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Risk of Low Birth Weight and Stillbirth Associated With Indoor Air Pollution From Solid Fuel Use in Developing Countries

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Exposure to indoor air pollution from solid fuel use (IAP) has been linked to approximately 1.5 million annual deaths (World Health Organization (http://www.who.int/indoorair/publications/fuelforlife/en/index.html)) due to acute lower respiratory infections in children <5 years of age and chronic obstructive lung disease and lung cancer in adults. Emerging evidence suggests that IAP increases the risk of other conditions, including adverse pregnancy outcomes. To establish the relation of IAP with birth weight and stillbirth, systematic reviews with meta-analyses were conducted. Studies reporting outcomes of mean birth weight, percentage of low birth weight (LBW; <2,500 g), and/or stillbirth and assessing IAP were identified. Five LBW studies (of 982) and 3 stillbirth studies (of 171) met inclusion criteria for the reviews. Fixed-effect meta-analyses ($I^2 = 0\%$) found that IAP was associated with increased risk of percentage LBW (odds ratio = 1.38, 95% confidence interval: 1.25, 1.52) and stillbirth (odds ratio = 1.51, 95% confidence interval: 1.23, 1.85) and reduced mean birth weight (−95.6 g, 95% confidence interval: −68.5, −124.7). Evidence from secondhand smoke, ambient air pollution, and animal studies—and suggested plausible mechanisms—substantiate these associations. Because a majority of pregnant women in developing countries, where rates of LBW and stillbirth are high, are heavily exposed to IAP, increased relative risk translates into substantial population attributable risks of 21% (LBW) and 26% (stillbirth).

air pollution, indoor; fetal growth retardation; infant, low birth weight; meta-analysis; stillbirth

Abbreviations: CI, confidence interval; IAP, indoor air pollution from solid fuel use; LBW, low birth weight; OR, odds ratio; PM_{10}, particulate matter ≤10 μm in diameter.

BACKGROUND

Approximately 3 billion people worldwide use solid fuels (including biomass and coal) for their household energy needs (1). The World Health Organization has estimated that indoor air pollution from solid fuel use (IAP) accounted for 2.7% of the global burden of disease in 2000 (2), with 1.5 million excess deaths in 2002 (3). Such estimates are based on the relation between IAP and acute lower respiratory infections (children <5 years of age) and chronic obstructive lung disease (adults) and lung cancer (adults, coal only). However, emerging is evidence that IAP also increases the risk of other health conditions, including adverse pregnancy outcomes (4). Pregnancy outcomes including fetal mortality, low birth weight (LBW), preterm birth, small for gestational age, intrauterine growth retardation, and birth defects have been linked to exposure to secondhand smoke (5) and ambient air pollution (6, 7) in recent systematic reviews. Adverse pregnancy outcomes were not included in the 2000 burden of disease estimates for IAP because of the paucity of epidemiologic evidence (2–4).

It is therefore timely and important to review the available evidence. The goals were to 1) synthesize the extent and quality of evidence regarding the relation between IAP and adverse pregnancy outcomes, 2) quantify these associations by meta-analyses, and 3) identify future research needs.

METHODS

Two systematic reviews were carried out to summarize the relation between IAP and 1) LBW and 2) stillbirths. Other adverse pregnancy outcomes (intrauterine growth

Table 1. Electronic Databases Searched for the Systematic Reviews[a]

MEDLINE[b]
EMBASE[c]
Cochrane Controlled Trials Register[d]
Cumulative Index to Nursing and Allied Health Literature[e]
Latin American and Caribbean Health Sciences Information System[f]
System for Information on Grey Literature in Europe[g]
Index to Conference Proceedings[h]
PASCAL (conference proceedings, dissertations, patents and reports)[i]

[a] All databases were searched from 1966 to 2008. Foreign language abstracts from Europe and the Americas were translated.
[b] National Library of Medicine, Bethesda, Maryland.
[c] Elsevier B. V., Amsterdam, the Netherlands.
[d] The Cochrane Collaboration Secretariat, Oxford, United Kingdom.
[e] EBSCO Publishing, Glendale, California.
[f] BIREME, São Paulo, Brazil.
[g] European Association for Grey Literature Exploitation, The British Library, London, United Kingdom.
[h] The British Library, London, United Kingdom.
[i] Institute of Scientific and Technical Information, Nancy, France.

retardation, small for gestational age, preterm births) were not used as primary outcomes because of the lack of available evidence, although, for studies that provided this information, estimates have been presented separately for term and preterm LBW. Inclusion criteria were studies of humans that reported 1) percentage of LBW or mean birth weight and/or stillbirth or perinatal/early neonatal deaths and 2) assessment of IAP exposure. All epidemiologic study designs were eligible.

Table 1 shows the electronic databases searched. Search terms that were used are detailed in Table 2. Information was also obtained from 1) a World Health Organization report including unpublished data describing the relation between IAP and LBW and stillbirth based on an expert symposium (8) and 2) contact with investigators in the field of IAP and child health.

The process of selecting studies for data extraction is shown in Figure 1. Two reviewers (D. P. and N. B.) independently conducted literature searches and rejected studies not meeting inclusion criteria after reviewing titles, abstracts, and, finally, the full text.

Methodological quality was assessed by using design-specific forms developed from the Newcastle-Ottawa scale (9) to meet the needs of this evidence base, awarding a star rating for each study (this approach has been successfully used in other systematic reviews of IAP (10)). Quality criteria focused on any major bias/error and adequacy of adjustment for confounding (Table 3).

Data extraction and quality assessment were carried out independently by two reviewers (D. P. and N. B.). Disagreement was resolved through discussion.

Three meta-analyses provided pooled estimates of the effect of IAP on 1) LBW (<2,500 g), 2) mean birth weight in the high and low exposure groups, and 3) stillbirth (≥24 weeks of gestation). An additional meta-analysis was conducted by separating term from preterm births (where estimates were available). Study heterogeneity was assessed by using Cochrane's Q and I^2 statistics (moderate heterogeneity indicated by a value of >50%). Fixed-effect meta-analyses were used in the absence of statistical heterogeneity. To assess the effect of study quality on pooled effect estimates, sensitivity analyses were conducted by excluding studies with a star rating of less than 60% for respective study designs (a value representing a ''good'' score on more than half of the methodological quality items). To test for publication bias, funnel plots were visually inspected, and statistical tests for asymmetry (Egger's and Begg's tests using a conservative P value of <0.1) were used.

Table 2. Search Terms Used to Identify Relevant Studies for the Reviews

IAP and Low Birth Weight	IAP and Stillbirth
Outcome	Outcome
1. "birth weight"	1. "still*birth"
2. "pre*term"	2. "perinatal mortality"
3. "premature"	3. "perinatal death"
4. "small for dates"	4. "1 OR 2 OR 3"
5. "growth retardation"	
6. "lbw"	
7. "1 OR 2 OR 3 OR 4 OR 5 OR 6"	
Exposure*	
8. "biomass"	
9. "wood smoke"	
10. "indoor air"	
11. "iap"	
12. "particulate*"	
13. "solid fuel"	
14. "dung"	
15. "cooking fuel"	
16. "heating fuel"	
17. "coal"	
18. "chuj*"	
19. "8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18"	
Combined terms	Combined terms
20. "7 AND 19"	5. "4 AND 19"

Abbreviation: IAP, indoor air pollution from solid fuel use.

RESULTS

Figure 1 shows the number of articles/studies at each stage of the search and selection process. The literature searches identified 982 papers for birth weight and 171 papers for stillbirth. Of these, 978 and 169, respectively, were excluded because they were not relevant after screening titles (953 and 159), abstracts (22 and 9), and the full paper (3 and 1); reasons for exclusion were that they were studies of animals, ambient air pollution, and outcomes other than those concerning pregnancy. Four papers were

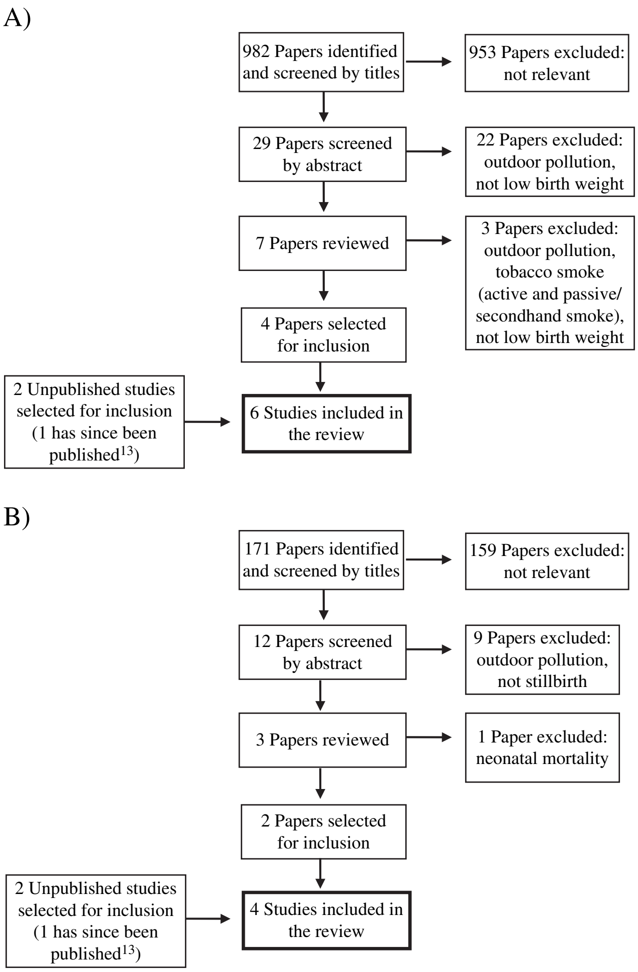

Figure 1. Flowchart of the process of selecting studies for data extraction. A) Indoor air pollution and birth weight; B) indoor air pollution and stillbirth.

appropriate for birth weight and 2 for stillbirth/perinatal mortality. In addition, 3 unpublished studies were included: 1 on birth weight (11), 1 on stillbirth (12), and 1 on both (13). Thus, 10 studies (6 for birth weight and 4 for stillbirth) were selected for data extraction and quality appraisal.

Table 3. Confounding Variables Looked for in Assessing Methodological Quality

IAP and Birth Weight	IAP and Stillbirth
Active smoking	Active smoking
Passive smoking	Passive smoking
Maternal age	Obstetric care
Parity	Maternal age
Socioeconomic status	Parity
Maternal malnutrition	Socioeconomic status
Vitamin supplementation	

Abbreviation: IAP, indoor air pollution from solid fuel use.

IAP and birth weight

Studies included 2 cross-sectional surveys, 2 cohort studies, 1 case-control study, and 1 randomized controlled trial. Refer to Table 4.

The studies were conducted in 4 countries (Guatemala, India, Zimbabwe, and Pakistan) where a significant proportion of the populations use solid fuel in open fires. The cross-sectional studies (14, 15) and cohort studies (13, 16) considered self-reported use of wood, coal, dung, or straw for IAP exposure compared with cleaner fuels (electricity or gas, although one of the cohort studies used gas and kerosene for comparison (13)). The case-control study (17) assessed self-reported cooking smoke during pregnancy. Only the Guatemalan randomized controlled trial (11), allocating women to either a plancha (wood stove with a chimney) or a traditional open fire, conducted personal IAP measurements. In this trial, 48-hour carbon monoxide exposures, used as a proxy for particulate matter (18), were significantly lower (41%) in pregnant women with a plancha compared with those using open fires.

Birth weights were measured by trained research staff using scales for most studies, the cross-sectional study in Zimbabwe recorded weight from mother's recall for 1,220 (46.7%) births, and the remainder of the information was obtained directly from available health card records (15). Although all observational studies collected information on important confounders, only the cohort studies (13, 16) presented an adjusted multivariable analysis for LBW; the case-control study (17) and cross-sectional surveys (14, 15) reported only univariate data. The intervention study (11) used a randomized design, but results were adjusted for maternal age, primiparity, more than 5 births, socioeconomic status, and passive smoking because of an imbalance in randomization that arose for women who used the intervention stove early in the study. Five studies provided adjusted estimates for IAP and mean birth weight (11, 13–16).

Risk of LBW. Figure 2 shows the forest plot for risk of LBW. Two estimates were provided by the Indian case-control (17) and cohort (13) studies, one for "term" and one for "preterm" LBW (based on small for gestational age estimated from women's last menstrual period). The other studies did not distinguish between term and preterm births.

All studies identified an increased risk of LBW with higher exposure to IAP. The strongest effect, comparing biomass with natural gas, was observed for the cohort study in Pakistan (16) (adjusted odds ratio (OR) = 1.77, 95% confidence interval (CI): 1.09, 2.88). No evidence of statistical heterogeneity was observed ($I^2 = 0\%$; chi^2 (df = 5) = 5.54, $P = 0.59$). Fixed-effect meta-analysis identified a statistically significant pooled odds ratio of 1.38 (95% CI: 1.25, 1.52). The cross-sectional study from Zimbabwe had a quality star rating of less than 60% (15). Sensitivity analysis excluding this study slightly increased the pooled effect estimate (OR = 1.41, 95% CI: 1.27, 1.56).

Although there are few studies ($n = 6$; 8 estimates), there was no visual evidence of funnel plot asymmetry indicating publication bias. This finding was confirmed by Begg's ($P =$ 0.536) and Egger's ($P = 0.781$) tests. A larger pooled effect

(OR = 1.51, 95% CI: 1.25, 1.83) was observed for the 2 studies looking at preterm LBW (13, 17) compared with that of term LBW alone (OR = 1.33, 95% CI: 1.19, 1.50).

Impact on mean birth weight. Five studies provided adjusted estimates of mean birth weight. Fixed-effect meta-analysis (in the absence of statistical heterogeneity: $I^2 = 0\%$) provided a weighted mean difference (lower exposure group mean minus higher exposure group mean) of 96.6 g (95% CI: 68.5, 124.7). Refer to Figure 3. Only 3 studies (13, 14, 16) adjusted for gestational age.

A sensitivity analysis was carried out by excluding mother's recalled birth weight from the Zimbabwe study (15) because of a propensity for overestimation (19). The weighted mean difference was attenuated slightly to 93.1 g (95% CI: 64.6, 121.6). Exclusion of this study from the meta-analysis because of weaker methodological quality had little additional effect on the pooled estimate (weighted mean difference = 92.4 g, 95% CI: 63.6, 121.2).

There was no visual evidence of publication bias from the funnel plot and from statistical tests for funnel plot asymmetry (Begg's test ($P = 0.308$) and Egger's test ($P = 0.479$)).

IAP and stillbirth

Four studies investigated stillbirth: 2 cohort studies in southern Pakistan (12) and India (13), 1 case-control study in India (20), and 1 cross-sectional study in India (21). Refer to Table 5.

Studies classified IAP as self-reported exposure to smoke from cooking (20) or from solid fuel use compared with cleaner fuels (electricity or gas or gas/kerosene) (12, 13, 21). Two studies defined stillbirth as "delivery after 28 weeks in which the fetus was born dead" (13, 21), whereas, for other studies, the definition was less clear: "reproductive loss through stillbirth" (12) and "stillbirths occurring in hospital" (20). Three studies adjusted for important confounding factors and presented adjusted effect estimates (13, 20, 21). The cohort study was adjusted for area of residence (rural vs. urban) only (12).

All studies reported an increased risk of stillbirth in the higher exposure group, with 3 estimates being statistically significant. There was no evidence of statistical heterogeneity between studies ($I^2 = 0\%$; chi^2 (df = 3) = 0.98, $P = 0.81$). Fixed-effect meta-analysis identified a significant pooled effect (OR = 1.51, 95% CI: 1.23, 1.85) (Figure 4). Sensitivity analysis excluding the cohort study (12) with a low star rating slightly attenuated the pooled estimate (OR = 1.45, 95% CI: 1.16, 1.80).

Because of the small number of studies, the funnel plot was difficult to interpret. However, there was no evidence of funnel plot asymmetry when Egger's ($P = 0.644$) and Begg's ($P = 0.989$) tests were used.

DISCUSSION

To our knowledge, this study is the first to carry out systematic reviews and meta-analyses on risk of LBW and stillbirth associated with IAP in developing countries. The strength of the reviews is inevitably limited by the small number of studies and heterogeneity of designs across a range of settings. Despite this limitation, results for individual studies were remarkably consistent, with no evidence of statistical heterogeneity. One explanation could be the presence of substantial residual confounding in the observational studies. However, given the variability regarding degree of adjustment across studies, it is more likely that the findings indicate a real effect.

Another difficulty in interpreting the results relates to variability in exposure assessment and lack of direct exposure measurement. Only 1 study (11) directly measured exposure by using home and personal carbon monoxide monitors, and a cohort study (16) measured particulate and carbon monoxide exposure in a small subsample. However, neither study analyzed these exposure data directly in relation to adverse pregnancy events. When exposure was measured in a consistent way (e.g., solid fuel compared with gas/electricity) (13–16), it is likely that absolute levels differed between settings, as did the relative differences between higher and lower exposure comparison groups. Such variable exposure classification is likely to lead to underestimation of the relation between IAP and adverse pregnancy outcomes. Accurate quantification requires an exposure-response analysis using objectively measured exposure data during all trimesters to identify periods of maximum risk.

A further problem for community studies is the difficulty in obtaining timely (within 24–48 hours) measurements of birth weight when most deliveries occur at home. Unfortunately, among poor populations, where solid fuels constitute the primary cooking fuel, systematic measurement of birth weight is rare. This issue was identified as a particular problem for the Indian cohort study (13), which had a median delay of 28.3 hours before measurement of birth weight, with 18% of babies not being weighed within 72 hours. In addition, assessment of gestational age by specially trained field staff is important for distinguishing small-for-gestational-age babies from preterm babies of normal weight for gestational age. For community studies, the logistics involved in ensuring that trained staff either attend the birth or are informed about new deliveries and can reach the home within 24–48 hours can be very demanding. As a result, the few studies that have been carried out often provide suboptimal data on birth weight. Finally, clearly in these settings, birth weight will be measured for livebirths only. Consequently, babies who die within a short time after birth and who are of LBW will not be recorded, which could lead to underestimation of the true burden of exposure to IAP on reduced birth weight.

Relation between IAP and birth weight

We identified a significantly increased risk of LBW of 38% (OR = 1.38, 95% CI: 1.25, 1.52) from exposure to IAP and an associated reduction in birth weight of 96.6 g (95% CI: 68.5, 124.7). It is possible that this association was underestimated given poor exposure classification. Alternatively, there could also be a degree of residual confounding given the observational epidemiology and the strong linkage between LBW, IAP exposure, and poverty.

Table 4. Summary of Studies on Risk of Low Birth Weight Associated With Solid Fuel Use

First Author, Year (Reference No.); Design	Location	Population/Setting	Exposure	Measurement of Outcome	Adjustment for Confounding	Results for Risk of Low Birth Weight	Results for Mean Birth Weight	Quality
Boy, 2002 (14); cross-sectional survey (6-month recruitment)	Quetzal-tenango province, western Guatemala	Rural. Home births referred by traditional birth attendants or identified by field-worker in larger villages. Included if alive at 72 hours. Hospital singleton births (all births in public regional hospital in the same period).	Interview. 871 cooking with wood or coal, with no chimney; 489 cooking with wood or coal, with a chimney; 357 cooking with electricity or gas.	Trained staff used Salter spring scales (Melbourne, Australia) (to nearest 50 g for home births, 25 g for hospital) to weigh babies, singleton births only. For home births ($n = 572$), majority visited within 72 hours of delivery; hospital births ($n = 1,145$), within 24 hours.	Parity, gestational age <37 weeks, mother's age, floor material (socioeconomic status measure), area of residence, vitamins in the third trimester, mother's calf circumference.	Unadjusted analysis: wood/coal fuel (no chimney): LBW, $n = 173$ (19.9%). Electricity/gas: LBW, $n = 57$ (16%). OR = 1.3, 95% CI: 0.92, 1.83.	Adjusted difference in mean birth weight: 63 g, 95% CI: 0.4, 126	9 stars (82% of the maximum 11 stars for design)
Mavalankar, 1992 (17); case-control study	Ahmedabad, western India	Three government teaching hospitals. 1,317 cases (systematic sample of 20% of surviving LBW infants and all LBW deaths). 1,465 controls (infants >2,500 g surviving until discharge or up to 7 days). Singleton births.	Interview. Reported "exposure to cooking fire smoke" during pregnancy. 30% of mothers of controls exposed.	Study physicians collected data by interview, case note extraction, and anthropometry. Gestational age by last menstrual period and Capurro method. Measurement technique for birth weight not reported.	Maternal education, religion, parity, prior stillbirth, prior child health, gestational age, interpregnancy interval, maternal weight, clinical anemia, antenatal care, blood pressure, sex of baby.	Unadjusted analysis: cases, term ($n = 673$); exposed = 234 (34.8%). Cases, preterm ($n = 644$); exposed = 252 (39.1%). Controls ($n = 1,465$); exposed = 442 (30.2%). OR (term) = 1.23, 95% CI: 1.01, 1.50. OR (preterm[a]) = 1.49, 95% CI: 1.22, 1.82. Adjustment carried out, but estimates for cook smoke not reported so presumed nonsignificant).	Not available	6 stars (60% of the maximum 10 stars for design)
Mishra, 2004 (15); cross-sectional survey	Zimbabwe	Nationally representative 2-stage cluster sample: 3,559 births in the past 5 years, with 2,610 singletons weighed at birth. At time of study, 75% of births in Zimbabwe took place in a health facility and the babies were weighed.	Interview asked about main cooking fuel. Pollution rated as high (fuel is wood, dung, straw) and low (fuel is electricity/gas). Medium-rated fuels (mixed fuels, kerosene, charcoal) were excluded.	Weight recorded from health card if available ($n = 1,390$). Otherwise, weight from mother's recall ($n = 1,220$). Scales to nearest 100 g (more for recalled weights). Gestational age not available.	Sex, birth order of child, mother's age at birth, mother's body mass index, iron supplements during pregnancy; mother's education, religion, household standard of living, region of residence, malaria drug taken during pregnancy. Smoking data not available.	Unadjusted analysis—high pollution: LBW, $n = 132$ (8.6%); low pollution: LBW, $n = 59$ (7.7%). OR = 1.12, 95% CI: 0.80, 1.56.	Adjusted mean differences (low pollution minus high pollution)—subjects with health cards: 120 g, 95% CI: 301, −61; subjects recalling weight: 183 g, 95% CI: 376, −10; all subjects: 175 g, 95% CI: 50, 300.	6 stars (55% of the maximum 11 stars for design)

Siddiqui, 2008 (16); cohort study	Southern Pakistan	Rehri Goth, a coastal fishing village (approximately 50% using wood for cooking/heating). 634 women were followed through pregnancy until birth. Enrolled through child health surveillance program. Singleton births only.	Interview. Wood for cooking ($n = 366$) or natural gas for cooking ($n = 268$). Separate study (unpublished) of 13 homes in Bilal and Rehri Goth reported 7-hour daytime winter levels of 1) $PM_{2.5}$ at 9.7 mg/m^3 (wood) and 0.26 mg/m^3 (gas); and 2) carbon monoxide 12–33.3 ppm (wood) and 0.7–6.0 ppm (gas).	Babies weighed on infant scale (100 g precision) by trained field-workers. 91% measured within 48 hours. Gestational age data available for only 221 infants, not used for analysis.	Propensity score (including separate kitchen, absence of window in kitchen, spouse illiterate, mother illiterate, house construction, income level, sleep/rest during pregnancy, gravidity, body mass index); prenatal examination at hospital.	Unadjusted analysis—wood as fuel: LBW, $n = 83$ (22.7%); gas as fuel: LBW, $n = 40$ (15%). OR = 1.65, 95% CI: 1.09, 2.51. Adjusted analysis: OR = 1.77, 95% CI: 1.09, 2.88.	Adjusted analysis: difference in mean birth weight (gas minus wood) = 82 g, 95% CI: −9, 170	7 stars (70% of the maximum 10 stars for design)
Tielsch, 2009 (13); cohort study	Southern India	Tamil Nadu, a rural area (92% of households use wood and/or dung as primary cooking fuel). 11,728 liveborn infants. Recruited for intervention study of vitamin A supplement given to newborns. Not specified whether singleton births.	Interview. Wood or dung as primary cooking fuel ($n = 8,958$) compared with gas or kerosene ($n = 646$). "Vast majority" used open fire with no ventilation.	Babies were weighed on electronic infant scale. Median delay, 28.3 hours. 82% measured within 72 hours ($n = 9,604$); the rest were excluded. Gestational age estimated from last menstrual period.	Head of household occupation, literacy, number of children in household, place of delivery, roof material, religion, maternal age, education, night blindness, parity, tv/radio ownership, electricity in house, SHTS.	Unadjusted analysis—wood/dung as fuel: LBW, $n = 3,052$ (34.1%); gas/kerosene as fuel: LBW, $n = 120$ (18.6%). RR = 1.83, 95% CI: 1.56, 2.16.	Adjusted analysis: Difference in mean birth weight (gas/kerosene minus wood/dung) = 104.5 g, 95% CI: 68.9, 140.1.	7 stars (70% of the maximum 10 stars for design)
						Adjusted analysis: RR (term) = 1.49, 95% CI: 1.25, 1.77; RR (preterm[a]) = 1.70, 95% CI: 0.93, 3.10.	Adjusted analysis—difference in mean birth weight: 1) no SHTS minus 1–10 cigarettes/day = 22.3 g, 95% CI: 4.6, 40.1; 2) no SHTS minus >10 cigarettes/day = 69.8 g, 95% CI: 43.7, 95.9.	
						Adjusted analysis for risk of LBW with SHTS found RR (1–10 cigarettes/day) = 1.05, 95% CI: 0.99, 1.12; RR (>10 cigarettes/day) = 1.22, 95% CI: 1.13, 1.32.	Adjusted analysis for risk of premature birth (<37 weeks) found RR = 1.43, 95% CI: 1.11, 1.84.	
Thompson, 2005 (11); randomized controlled trial	Western Guatemala	Rural. 23 Mayan communities in highlands. 534 households (women pregnant or with young children) randomly assigned to intervention (stove with chimney) or control (open fire). 225 singleton births.	Plancha (improved cooking stove with chimney): 104 births included. Open fire (using traditional fuel): 121 births included.	Trained field-workers visited home as soon as possible after birth to measure weight. Scales accurate to 100 g. 188 babies (65.7%) measured within 48 hours. 225 babies (78.7%) measured within 1 week.	Randomization balanced. Some women allocated to intervention stove could not use it before giving birth (5 weeks required for drying of stove); therefore, adjustment per protocol analysis also carried out for mother's age, primiparity, >5 births, socioeconomic status, father's smoking (results shown).	Unadjusted analysis—open fire (control): LBW, $n = 26$ (25%); plancha (intervention): LBW, $n = 24$ (19.8%). RR = 1.16, 95% CI: 0.85, 1.60. Adjusted analysis: RR = 1.30, 95% CI: 0.72, 2.35.	Adjusted analysis: Difference in mean birth weight (plancha minus open fire) = 82 g, 95% CI: −32, 197.	8 stars (62% of the maximum 13 stars for design)

Abbreviations: CI, confidence interval; LBW, low birth weight; OR, odds ratio; $PM_{2.5}$, particulate matter $\leq$2.5 µm in diameter; RR, relative risk; SHTS, secondhand tobacco smoke.

[a] Preterm LBW was based on being small for gestational age for premature birth (<37 weeks) based on the last menstrual period. (This estimate was obtained from James Tielsch, Johns Hopkins Bloomberg School of Public Health, personal communication, 2009.)

Study or Subgroup	log(Odds Ratio)	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Boy, 2002 (14)	0.26236	0.17543	8.3%	1.30 (0.92, 1.83)
Mavalankar, 1992(a) (17)	0.20701	0.10091	25.0%	1.23 (1.01, 1.50)
Mavalankar, 1992(b) (17)	0.39878	0.10321	23.9%	1.49 (1.22, 1.82)
Mishra, 2004 (15)	0.11333	0.17036	8.8%	1.12 (0.80, 1.56)
Siddiqui, 2008 (16)	0.57098	0.24786	4.1%	1.77 (1.09, 2.88)
Thompson, 2005 (11)	0.26236	0.30285	2.8%	1.30 (0.72, 2.35)
Tielsch, 2009(a) (13)	0.39878	0.10204	24.4%	1.49 (1.22, 1.82)
Tielsch, 2009(b) (13)	0.53063	0.30691	2.7%	1.70 (0.93, 3.10)
Total (95% CI)			100.0%	1.38 (1.25, 1.52)

Heterogeneity: chi² = 5.54, df = 7 (P = 0.59); I^2 = 0%
Test for overall effect: z = 6.37 (P < 0.00001)

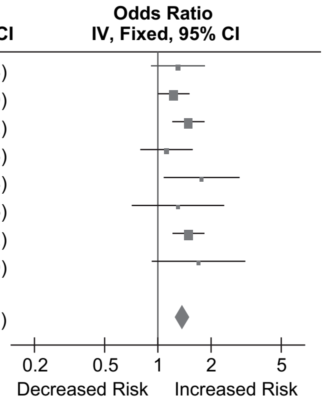

Figure 2. Effect of exposure to indoor air pollution from solid fuel use compared with cleaner fuels, or for users of improved chimney stoves, on risk of low birth weight. Sizes of the boxes in the forest plot are proportional to the sample sizes of the included studies. (a) Term births (low birth weight <2,500 g); (b) preterm births (small for gestational age). CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error.

Levels of respirable particulate matter (particulate matter ≤10 μm in diameter (PM_{10})) from IAP deriving from solid fuel use in developing countries are quantitatively similar to those of secondhand smoke and greater than those of ambient air pollution. Compiled data from studies of homes using solid fuel in developing countries found 24-hour PM_{10} concentrations ranging from 300 μg/m^3 to 3,000 μg/m^3 (22), similar to time-weighted room mean PM_{10} concentrations of 3,000 μg/m^3 to 4,000 μg/m^3 found after 8 hours of secondhand smoke exposure (23).

Our pooled effect estimate resembles that from a recent meta-analysis of 9 prospective cohort studies of LBW and secondhand smoke (5), which reported a 32% increase in risk of LBW (OR = 1.32, 95% CI: 1.07, 1.63) from secondhand smoke exposure. Seventeen prospective cohort studies found secondhand smoke exposure to be significantly associated with a reduction of 33.0 g (95% CI: 15.7, 51.3) in birth weight—a reduction smaller than that observed in our study. In addition, one of the studies included in our review also looked at the relation of secondhand smoke with LBW (13) and found a weaker association than with IAP from solid fuel use: risk of exposure to more than 10 cigarettes a day compared with no secondhand smoke was associated with a 22% increase in risk of LBW (adjusted relative risk = 1.22, 95% CI: 1.13, 1.32).

A number of studies reported a statistically significant association of sulfur dioxide and total suspended particles in ambient air pollution with birth weight, summarized in a recent systematic review (6). Refer to Table 6.

The Beijing study also identified significant reductions of 7.3 g and 6.9 g in birth weight associated with maternal exposure to unit increases of 100 μg/m^3 of sulfur dioxide and total suspended particles, respectively (24). In addition, maternal exposure to ambient carbon monoxide was found to be associated with LBW in studies conducted in Southern California (carbon monoxide >5.5 ppm in the third trimester; relative risk = 1.22, 95% CI: 1.03, 1.44) (25) and South Korea (increased carbon monoxide; relative risk = 1.08, 95% CI: 1.04, 1.12) (26). Studies conducted in Nevada and São Paulo, Brazil, found significant reductions in birth weight with a 10-μg/m^3 increase in mean PM_{10} concentration during the third trimester (11 g, 95% CI: 2.3, 19.8) and

	Lower Exposure			Higher Exposure				
Study or Subgroup	Mean	(SD)	Total	Mean	(SD)	Total	Weight	Mean Difference IV, Fixed, 95% CI
Boy, 2002 (14)	2,835	(533)	357	2,772	(525)	871	18.5%	63.0 (0.40, 126.0)
Mishra, 2004 (15)	3,271	(1,448)	766	3,096	(1,429)	1,535	5.0%	175.0 (50.0, 300.0)
Siddiqui, 2008 (16)	2,812	(404)	80	2,730	(385)	108	6.0%	82.0 (–9.0, 170.0)
Thompson, 2005 (11)	2,805	(579)	366	2,723	(573)	268	9.6%	82.0 (–32.0, 197.0)
Tielsch, 2009 (13)	2,819	(453)	646	2,715	(420)	8,958	60.9%	104.0 (68.9, 140.1)
Total (95% CI)			2,215			11,740	100.0%	96.6 (68.5, 124.7)

Heterogeneity: chi² = 2.85, df = 4 (P = 0.58); I^2 = 0%
Test for overall effect: z = 6.74 (P < 0.00001)

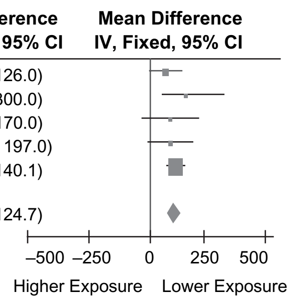

Figure 3. Effect of exposure to indoor air pollution from solid fuel use compared with cleaner fuels, or for users of improved chimney stoves, on mean birth weight. For adjusted mean difference in birth weight (grams), actual birth weights and associated standard deviations are estimated. Sizes of the boxes in the forest plot are proportional to the sample sizes of the included studies. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SD, standard deviation.

Table 5. Summary of Studies on Stillbirth Associated With Solid Fuel Use

First Author, Year (Reference No.); Design	Location	Population/Setting	Exposure	Measurement of Outcome	Adjustment for Confounding	Results	Quality
Mavalankar, 1991 (20); case-control study	Western India, Ahmedabad	Three government teaching hospitals. Cases: 451 stillbirths and 160 early neonatal deaths. Controls: 1,465 infants >2,500 g surviving until discharge or up to 7 days. Singleton births only.	Interview. Reported "exposure to cooking smoke" during pregnancy. 30% of mothers of controls exposed.	Trained physicians collected data (maternal interview, medical records, anthropometry). Stillbirth (occurring in hospital). Early neonatal death (occurring in hospital within first week of life).	Maternal age, previous stillbirth, >1 previous child death, last birth premature, maternal weight, anemia, antenatal factors, intrapartum factors, maternal education, caste, place of residence, toilet facilities, parity.	Unadjusted analysis—cases: stillbirth ($n = 451$); exposed, $n = 185$ (41.0%). Cases: early neonatal death ($n = 160$); exposed, $n = 62$ (38.8%). Controls ($n = 1,465$); exposed, $n = 442$ (30.2%). Adjusted analysis: OR (stillbirth) = 1.5, 95% CI: 1.0, 2.1; $P < 0.05$. OR (neonatal death) = not given; $P > 0.05$.	6 stars (60% of the maximum 10 stars for design)
Mishra, 2005 (21); cross-sectional survey	India	Nationally representative sample of 19,189 ever-married women aged 40–49 years with complete birth histories. 96% response rate. Singleton births only.	Interview. Pollution rated as high (wood, dung, straw) and low (electricity/liquefied propane gas/natural gas). Medium rating excluded.	Stillbirth defined as delivery of dead baby after 28th week of pregnancy.	Full model includes tobacco smoking, anemia, body mass index, education, caste/religion, house/kitchen type, crowding, standard of living, area of residence, region.	Unadjusted analysis—high pollution: stillbirth, $n = 1,634$ (8.8%); low pollution: LBW, $n = 817$ (4.4%). Adjusted analysis: OR (stillbirth) = 1.44, 95% CI: 1.04, 1.97.	7 stars (64% of the maximum 11 stars for design)
Siddiqui, 2005 (12); cohort study	Southern Pakistan	Urban and rural. Nara (90% wood fuel), Kotdiji (80% wood fuel), and Bilal (15% wood fuel) provinces. 1,102 women followed through pregnancy until birth. Enrolled through child health surveillance program. Singleton births only.	Interview. Wood for cooking ($n = 584$) vs. gas for cooking ($n = 518$). 53% of sample used wood.	Reproductive loss through stillbirth ($n = 85$).	Location (urban vs. rural).	Unadjusted analysis—wood as fuel: stillbirth, $n = 60$ (10.2%); gas as fuel: stillbirth, $n = 25$ (4.8%). Adjusted analysis: OR = 1.90, 95% CI: 1.10, 3.20.	5 stars (50% of the maximum 10 stars for design)
Tielsch, 2009 (13); cohort study	Southern India	Tamil Nadu, a rural area (92% of households use wood and/or dung as primary cooking fuel). 11,728 liveborn infants. Recruited for intervention study of vitamin A supplement given to newborns. Not specified whether singleton births.	Interview. Wood or dung as primary cooking fuel ($n = 8,958$) compared with gas or kerosene ($n = 646$). "Vast majority" used open fire with no ventilation.	Delivery after 28 weeks in which fetus was born dead ($n = 358$). Trained interviewers excluded early neonatal deaths.	Head of household occupation, number of children in household, place of delivery, roof material, religion, maternal age, education, night blindness, parity, tv/radio ownership, electricity in house, SHTS.	Unadjusted analysis—wood/dung as fuel: stillbirth, $n = 343$ (2.8%); gas/kerosene as fuel: stillbirth, $n = 15$ (1.5%). RR = 1.92, 95% CI: 1.15, 3.21. Adjusted analysis: RR = 1.34, 95% CI: 0.76, 2.36. Adjusted analysis for risk of stillbirth with SHTS found RR (1–10 cigarettes/day) = 1.05, 95% CI: 0.83, 1.33; RR (>10 cigarettes/day) = 1.52, 95% CI: 1.13, 2.04.	7 stars (70% of the maximum 10 stars for design)

Abbreviations: CI, confidence interval; LBW, low birth weight; OR, odds ratio; RR, relative risk; SHTS, secondhand tobacco smoke;

Study or Subgroup	log(Odds Ratio)	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Mavalankar, 1991 (20)	0.40547	0.18763	30.8%	1.50 (1.04, 2.17)
Mishra, 2005 (21)	0.36464	0.16181	41.4%	1.44 (1.05, 1.98)
Siddiqui, 2005 (12)	0.64185	0.27019	14.8%	1.90 (1.12, 3.23)
Tielsch, 2009 (13)	0.29267	0.28906	13.0%	1.34 (0.76, 2.36)
Total (95% CI)			100.0%	1.51 (1.23, 1.85)

Heterogeneity: chi² = 0.98, df = 3 (P = 0.81); I^2 = 0%

Test for overall effect: z = 3.93 (P < 0.0001)

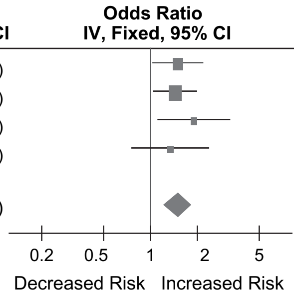

Figure 4. Effect of stillbirth on exposure to indoor air pollution from solid fuel use compared with cleaner fuels. Sizes of the boxes in the forest plot are proportional to the sample sizes of the included studies. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error.

a 1-ppm increase in mean carbon monoxide concentration in the first trimester (23 g, 95% CI: 5, 41), respectively (27, 28).

Relation between IAP and stillbirth

We observed a 51% increase in risk of stillbirth associated with IAP (OR = 1.51, 95% CI: 1.23, 1.85). In addition to exposure misclassification and residual confounding, a particular concern for population-based studies of stillbirth is underreporting of events (29). This is more likely to occur in poorer rural biomass-using communities and is expected to dilute effect estimates. The hospital-based case-control study (20) and the cohort studies with trained community health workers (12, 13) are unlikely to have been biased in this way, but the interview-based cross-sectional study (21) may well have been. This study was the largest in the meta-analysis and also reported one of the smallest effect sizes (OR = 1.44, 95% CI: 1.04, 1.97). The pooled estimate we report might therefore be underestimated.

There is little published evidence regarding the relation between secondhand smoke and stillbirth; most studies focus on active smoking by pregnant women. However, our estimate of risk is similar to that observed in a Swedish prospective cohort study of 678 working, pregnant women nonsmokers (30) that reported a 53% increase in risk of stillbirth (relative risk = 1.53, 95% CI: 0.98, 2.38) associated with secondhand smoke, adjusted for all major confounders. In addition, one of the studies included in our review also looked at the relation of secondhand smoke with stillbirth (13) and found a relation similar to that for IAP: risk of exposure to more than 10 cigarettes a day compared with no secondhand smoke was associated with a 52% increase in risk of LBW (adjusted relative risk = 1.52, 95% CI: 1.13, 2.04).

A systematic review of ambient air pollution and fetal health (6) identified only 3 studies of ambient air pollution and stillbirth. A Brazilian time-series study, investigating the association between daily counts of intrauterine mortality and measurements of several pollutants, found an association with combined exposure to nitrogen dioxide, sulfur dioxide, and carbon monoxide ($P < 0.01$) (31). A Czech ecologic study found no relation between stillbirth and ambient air pollution including sulfur dioxide, nitrogen dioxide, and maternal exposure to total suspended particles (10-$\mu g/m^3$ increase in total suspended particles (OR = 0.99, 95% CI: 0.95, 1.04)) (32). Another ecologic study conducted in Japan found no evidence of a correlation between annual mean dust particle levels and rate of spontaneous fetal death (correlation coefficient = −0.351, $P > 0.1$) (33).

Although there is a lack of evidence investigating how environmental pollution is associated with stillbirth, it appears that exposure to secondhand smoke and IAP increases the risk. However, the relation with ambient air pollution is less clear.

Table 6. Studies Summarizing the Association of Maternal Exposure to Sulfur Dioxide and Total Suspended Particles With Low Birth Weight

First Author, Year (Reference No.)	Location	Exposure	Relative Risk	95% CI
Wang, 1997 (24)	Beijing, China	100-$\mu g/m^3$ increase in sulfur dioxide	1.11	1.06, 1.16
		100-$\mu g/m^3$ increase in total suspended particles	1.10	1.05, 1.14
Bobak, 2000 (45)	Czech Republic	50-$\mu g/m^3$ increase in sulfur dioxide	1.20	1.11, 1.30
		50-$\mu g/m^3$ increase in total suspended particles	1.15	1.07, 1.24
Ha, 2001 (26)	South Korea	"Increased concentration" of sulfur dioxide	1.06	1.02, 1.10
		"Increased concentration" of total suspended particles	1.05	1.00, 1.08

Abbreviation: CI, confidence interval.

Biologic plausibility

Smoke from solid fuel combustion produces pollutants, including particulate matter, carbon monoxide, and hundreds of other organic compounds, detrimental to health (34, 35). These pollutants may be absorbed into maternal blood, cross the placental barrier, and have direct toxic effects on the fetus. The exact biologic mechanisms through which IAP influences birth weight and stillbirth remain to be confirmed, but much can be learned from the evidence on ambient air pollution and smoking.

The mechanism through which carbon monoxide might affect the fetus is best understood (6). Exposure to high levels of carbon monoxide, which binds to hemoglobin to form carboxyhemoglobin, reduces the capacity of the blood to carry oxygen to body tissues. Carbon monoxide crosses the placental barrier, and hemoglobin in fetal blood has 10 times more affinity for binding carbon monoxide than for adults (25). Furthermore, fetal elimination of carbon monoxide is slower than in the mother (36). Thus, a developing fetus can be deprived of adequate oxygen, leading to intrauterine growth retardation and risk of LBW and stillbirth (21). Carbon monoxide exposure has been directly related to fetal development and adverse pregnancy outcomes including LBW (37, 38). Animal studies have demonstrated the association between retarded fetal growth by direct toxic effects of carbon monoxide and other substances generated by burning cigarettes (39). Inhaled carbon monoxide of 90 ppm in pregnant rabbits (resulting in a carboxyhemoglobin level of 8%–9%) reduced mean birth weight by 11% (40). However, similar levels of inhaled carbon monoxide in pregnant rats was not associated with a reduction in birth weight (38). Biomass combustion has been shown to be qualitatively similar to tobacco burning, with carboxyhemoglobin levels of 2.5%–13% (41), covering the range for passive to heavy active smoking (23).

The role of maternal particulate matter exposure in relation to pregnancy outcomes is less clear. Such exposure can result in decreased efficiency of transplacental function, with consequent deterioration of fetal growth and development (6), although it is not known which toxic components of particulate matter are involved. Transplacental transfer of polyaromatic hydrocarbons and other constituents of secondhand smoke from mother to fetus has been reported (42). In addition, increased polyaromatic hydrocarbons–DNA adduct levels from exposure to polyaromatic hydrocarbons in ambient air pollution, which increase the potential for genetic fetal damage, have been reported in maternal and newborn white blood cells (43). Another postulated mechanism is through effects on maternal respiratory or general health, which can impair uteroplacental and umbilical blood flow, transplacental glucose, and total insulin, the major determinants of fetal growth (44).

CONCLUSIONS

Given that pregnant women in countries with high rates of solid fuel use and of LBW and stillbirth are rarely able to avoid activities that expose them and their unborn children to IAP, even a modest increase in relative risk of these conditions could translate into a substantial population attributable risk. We calculated population attributable risks for LBW and stillbirth associated with IAP by using a 70% prevalence of solid fuel use (16). Taking the pooled odds ratios of 1.38 and 1.51 from the meta-analyses of LBW and stillbirth, the respective population attributable risks were 21.0% and 26.3%.

Although there is good reason to minimize exposure of pregnant mothers to IAP, there is a need for further research to strengthen and refine the evidence reported here. Intervention trials are valuable, but well-planned observational studies with careful exposure assessment, including direct measurement in at least a subsample, are also important. Assessment across all trimesters will help identify the most vulnerable periods; however, first-trimester recruitment remains a challenge for women in developing countries who may not seek early prenatal care or volunteer that they are pregnant if asked. For studies of birth weight, it is important to obtain valid measures of weight and gestational age as soon as possible after birth. For studies of stillbirth, it is important to ensure that outcomes are accurately reported and are not confused with early neonatal deaths.

Despite limitations in the extent and quality of available evidence, the consistency of findings across settings and findings regarding exposure to secondhand smoke and ambient air pollution (to date, LBW only) and biologic plausibility point toward a causal relation. The results of these reviews present a strong case for moving swiftly to conduct high-quality studies in a variety of developing-country settings.

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