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Biomass smoke exposure and somatic growth among children: The RESPIRE and CRECER prospective cohort studies in rural Guatemala

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ABSTRACT

Background: Cooking-related biomass smoke is a major source of household air pollution (HAP) and an important health hazard. Prior studies identified associations between HAP exposure and childhood stunting; less is known for underweight and wasting. Few studies had personal HAP measurements.

Methods: 557 households in rural Guatemala were enrolled in the CRECER study, the follow-up study of the RESPIRE randomized intervention trial. They were assigned to three groups that received chimney stoves at different ages of the study children. Multiple personal carbon monoxide (CO) exposure measurements were used as proxies for HAP exposures. Children's heights and weights were measured from 24 to 60 months of age. Height-for-age z-score (HAZ), weight-for-age z-score (WAZ), and weight-for-height z-score (WHZ) were calculated based on the World Health Organization's Multicentre Growth Reference Study. HAZ, WAZ, and WHZ below −2 were classified as stunting, underweight, and wasting, respectively. Generalized linear models and mixed effects models were applied.

Results: 541 children had valid anthropometric data, among whom 488 (90.2 %) were stunted, 192 (35.5 %) were underweight, and 2 (0.3 %) were wasted. A 1 ppm higher average CO exposure was associated with a 0.21 lower HAZ (95 % CI: 0.17–0.25), a 0.13 lower WAZ (95 % CI: 0.10–0.17) and a 0.06 lower WHZ (95 % CI: 0.02–0.10). The associations for HAZ were stronger among boys (coefficient = −0.29, 95 % CI: −0.35 – −0.22) than among girls (coefficient = −0.15, 95 % CI: −0.20 – −0.10). A 1 ppm-year higher cumulative CO exposure was associated with a higher risk of moderate stunting among boys (OR = 1.27, 95 % CI: 1.05-1.59), but not among girls.

Discussion: In this rural Guatemalan population, higher HAP exposure was associated with lower HAZ and WAZ. The associations between HAP and HAZ/stunting were stronger among boys. Reducing HAP might benefit childhood somatic growth in rural populations of low-income countries.

1. Introduction

Household air pollution (HAP) is a common source of environmental exposure that arises primarily from indoor activities such as cooking and heating. For 2022, the World Health Organization (WHO) estimates that 2.4 billion people (a third of the world's population), most in low- and middle-income countries, use polluting cooking fuels and are exposed to high levels of cooking-related biomass smoke (WHO, 2022). Infants and

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young children are highly vulnerable to the adverse health effects of biomass smoke because they spend most of their time indoors; they have higher ventilation rates and metabolic rates per kg body weight; and their biological systems are still under development and thus more susceptible to disruptions from environmental toxicants. In 2020, HAP from solid fuel and kerosene combustion contributed to an estimated 3.2 million premature deaths, including 273,000 deaths in children before the age of 5 years (WHO, 2022). Apart from premature death, studies have also linked prenatal and early-life HAP exposure with other adverse health effects in children, including preterm birth, low birth weight, stunting, allergy, acute lower respiratory infections, asthma, and pneumonia (Breysse et al., 2010; Bruce et al., 2013; Lu et al., 2022; Smith et al., 2011; Suryadhi et al., 2019; Yu, 2011).

Somatic growth outcomes including height, weight, and body mass index (BMI) are used to evaluate nutritional adequacy and general health status among children. Indicators for somatic growth impairments include stunting (low height-for-age), underweight (low weight-for-age), and wasting (low weight-for-height). Stunting is an indicator of chronic malnutrition, wasting mostly results from acute food shortages and diseases, while underweight can result from a combination of both chronic and acute malnutrition (de Onis & Blössner, 2003; De Sanctis et al., 2021). Children from rural low-income indigenous communities may have higher risks of stunting and being underweight, contributed by factors including malnutrition, high rates of infectious diseases, socioeconomic disparities, and environmental exposures (Martorell & Young, 2012; Mazariegos et al., 2020). Childhood malnutrition and stunting can have long-term impacts on health, cognitive development, educational and economic development, and maternal reproductive outcomes (Dewey & Begum, 2011; Hoddinott et al., 2013).

Environmental exposures, such as air pollution, have been linked with poor somatic growth (Kim et al., 2017; Sinharoy et al., 2020). Several observational studies from different countries have found that HAP and cooking-related biomass smoke exposure can increase the risk of childhood stunting (Adjei-Mantey and Takeuchi, 2021; Boamah-Kaali et al., 2021; Caleyachetty et al., 2022; Islam et al., 2021b; Lamichhane et al., 2020; Liang et al., 2020; Pun et al., 2021). A study in Ghana using nationally representative panel data found that switching fuels during the prenatal period from biomass fuels to liquified petroleum gas was associated with improvements in children's height-for-age z-score before 5 years old (HAZ improving from −1.26 to −0.43); this effect was more pronounced among boys compared to girls (Adjei-Mantey & Takeuchi, 2021). A large Indian study using National Family Health Survey data found that children from households that cook with biomass fuel have a 16 % higher likelihood of stunting (Islam et al., 2021b). A cross-sectional study in Nepal using Demographic and Health Survey data found that cooking with polluting fuels was associated with higher risks of both stunting and underweight, but not wasting, among children less than 5 years old (Lamichhane et al., 2020). Fewer studies have examined the effects of HAP on other somatic growth outcomes such as underweight and wasting. The only randomized trial published to date that examined the relationship between somatic growth in children and HAP is the GRAPHS study in Ghana. They found that children exposed to prenatal cooking-related HAP had higher risk of stunting; children exposed to higher postnatal cooking-related HAP during the first year of life had higher risk of wasting; compared to the control group with open fire stoves, children in families assigned to liquefied petroleum gas stoves had lower risks of small head circumference and small mid-upper arm circumference (Boamah-Kaali et al., 2021). Other published studies were observational, with no assignment of stove or fuel usage to the study households. In addition, most studies on HAP and child growth outcomes examined prenatal exposure, early life exposure, or fuel and stove types as exposure proxies. No study has quantified cumulative lifetime HAP exposure and examined its effect on somatic growth outcomes.

This study investigates the relationship between cooking-related biomass smoke exposure and somatic growth outcomes among a cohort of children under 5 years of age in rural Guatemala. We hypothesize that (i) the use of an introduced vented chimney stove (*plancha*) can reduce cooking-related biomass smoke levels and HAP exposure in these households compared to households using open fires for cooking, and (ii) children with lower biomass smoke exposure may have lower risks of somatic growth impairment. We tested the first hypothesis by comparing carbon monoxide (CO) levels as a proxy for cooking related HAP across study groups that were provided *plancha* at different times. The second hypothesis was tested by analyzing the associations between average/cumulative CO exposures and the children's somatic growth outcomes. We also stratified the analyses by sex to explore potential effect measure modifications (EMM).

2. Methods

2.1. Study design and participants

We used data collected from the Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE) from 2002 to 2004, and its follow-up study: the Chronic Respiratory Effects of Early Childhood Exposure to Respirable PM Cohort (CRECER) from 2006 to 2009. The structure and timeline of these two studies are summarized in Fig. 1, with details published elsewhere (Heinzerling et al., 2016; Lu et al., 2022; Smith et al., 2011; Smith-Sivertsen et al., 2009). Briefly, in October 2002, the RESPIRE study recruited 534 households from rural highlands of Guatemala that cooked exclusively using open indoor wood fires and had a young infant or pregnant woman. Participating families were randomized to receive a *plancha* (wood-fueled chimney stove) either at the beginning of the trial (group 1) or 18 months later at the end of the trial (group 2). After excluding 19 families that were lost to follow-up during chimney stove construction and including three sets of twins born after initial recruitment, 518 children participated in the RESPIRE study. The follow-up CRECER study revisited RESPIRE households, among whom 194 households from each group agreed to participate. The CRECER study also recruited 169 new households (group 3) from the same geographical region that cooked exclusively using open indoor wood fires, had a child within the same age range as the RESPIRE study children, and had one infant less than 6 months old. Group 3 households also received chimney stoves at the end of the CRECER study in 2009, when we had completed all exposure and outcome assessments. Overall, the three groups of participating households received the chimney stoves at different points in time: Group 1 households received the stoves when the study children were < 6 months old; Group 2 households received the stoves when the study children were 18–24 months old; Group 3 households received the stoves when the study children were around 57 months old.

2.2. Carbon monoxide exposure

Cooking-related biomass smoke exposure is the major source of HAP in this rural Guatemalan population where the RESPIRE and CRECER studies were conducted, followed by *temazcal* (wood-fueled sauna bath) use (Lam et al., 2011; Thompson et al., 2011). The locally produced biomass chimney stoves provided in the study improved fuel combustion and vented biomass smoke outdoors, thus reducing household concentrations (Smith et al., 2010). Although venting smoke outdoors will increase ambient air pollution concentrations, the overall air pollution exposures of the study children were expected to decrease because indoor air pollution is experienced for a longer duration and at higher concentrations. Thus, we hypothesized that group 1 children had the lowest lifetime biomass smoke exposure because they were provided the chimney stoves the earliest, followed by groups 2 and 3.

To test this hypothesis, the study children's personal CO exposures were measured as a proxy for their overall biomass smoke exposures: previous studies have shown that CO concentrations correlate well with fine particulate matter ($PM_{2.5}$) concentrations in this Guatemalan rural

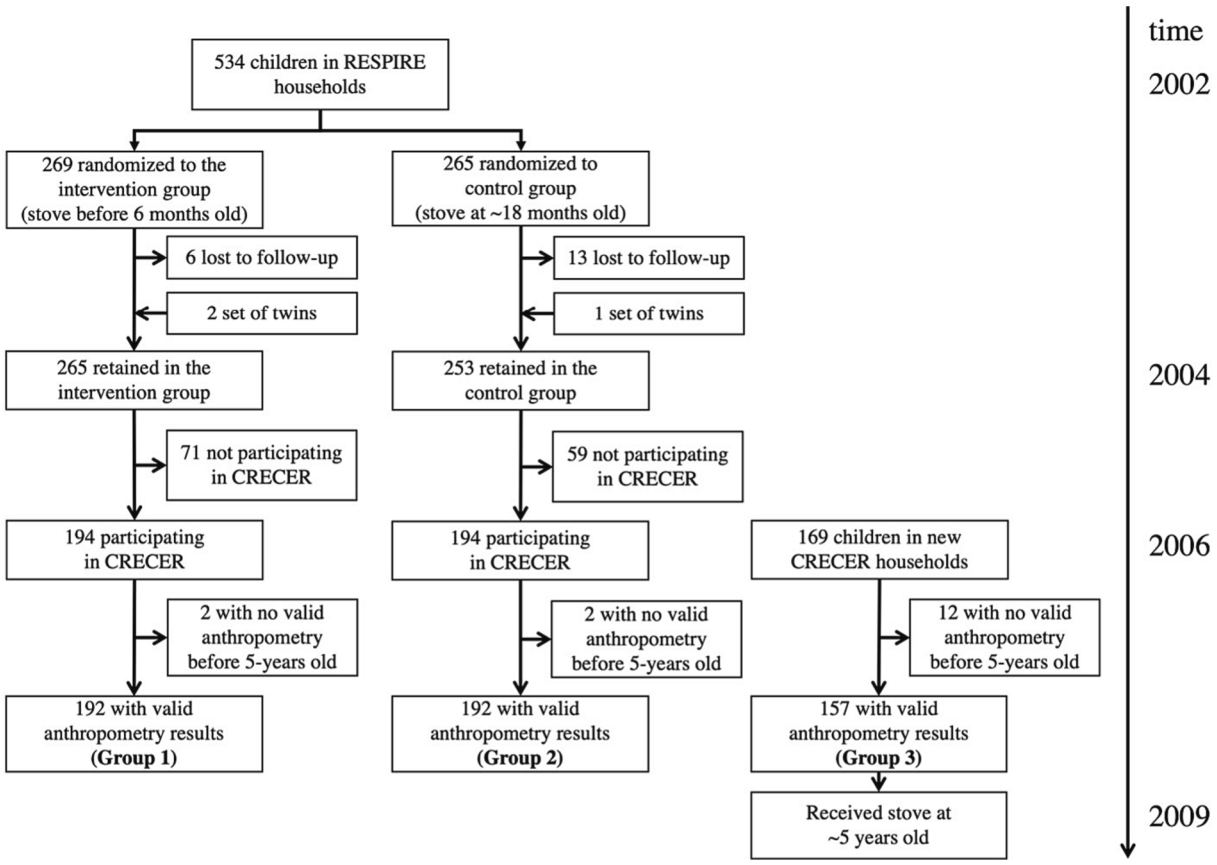

Fig. 1. Study diagram and the timeline for the Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE) and the Chronic Respiratory Effects of Early Childhood Exposure to Respirable PM cohort study (CRECER).

population, in households with or without the chimney stoves (McCracken et al., 2013; Naeher et al., 2001; Northcross et al., 2010). Study children wore small, passive CO diffusion tubes (Gastec Corp., Japan) for 48 hours every 3 months during the RESPIRE study and every 3–6 months during the CRECER study. The CO-exposure assessment timelines and data completeness by study group are summarized in Supplementary Table S1. The CO diffusion tubes display a brownish-grey stain due to chemical reactions between CO and sodium palladosulfite. The length of the stain indicates the cumulative CO levels (ppm-h) during the measuring period. The average CO concentrations during each measurement (ppm) were calculated by dividing the cumulative CO levels by the length of the measuring period. To address missing exposure information for group 3 study children during the RESPIRE study stage (<18 months of age), their infant siblings' personal CO exposure during the CRECER study was measured and used as a proxy for group 3 early life CO exposure, based on the assumption that children who grew up in the same household raised by the same parents will have similar early life activity patterns and comparable early life biomass smoke exposure. More details on exposure assessment methodology, validation, and quality assurance of the CO tubes have been extensively described in previous publications (McCracken et al., 2009; Smith et al., 2010).

For each round of valid anthropometric outcome assessment for each child, we calculated an average CO exposure (ppm) as an arithmetic mean of all valid CO measurements from both RESPIRE and CRECER studies before the date of the outcome assessment. We also combined these personal CO measurements (ppm) from both RESPIRE and CRECER studies to construct a lifetime cumulative CO exposure (ppm-year) before 1675 days old (4.59 years old), the median age of the children's last valid anthropometry. Seven children with no valid CRECER-stage CO measurement before 1675 days old were excluded. Exposures from birth to 600 days old were estimated based on measurements during the RESPIRE study for groups 1 and 2, or proxy sibling measurement for group 3; exposures from 600 to 1675 days old were estimated based on the measurements during the CRECER study. The 600-day-old cut point was chosen to reflect a behavioral pattern: women in this population tend to carry their newborn children on their backs while cooking before the children reach approximately 18 months old. Thus, younger children have higher biomass smoke exposure compared to older children. We conducted sensitivity analyses using alternative calculations of the cumulative CO exposure. Similar methods have been used in a previously published analysis (Lu et al., 2022). Details of these calculations are presented in Supplementary Table S2.

2.3. Anthropometry

The study children's heights and weights were measured every 6 months for 4 rounds during the CRECER study stage. Each study child had on average 3.44 valid measurements. Children were dressed in a standard shirt and underwear for the measurements. Height was measured using a SECA Model 214 portable stadiometer. If the two measurements differed by more than 0.1 cm, a third measurement was taken, and the two closest measurements were averaged. Weight was measured using the SECA 881 Digital floor Uniscale, measuring weight two times to the nearest 100 g, and using the TARE function for infants held by their mothers during the weighing. We took the average of the two closest measures. BMI was calculated as the children's weight in kilograms divided by the square of height in meters. Anthropometric z-scores, including height-for-age z-score (HAZ), weight-for-age z-score (WAZ), weight-for-height z-score (WHZ), and BMI z-score, were standardized by sex, calculated based on the WHO Child Growth Standards for children 0–5 years (WHO, 2023) as:

$$z-score=\frac{observed\ value-median\ value\ in\ reference\ population}{standard\ deviation(SD)\ of\ reference\ population}$$

The WHO child growth standard was developed from the WHO Multicentre Growth Reference Study (MGRS), which collected growth information from more than 8,000 children in Brazil, Ghana, India, Norway, Oman and the United States (WHO, 2023). It is the most representative international child growth standard due to its large sample size and diverse geographical, ethnic and cultural settings of the reference population. The z-score calculations were conducted with the R package "anthro" provided by the WHO, standardized on age in days. Children with HAZ < -2 or HAZ < -3 were recorded as moderately or severely stunted; children with WAZ < -2 or WAZ < -3 were recorded as moderately or severely underweight; children with WHZ < -2 or WHZ < -3 were recorded as moderately or severely wasted. These categorical definitions of stunting, underweight and wasting have been commonly used in previous studies on child somatic growth (Adjei-Mantey & Takeuchi, 2021; Boamah-Kaali et al., 2021; Caleyachetty et al., 2022).

2.4. Statistical analysis and covariates

Anthropometric z-scores were analyzed with multivariable linear regression models. Binary growth indicators (e.g., moderate stunting) were analyzed using multivariable logistic regression models. We conducted three sets of analyses:

(1) An intention-to-treat analysis using study groups (groups 1, 2, and 3) as a categorical variable with group 1 as the reference level, and the last round of valid measurements (z-scores and binary growth indicators) before 60 months old as the final growth outcomes. Groups 1, 2 and 3 received chimney stoves (*plancha*) when the study children were < 3, ~18 and ~ 57 months old, respectively.
(2) A single measure analysis using the cumulative CO exposure as a continuous independent variable, and the last round of valid measurements (z-scores and binary growth indicators) before age 60 months old as the final growth outcome.
(3) A repeated measures analysis using average CO exposure as independent variable, and all valid anthropometric z-scores before 60 months old as repeated growth outcomes. Linear mixed-effect models with random intercepts for child IDs were applied to account for the non-independence of multiple observations from the same child. Average CO exposure was treated as a continuous variable to explore the overall linear association, and also categorized into quartiles to explore potential exposure–response relationships.

For all analyses, we tested bivariate models that only included exposure variables, and multivariable models that adjusted for covariates associated with either biomass smoke exposure or anthropometric outcomes. These covariates were selected based on a directed acyclic graph representing the causal relationships between HAP exposure and child somatic growth (Supplementary Fig. S3). Adjusted covariates include sex, second-hand tobacco smoke, number of children alive in the family, average weekly *temazcal* (wood-fueled sauna bath) used by the child, kitchen location and type, maternal height, maternal and paternal education, and socioeconomic status (SES). SES variables include whether the family indicated that they owned land, owned houses, and the number of major assets owned (radios, televisions, refrigerators, bikes, motorcycles, automobiles, and cellphones). Age was not adjusted in the models because the anthropometric z-scores calculated from the WHO child growth standard were standardized by age in days, and that all study children were similar in age. Similar covariates such as maternal height, parental education, SES, and alternative sources of HAP were also adjusted in previous studies on HAP exposure and child growth (Adjei-Mantey & Takeuchi, 2021; Caleyachetty et al., 2022).

Among these variables, maternal height was measured together with the children's height during repeated visits in the CRECER study stage. The final maternal height adjusted in the models were averaged across all valid measurements as a time-invariant variables, because the mothers' heights had little variation during the CRECER study stage. Maternal weight was not included in the models because some of the participating mothers were pregnant during the study. All other covariates were collected in February and March of 2006 from the CRECER study baseline questionnaire, which was given to the participating mothers by field workers fluent in their primary language (*Mam*). The kitchen structure (whether the kitchen was a single structure or in the same building structure with the main living area, and whether the kitchen was open or partitioned from other areas) was determined by the field workers during the baseline household visits. In terms of *temazcal* use, the participating mothers were asked whether and how frequently they used *temazcal* baths, whether they brought the study children with them, and approximately how long the study children stayed in the *temazcal* each time. An average weekly *temazcal* use time (minutes) were calculated for each study child based on these information.

Among the three households with twins, two households participated in the CRECER study stage. For these two pairs of twins, we dropped the second child on the record to ensure independence among observations. In addition, we conducted three sets of sensitivity analyses:

First, for analysis (2) with cumulative CO exposure, we repeated the analysis with alternative cauculations of cumulative CO, which had been described above and in Supplementary Table S2.

Second, for both analysis (2) with cumulative CO exposure and analysis (3) with average CO exposure, we stratified the analyses by sex to explore the potential EMM. The sex-stratified analyses adjusted for the same set of covariates as the corresponding multivariable models, except for sex.

Third, for both analysis (2) and (3), we repeated the analyses after restricting to groups 1 and 2. This is to test whether group 3 was systematically different from groups 1 and 2 due to its later recruitment. If so, the analyses restricted to groups 1 and 2 would yield different results compared to the unrestricted analyses with children from all groups.

All statistical analyses were conducted using software R version 4.2.2.

3. Results

After restricting to children with valid measurements before 5 years of age, 541 children (192 in group 1, 192 in group 2, and 157 in group 3) remained in the analysis (Fig. 1). The distributions of their demographic characteristics are summarized in Table 1. The study population is racially homogenous, with 98.9 % identifying as indigenous Mam of Mayan descent. There are no apparent differences in characteristics across the three groups except for the SES variables: group 3 households were slightly less likely to own land or a house, and on average owned fewer major assets, compared to groups 1 and 2.

The distributions of average CO concentrations by study groups and study stages, as well as baseline and cumulative CO exposures by study groups, are summarized in Fig. 2 and Supplementary Table S4. Group 1 baseline CO levels before *plancha* installation were higher than their average CO exposure during both the RESPIRE and CRECER study stages. Group 2 baseline CO levels and RESPIRE stage CO exposure were similar in magnitude and higher than their CRECER stage CO exposure. Group 3 children's CO exposure levels at baseline, during the RESPIRE stage, and the CRECER stage were comparable. These comparisons across study stages were consistent with our assumption that the availability of the *plancha* is associated with reduced CO exposure. For all three groups, the children's estimated CO exposure levels during the RESPIRE stage were higher than during the CRECER stage, which was

Table 1
Child-level and household-level demographic characteristics by study group.

Plancha installation	Group 1 (<6 months)	Group 2 (~18 months)	Group 3 (~57 months)
Number of children	n = 192	n = 192	n = 157
Child Sex			
Female	102 (53.1 %)	101 (52.6 %)	82 (52.2 %)
Age (years) at final anthropometry measurement			
Mean (SD)	4.72 (0.42)	4.70 (0.44)	4.67 (0.78)
Race			
Maternal indigenous race	189 (98.4 %)	190 (99.0 %)	156 (99.4 %)
Paternal indigenous race	181 (94.3 %)	186 (96.9 %)	156 (99.4 %)
Number of children in household			
Mean (SD)	5.02 (2.37)	4.98 (2.41)	4.69 (2.42)
Second-hand smoke			
Smoker in household	14 (7.3 %)	22 (11.5 %)	16 (10.2 %)
Kitchen type			
Single structure, open kitchen	33 (17.2 %)	31 (16.1 %)	17 (10.8 %)
Single structure, partitioned kitchen	12 (6.3 %)	8 (4.2 %)	7 (4.5 %)
Separate structure, open kitchen	19 (9.9 %)	18 (9.4 %)	30 (19.1 %)
Separate structure, partitioned kitchen	128 (66.7 %)	135 (70.3 %)	103 (65.6 %)
Temazcal (native steam bath) use			
Temazcal at home	150 (78.1 %)	147 (76.6 %)	117 (74.5 %)
Average weekly *temazcal* use time of the child (minutes): mean (SD)	26.3 (17.3)	26.8 (19.9)	27.6 (17.0)
Maternal height (cm)			
Mean (SD)	144 (4.64)	145 (4.59)	144 (5.00)
Maternal education			
None	67 (34.9 %)	73 (38.0 %)	46 (29.3 %)
Primary school	118 (61.5 %)	116 (60.4 %)	109 (69.4 %)
Middle school or higher	7 (3.6 %)	3 (1.6 %)	2 (1.3 %)
Paternal education			
None	23 (12.0 %)	26 (13.5 %)	19 (12.1 %)
Primary school	135 (70.3 %)	130 (67.7 %)	110 (70.1 %)
Middle school or higher	25 (13.0 %)	28 (14.6 %)	27 (17.2 %)
Unknown	9 (4.7 %)	8 (4.2 %)	1 (0.6 %)
Socioeconomics (SES)			
Land-owning	173 (90.1 %)	172 (89.6 %)	125 (79.6 %)
Home-owning	162 (84.4 %)	167 (87.0 %)	120 (76.4 %)
Number of major assets*: mean (SD)	1.67 (1.01)	1.71 (1.13)	1.59 (1.08)

* Major assets include radios, televisions, refrigerators, bikes, motorcycles, automobiles, and cellphones.

consistent with the behavioral pattern that young children and infants were carried on their mothers' backs before 18 months old, exposed to higher levels of biomass smoke. During the RESPIRE study stage, group 2 children had the highest CO exposure (mean = 2.87 ppm, SD = 1.72 ppm) followed by group 3 proxy siblings (mean = 1.67 ppm, SD = 0.88 ppm) and group 1 study children (mean = 1.47 ppm, SD = 0.93 ppm). During the CRECER study stage, group 3 study children had higher CO exposure (mean = 1.30 ppm, SD = 0.55 ppm) than group 1 (mean = 0.89 ppm, SD = 0.72 ppm) and group 2 (mean = 0.89 ppm, SD = 0.55 ppm). Overall, group 2 children had the highest cumulative CO exposure (mean = 7.16 ppm-year, SD = 3.51 ppm-year) followed by group 3 (mean = 6.64 ppm-year, SD = 3.30 ppm-year) and group 1 (mean = 4.98 ppm-year, SD = 2.91 ppm-year). All comparisons between groups were statistically significant based on one-way analysis of variance (ANOVA) tests.

The density distributions of average CO exposure (ppm) before each valid anthropometric outcome assessment, stratified by child sex, are illustrated in Fig. S5. Among the 1860 valid measurements from 541 children, the mean of the average CO exposure is 1.90 ppm (SD = 1.25 ppm, min = 0.30 ppm, max = 13.84 ppm). Girls have slightly higher average CO exposure (mean = 1.97 ppm, SD = 1.25 ppm) compared to boys (mean = 1.82 ppm, SD = 1.25 ppm). The overall distribution of average CO exposure is skewed to the right with some large outliers. For the exposure-response analysis, we categorized the average CO exposures into quartiles, with cutpoints of 1.09, 1.62, and 2.29 ppm.

The study children's final measurements before 5 years old are summarized in Table 2. Study children were on average 53.9 months old (SD = 4.6 months), 92.0 cm tall (SD = 5.0 cm), and weighed 13.7 kg (SD = 1.5 kg) at their last valid anthropometric assessment, with no apparent differences across groups. Their average HAZ was −3.2, with 90.4 % of the children classified as at least moderately stunted and 59.7 % severely stunted. 35.5 % of the study children were moderately underweight and 5 % were severely underweight. Only 2 children were moderately wasted, and none were severely wasted; indicators for wasting were thus not included in the following regression analysis. The high prevalence of stunting indicates severe chronic malnutrition in this population.

The sex-stratified age trends of z-scores calculated from all valid anthropometric assessments during the CRECER study stage are illustrated in Fig. S6. As the children grew between 25 and 59 months old, there were slightly increasing trends for HAZ, WAZ, and HWZ, but not for BMI z-score. There is no apparent difference in somatic growth trends between boys and girls in this sample.

Table 3 presents point estimates and 95 % confidence intervals (CIs) of the associations between the last valid anthropometric outcomes before 60 months old and study groups. Compared with group 1 children whose household received the *plancha* around their birth, group 2 children whose household received the *plancha* around when they were 1.5 years old had on average 0.02 higher HAZ (95 % CI: −0.14, 0.19), 0.05 higher WAZ (95 % CI: −0.09, 0.19), 0.06 higher WHZ (95 % CI: −0.09, 0.21) and 0.05 higher BMI z-score (95 % CI: −0.09, 0.19); group 3 children whose household received the *plancha* when they were around 5 years old had on average 0.07 lower HAZ (95 % CI: −0.11, 0.25), 0.01 lower WAZ (95 % CI: −0.14, 0.16), 0.06 higher WHZ (95 % CI: −0.09, 0.22) and 0.04 higher BMI z-score (95 % CI: −0.11, 0.19). All 95 % CIs covered the null and were relatively wide compared to the magnitudes of the point estimates. Despite the different *plancha* installation timelines, the results from this intent-to-treat analysis suggest no apparent difference in somatic growth outcomes across groups.

The point estimates and 95 % CIs of the associations between the last valid growth outcomes before 60 months old and cumulative CO exposures, as well as the sex-stratified results, are summarized in Table 4. The bivariate model found a 1 ppm-year higher cumulative CO exposure was associated with a 0.03 lower HAZ (95 % CI: 0.007, 0.05). After adjusting for relevant covariates, this association was slightly attenuated to a 0.02 lower HAZ (95 % CI: −0.004, 0.04). The unstratified multivariable model for all children found no association between cumulative CO exposure and the risk of moderate stunting (OR = 1.01, 95 % CI: 0.92–1.13). But after stratifying for sex, we found a 1 ppm-year higher cumulative CO was associated with higher risks of moderate stunting among boys (OR = 1.27, 95 % CI: 1.05–1.09) and slightly lower risk among girls (OR = 0.89, 95 % CI: 0.78–1.03). We also found suggestive evidence that higher cumulative CO exposure might be associated with higher risks of moderate underweight (OR = 1.03, 95 % CI: 0.98 – 1.09) and severe underweight (OR = 1.05, 95 % CI: 0.92–1.16). The association for moderate underweight risk was consistent for both boys and

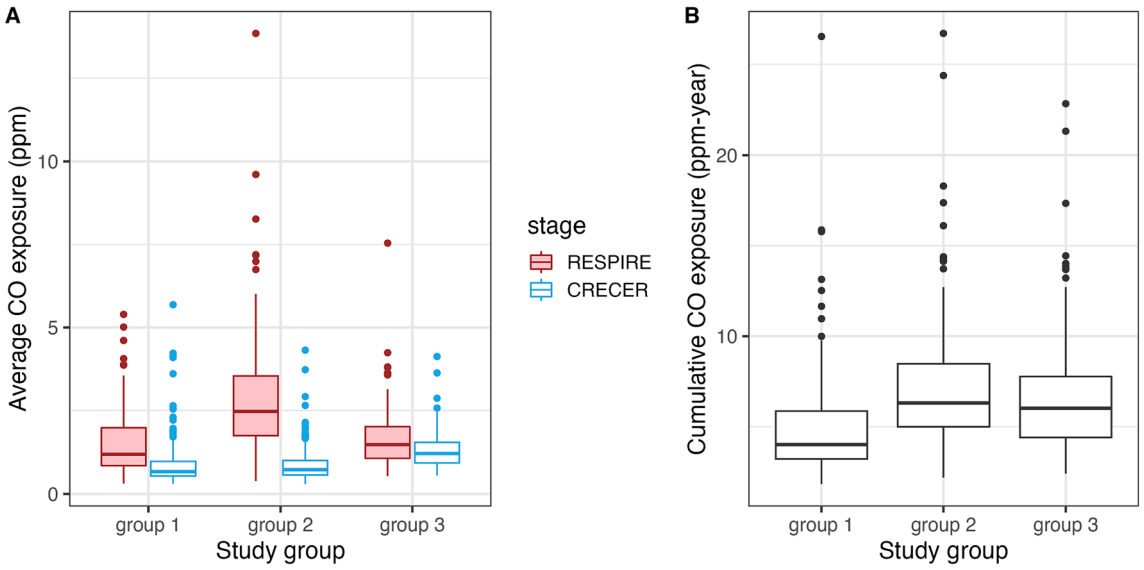

Fig. 2. Distribution of average CO exposure levels (ppm) by study groups and stages (A) and cumulative CO exposure at 4.6 years old (ppm-year) by study groups (B) during Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE) and Chronic Respiratory Effects of Early Childhood Exposure to Respirable PM cohort study (CRECER) study stages.

Table 2
Distribution of children's somatic growth outcomes by study groups.

	Group 1 (<6 months) n = 192	Group 2 (~18 months) n = 192	Group 3 (~57 months) n = 157	Tests for equal distribution across groups
Age (years) at final anthropometry measurement	Mean (SD) 4.52 (0.41)	4.55 (0.34)	4.39 (0.40)	One-way ANOVA p-value 0.0002
Final anthropometry	Mean (SD)			One-way ANOVA p-value
Height (cm)	92.2 (5.06)	92.4 (4.76)	91.3 (5.23)	0.08
Weight (kg)	13.7 (1.51)	13.8 (1.47)	13.5 (1.55)	0.09
BMI (kg/m^2)	16.1 (0.99)	16.2 (1.10)	16.2 (1.06)	0.60
Z-score growth indicators*	Mean (SD)			One-way ANOVA p-value
Height for age z-score (HAZ)	−3.20 (0.85)	−3.18 (0.91)	−3.25 (0.94)	0.73
Weight for age z-score (WAZ)	−1.79 (0.70)	−1.73 (0.73)	−1.80 (0.75)	0.60
Weight for height z-score (WHZ)	0.30 (0.70)	0.37 (0.75)	0.33 (0.73)	0.61
Binary growth indicators	n (%)			Test for equal proportions p-values
Moderate stunting (HAZ < −2)	176 (91.7 %)	170 (88.5 %)	143 (91.1 %)	0.55
Severe stunting (HAZ < −3)	118 (61.5 %)	114 (59.4 %)	91 (58.0 %)	0.80
Moderate underweight (WAZ < −2)	63 (32.8 %)	66 (34.4 %)	63 (40.1 %)	0.34
Severe underweight (WAZ < −3)	10 (5.2 %)	7 (3.6 %)	10 (6.4 %)	0.50
Moderate wasting (WHZ < −2)	1 (0.5 %)	0 (0 %)	1 (0.6 %)	–
Severe wasting (WHZ < −3)	0 (0 %)	0 (0 %)	0 (0 %)	–

* Z-score growth indicators were calculated using WHO Multicentre Growth Reference Study (MGRS) international reference population.

Table 3
Point estimates and 95 % confidence intervals (CIs) of the associations between the last valid somatic growth outcomes before 60 months old and study groups (Group 1 as the reference group).

	Group 2 (*Plancha* installation ~ 18 months)		Group 3 (*Plancha* installation ~ 57 months)	
	Bivariate model	Multivariate model	Bivariate model	Multivariate model
Z-score growth indicators: coefficient (95 % CI)				
Height for age z-score (HAZ)	0.02 (−0.16, 0.21)	0.02 (−0.14, 0.19)	−0.05 (−0.24, 0.14)	−0.07 (−0.25, 0.11)
Weight for age z-score (WAZ)	0.06 (−0.09, 0.21)	0.05 (−0.09, 0.19)	−0.01 (−0.16, 0.14)	−0.01 (−0.16, 0.14)
Weight for height z-score (WHZ)	0.07 (−0.07, 0.22)	0.06 (−0.09, 0.21)	0.03 (−0.12, 0.19)	0.06 (−0.09, 0.22)
BMI z-score	0.06 (−0.08, 0.20)	0.05 (−0.09, 0.19)	0.06 (−0.09, 0.20)	0.04 (−0.11, 0.19)
Binary growth indicators: OR (95 % CI)				
Moderate stunting (HAZ < −2)	0.70 (0.35, 1.38)	0.67 (0.31, 1.41)	0.93 (0.44, 1.99)	0.86 (0.37, 2.03)
Severe stunting (HAZ < −3)	0.92 (0.61, 1.38)	0.92 (0.60, 1.42)	0.86 (0.56, 1.33)	0.85 (0.53, 1.34)
Moderate underweight (WAZ < −2)	1.07 (0.70, 1.64)	1.09 (0.70, 1.72)	1.37 (0.88, 2.13)	1.39 (0.87, 2.24)
Severe underweight (WAZ < −3)	0.69 (0.25, 1.83)	0.81 (0.28, 2.30)	1.24 (0.50, 3.09)	1.44 (0.53, 3.94)

Multivariate models adjusted for sex, second-hand smoke, number of children in the family, average weekly *temazcal* use time of the child, kitchen location and type, maternal height, maternal and paternal education, and SES (land-owning, house-owning, and number of major assets).

girls (OR = 1.05 for boys and 1.02 for girls), while the association between cumulative CO and risk of severe underweight was stronger among girls (OR = 1.12, 95 % CI: 0.95–1.31). We conducted sensitivity analyses with the alternative calculations of cumulative CO exposure described the Supplementary Table S2. The results were consistent in

Table 4
Point estimates and 95 % confidence intervals (CIs) of the associations between the last valid anthropometry outcomes before 60 months old and cumulative CO exposure (ppm-year).

	Bivariate model, all children	Multivariable model, all children	Multivariable model, male only	Multivariable model, female only
Z-score growth indicators: coefficient (95 % CI)				
Height for age z-score	−0.03 (−0.05, −0.007)	−0.02 (−0.04, 0.004)	−0.03 (−0.06, 0.007)	−0.006 (−0.03, 0.02)
Weight for age z-score	−0.01 (−0.03, 0.006)	−0.005 (−0.02, 0.01)	−0.007 (−0.03, 0.02)	−0.004 (−0.03, 0.02)
Weight for height z-score	0.01 (−0.01, 0.02)	0.01 (−0.01, 0.03)	0.02 (−0.01, 0.04)	−0.001 (−0.03, 0.02)
BMI z-score	0.01 (−0.005, 0.03)	0.01 (−0.007, 0.03)	0.02 (−0.01, 0.05)	0.001 (−0.02, 0.03)
Binary growth indicators: OR (95 % CI)				
Moderate stunting	1.06 (0.97, 1.18)	1.01 (0.92, 1.13)	1.27 (1.05, 1.59)	0.89 (0.78, 1.03)
Severe stunting	1.03 (0.98, 1.09)	1.003 (0.95, 1.06)	1.01 (0.93, 1.10)	0.98 (0.91, 1.07)
Moderate underweight	1.04 (0.99, 1.10)	1.03 (0.98, 1.09)	1.05 (0.97, 1.15)	1.02 (0.94, 1.10)
Severe underweight	1.02 (0.90, 1.12)	1.05 (0.92, 1.16)	1.00 (0.75, 1.24)	1.12 (0.95, 1.31)
number of children (n)	527	522	248	274

Multivariable models adjusted for sex, second-hand smoke, number of children in the family, average weekly temazcal use time of the child, kitchen location and type, maternal height, maternal and paternal education, SES (land-owning, house-owning, and number of major assets). Sex-stratified models adjusted for the same covariates as the multivariable model, except for sex.

directions and similar in magnitudes compared to the main analysis (Supplementary Table S7). In addition, we repeated the analyses after restricting to groups 1 and 2. The point estimates are similar to the results from all three groups, with slightly wider CIs due to the reduced sample size (Supplementary Table S8).

Table 5 summarizes the associations between average CO exposure (ppm) and anthropometric z-scores, estimated from the linear mixed effects models. We found that a 1 ppm higher average CO exposure was associated with a 0.21 lower HAZ (95 % CI: 0.17 – 0.25), a 0.13 lower WAZ (95 % CI: 0.10 – 0.17) and a 0.06 lower WAZ (95 % CI: 0.02 – 0.10). After stratifying by sex, these associations persisted among both boys and girls. The association between average CO exposure and HAZ was stronger among boys (coefficient = −0.29, 95 % CI: −0.35 – −0.22) compared to girls (coefficient = −0.15, 95 % CI: −0.20 – −0.10), which is consistent with the EMM found in the analyses with cumulative CO exposure. We did not find an association between average CO exposure and BMI z-score. The sensitivity analysis restricting to groups 1 and 2 produced almost identical results (Supplementary Table S9), suggesting no systematic difference between groups 3 and groups 1 and 2.

Fig. 3 and Supplementary Table S10 present the point estimates and 95 % CIs of the associations between repeated anthropometric z-scores and average CO exposure quartiles, estimated from the linear mixed effect models. We found that higher average CO exposure quartiles are associated with monotonically decreasing HAZ and WAZ, and are consistent among both girls and boys. Being in the highest exposure quartile is associated with a 0.44 (95 % CI: 0.32, 0.54) lower HAZ and a 0.29 (95 % CI: 0.18, 0.40) lower WAZ, compared to being in the lowest exposure quartile. In addition, the reduction in HAZ associated with being in higher average CO quartiles compared to the first quartile is also consistently larger among boys (coefficient = −0.62, 95 % CI: −0.79 – −0.44 for the 4th quartile), compared with among girls (coefficient = −0.26, 95 % CI: −0.42 – −0.11 for the 4th quartile). This suggests an EMM of the relationship between HAP exposure and HAZ by sex. For WHZ and BMI z-score, the exposure–response relationship is less clear with most CIs covering the null, except for the association between average CO exposure and WHZ among girls (coefficient = −0.21, 95 % CI: −0.37 – −0.05 for the 4th quartile).

4. Discussion

This prospective cohort study assessed cooking-related biomass smoke exposure and somatic growth outcomes among 541 children in rural Guatemala between 25 and 60 months of age. We found that older children and children in households with wood-fueled chimney stoves (*plancha)* tended to have lower CO exposure compared to their counterparts who were younger or from households cooking with open wood fires. The study population had a very high prevalence of childhood stunting (90.2 %) and underweight (35.5 %), suggesting severe chronic malnutrition contributed by both environmental and social deprivation factors.

We measured personal CO exposures, which were highly correlated with fine particulate matter exposures in this study population, as a proxy for the study children's overall HAP exposure (McCracken et al., 2013). We compared the distributions of CO exposures across groups and study periods and found that older children tend to have lower HAP exposure, which corresponds with the behavioral pattern that mothers often carry newborns on their back while cooking. Among children of similar ages, those from households assigned to plancha stoves had on average higher CO exposures, except for the exposures of group 3 proxy infant siblings (Fig. 2). This suggest that the availability of *plancha* stoves can reduce HAP levels to some extent in real world settings, although the group-level distributions of HAP exposures overlapped with relatively large within-group variations. The potential underestimation of group 3 RESPIRE stage HAP exposure with proxy infant

Table 5
Point estimates and 95% confidence intervals (CIs) of anthropometry z-score outcomes associated with average CO exposure (ppm).

	Bivariate model, all children	Multivariable model, all children	Multivariable model, male only	Multivariable model, female only
Z-score growth indicators: coefficient (95 % CI)				
Height for age z-score	−0.21 (−0.24, −0.17)	−0.21 (−0.25, −0.17)	−0.29 (−0.35, −0.22)	−0.15 (−0.20, −0.10)
Weight for age z-score	−0.14 (−0.17, −0.10)	−0.13 (−0.17, −0.10)	−0.15 (−0.20, −0.09)	−0.12 (−0.16, −0.07)
Weight for height z-score	−0.05 (−0.09, −0.02)	−0.06 (−0.10, −0.02)	−0.06 (−0.12, −0.00)	−0.07 (−0.11, −0.01)
BMI z-score	0.01 (−0.02, 0.05)	0.01 (−0.03, 0.05)	0.01 (−0.04, 0.06)	0.01 (−0.04, 0.05)
number of children	541	490	235	285
number of observation	1859	1699	808	982

All models included random intercepts for child id. Multivariable models adjusted for sex, second-hand smoke, number of children in the family, average weekly temascal use time of the child, kitchen location and type, maternal and paternal education, SES (land-owning, house-owning and number of major assets). Multivariable models of HAZ adjusted for maternal height. Sex-stratified models adjusted for the same covariates as the multivariable model, except for sex.

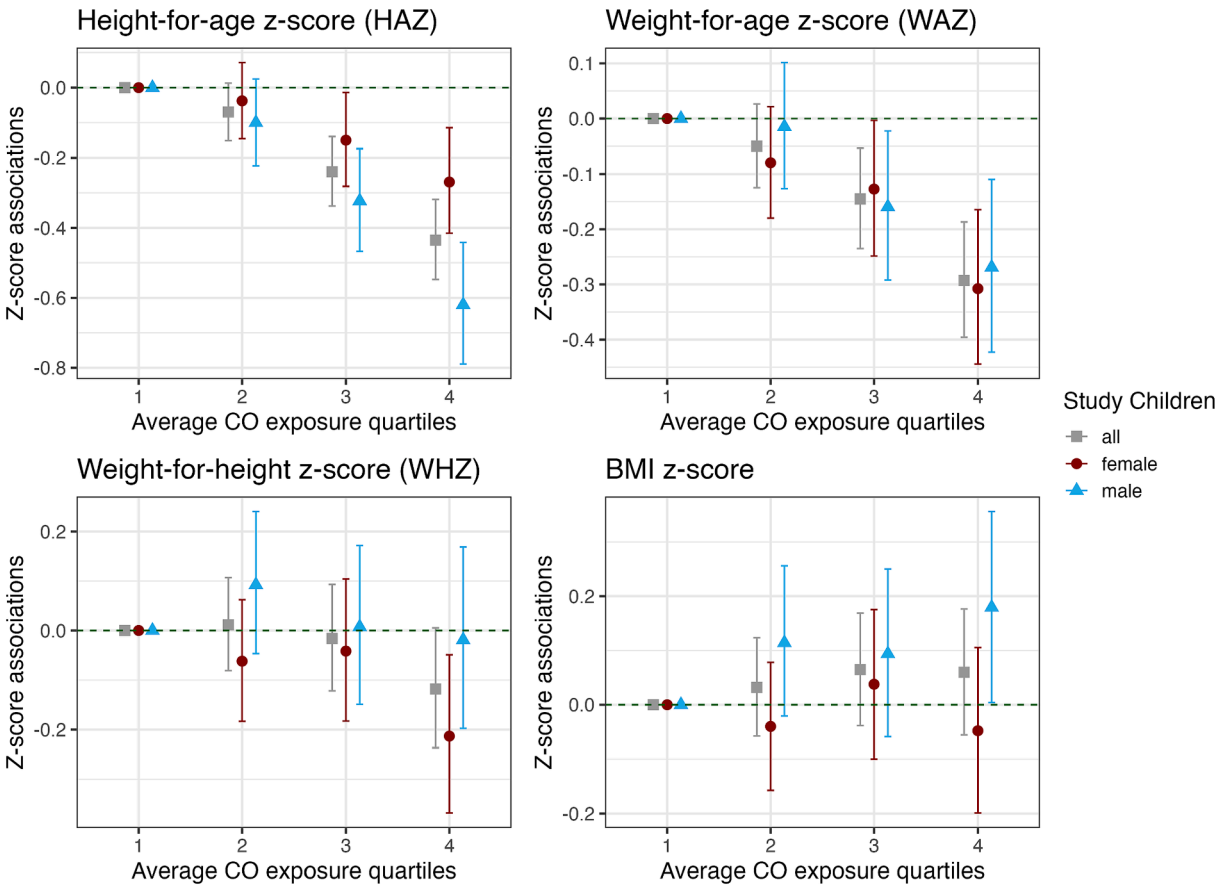

Fig. 3. Point estimates and 95% confidence intervals (CIs) of the associations between repeated measurements of anthropometric z-scores and average CO exposure quartiles.

siblings will be discussed in detail later.

Although *plancha* availability at different ages did not directly predict childhood somatic growth outcomes, we found that higher average CO exposure was associated with lower HAZ, WAZ, and WHZ (Table 5). The associations for HAZ and WAZ were also monotonically decreasing across exposure quartiles (Fig. 3). The association between being in a higher average CO exposure quartile and having a lower HAZ score is also consistently stronger among boys compared to girls. A 1 ppm-year increase in cumulative CO exposure was associated with a higher risk of moderate stunting among boys but not among girls (Table 4). Analyses with both average CO and cumulative CO showed consistent EMM by sex. Higher cumulative CO exposure appeared to be slightly protective of stunting among girls with an OR of 0.89 (Table 4), and the protective association was even stronger (OR = 0.80) in the sensitivity analysis restricted to groups 1 and 2 (Supplementary Table S8). This might be due to the an overestimation of group 2 cumulative CO exposure caused by extrapolating RESPIRE and CRECER stages CO measurements to the ~ 1.5-year gap in-between: Group 2 households were provided *plancha* stoves at the end of RESPIRE, therefore their CO exposure should be the lowest during the 1.5-year gap when there was no exposure measured, compared with the RESPIRE stage when they used open wood fire, and the CRECER stage when their *plancha* stoves might have deteriorated. The repeated measures analysis with average CO exposures was less sensitive to the inaccurate extrapolation of exposures, and showed that higher average CO exposure was associated with lower HAZ among girls, although not as strongly as among boys (Fig. 3).

The study children's WHZs and BMI fell within the normal range (Supplementary Fig. S6) with only two cases of moderate wasting (Table 2). We also did not find clear associations between higher average CO exposure quartiles and WHZ or BMI z-scores. However, we would suggest interpretation with caution on whether children in the study population are at acute risk due to diseases or food shortages, which we did not examine in-depth, and which are common causes of wasting and low BMI. The study children are both much thinner and much shorter compared to the international reference population, as reflected by their low HAZ and WAZ (Supplementary Fig. S6). Thus, both WHZ, which is standardized by child height, and BMI, which has height in the denominator, may not be indicative of health status in this particular study population. For example, we found that being in the highest average CO exposure quartile is associated with a 0.21 lower WHZ (95 % CI: 0.05, 0.37) among girls but not among boys. This difference does not suggest that boys are less vulnerable to low WHZ or wasting: boys had a higher decrease in height associated with higher CO exposure, reflected in the larger reduction in HAZ associated with higher CO exposures (Fig. 3, Supplementary Table S10), thus the associations between CO exposure and WHZ among boys was attenuated after standardizing by height. Future studies may consider investigating populations with adequate nutrition and health conditions to examine the relationship between HAP exposure and wasting as an indicator of acute malnutrition.

Our findings that cooking-related HAP exposure is associated with lower HAZ and WAZ are consistent with previous studies (Adjei-Mantey and Takeuchi, 2021; Boamah-Kaali et al., 2021; Caleyachetty et al., 2022; Islam et al., 2021b; Lamichhane et al., 2020; Liang et al., 2020). Our finding that the associations between air pollution exposure and HAZ/stunting are stronger among boys compared to girls has also been observed in previous studies. A study in Ghana found that prenatal HAP exposure from polluting fuels had a greater negative impact on HAZ among boys than girls before 5 years old (Adjei-Mantey & Takeuchi, 2021). Another study in Bangladesh also reported prenatal ambient fine

particulate ($PM_{2.5}$) was associated with stunting among boys but not girls before 5 years old (Kurata et al., 2020). This EMM by sex might be related to the different growth rates of height betwen boys and girls, but the underlying biological mechanism remains unclear.

We did not find differences in growth outcomes across study groups that received *plancha* stoves at different ages. This might be due to the relatively small sample size in each group. Another possible reason is insufficient exposure reduction due to at least three factors. Firstly, the *plancha* stoves used the same fuel types as the open wood fires and only vented biomass smoke outdoors, which might still be inhaled by older children as they spend time outdoors. Secondly, the stoves were not regularly maintained during the 2-year gap between the RESPIRE and CRECER study stages, during which group 1 might have had higher HAP exposure than group 2 because of the older deteriorated stoves. Thirdly, compliance with the stove assignment was not assessed: groups assigned to *plancha* may still have continued to use open wood fires for some cooking. Overall, the moderate exposure difference across groups may be insufficient to yield significant reductions in health outcome risks, which was also observed in previous analyses of other outcomes in the RESPIRE and CRECER cohorts (Lu et al., 2022; Smith et al., 2011). The compromised efficiency of improved stoves due to non-ideal combustion and imperfect compliance are also commonly observed in other cookstove intervention studies in rural areas of developing countries. For example, an Indian study found that the emission produced by liquefied petroleum gas stoves were substantially higher in homes compared to in laboratories due to non-ideal combustion performance (Islam et al., 2021a). Other cookstove intervention trials in Malawi, India and Ghana also found no significant evidence of direct health improvement after providing cleaner biomass-fueled stoves (Asante et al., 2019; Aung et al., 2018; Darby et al., 2021; Mortimer et al., 2017). Future studies should consider practical methods to improve the efficiency of clean stove in real world settings, such as improving stove robustness, providing long-term repair and replacement services, and designing the stoves to fit the everyday cooking conditions in specific study populations.

The biological mechanisms of exposure to air pollution and poor somatic growth might involve oxidative stress, epigenetic changes, and immune dysfunction. Previous studies have found that prenatal exposure to air pollution can increase maternal mitochondrial copy number, reduce telomere length, and affect infant DNA methylation levels; these cellular changes are also associated with poor fetal growth outcomes such as low birth weight and small for gestational age (Burris & Baccarelli, 2017; Iodice et al., 2018). Studies have also found that air pollution exposure can cause epigenetic changes that downregulate immune responses among children (van Leeuwen et al., 2008), which will then contribute to recurrent infections, chronic inflammation, and the subsequent development of chronic malnutrition and poor childhood growth outcomes (Bourke et al., 2016).

This is the first randomized stove intervention trial followed by a prospective cohort study that examined cumulative postnatal HAP exposure and somatic growth outcomes among children. We also examined less studied growth outcomes such as being underweight and wasting. We collected extensive data on household and family information, building structure, SES, and alternative exposure sources that allowed for adequate control of potential confounding factors. The randomization of groups 1 and 2 to chimney stove intervention and continued open fire use during the RESPIRE study stage further reduced the risk of residual confounding. The sensitivity analyses restricting to only groups 1 and 2 (Supplementary Table S8, Supplementary Table S9) produced similar results to the corresponding main analyses for all groups (Table 4, Table 5), which also reduces the risk of residual confounding due to different recruitment processes. This is also the first study to quantify cumulative lifetime HAP exposure and analyze its effect on somatic growth outcomes. We estimated average and cumulative CO exposures based on repeated personal CO tube measurements, which may be more accurate than short-term, periodic personal measurements, use of microenvironmental household air pollution monitors or questionnaire-based use of stove and fuel types commonly used in other studies.

One limitation of the study is the less accurate early-life exposure measurement for group 3. Since group 3 children were not recruited during the RESPIRE study stage, using their infant siblings' exposure levels during the CRECER study stage as a proxy was the best plausible estimation. This approximation assumed that siblings who grew up in the same household have similar activity patterns and HAP exposure. However, the comparability of this proxy measurement might have been compromised. Firstly, personal CO exposure measurement was conducted less frequently for groups 1 and 2 compared to group 3 during the CRECER study stage (Supplementary Table S1). Thus, group 3 infant siblings' exposure during CRECER and the RESPIRE stage CO measurements of groups 1 and 2 had different approximations of cumulative exposure. Secondly, secular changes in biomass fuel types and household cooking conditions were not considered. Finally, group 3 study children were on average 2.8 years older than their proxy infant siblings, and thus were less likely to have an older sibling who could take care of them while their parents were cooking. They were more likely to be carried on their mothers' backs while cooking and exposed to higher levels of HAP. Using the younger siblings' exposure as a proxy may underestimate their early-life HAP exposures. Our finding that group 3 RESPIRE stage CO exposure was much lower than group 2 (Fig. 2) is evidence for this potential underestimation. Overall, the average and cumulative CO exposures for group 3 were likely measured less accurately than for groups 1 and 2 and thus may have been underestimated. Since the distributions of somatic growth outcomes were similar across groups (Table 2), this exposure misclassification was non-differential with regard to the outcomes and was likely to cause a bias towards the null.

Our finding that cooking-related biomass smoke exposure was associated with slower somatic growth for both height and weight provides evidence for stove and fuel upgrade interventions in rural communities of low-income countries. We found evidence consistent with existing literature that young boys are more vulnerable to the adverse impacts of air pollution on stunting, which suggests potential policy priorities. Future studies may consider larger sample sizes; more efficient HAP reduction interventions with cleaner fuels and better-combusting, more efficient stoves; and populations with a higher prevalence of acute malnutrition and wasting.

CRediT authorship contribution statement

Wenxin Lu: Formal analysis, Visualization, Writing – original draft. **Alisa Jenny:** Project administration, Resources, Supervision. **Carolina Romero:** Investigation, Supervision. **Anaite Diaz-Artiga:** Investigation, Supervision, Writing – review & editing. **Andrea Kuster:** Investigation, Supervision. **Eduardo Canuz:** Investigation. **Ajay Pillarisetti:** Data curation, Writing – review & editing. **John P. McCracken:** Data curation, Investigation, Writing – review & editing. **Wenzhong Huang:** Methodology, Writing – review & editing. **Kirk R. Smith:** Funding acquisition, Methodology, Resources, Supervision, Validation. **John Balmes:** Data curation, Investigation, Writing – review & editing. **Lisa M. Thompson:** Conceptualization, Data curation, Methodology, Supervision, Validation, Writing – review & editing.

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

Data will be made available on request.

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Data sharing

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy concerns.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108401.

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