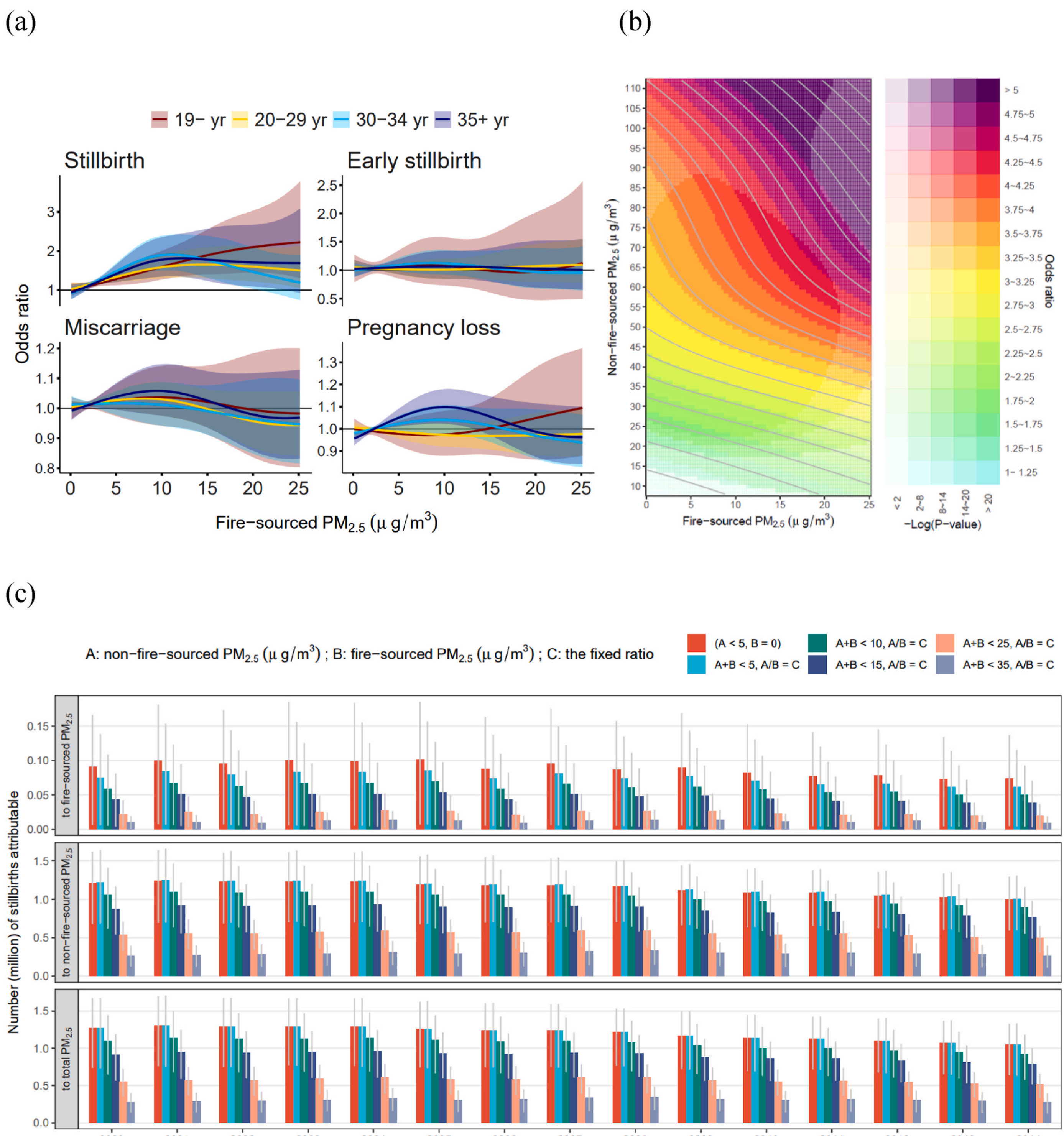

Fig. 2. The function to link stillbirth with $PM_{2.5}$ mixture, and the attributable numbers of stillbirths across the 136 Non-Western countries. (a) the single-pollutant exposure-response functions between fire-sourced $PM_{2.5}$ and pregnancy loss or its subtype; (b) the joint-exposure-response function (JERF) to link stillbirth with fire- and non-fire-sourced $PM_{2.5}$, simultaneously; (c) the number of stillbirths attributable to $PM_{2.5}$ mixture, estimated by the JERF.

Population characteristics and the levels of environmental exposure are summarized in Table 1. Fig. 1 shows the spatial distribution of $PM_{2.5}$ across the 136 non-Western countries. For total $PM_{2.5}$, the pollution hotspots included northern Africa, India and China. However, fire-sourced $PM_{2.5}$ exhibited a distinguishable spatial pattern, and was highly clustered in low-latitude forest regions, such as the Congo Basin (Central Africa), Amazon Basin (Brazil) and the Malaysian rainforest.

3.2. Associations

We examined the association between total $PM_{2.5}$ and stillbirths in previous studies (Xue et al., 2021c; Xue et al., 2022). Here, we focused on the effect of fire-sourced $PM_{2.5}$ on stillbirth. First, we explored the potential confounders for the association between fire-sourced $PM_{2.5}$ and stillbirth using linear models (Fig. S1a). The estimator for the average effect of fire-sourced $PM_{2.5}$ on stillbirth was sensitive to the choice of adjusted covariates, particularly for the control of country-specific trends in maternal health improvement. According to the fully-adjusted model, each 10 μg/m^3 increment in fire-sourced $PM_{2.5}$ was associated with a 17.4% (95% confidence interval [CI]: 1.6, 35.7) increased risk of stillbirth. Among all subtypes of pregnancy loss, stillbirth was most strongly associated with fire-sourced $PM_{2.5}$ exposure. Additionally, exposure to fire-sourced $PM_{2.5}$ during the first trimester was more strongly associated to stillbirth, compared to exposure during the second or third trimester (Fig. S1b). Furthermore, the linear association between fire-sourced $PM_{2.5}$ and stillbirth was not significantly modified by any subpopulation indicator (Fig. S2). We also explored how the estimated effect of fire-sourced $PM_{2.5}$ varied with different exposure levels (i.e. the nonlinear exposure-response function). The results suggested that the effect was significantly nonlinear, which was consistent between subpopulations, such as maternal age subgroups (Fig. 2a). Accordingly, the curvature of the nonlinear association was sublinear, suggesting that the effect of fire-sourced $PM_{2.5}$ was saturated for a high-concentration exposure (>15 μg/m^3).

Considering the nonlinearity in the estimated results (Fig. 2a), we developed a JERF that linked stillbirth to fire- and non-fire-sourced $PM_{2.5}$ using a two-dimensional nonlinear approach (Fig. 2b). Generally, odds ratio (OR) of stillbirth increased with an increment in either fire- or non-fire-sourced $PM_{2.5}$. The contour lines in Fig. 2b represent different fire- and non-fire-sourced $PM_{2.5}$ combinations, associated with an equal OR of stillbirth. Based on the contour lines, fire-sourced $PM_{2.5}$ was slightly more toxic than non-fire-sourced $PM_{2.5}$ at low-concentration levels (total $PM_{2.5} \leq 20$ μg/m^3). However, due to large uncertainties embedded in the JERF, the unequal toxicity was inclusive and requires confirmation in future studies. In summary, the JERF derived in this study could characterize single-pollutant effects (Fig. 2b), their nonlinear curvature (Fig. S3)., and potential interactions for the mixture of fire- and non-fire-sourced $PM_{2.5}$ (Fig. S4).

3.3. Risk assessment

Across our study domain of 136 non-Western countries in 2014, the pregnancy-number-weighted averages of total, non-fire-sourced, and fire-sourced $PM_{2.5}$ were 42.01 μg/m^3, 39.76 μg/m^3, and 2.25 μg/m^3, respectively. Open fire burning contributed to 5.36% of the total $PM_{2.5}$ concentration. Since the distribution of fire-sourced $PM_{2.5}$ was highly concentrated (Fig. 1), the fraction varied from zero (in the places without open fires) to as high as 45.39% in the Republic of the Congo, followed by the Democratic Republic of the Congo (DR Congo: 44.56%), Angola (41.27%), Gabon (40.73%) and Zambia (39.76%). As shown in Fig. 1c, all these countries were within or surrounding the Congo rainforest.

In 2014, according to UN IGME estimates (Hug et al., 2021b) our study domain of 136 non-Western countries accounted for 98.08% (2, 135,781/2,177,493) of global stillbirths. If the fire-sourced fraction is assumed to be unchanged in counterfactual safety scenarios, on average, 48.90% (95% CI: 29.64, 62.08), 43.21% (95% CI: 27.01, 54.98), 36.81% (95% CI: 23.74, 46.63), 23.72% (95% CI: 15.20, 30.59) and 12.81% (95% CI: 5.70, 18.48) of these stillbirths were attributable to a $PM_{2.5}$ concentration exceeding the WHO AQG, IT4, IT3, IT2, and IT1, respectively. Under the same counterfactual safety scenarios, 47.24% (95% CI: 27.80, 60.79), 41.81% (95% CI: 25.29, 53.84), 35.70% (95% CI: 22.57, 45.92), 23.10% (95% CI: 14.36, 30.10) and 12.48% (95% CI: 5.13, 18.26) of stillbirths were respectivelyattributable to $PM_{2.5}$ produced by non-fire sources; while 2.92% (95% CI: 0.19, 5.38), 2.34% (95% CI: 0.17, 4.33), 1.78% (95% CI: 0.14, 3.31), 0.91% (95% CI: 0.09, 1.74) and 0.44% (95% CI: 0.03, 0.89) were respectivelyattributable to $PM_{2.5}$ produced by open fires (Fig. 2c). The country-level fractions of stillbirths attributable to fire-sourced $PM_{2.5}$ (IT1) are shown in Fig. 1e.

As the estimated effect of fire-sourced $PM_{2.5}$ was statistically comparable to that of non-fire-sourced components (Fig. 2b), the $PM_{2.5}$-associated impacts were not sensitive to the fire-sourced ratio in TMREL (Fig. 2c). However, different TMRELs considerably affected the estimated attributable numbers. Our JERF suggested that the effect of $PM_{2.5}$ has no threshold (Fig. 2b), but the samples did not include pregnancies exposed to $PM_{2.5}$ levels as low as AQG, which was based on evidence from Western countries. Therefore, we selected the IT4 (i.e. 10 μg/m^3) as the major TMREL in this study. Based on the estimated attributable fractions and UN IGME estimates, in 2014, 922,860 (95% CI: 578,451, 1,183,720), 892,955 (95% CI: 550,357, 1,156,098) and 49,951 (95% CI: 3,634, 92,629) stillbirths were attributable to total, non-fire-sourced, and fire-sourced $PM_{2.5}$, respectively. Given the uncertainties, we did not observe a clear trend in the estimated number of stillbirths attributable to either total, fire-sourced, or non-fire-sourced $PM_{2.5}$ between 2000 and 2014.

3.4. Geographic disparities

In 2014, the top six countries with the largest numbers of $PM_{2.5}$-related stillbirths were India (256,299 [95% CI: 173,018, 325,336]), Pakistan (119,970 [95% CI: 81,562, 151,745]), Nigeria (86,871 [95% CI: 42,811, 133,562]), China (79,809 [95% CI: 53,426, 97,875]), Bangladesh (55,385 [95% CI: 37,720, 68,642]) and DR Congo (38,874 [95% CI: 18,381, 54,717]). Meanwhile, the top five for fire-related stillbirths were DR Congo (16,341 [95% CI: 2,240, 28,783]), Nigeria (5873 [95% CI: 267, 12,709]), India (5873 [95% CI: 267, 12,709]), China (2795 [95% CI: 72, 5495]), Bangladesh (2157 [95% CI: 6, 4466]) and Indonesia (2148 [95% CI: 152, 4115]). According to the equation of risk assessment (equation-2), the heavy burden in these countries was due to either a large size of the population at risk, a poor baseline (i.e., a high stillbirth rate), a high exposure level, or its combination. For instance, among the analyzed countries, DR Congo had the 9th largest pregnancy number, 8th highest stillbirth rate, 28th highest total $PM_{2.5}$ concentration and the highest fire-sourced $PM_{2.5}$ concentration. Although the total $PM_{2.5}$ exposure level was not very high, the large size of the population at risk and the poor baseline made DR Congo the 6th largest country for $PM_{2.5}$-related stillbirths. Moreover, the high level of fire-sourced $PM_{2.5}$ caused the most fire-related stillbirths in DR Congo.

The spatial distribution of fire-related stillbirths showed a high degree of geographic disparity (Fig. 3). For instance, 10% of the stillbirths attributable to total $PM_{2.5}$ occurred within a 6.4% subset of all pregnancies, while 10% of stillbirths attributable to fire-sourced $PM_{2.5}$ occurred within a tiny subset of 0.6% of pregnancies. We showed two-dimensional probability distributions by fire- and non-fire-sourced $PM_{2.5}$ (Fig. 3a). Based on the comparison between two-dimensional distribution of all pregnancies and that of attributable stillbirths, a small subgroup of at-risk population exposed to high concentrations of both fire-sourced (>1 μg/m^3) and non-fire-sourced $PM_{2.5}$ (>70 μg/m^3) had a disproportionately high incidence of stillbirths. The high geographic disparity was quantified by Gini index. For stillbirths attributable to fire-sourced $PM_{2.5}$, the Gini index was 0.65, much higher than that for total $PM_{2.5}$ (0.28). The Lorenz curves corresponding to the

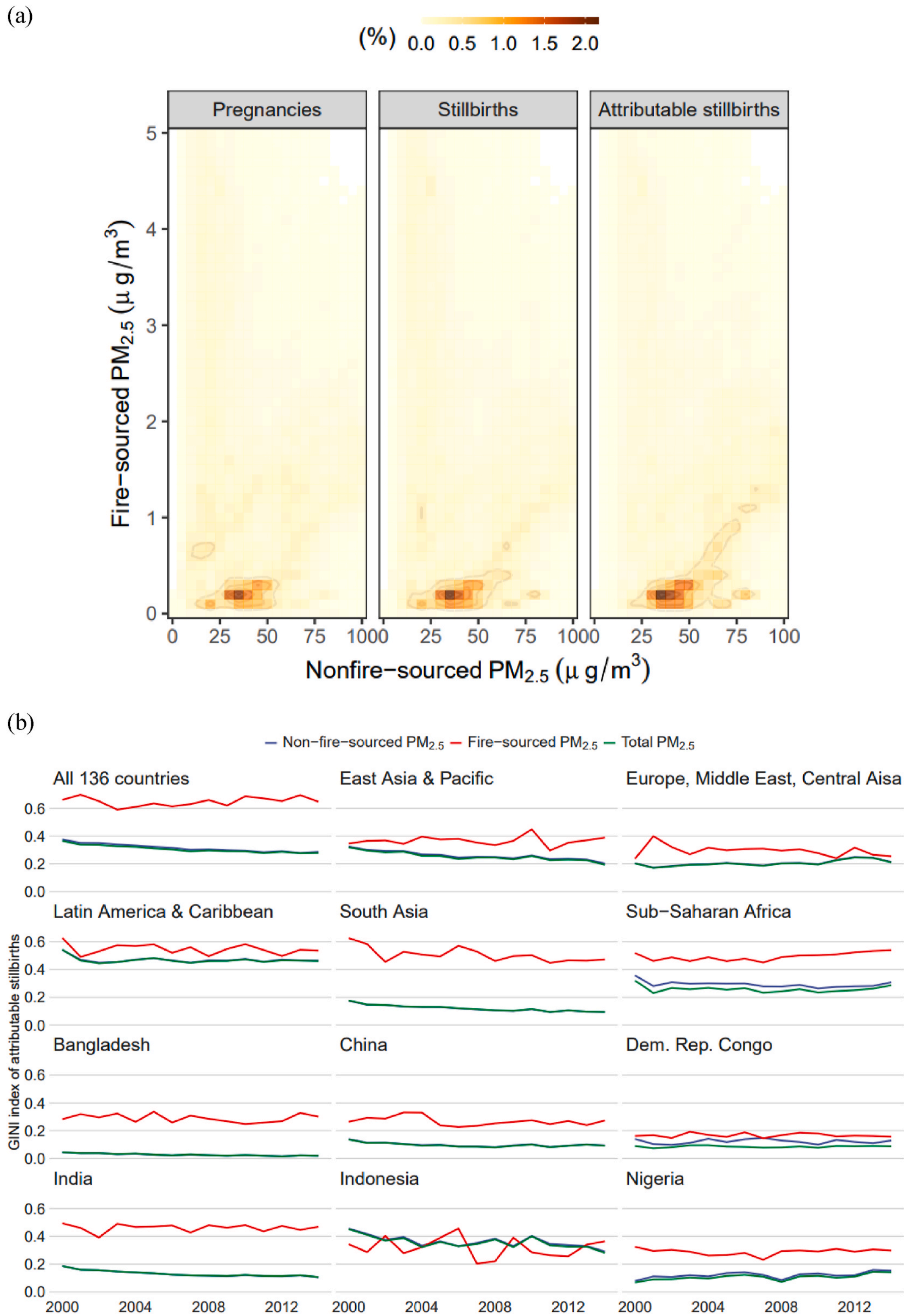

Fig. 3. Distributions of population at risk and attributable stillbirths, by different levels of $PM_{2.5}$ mixture, and the corresponding Gini indexes to measure geographic disparity. (a) Probability distributions by the two components of $PM_{2.5}$ mixture; (b) Gini indexes derived from those distributions. The Lorenz curves underlying Gini indexes are shown in Supplemental Fig. S5.

Gini indexes are also shown in Fig. S5. Furthermore, between 2000 and 2014, the Gini index for the whole study domain was slightly reduced for stillbirths attributable to non-fire-sourced $PM_{2.5}$, but remained stable for those attributable to fire-sourced $PM_{2.5}$ (Fig. 3b). The Gini indexes for the five subregions of the study domain and the top six countries with the most fire-related stillbirths between 2000 and 2014 are shown in Fig. 3c. Except for regions or countries (e.g., DR Congo and Indonesia) where open fires contributed considerably to the total $PM_{2.5}$ concentration, the geographic disparity embedded in fire-related stillbirths remains higher than for non-fire-related cases. Unlike anthropogenic sources, which might increase both $PM_{2.5}$ and SES, open fires are more frequent in regions with lower SES levels, an additional risk factor for stillbirth. This could explain the high degree of geographic disparity in our study domain.

4. Discussion

This was the first study to assess stillbirths attributable to fire-sourced $PM_{2.5}$ and the associated geographic disparity. Based on samples from multiple LMICs, we found a nonlinear association between fire-sourced $PM_{2.5}$ and stillbirth, with adjustments for the effect of non-fire-sourced $PM_{2.5}$. Within 136 non-Western countries in 2014, fire-sourced $PM_{2.5}$ contributed to 49,951 (95% CI: 3,634, 92,629) stillbirths, which accounted for 2.34% (95% CI: 0.17, 4.33) of all stillbirths or 5.41% (95% CI: 0.50, 10.96) of stillbirths attributable to total $PM_{2.5}$ mixture. We also found that 10% of fire-related stillbirths occurred within a small group of 0.6% pregnancies, which suggested a large degree of geographic disparity. Although fire-related stillbirths were fewer than those attributable to $PM_{2.5}$ from non-fire sources, the high level of geographic disparity embedded in the fire-related stillbirths made the problem locally important, and could further contribute to the unequal progress in stillbirth prevention between LMICs and high-income countries.

Although few studies have specifically investigated the association between fire-sourced $PM_{2.5}$ and stillbirth, there is a lot of evidence for the adverse effects of total $PM_{2.5}$. *Zhang* et al. *(2021)* reported a pooled OR of 1.103 (95% CI 1.074, 1.131) per 10 μg/m^3 increment in $PM_{2.5}$ during pregnancy, based on a meta-analysis of seven independent studies. Xie et al. (2021) reported a value of 1.15 (95% CI 1.07, 1.25) based on six of the seven studies in another meta-analysis. Studies confirming the association between $PM_{2.5}$ and stillbirth or similar outcomes (*e.g.* miscarriage) covered different populations of North America (Gaskins et al., 2019; Tong et al., 2022), Europe (Smith et al., 2020), East Asia (Kim et al., 2021; Liang et al., 2021; Xue et al., 2019b), South Asia (Xue et al., 2021a), and Africa (Xue et al., 2019a). Additionally, previous studies have reported that fire-sourced $PM_{2.5}$ was associated with several other adverse birth outcomes, including low birthweight (Li et al., 2021a; Li et al., 2022), preterm birth (Heft-Neal et al., 2022; Requia et al., 2022), gestational diabetes mellitus (Melody et al., 2019), and fetal gastroschisis (Park et al., 2022). Therefore, in general, the findings of this study were in agreement with previous studies. However, our secondary findings, which suggested pregnant women during their first trimester as susceptible to fire-sourced $PM_{2.5}$, are incomparable with previous findings (Xie et al., 2021; Zhang et al., 2021). The inconsistency should be investigated by future studies with accuracy measurements on gestational length and specific causes of stillbirths.

A few global assessments have demonstrated that $PM_{2.5}$ exposure contributes to a heavy burden of poor maternal health outcomes. Annually, 0.92 million infants born with a low birthweight and 2.03 million infants born prematurely are attributable to exposure to ambient $PM_{2.5}$ (Ghosh et al., 2021). According to the global burden of diseases assessment 2019, 0.21 million infant deaths were attributable to total ambient $PM_{2.5}$ (GBD 2019 Diseases and Injuries Collaborators, 2020). Pullabhotla et al. reported that biomass fire burning contributes to 0.13 million infant deaths per year globally (Pullabhotla et al., 2023). Since stillbirth is a burden in addition to the adverse outcomes that occur in livebirths, our findings enrich the evidence on health impacts from air pollution on maternal health. Additionally, fire-related infant deaths were also found to be highly spatially clustered. Pullabhotla et al. reported that 75% of global fire-related infant deaths occur in Africa (Pullabhotla et al., 2023). The unique spatial pattern of fire-related burdens, including infant deaths and stillbirth, adds to the geographic disparity of global maternal health (Burstein et al., 2019).

Geographic disparity in maternal health has been widely reported, but was previously attributed to SES-related factors, such as unequal inputs to improve coverage of vaccination or water sanitation (Burstein et al., 2019). Our findings suggest that open fires, resulting from interactions between human activities and nature, may also contribute to the disparity. Additionally, open fire burning is considered a key pathway for explaining the health impacts of climate change (Rossiello and Szema, 2019; Xu et al., 2020), which has also been reported to increase the degree of geographic disparity by affecting income and other SES indicators (Peck and Pressman, 2013). Therefore, our findings provide a new explanation for climate-change-related disparities. Therefore, to improve maternal health further and to minimize global disparity, interventions against fire-related stillbirths are warranted. Since open fires and wildfires occur rarely, costly personal prevention, such as temporary migration, should be considered, particularly for pregnant women.

There were some limitations of this study to develop the JERF. Our previous studies that estimated the association of $PM_{2.5}$ with stillbirth, miscarriage and pregnancy loss documented limitations regarding (1) data quality, (2) epidemiological design, and (3) exposure assessment in details. Therefore, those limitations are only mentioned here briefly. First, data quality might be questionable due to underreported stillbirth rates or misclassified outcomes which might be caused by stigma or recall bias. Second, the epidemiological design could have led to a bias due to omitted longitudinal covariates. Furthermore, since $PM_{2.5}$ exposure has been associated to decreased human fecundity or infertility (Li et al., 2021b; Xue and Zhang, 2018; Xue and Zhu, 2018a,b), this study might ignore the susceptible women, which resulted in a selection bias. Third, exposure assessment might be inaccurate because of uncertainties in GEOS-Chem simulations or limited spatial and temporal resolutions in both concentration and duration of exposure. For instance, the inventory of fire emissions inputted into the CTM may be inaccurate due to a few aspects, such as the simplified emission factors and limited capability to characterize small-fire emissions. Using alternative inventories can generate different levels of exposure. How uncertainties in GEOS-Chem simulations affect the estimated JERF should be investigated by future studies. Additionally, the lack of residential address or daily mobility pattern in DHS could also contribute to misclassifications in exposure. Particularly, the spatial misalignments couldn't be completely avoided, and might lead to an oversmoothed exposure. The misclassification could underestimate the variation in exposure and thus decreased the statistical power of our study. Specifically, in our previous study (Xue et al., 2021c), we performed a theorical simulation to explore the direction of some above-mentioned limitations.

Besides these limitations of JERF, our risk assessment also had the following limitations. First, generalizability of the JERF was questionable. Although our subpopulation-specific analyses did not detect significant heterogeneity in the estimated effects of fire-sourced $PM_{2.5}$, we could not completely rule it out. If the effects of $PM_{2.5}$ were heterogenous, our JERF could not be applied directly to the general population because mothers who suffered from stillbirths were highly selective. Additionally, ignoring differential adaptability (a reason to explain the heterogenous effects) to open fires could result in an underestimated degree of inequality in the fire-related stillbirths. Second, the risk presented by $PM_{2.5}$-related stillbirths was not additive with the risk estimated from previous studies, such as on premature births. For instance, stillbirth and premature birth are affected by some common biological pathways (i.e., fetal growth restriction), and risks embedded in the two outcomes partially overlap. Finally, in our disparity assessment, we ignored the within-country variance in baseline stillbirth rate, which could have led to a bias. If within-country variance in baseline stillbirth rate was correlated with level of fire-sourced $PM_{2.5}$ (which is possible because both these variables were negatively correlated with SES), the disparity would be underestimated.

5. Conclusions

Based on a multi-national study, we developed a model to link stillbirth with joint exposure to $PM_{2.5}$ produced by fire- and non-fire sources, and applied it to assess the burden of fire-related stillbirths and its allocation in 136 non-Western countries. We found that fire-sourced $PM_{2.5}$ contributed to 49,951 (95% CI: 3,634–92,629) stillbirths per year, and 10% of fire-related stillbirths were disproportionally distributed within a small high-exposure subgroup, which only accounted for 0.6% of all pregnancies. Our findings suggest that open fire burning not only harms maternal health but also contributes to disparities between countries.

Funding

This work was supported by National Natural Science Foundation of China (42175182, and 42293324), Ministry of Science and Technology of the People's Republic of China (2022YFC3703000), and the Energy Foundation (G-2208-34045, G-2107-33169, and R-2109-33379). Study sponsors were not involved in study design, data interpretation, writing, or the decision to submit the article for publication.

Authorstatement

Tao Xue: Conceptualization; Methodology; Formal analysis; Writing - Original Draft, Jiajianghui Li: Formal analysis; Validation; Writing - Original Draft, Mingkun Tong: Validation; Writing - Original Draft, Xinguang Fan: Methodology: Writing - Review & Editing, Pengfei Li: Validation, Ruohan Wang: Data Curation, Yanshun Li: Resources, Yixuan Zheng: Writing - Review & Editing, Jiwei Li: Writing - Review & Editing, Tianjia Guan: Writing - Review & Editing, Tong Zhu: Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data analyzed in this study is public.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2023.122170.

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