ORIGINAL ARTICLE

Effects of Cooking with Liquefied Petroleum Gas or Biomass on Stunting in Infants

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ABSTRACT

BACKGROUND

Household air pollution is associated with stunted growth in infants. Whether the replacement of biomass fuel (e.g., wood, dung, or agricultural crop waste) with liquefied petroleum gas (LPG) for cooking can reduce the risk of stunting is unknown.

METHODS

We conducted a randomized trial involving 3200 pregnant women 18 to 34 years of age in four low- and middle-income countries. Women at 9 to less than 20 weeks' gestation were randomly assigned to use a free LPG cookstove with continuous free fuel delivery for 18 months (intervention group) or to continue using a biomass cookstove (control group). The length of each infant was measured at 12 months of age, and personal exposures to fine particulate matter (particles with an aerodynamic diameter of ≤2.5 μm) were monitored starting at pregnancy and continuing until the infants were 1 year of age. The primary outcome for which data are presented in the current report — stunting (defined as a length-for-age z score that was more than two standard deviations below the median of a growth standard) at 12 months of age — was one of four primary outcomes of the trial. Intention-to-treat analyses were performed to estimate the relative risk of stunting.

RESULTS

Adherence to the intervention was high, and the intervention resulted in lower prenatal and postnatal 24-hour personal exposures to fine particulate matter than the control (mean prenatal exposure, 35.0 μg per cubic meter vs. 103.3 μg per cubic meter; mean postnatal exposure, 37.9 μg per cubic meter vs. 109.2 μg per cubic meter). Among 3061 live births, 1171 (76.2%) of the 1536 infants born to women in the intervention group and 1186 (77.8%) of the 1525 infants born to women in the control group had a valid length measurement at 12 months of age. Stunting occurred in 321 of the 1171 infants included in the analysis (27.4%) of the infants born to women in the intervention group and in 299 of the 1186 infants included in the analysis (25.2%) of those born to women in the control group (relative risk, 1.10; 98.75% confidence interval, 0.94 to 1.29; P=0.12).

CONCLUSIONS

An intervention strategy starting in pregnancy and aimed at mitigating household air pollution by replacing biomass fuel with LPG for cooking did not reduce the risk of stunting in infants. (Funded by the National Institutes of Health and the Bill and Melinda Gates Foundation; HAPIN ClinicalTrials.gov number, NCT02944682.)

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*A complete list of the HAPIN Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Household air pollution is a leading environmental risk factor in low- and middle-income countries, accounting for an estimated 2.3 million premature deaths and 91.5 million disability-adjusted life years lost in 2019.[1] Household air pollution results from the incomplete combustion of biomass fuels (e.g., wood, dung, or agricultural crop waste), which were used as energy sources for cooking by 36% of the worldwide population in 2020.[2]

Women and children younger than 5 years of age are at highest risk for exposure to indoor air pollution owing to their time spent in the kitchen. In 2019, an estimated 9% of childhood deaths worldwide were attributed to exposures to household air pollution.[3] Moreover, regular exposure to household air pollution is linked to poor health outcomes, including stunted growth in children.[4-7] Stunting in childhood is defined by the World Health Organization (WHO) as a length or height that is more than two standard deviations below the median of the Multicentre Growth Reference Study (MGRS) standard for a given age and sex.[8] Mechanisms linking exposure to household air pollution and childhood stunting are not well elucidated and may include prenatal and postnatal oxidative stress and inflammation and impaired immune function leading to a higher burden of clinical and subclinical infections and increased nutrient requirements.[4]

Despite a better understanding of the environmental and nutritional factors that contribute to faltering of linear growth in children, stunting remains a substantial public health problem in low- and middle-income countries.[9-12] In 2019, an estimated 144 million children younger than 5 years of age worldwide had stunted growth.[13] Stunting that reflects chronic undernutrition is not only associated with short-term medical complications and death from acute illnesses and impaired cognitive development; it may also contribute to lower educational attainment in childhood and adolescence, with subsequent reduced economic performance in adulthood.[14-18] Therefore, environmental interventions that reduce the burden of childhood stunting are likely to have a major effect on health in low- and middle-income countries.[19]

The Household Air Pollution Intervention Network (HAPIN) trial was designed to assess the effects of replacing biomass cookstoves with liquefied petroleum gas (LPG) cookstoves on four primary outcomes, including stunting in infants. We reported previously that there was no significant effect of the intervention on infant birth weight.[20] Here, we report the effects of the intervention on stunting in infants.

METHODS

TRIAL SETTING AND DESIGN

We conducted a randomized, controlled trial to evaluate the effect of an LPG cookstove intervention on four primary outcomes: infant birth weight, stunting in infants, severe pneumonia in infants, and blood pressure in adult women 40 to 79 years of age.[21] A total of 3200 women across four low- and middle-income countries were randomly assigned in a 1:1 ratio to the intervention group or the control group; the groups are described below. Randomization was stratified according to geographic region, of which there were 10 in the trial: one district in Jalapa, Guatemala; two districts in Tamil Nadu, India; six provinces in Puno, Peru; and one district in Kayonza, Rwanda.

We enrolled pregnant women 18 to 34 years of age with a singleton pregnancy at 9 to less than 20 weeks' gestation, as confirmed by ultrasonography; eligible women were identified at prenatal clinics.[21] Women randomly assigned to the intervention group received an LPG cookstove, along with continuous free fuel delivery and behavioral reinforcement for 18 months (starting during pregnancy and continuing until the infants were 1 year of age). Those assigned to the control group were asked to continue their usual cooking practices and received periodic compensation, which varied by country,[22] to offset the economic benefits of the intervention; at the end of the 18-month trial period, they were also offered either an LPG stove and a 1-month supply of fuel or another household item.[22] Total compensation over the course of the trial in the control households ($141 [U.S. dollars] in Peru, $268 in Guatemala, $313 in Rwanda, and $363 in India) was one half to one fifth the cost of the intervention in Peru, Guatemala, and Rwanda ($473, $1,414, and $638, respectively) but was equal to the cost in India ($363).

We used temperature sensors on the biomass-burning stoves in the intervention households to monitor adherence to LPG stove use.[23] We conducted additional home visits to deliver LPG fuel tanks to the intervention households and provided behavioral reinforcement if the stove-use monitors indicated that the biomass stoves had been used.[24-26]

The trial was approved by the applicable ethics committees; details are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org. The first and last two authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol, available at NEJM.org.

Assessment of Personal Exposures to Air Pollutants

We measured 24-hour personal exposures to fine particulate matter (particles with an aerodynamic diameter of ≤2.5 μm [$PM_{2.5}$]) using the Enhanced Children's MicroPEM monitor (RTI International) and to carbon monoxide using the Lascar EL-USB-CO300 (Lascar Electronics). Measurements of these pollutants were obtained three times in the women during pregnancy — at 9 to 19 weeks' gestation (before randomization) and at 24 to 28 weeks' and 32 to 36 weeks' gestation (after randomization) — and three times in the infants, at 3, 6, and 12 months of age[26]; details are provided in the Supplementary Appendix. The women carried the monitors in a vest or apron. We assessed personal exposures indirectly in the infants using beacon emitters and receivers.[27] Black carbon concentrations were estimated from $PM_{2.5}$ filter samples at baseline and during pregnancy but not when the Enhanced Children's MicroPEMs were used for indirect assessment in infants. Differences between the trial groups in prenatal and postnatal exposures have been reported previously.[28,29] Here, we report personal exposures to fine particulate matter, black carbon, and carbon monoxide for live births only.

Outcomes

The primary outcome for this report was stunting at 12 months of age (defined as a length-for-age z score that was more than two standard deviations below the median of the WHO MGRS standard for a given age and sex[8]). Secondary outcomes were the length-for-age z score at 12 months of age, severe stunting (defined as a length-for-age z score that was more than three standard deviations below the median of a growth standard) at 12 months of age, and stunting at 6 months of age.

Persons who were trained in anthropometry measured the recumbent length of the infants to the nearest 1 mm with the use of a seca 417 measuring board (Seca) at birth and at 3, 6, 9, and 12 months of age in accordance with standard methods.[30] They measured the infants in the homes where the infants resided and thus were aware of the trial-group assignments. We developed a longitudinal training and quality-control program to ensure high-quality anthropometric assessments (see the Supplementary Appendix), and we tracked precision, as described elsewhere.[31]

Interruptions in Data Collection Owing to the Covid-19 Pandemic

The coronavirus disease 2019 (Covid-19) pandemic led to some interruptions in in-home visit schedules between March 2020 and October 2020; however, LPG fuel delivery was considered to be essential and continued uninterrupted during the pandemic. As restrictions eased, we adapted to local regulations by increasing the number of staff to accommodate shorter workdays because of curfews or by shifting tasks when staff had to quarantine. We followed a safety protocol as described elsewhere.[32] We compared the percentages of women and infants with missed assessments before and after March 17, 2020.

Statistical Analysis

We estimated that 1440 participants per trial group would be needed to provide the trial with 80% power to detect a relative risk of stunting of 0.81 favoring the intervention, with a baseline incidence of stunting of 30% among participants in the control group, at an alpha level of 0.0125 (adjusted for the four primary outcomes to preserve the family-wise type I error rate at 0.05).[21] The statistical analysis plan was finalized before the unblinding of the trial-group assignments (see the Supplementary Appendix). Analyses that included unblinded data were performed independently by two statisticians.

The primary-outcome analysis was based on the intention-to-treat principle, with stunting as a dichotomous variable. We used a log-binomial regression model, with stunting at 12 months of age as the outcome and the trial-group assignment (with the control group as the reference) as the main covariate, adjusted for randomization strata. We present a 98.75% confidence interval for the relative risk of the intervention on stunting to account for the four primary outcomes. For the secondary-outcome analyses, which were also based on the intention-to-treat principle, we used a linear regression model for the length-for-age z score at 12 months of age and either a log-binomial or Poisson regression model with a robust variance estimator (as an approximation if the log-binomial model did not converge) for severe stunting at 12 months of age and stunting at 6 months of age as a function of the trial-group assignment (with the control group as the reference) and randomization strata. We performed prespecified subgroup analyses of the primary outcome with no adjustment for multiplicity (see the Supplementary Appendix).

Participants with missing length-for-age z scores were excluded from the analyses. In sensitivity analyses, we evaluated whether differential missingness affected the results of the primary analysis by using a log-binomial model with adjustment for key potential confounders (see the Supplementary Appendix). We analyzed repeated measurements of stunting at birth and at 3, 6, 9, and 12 months of age using a Poisson regression model as a function of age, the trial-group assignment (with the control group as the reference), and randomization strata with infant-specific random intercepts and robust variance estimation at the level of each observation.[33] We performed the statistical analyses using R software, version 4.1.2 (R Project for Statistical Computing),[34] and Stata SE software, version 15.1 (StataCorp).

RESULTS

PARTICIPANT CHARACTERISTICS

Between May 7, 2018, and February 29, 2020, a total of 3200 pregnant women underwent randomization: 1593 to the intervention group and 1607 to the control group. Five women were determined to be ineligible after randomization and were withdrawn from the trial. A total of 36 women (2.3%) in the intervention group and 31 women (1.9%) in the control group had a pregnancy loss. Among the 3200 women who had undergone randomization, 3061 (95.7%) had live births (1536 in the intervention group and 1525 in the control group). A total of 28 (1.8%) of the 1536 women in the intervention group and 36 (2.4%) of the 1525 women in the control group had infants who died before 12 months of age (Fig. 1 and Table S2 in the Supplementary Appendix).

Length measurements at 12 months of age were obtained in 2359 infants (77.1%), with the last measurement obtained on September 21, 2021. There were no substantive differences in the percentages of infants who were missing a length measurement either before March 17, 2020 (intervention group, 9.9%; control group, 6.0%) or after March 17, 2020 (intervention group, 26.6%; control group, 25.4%) (Fig. S1). Length-for-age z scores of more than six standard deviations below the median were considered to be erroneous; there were seven such scores at 3 months of age, two at 6 months of age, three at 9 months of age, and two at 12 months of age. There were no length-for-age z scores greater than 6. Therefore, our analyses included valid z scores for 2357 infants (77.0%).

The characteristics of the infants born to women in the intervention group and the characteristics of those born to women in the control group were similar at baseline, as were the characteristics of the infants who were included in the analysis and the characteristics of those who were excluded from the analysis because of a missing or erroneous length-for-age z score (Table 1). Additional baseline information is provided in Table S3. Background information on the broader population affected by household air pollution and comments on the representativeness of the participants in the trial are provided in Table S1.

Adherence to the intervention was high; the median percentage of monitored days that intervention households used their biomass cookstove rather than the LPG cookstove during the trial period was 0.4% (interquartile range, 0 to 2.3). The intervention resulted in lower prenatal and postnatal exposures to air pollutants in the first year of life than the control (Table 2). Specifically, after randomization, the mean prenatal 24-hour personal exposure to fine particulate matter was 35.0 μg per cubic meter in the intervention group and 103.3 μg per cubic meter in the control group, and the mean postnatal exposures were 37.9 μg per cubic meter and 109.2 μg per cubic meter, respectively. The median and interquartile range values, as well as the geometric mean and geometric standard deviation values, for personal exposures to air pollutants are provided in Table S3.

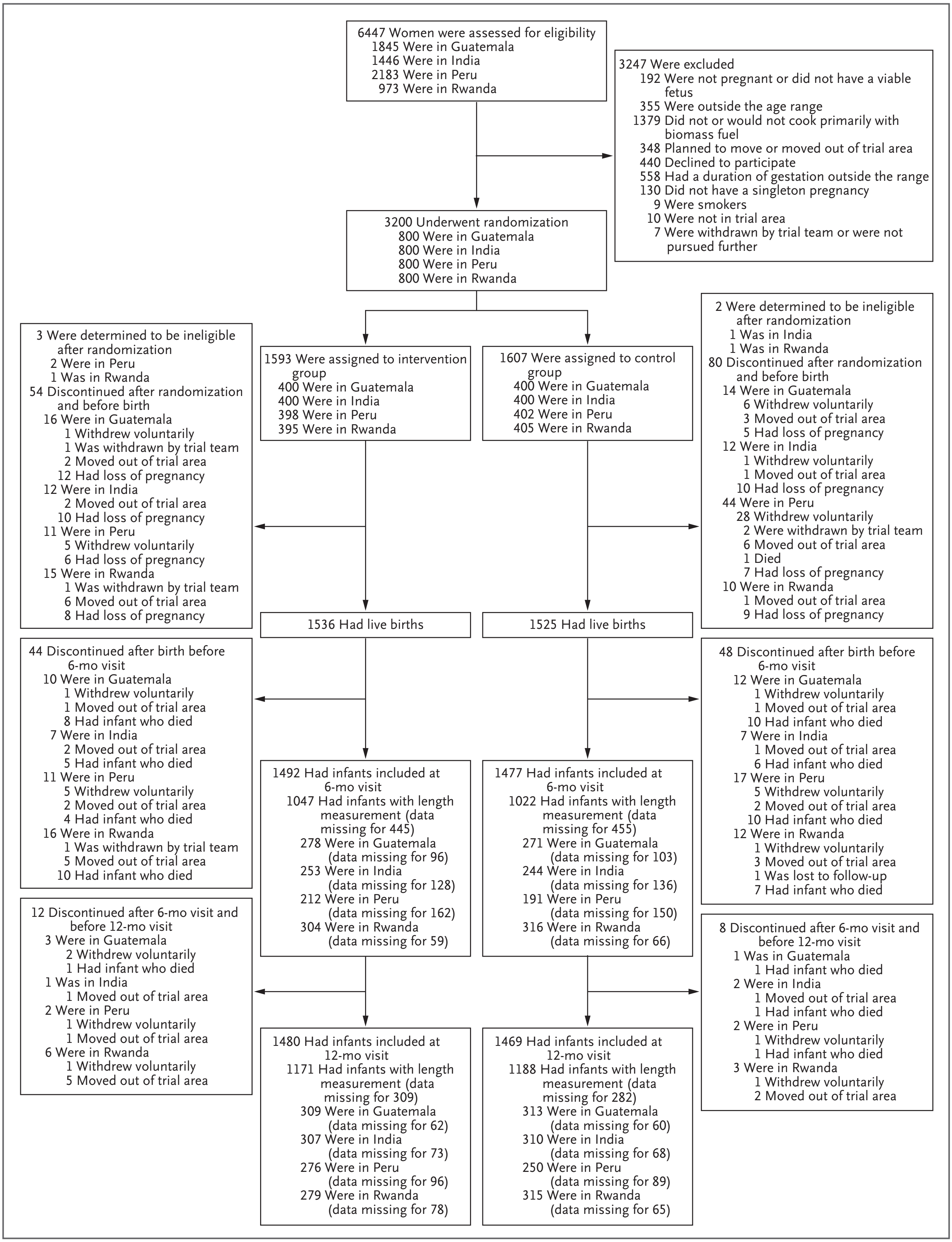
6447 Women were assessed for eligibility
1845 Were in Guatemala
1446 Were in India
2183 Were in Peru
973 Were in Rwanda
3247 Were excluded
192 Were not pregnant or did not have a viable fetus
355 Were outside the age range
1379 Did not or would not cook primarily with biomass fuel
348 Planned to move or moved out of trial area
440 Declined to participate
558 Had a duration of gestation outside the range
130 Did not have a singleton pregnancy
9 Were smokers
10 Were not in trial area
7 Were withdrawn by trial team or were not pursued further
3200 Underwent randomization
800 Were in Guatemala
800 Were in India
800 Were in Peru
800 Were in Rwanda
1593 Were assigned to intervention group
400 Were in Guatemala
400 Were in India
398 Were in Peru
395 Were in Rwanda
1607 Were assigned to control group
400 Were in Guatemala
400 Were in India
402 Were in Peru
405 Were in Rwanda
3 Were determined to be ineligible after randomization
2 Were in Peru
1 Was in Rwanda
54 Discontinued after randomization and before birth
16 Were in Guatemala
1 Withdrew voluntarily
1 Was withdrawn by trial team
2 Moved out of trial area
12 Had loss of pregnancy
12 Were in India
2 Moved out of trial area
10 Had loss of pregnancy
11 Were in Peru
5 Withdrew voluntarily
6 Had loss of pregnancy
15 Were in Rwanda
1 Was withdrawn by trial team
6 Moved out of trial area
8 Had loss of pregnancy
2 Were determined to be ineligible after randomization
1 Was in India
1 Was in Rwanda
80 Discontinued after randomization and before birth
14 Were in Guatemala
6 Withdrew voluntarily
3 Moved out of trial area
5 Had loss of pregnancy
12 Were in India
1 Withdrew voluntarily
1 Moved out of trial area
10 Had loss of pregnancy
44 Were in Peru
28 Withdrew voluntarily
2 Were withdrawn by trial team
6 Moved out of trial area
1 Died
7 Had loss of pregnancy
10 Were in Rwanda
1 Moved out of trial area
9 Had loss of pregnancy
1536 Had live births
1525 Had live births
44 Discontinued after birth before 6-mo visit
10 Were in Guatemala
1 Withdrew voluntarily
1 Moved out of trial area
8 Had infant who died
7 Were in India
2 Moved out of trial area
5 Had infant who died
11 Were in Peru
5 Withdrew voluntarily
2 Moved out of trial area
4 Had infant who died
16 Were in Rwanda
1 Was withdrawn by trial team
5 Moved out of trial area
10 Had infant who died
48 Discontinued after birth before 6-mo visit
12 Were in Guatemala
1 Withdrew voluntarily
1 Moved out of trial area
10 Had infant who died
7 Were in India
1 Moved out of trial area
6 Had infant who died
17 Were in Peru
5 Withdrew voluntarily
2 Moved out of trial area
10 Had infant who died
12 Were in Rwanda
1 Withdrew voluntarily
3 Moved out of trial area
1 Was lost to follow-up
7 Had infant who died
1492 Had infants included at 6-mo visit
1047 Had infants with length measurement (data missing for 445)
278 Were in Guatemala (data missing for 96)
253 Were in India (data missing for 128)
212 Were in Peru (data missing for 162)
304 Were in Rwanda (data missing for 59)
1477 Had infants included at 6-mo visit
1022 Had infants with length measurement (data missing for 455)
271 Were in Guatemala (data missing for 103)
244 Were in India (data missing for 136)
191 Were in Peru (data missing for 150)
316 Were in Rwanda (data missing for 66)
12 Discontinued after 6-mo visit and before 12-mo visit
3 Were in Guatemala
2 Withdrew voluntarily
1 Had infant who died
1 Was in India
1 Moved out of trial area
2 Were in Peru
1 Withdrew voluntarily
1 Moved out of trial area
6 Were in Rwanda
1 Withdrew voluntarily
5 Moved out of trial area
8 Discontinued after 6-mo visit and before 12-mo visit
1 Was in Guatemala
1 Had infant who died
2 Were in India
1 Moved out of trial area
1 Had infant who died
2 Were in Peru
1 Withdrew voluntarily
1 Had infant who died
3 Were in Rwanda
1 Withdrew voluntarily
2 Moved out of trial area
1480 Had infants included at 12-mo visit
1171 Had infants with length measurement (data missing for 309)
309 Were in Guatemala (data missing for 62)
307 Were in India (data missing for 73)
276 Were in Peru (data missing for 96)
279 Were in Rwanda (data missing for 78)
1469 Had infants included at 12-mo visit
1188 Had infants with length measurement (data missing for 282)
313 Were in Guatemala (data missing for 60)
310 Were in India (data missing for 68)
250 Were in Peru (data missing for 89)
315 Were in Rwanda (data missing for 65)

Figure 1 (facing page). Screening, Randomization, and Follow-up.
Women could have had more than one reason for exclusion (i.e., categories are not mutually exclusive). Data are presented according to country in Table S2.

EFFECTS OF THE INTERVENTION ON THE PRIMARY AND SECONDARY OUTCOMES

At 12 months of age, 27.4% of the infants born to women in the intervention group and 25.2% of the infants born to women in the control group were stunted (relative risk, 1.10; 98.75% confidence interval [CI], 0.94 to 1.29; P=0.12) (Table 3). The results were similar when the intention-to-treat analysis was adjusted for maternal height, maternal age, infant sex, socioeconomic status index, and food security (relative risk, 1.11; 98.75% CI, 0.95 to 1.31).

There was no appreciable difference in the mean length-for-age z scores at 12 months of age between the infants born to women in the intervention group and those born to women in the control group (mean difference, −0.03; 95% CI, −0.11 to 0.05) (Table 3). The percentage of infants with severe stunting at 12 months of age was 8.1% in the intervention group and 6.1% in the control group (relative risk, 1.36; 95% CI, 1.02 to 1.82) (Table 3). The percentage of infants with stunting at 6 months did not differ appreciably between the trial groups (relative risk, 1.01; 95% CI, 0.86 to 1.19) (Table 3). The sensitivity analysis, in which a model for repeated measurements of stunting at 3, 6, 9, and 12 months of age was used, included data from 3026 infants (98.9% of the live births); the results in the intervention group were similar to those in the control group (relative risk, 1.05; 95% CI, 0.94 to 1.18). In the subgroup analyses of the primary and secondary outcomes, no subgroup appeared to benefit from the intervention more than others (Fig. 2 and Figs. S2, S3, and S4).

Three infants (0.2%) born to women in the intervention group and 7 infants (0.5%) born to women in the control group had burns related to stoves. Analyses of participants with missing data are provided in the Supplementary Appendix.

DISCUSSION

In this multicountry, randomized, controlled trial involving women in households in which biomass cookstoves were used at baseline, the provision of an LPG cookstove, continuous fuel delivery, and longitudinal behavioral messaging starting in pregnancy and continuing until infants were 1 year of age did not result in a lower risk of growth stunting at 12 months of age than households in which biomass cookstoves continued to be used. This lack of benefit was observed despite high levels of adherence to the LPG cookstove intervention and evidence that the intervention reduced prenatal and infant exposures to air pollutants. Secondary analyses that focused on stunting at other time points and on severe stunting also did not show a benefit of the intervention.

Associations between exposures to household air pollution and stunting have been reported in observational studies. For example, a review of two studies showed a 27% higher risk of stunting among children younger than 5 years of age who were exposed to household air pollution than among those who were not exposed.[7] A meta-analysis of 11 studies showed a 19% higher risk of stunting among children younger than 5 years of age who were exposed to household air pollution than among those who were not exposed.[37] In contrast, the results of the current report and the results of the Ghana Randomized Air Pollution and Health Study (in which LPG stoves and improved biomass stoves were compared with open-fire stoves)[38] did not support reductions in childhood stunting despite evidence of reduced household air pollution. Our recently reported analysis of the intervention on birth weight,[20] as well as our analysis of the intervention on severe infant pneumonia (reported in another article in this issue of the *Journal*),[39] in the HAPIN trial also failed to show a protective effect.

We propose several possible explanations for the lack of an observed effect of the intervention on stunting. First, our intervention may have needed to begin earlier during pregnancy or before conception in order to be effective. Second, our intervention, which used LPG, may not have been clean enough. Despite substantial reductions in personal exposures to fine particulate matter in the intervention group, the measured exposures were still higher than the value recommended by the WHO annual guidelines (5 μg per cubic meter).[40] Other pollutants resulting from the combustion of LPG, such as nitrogen dioxide, may also be present when unvented stoves are used.

Table 1. Baseline Characteristics of the Infants Who Were Included in or Excluded from the Primary-Outcome Analysis.*

Characteristic	Infants Included in Analysis		Infants Excluded from Analysis	
	Intervention (N=1171)	Control (N=1186)	Intervention (N=365)	Control (N=339)
Demographic data				
Maternal age — yr	25.4±4.4	25.5±4.5	25.2±4.4	25.3±4.7
Maternal height — cm	152.2±6.4	152.3±5.9	152.5±5.7	151.5±6.6
Male sex — no. (%)	608 (51.9)	605 (51.0)	192 (52.6)	182 (53.7)
Household socioeconomic status indicators				
Bank account — no. (%)	508 (43.4)	466 (39.3)	169 (46.3)	141 (41.6)
Television — no. (%)	586 (50.0)	582 (49.1)	167 (45.8)	157 (46.3)
Radio — no. (%)	528 (45.1)	491 (41.4)	183 (50.1)	179 (52.8)
Cellular telephone — no. (%)	1017 (86.8)	1016 (85.7)	325 (89.0)	303 (89.4)
Maternal education — yr	8.2±3.8	7.9±3.6	8.3±3.7	8.3±3.5
No. of persons living in the house	4.3±2.0	4.2±2.0	4.2±2.1	4.4±2.0
Socioeconomic status index†	0.1±1.0	−0.1±1.1	0.0±1.0	−0.1±1.0
Pregnancy factors				
Gestational age — wk	15.4±3.1	15.1±3.2	15.9±3.1	15.8±3.0
Nulliparous — no. (%)	470 (40.1)	421 (35.5)	147 (40.3)	129 (38.1)
Hypertension during pregnancy — no. (%)	22 (1.9)	24 (2.0)	3 (0.8)	5 (1.5)
Preterm birth — no. (%)	60 (5.1)	58 (4.9)	30 (8.2)	25 (7.4)
Minimum dietary diversity score — no. (%)‡				
<4, Low diversity	653 (55.8)	681 (57.4)	200 (54.8)	190 (56.0)
4 or 5, Medium diversity	364 (31.1)	393 (33.1)	119 (32.6)	108 (31.9)
>5, High diversity	154 (13.2)	111 (9.4)	46 (12.6)	41 (12.1)
Household food insecurity score — no. (%)§				
0, Food secure	697 (59.5)	662 (55.8)	207 (56.7)	158 (46.6)
1–3, Mild insecurity	309 (26.4)	313 (26.4)	94 (25.8)	111 (32.7)
4–8, Moderate or severe insecurity	147 (12.6)	193 (16.3)	61 (16.7)	66 (19.5)
Smoking in the household — no. (%)	115 (9.8)	138 (11.6)	31 (8.5)	36 (10.6)
Exclusive breast-feeding through 6 mo of age — no. (%)	558 (47.7)	602 (50.8)	144 (39.5)	145 (42.8)

* Plus–minus values are means ±SD. This table shows the baseline characteristics of infants born to women in the intervention or control group according to whether the infants were included in or excluded from the analysis of the primary outcome, stunting at 12 months of age. Infants were excluded from the primary-outcome analysis if their length-for-age z scores were either missing or considered to be erroneous. In total, 2357 infants were included in the analysis, and 704 were excluded from the analysis.

† Scores range from −0.22 to 0.21, with higher scores indicating a higher socioeconomic status.

‡ Minimum dietary diversity during the previous 30 days was assessed with the use of an adapted version of the Food and Agriculture Organization Minimum Dietary Diversity for Women indicator.[35]

§ Household food insecurity during the previous 30 days was assessed with the use of the Food and Agriculture Organization Food Insecurity Experience Scale.[36]

Table 2. Personal Exposures to Fine Particulate Matter, Black Carbon, and Carbon Monoxide.*

Variable	Intervention		Control	
	value	*no.*	*value*	*no.*
Personal exposure to fine particulate matter — μg/m³				
Prenatal maternal exposure at baseline†	119.5±133.6	1352	111.9±110.9	1352
Prenatal maternal exposure after randomization‡	35.0±37.2	1437	103.3±97.9	1409
Postnatal infant exposure§	37.9±97.4	848	109.2±122.7	933
Personal exposure to black carbon — μg/m³				
Prenatal maternal exposure at baseline†	12.6±10.9	1223	12.4±9.2	1211
Prenatal maternal exposure after randomization‡	4.1±5.6	1413	11.2±9.3	1376
Personal exposure to carbon monoxide — ppm				
Prenatal maternal exposure at baseline†	2.7±4.5	1384	2.3±4.0	1375
Prenatal maternal exposure after randomization‡	0.7±1.2	1450	2.2±3.6	1430
Postnatal infant exposure§	0.9±2.0	965	2.6±4.1	916

* Plus–minus values are means ±SD. Personal exposures to fine particulate matter, black carbon, and carbon monoxide were measured over a period of 24 hours at baseline and after randomization. The abbreviation ppm denotes parts per million.
† These exposures were measured at enrollment in pregnant women before randomization.
‡ These values are the means of exposures measured during the first and second visits during pregnancy by means of a direct method (i.e., women wore the monitors).
§ These values are the means of exposures measured when infants were 3, 6, and 12 months of age by an indirect method (i.e., infants wore a beacon emitter).

Table 3. Primary and Secondary Outcomes.*

Outcome	Intervention	Control	Intervention Effect (98.75% CI or 95% CI)†
Primary outcome			
Stunting at 12 mo of age — no./total no. (%)	321/1171 (27.4)	299/1186 (25.2)	1.10 (0.94 to 1.29)
Secondary outcomes			
Length-for-age z score at 12 mo of age‡	−1.32±1.17	−1.30±1.10	−0.03 (−0.11 to 0.05)
Severe stunting at 12 mo of age — no./total no. (%)§	95/1171 (8.1)	72/1186 (6.1)	1.36 (1.02 to 1.82)
Stunting at 6 mo of age — no./total no. (%)	219/1046 (20.9)	211/1021 (20.7)	1.01 (0.86 to 1.19)

* Plus–minus values are means ±SD.
† Relative risks are shown for the dichotomous outcomes, and mean differences are shown for the continuous outcomes. A 98.75% confidence interval was used for the primary outcome, and a 95% confidence interval was used for the secondary outcomes. The 95% confidence intervals for the secondary outcomes and other measurements were not adjusted for multiplicity and should not be used in place of hypothesis testing.
‡ This analysis included 1171 infants born to women in the intervention group and 1186 infants born to women in the control group.
§ Severe stunting was defined as a length-for-age z score that was more than three standard deviations below the median of the World Health Organization Multicentre Growth Reference Study standard for a given age and sex.

For example, in a previous randomized, controlled trial in which unvented LPG stoves were compared with biomass stoves in Peru, kitchen concentrations of nitrogen dioxide, as well as personal exposures to nitrogen dioxide, were found to be higher on average than those recommended by the WHO 2021 annual air quality guidelines, although the values were lower among participants in the intervention group than among those in the control group, in which biomass stoves were used.[40,41] In future studies, evaluation of LPG stoves with ventilation hoods should be consid-

Subgroup	Intervention	Control	Relative Risk (95% CI)
	no. with stunting/total no. (%)		
Overall	321/1171 (27.4)	299/1186 (25.2)	1.10 (0.94–1.29)
Country			
Guatemala	155/309 (50.2)	136/311 (43.7)	1.15 (0.97–1.36)
India	97/307 (31.6)	93/310 (30.0)	1.05 (0.83–1.33)
Peru	22/276 (8.0)	17/250 (6.8)	1.17 (0.64–2.16)
Rwanda	47/279 (16.8)	53/315 (16.8)	1.00 (0.70–1.43)
Maternal height			
<151 cm	206/495 (41.6)	179/485 (36.9)	1.16 (0.99–1.34)
151–154 cm	71/307 (23.1)	71/331 (21.5)	1.10 (0.84–1.45)
≥155 cm	44/364 (12.1)	49/369 (13.3)	0.90 (0.62–1.31)
Infant sex			
Male	185/608 (30.4)	182/605 (30.1)	1.05 (0.90–1.22)
Female	136/563 (24.2)	117/581 (20.1)	1.19 (0.98–1.46)
Socioeconomic status index			
<Median	190/557 (34.1)	175/622 (28.1)	1.18 (1.01–1.38)
≥Median	131/614 (21.3)	124/564 (22.0)	1.00 (0.82–1.23)
Food insecurity			
<Median	196/697 (28.1)	158/662 (23.9)	1.20 (1.02–1.42)
≥Median	120/456 (26.3)	135/506 (26.7)	0.99 (0.82–1.20)
Gestation at time of intervention			
<18 wk	157/592 (26.5)	299/1186 (25.2)	1.05 (0.90–1.22)
≥18 wk	164/579 (28.3)	299/1186 (25.2)	1.16 (1.00–1.35)
Small size for gestational age			
<−1.28 z scores	172/375 (45.9)	168/401 (41.9)	1.10 (0.94–1.28)
≥−1.28 z scores	144/786 (18.3)	122/766 (15.9)	1.15 (0.94–1.42)
Exclusive breast-feeding			
No	184/566 (32.5)	149/531 (28.1)	1.15 (0.97–1.36)
Yes	129/558 (23.1)	142/602 (23.6)	1.02 (0.84–1.24)

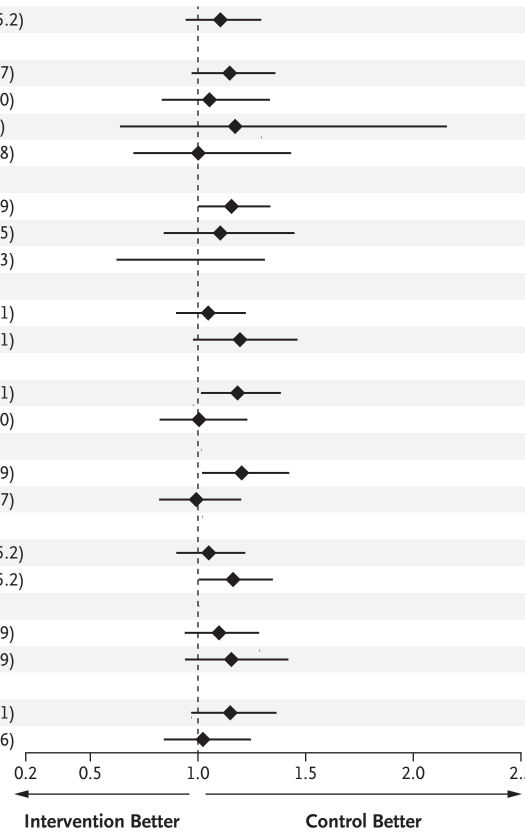

Figure 2. Subgroup Analyses of the Effects of the Intervention on the Risk of Stunting at 12 Months of Age.

Shown is the analysis of the effects of the intervention on the risk of stunting at 12 months of age in the overall sample and in prespecified subgroups. Household food insecurity during the previous 30 days was assessed with the use of the Food and Agriculture Organization Food Insecurity Experience Scale.[36] Gestation at the time of intervention refers to the time at which the women in the intervention group received an LPG cookstove. Exclusive breast-feeding refers to the first 6 months of life. We defined stunting as a length-for-age z score that was more than two standard deviations below the median of the World Health Organization Multicentre Growth Reference Study standard for a given age and sex. We estimated the relative risk using a log-binomial regression model for stunting at 12 months of age as a function of the trial-group assignment and randomization strata. The number of stunted infants with length measurements and the total number of infants with length measurements who were born to women in each trial group are presented. A 98.75% confidence interval was used for the total sample included in the analysis (primary outcome), and 95% confidence intervals were used for each subgroup. The 95% confidence intervals for the subgroup analyses were not adjusted for multiplicity and should not be used in place of hypothesis testing.

ered as a strategy to reduce exposures to pollutants still present in LPG stove emissions.

Another possible explanation for the lack of an observed effect on stunting is related to the fact that child growth is a complex and multifactorial process. Household air pollution may have only minor effects on stunting as compared with other factors such as nutritional status. It is possible that household air pollution is not causally related to stunting but rather is associated with low socioeconomic status, poor nutrition and sanitation, coexisting illnesses, and other effects of poverty that themselves lead to stunting.

Although adherence to the intervention was extremely high across four low- and middle-income countries, and personal exposures to fine particulate matter were lowered to levels near or below the WHO Annual Interim Target 1 recommendation of 35 μg per cubic meter[42] among infants born to women in the intervention group, our trial had limitations. First, we were unable to measure linear growth in approximately 20% of the infants because of challenges during the Covid-19 pandemic. However, a sensitivity analysis, in which a model for repeated measurements of stunting between birth and 12 months of age was used, also did not show a benefit of the intervention. Second, we were unable to measure direct personal exposures to household air pollutants in the infants and thus used indirect methods instead. As a result, our estimates of exposure reduction in the infants may not be entirely accurate; however, our formative research indicated a high degree of agreement between direct and indirect measures.[27]

Whereas LPG has been considered to be a near-term solution for energy needs in low- and middle-income countries, an LPG cookstove intervention starting in pregnancy and continuing until infants were 1 year of age did not reduce stunting at 1 year despite high adherence and large reductions in household air pollution. These findings do not support the use of unventilated LPG cookstoves to achieve reductions in childhood stunting.

The views expressed here are those of the authors and do not necessarily represent the official position of the National Institutes of Health or the Department of Health and Human Services.

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APPENDIX

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REFERENCES

1. Bennitt FB, Wozniak SS, Causey K, Burkart K, Brauer M, GBD Risk Factor Collaborators. Estimating disease burden attributable to household air pollution: new methods within the Global Burden of Disease study. Lancet Glob Health 2021;9:S18 (https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00126-1/fulltext).

2. Stoner O, Lewis J, Martínez IL, Gumy S, Economou T, Adair-Rohani H. Household cooking fuel estimates at global and country level for 1990 to 2030. Nat Commun 2021;12:5793.

3. The Institute for Health Metrics and Evaluation. GBD compare. Visualization hub (http://vizhub.healthdata.org/gbd-compare).

4. Sinharoy SS, Clasen T, Martorell R. Air pollution and stunting: a missing link? Lancet Glob Health 2020;8(4):e472-e475.

5. Bobak M, Richards M, Wadsworth M. Relation between children's height and outdoor air pollution from coal-burning sources in the British 1946 birth cohort. Int Arch Occup Environ Health 2004;77:383-6.

6. Bruce NG, Dherani MK, Das JK, et al. Control of household air pollution for

child survival: estimates for intervention impacts. BMC Public Health 2013;13: Suppl 3:S8.
7. Spears D, Dey S, Chowdhury S, Scovronick N, Vyas S, Apte J. The association of early-life exposure to ambient $PM_{2.5}$ and later-childhood height-for-age in India: an observational study. Environ Health 2019; 18:62.
8. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. Geneva: World Health Organization, 2006.
9. MAL-ED Network Investigators. Childhood stunting in relation to the pre- and postnatal environment during the first 2 years of life: the MAL-ED longitudinal birth cohort study. PLoS Med 2017;14(10): e1002408.
10. Victora CG, Christian P, Vidaletti LP, Gatica-Domínguez G, Menon P, Black RE. Revisiting maternal and child undernutrition in low-income and middle-income countries: variable progress towards an unfinished agenda. Lancet 2021;397:1388-99.
11. Vaivada T, Akseer N, Akseer S, Somaskandan A, Stefopulos M, Bhutta ZA. Stunting in childhood: an overview of global burden, trends, determinants, and drivers of decline. Am J Clin Nutr 2020; 112:Suppl 2:777S-791S.
12. Keats EC, Das JK, Salam RA, et al. Effective interventions to address maternal and child malnutrition: an update of the evidence. Lancet Child Adolesc Health 2021; 5:367-84.
13. United Nations Childrens Fund (UNICEF), World Health Organization, World Bank Group. Child malnutrition estimates: key findings of the 2020 Joint Child Malnutrition Estimates: UNICEF regions. 2020 (https://data.unicef.org/wp-content/uploads/2020/03/JME-2020-UNICEF-regions-new.pdf).
14. Hoddinott J, Maluccio JA, Behrman JR, Flores R, Martorell R. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. Lancet 2008;371:411-6.
15. Stein AD, Wang M, Martorell R, et al. Growth patterns in early childhood and final attained stature: data from five birth cohorts from low- and middle-income countries. Am J Hum Biol 2010;22:353-9.
16. Dewey KG, Begum K. Long-term consequences of stunting in early life. Matern Child Nutr 2011;7:Suppl 3:5-18.
17. Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013;382:427-51.
18. Akseer N, Tasic H, Nnachebe Onah M, et al. Economic costs of childhood stunting to the private sector in low- and middle-income countries. EClinicalMedicine 2022;45:101320.
19. Bhutta ZA, Akseer N, Keats EC, et al. How countries can reduce child stunting at scale: lessons from exemplar countries. Am J Clin Nutr 2020;112:Suppl 2:894S-904S.
20. Clasen TF, Chang HH, Thompson LM, et al. Liquefied petroleum gas or biomass for cooking and effects on birth weight. N Engl J Med 2022;387:1735-46.
21. Clasen T, Checkley W, Peel JL, et al. Design and rationale of the HAPIN study: a multicountry randomized controlled trial to assess the effect of liquefied petroleum gas stove and continuous fuel distribution. Environ Health Perspect 2020;128: 47008.
22. Quinn AK, Williams K, Thompson LM, et al. Compensating control participants when the intervention is of significant value: experience in Guatemala, India, Peru and Rwanda. BMJ Glob Health 2019; 4(4):e001567.
23. Quinn AK, Williams KN, Thompson LM, et al. Fidelity and adherence to a liquefied petroleum gas stove and fuel intervention during gestation: the multi-country Household Air Pollution Intervention Network (HAPIN) randomized controlled trial. Int J Environ Res Public Health 2021; 18:12592.
24. Williams KN, Thompson LM, Sakas Z, et al. Designing a comprehensive behaviour change intervention to promote and monitor exclusive use of liquefied petroleum gas stoves for the Household Air Pollution Intervention Network (HAPIN) trial. BMJ Open 2020;10(9):e037761.
25. Williams KN, Quinn A, North H, et al. Fidelity and adherence to a liquefied petroleum gas stove and fuel intervention: the multi-country Household Air Pollution Intervention Network (HAPIN) trial. Environ Int 2023;179:108160.
26. Johnson MA, Steenland K, Piedrahita R, et al. Air pollutant exposure and stove use assessment methods for the Household Air Pollution Intervention Network (HAPIN) trial. Environ Health Perspect 2020;128(4):47009.
27. Liao J, McCracken JP, Piedrahita R, et al. The use of bluetooth low energy Beacon systems to estimate indirect personal exposure to household air pollution. J Expo Sci Environ Epidemiol 2020;30:990-1000.
28. Johnson M, Pillarisetti A, Piedrahita R, et al. Exposure contrasts of pregnant women during the Household Air Pollution Intervention Network randomized controlled trial. Environ Health Perspect 2022;130(9):97005.
29. Pillarisetti A, Ye W, Balakrishnan K, et al. Post-birth exposure contrasts for children during the Household Air Pollution Intervention Network randomized controlled trial. July 6, 2023 (https://www.medrxiv.org/content/10.1101/2023.07.04.23292226v1). preprint.
30. Lohman TG, Roche AF, Martorell R, eds. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books, 1988.
31. de Onis M, Onyango AW, Van den Broeck J, Chumlea WC, Martorell R. Measurement and standardization protocols for anthropometry used in the construction of a new international growth reference. Food Nutr Bull 2004;25:Suppl:S27-S36.
32. Simkovich SM, Thompson LM, Clark ML, et al. A risk assessment tool for resumption of research activities during the COVID-19 pandemic for field trials in low resource settings. BMC Med Res Methodol 2021;21:68.
33. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004;159:702-6.
34. R Core Team. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing, 2021.
35. Minimum dietary diversity for women: a guide for measurement. Rome: Food and Agriculture Organization, 2016:82.
36. Swindale A, Bilinsky P. Development of a universally applicable household food insecurity measurement tool: process, current status, and outstanding issues. J Nutr 2006;136:1449S-1452S.
37. Pun VC, Dowling R, Mehta S. Ambient and household air pollution on early-life determinants of stunting — a systematic review and meta-analysis. Environ Sci Pollut Res Int 2021;28:26404-12.
38. Boamah-Kaali E, Jack DW, Ae-Ngibise KA, et al. Prenatal and postnatal household air pollution exposure and infant growth trajectories: evidence from a rural Ghanaian pregnancy cohort. Environ Health Perspect 2021;129(11):117009.
39. McCollum ED, McCracken JP, Kirby MA, et al. Liquefied petroleum gas or biomass cooking and severe infant pneumonia. N Engl J Med 2023;390:32-43.
40. WHO ambient air quality database, 2021 update. Geneva: World Health Organization, 2021 (https://cdn.who.int/media/docs/default-source/air-pollution-documents/air-quality-and-health/who-air-quality-database-2021_final.pdf).
41. Kephart JL, Fandiño-Del-Rio M, Williams KN, et al. Nitrogen dioxide exposures from LPG stoves in a cleaner-cooking intervention trial. Environ Int 2021;146: 106196.
42. WHO indoor air quality guidelines: household fuel combustion. Geneva: World Health Organization, 2014 (https://www.ncbi.nlm.nih.gov/books/NBK264291/).