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Kitchen $PM_{2.5}$ concentrations and child acute lower respiratory infection in Bhaktapur, Nepal: The importance of fuel type

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ABSTRACT

Background: Globally, solid fuels are used by about 3 billion people for cooking and a smaller number use kerosene. These fuels have been associated with acute lower respiratory infection (ALRI) in children. Previous work in Bhaktapur, Nepal, showed comparable relationships of biomass and kerosene cooking fuels with ALRI in young children, compared to those using electricity for cooking. We examine the relationship of kitchen $PM_{2.5}$ concentrations to ALRI in those households.

Methods: ALRI cases and age-matched controls were enrolled from a cohort of children 2–35 months old. 24-h $PM_{2.5}$ was measured once in each participant's kitchen. The main analysis was carried out with conditional logistic regression, with $PM_{2.5}$ measures specified both continuously and as quartiles.

Results: In the kitchens of 393 cases and 431 controls, quartiles of increasing $PM_{2.5}$ concentration were associated with a monotonic increase in odds ratios (OR): 1.51 (95% CI: 1.00, 2.27), 2.22 (1.47, 3.34), 2.48 (1.63, 3.77), for the 3 highest exposure quartiles. The general kitchen concentration-response shape across all stoves was supralinear. There was evidence for increased risk with biomass stoves, but the slope for kerosene stoves was steeper, the highest quartile OR being 5.36 (1.35, 21.3). Evidence for increased risk was also found for gas stoves.

Conclusion: Results support previous reports that biomass and kerosene cooking fuels are both ALRI risk factors, but suggests that $PM_{2.5}$ from kerosene is more potent on a unit mass basis. Further studies with larger sample sizes and preferably using electricity as the baseline fuel are needed.

1. Introduction

About 3 billion people use solid fuels, coal and biomass (crop residues, wood, charcoal and animal dung) for cooking (UNDP-WHO, 2009). Household combustion of these fuels, often with no chimneys and little ventilation, has been associated with a wide variety of health effects, particularly in women who typically cook for the household (Smith et al., 2004; Bruce et al., 2000). Young children who spend most of their time with their mothers are also highly exposed. Acute lower respiratory infection (ALRI) in young children is one of the leading causes of death in children under 5 years in developing countries, and considered responsible for an estimated 650,000 deaths in 2016. Estimates are that about 40% of these deaths globally were attributable to solid cookfuel use including about 20% of child ALRI deaths in Nepal (IHME GBD website: http://vizhub.healthdata.org/gbd-compare/).

We previously found, in a case-control study in Bhaktapur municipality, Nepal, that use of biomass and kerosene cooking fuels were associated with similar relative risks for ALRI among children 2–35 months of age (Bates et al., 2013). That investigation had the advantage that the study population contained an approximately equally balanced distribution of primary cooking fuel types–electricity, gas, kerosene, and biomass—permitting electricity to be used as the baseline situation to which the other cooking fuels could be compared. Here we investigate relationships with 24-h kitchen $PM_{2.5}$ concentrations in this

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study population.

2. Methods

Human subjects' approvals were obtained from the institutional review boards at the University of California–Berkeley, the Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal, and, the Regional Committee for Medical and Health Research Ethics (REK VEST), Norway. The work described was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Free and informed consent was obtained from guardians of all subjects before they participated in the research.

The underlying case-control study has previously been described (Mathisen et al., 2010a). Briefly, the study was carried out as part of a study designed primarily to investigate the causal role of respiratory viruses in children with and without ALRI. Cases and controls were enrolled from an open cohort containing at any one time about 4500 children less than 3 years of age under active surveillance for respiratory illness in Bhaktapur municipality (population ~ 72,000), 13 km east of Kathmandu.

Fieldworkers referred children with respiratory problems to the Siddhi Memorial Hospital inside Bhaktapur. Self-referrals from the study population were also accepted. Study physicians classified acute lower respiratory infections according to standard World Health Organization (WHO) criteria (WHO and UNICEF, 2005). ALRI was defined as cough or breathing difficulty combined with fast breathing (i.e., > 50 breaths/min for children 2–11 months of age or > 40 breaths/min for children $\geq$ 12 months of age). Excluded were cases with other severe illness, documented tuberculosis or congenital heart disease, dysentery, severe anemia (hemoglobin < 7 mg/L), severe malnutrition ($< 70\%$ NCHS median weight for height or length), cough for more than 14 days, or having received antibiotics within the last 48 h.

Potential controls, matched to cases by time (within a month of diagnosis) and age in months, were randomly selected from the list of children under surveillance. Fieldworkers visited homes of potential controls and requested parental consent for their child's participation. After consent, the child was examined to confirm that they did not have ALRI. The same exclusion criteria were applied as for cases.

During May 2006–June 2007 the study team was notified of confirmed cases of ALRI, as they were diagnosed, and about potential control households as they were identified. A questionnaire was administered to an adult household member, usually the mother, to obtain information on household characteristics, including cooking and heating appliances, both primary and secondary.

2.1. Indoor air pollution monitoring

$PM_{2.5}$ concentrations were measured in the kitchens using a light-scattering nephelometer, the UCB-PATS (University of California, Berkeley-Particle and Temperature monitoring System). After calibration of instruments, 24-h $PM_{2.5}$ levels were measured in households of the study participants, as previously described (Pokhrel et al., 2015). All $PM_{2.5}$ measurements were carried out within a week of recruitment. Household air pollution (HAP) was measured in 824 households (393 cases and 431 controls). Since HAP measurement began a month after study recruitment began, we did not measure $PM_{2.5}$ in the first 40 homes (24 cases and 16 controls), nor in a further 53 homes (35 cases and 18 controls) because of air pollution monitor malfunctioning.

2.2. Statistical procedures

Although a one-to-one age-in-months matching of cases and controls was originally sought, it was not exactly achieved, for logistical reasons and because of refusals to participate. To preserve study power, corresponding cases or controls were not eliminated from the study when a refusal occurred. Instead, we ran conditional logistic regression models using age in months as the matching variable. Adjusted conditional logistic regression was carried out across quartiles of $PM_{2.5}$ for each stove type and as a continuous measure with units of 10 $\mu g/m^3$, on both linear and natural log scales–for all participants combined and separately for participants whose families used the 4 primary stove types. Interaction terms were used, as appropriate, in models to confirm differences between slopes for stove types.

Since many of the households used secondary stoves, often kerosene or biomass stoves (Bates et al., 2013), we carried out some analyses after eliminating households with biomass, kerosene or unknown secondary stoves. Only kerosene secondary and unknown stoves were eliminated from the analysis with biomass and electric primary stoves combined, and only biomass secondary stove households were eliminated from the analysis with kerosene primary stoves. Building on this, we examined the relationship between primary stove type and whether the child was reported by their adult relative as being in the kitchen, "never", "sometimes", or "always" during cooking. This analysis excluded secondary stoves, as set out above, and children reported by their relatives as never being in the kitchen during cooking.

For consistency, covariates used in this paper were largely the same as those used in our previous analysis using stove types and the model-building process has previously been explained (Bates et al., 2013). Briefly, we selected covariates for the final model after investigating candidate variables by first selecting variables related directly to the exposure of the child (sources of $PM_{2.5}$ from cooking and heating). Then, for each remaining variable we examined associations: a) between primary cooking source of $PM_{2.5}$ and potential confounder in the control group, and b) between the candidate variable and the outcome (ALRI) in study participants. Any variable that predicted both primary cookstove source of $PM_{2.5}$ and ALRI with a p-value of $\leq$ 0.2 was included in the final model. Finally, the model was examined to ensure that we were not adjusting for anything on the causal pathway and not adjusting for a collider (Greenland et al., 1999). The variable for child in kitchen during cooking was not included because of concerns that it might be on the causal pathway between fuel type and ALRI. In addition, as a sensitivity analysis, we evaluated the influence on ORs of a wide range of covariates. The shape of the association between $PM_{2.5}$ and ALRI for all children was graphically examined with the use of restricted cubic splines with 3 degrees of freedom (Harrell et al., 1988). The estimated shape was visually compared to that of the Integrated Exposure-Response (IER) function that combines information on the risk of ALRI associated with $PM_{2.5}$ exposure from outdoor air pollution, second hand smoke, and indoor pollution from the burning of biomass for cooking (Burnett et al., 2014).

3. Results

The case and control refusal rates were about 8.5% and 8%, respectively (Mathisen et al., 2009, 2010b).

24-h air pollution monitoring was successfully carried out in the kitchens of a total of 824 houses. Table 1 shows demographic features of the cases and controls in the present study.

An arithmetic mean of the measured $PM_{2.5}$ concentration across the measurement period was calculated for the kitchen of each participant. For the main analysis, the distribution of these means across all participants was divided into quartiles. Table 2 shows the distribution of cases and controls across quartiles, by all participants combined and separately by the four primary stove types—electricity, gas, kerosene and biomass. For comparability, the same quartile cut-points were maintained across all analyses.

When study participants are stratified this way, many of the case and control cells represent small numbers of participants. For biomass primary stoves there are no participants in the lowest $PM_{2.5}$ quartile. For all stoves combined, there is an increasing case-to-control ratio of

Table 1
Distribution of demographic and exposure variables, with odds ratios for ALRI, using conditional logistic regression, while matching 393 cases and 431 controls for age in months, in Bhaktapur children, 2–35 months of age.

Variable	Controls (%)	Cases (%)	Unadjusted OR (95% CI)
Sex			
Female	197 (45.7)	166 (42.2)	1.00
Male	234 (54.3)	227 (57.8)	1.14 (0.86, 1.52)
Age (months)			
< 6 mo	122 (28.3)	111 (28.2)	–
6– < 12 mo	92 (21.4)	98 (24.9)	–
12– < 24 mo	161 (37.4)	133 (33.8)	–
24– < 36 mo	56 (13.0)	51 (13.0)	–
Ethnic group			
Not Newari	191 (44.3)	169 (43.0)	1.00
Newari	240 (55.7)	224 (57.0)	1.03 (0.78, 1.36)
Rooms in home			
1	210 (48.7)	192 (48.9)	1.00
2	39 (9.1)	51 (13.0)	1.41 (0.89, 2.25)
More than 2	182 (42.2)	149 (37.9)	0.89 (0.66, 1.19)
Missing	0	1	
Home ownership			
Own house	214 (49.7)	193 (49.1)	1.00
Rent	217 (50.4)	200 (50.9)	1.06 (0.80, 1.40)
House sharing			
Single family	225 (52.2)	217 (55.2)	1.00
Multiple families	206 (47.8)	175 (44.5)	0.89 (0.67, 1.18)
Missing	0	1	–
Domestic animals owned			
No	327 (75.9)	304 (77.4)	1.00
Yes	104 (24.1)	89 (22.7)	0.94 (0.67, 1.30)
Father's occupation			
Self-employed or salary earner	168 (39.0)	140 (35.6)	1.00
Factory worker/daily wage worker	209 (48.5)	207 (52.7)	1.20 (0.89, 1.61)
Other	54 (12.5)	46 (11.7)	1.01 (0.63, 1.60)
Father's education			
More than high school	56 (13.0)	44 (11.2)	1.00
High school	211 (49.0)	170 (43.3)	0.99 (0.63, 1.55)
Primary school	152 (35.3)	161 (41.0)	1.26 (0.79, 1.99)
No school (illiterate)	12 (2.8)	18 (4.6)	1.66 (0.72, 3.85)
Mother's work			
Outside home	87 (20.2)	116 (29.5)	1.00
Housework	344 (79.8)	277 (70.5)	0.61 (0.44, 0.84)
Mother's education			
More than high school	36 (8.4)	27 (6.9)	1.00
High school	146 (33.9)	114 (29.0)	0.97 (0.55, 1.71)
Primary school	168 (39.0)	168 (42.8)	1.27 (0.73, 2.20)
No school (illiterate)	81 (18.8)	84 (21.4)	1.29 (0.71, 2.34)
Incense or mosquito coils			
Not used	149 (34.6)	168 (42.8)	1.00
Used	282 (65.4)	225 (57.3)	0.73 (0.55, 0.97)
Number of smokers in household			
None	171 (39.7)	153 (38.9)	1.00
One	215 (49.9)	187 (47.6)	1.00 (0.74, 1.34)
2 or more	45 (10.4)	53 (13.5)	1.30 (0.82, 2.06)
Kitchen ceiling/roof			
Metal sheet	90 (20.9)	88 (22.4)	1.00
Concrete	172 (39.9)	185 (47.1)	1.06 (0.74, 1.53)
Wood and mud	167 (38.8)	118 (30.0)	0.68 (0.46, 1.00)
Other	2 (0.5)	2 (0.5)	1.29 (0.17, 9.49)
Land ownership			
No	242 (56.2)	235 (59.8)	1.00
Yes	189 (43.9)	158 (40.2)	0.83 (0.63, 1.10)
Space heating in winter			
None	362 (84.0)	317 (80.7)	1.00
Electric or gas[a]	15 (3.5)	9 (2.3)	0.74 (0.31, 1.72)
Wood, kerosene, or coal[a]	54 (12.5)	67 (17.1)	1.47 (0.99, 2.18)
Daily stove use (hours)			
< 2	302 (70.1)	271 (69.0)	1.00
2– < 3	90 (20.9)	91 (23.2)	1.20 (0.85, 1.68)
≥ 3	39 (9.1)	31 (7.9)	0.89 (0.53, 1.47)
Child in kitchen during cooking			
Never	109 (25.3)	74 (18.8)	1.00
Sometimes	94 (21.8)	86 (21.9)	1.34 (0.88, 2.05)
All the time	228 (52.9)	233 (59.3)	1.51 (1.06, 2.15)
Lighting when electricity fails			
Candles	233 (54.1)	226 (57.5)	1.00
Emergency light	19 (4.4)	13 (3.3)	0.67 (0.32–1.41)
Kerosene wick lamp	174 (40.4)	153 (38.9)	0.93 (0.70, 1.25)
None or other	5 (1.1)	1 (0.2)	0.18 (0.02, 1.60)
Kitchen size			
Large or medium	310 (71.9)	247 (62.9)	1.00
Small or very small	121 (28.1)	145 (36.9)	1.45 (1.09, 1.92)
Missing	0	1 (0.2)	
Usual kitchen ventilation			
Both doors & windows open	369 (85.6)	317 (80.7)	1.00
Either doors or windows open	58 (13.5)	73 (18.6)	1.58 (1.17, 2.14)
Neither open	4 (0.9)	3 (0.8)	–
Primary stove fuel			
Electricity	111 (25.8)	70 (17.8)	1.00
Gas	128 (29.7)	110 (28.0)	1.35 (0.90, 2.02)
Kerosene	83 (19.3)	104 (26.5)	2.13 (1.39, 3.27)
Biomass	109 (25.3)	109 (27.7)	1.65 (1.10, 2.49)
Secondary stove fuel			
Electricity/none	318 (73.8)	285 (72.5)	1.00
Gas	18 (4.2)	14 (3.6)	0.80 (0.38, 1.68)
Kerosene	43 (10.0)	49 (12.5)	1.23 (0.79, 1.91)
Biomass	50 (11.6)	45 (11.5)	1.03 (0.66, 1.60)
Other	2 (0.5)	0	–

95% CI, 95% confidence interval; ALRI, Acute lower respiratory infection; OR, odds ratio.

[a] Heating source: electric (n = 20); gas (n = 4); wood (n = 118); kerosene (n = 2); coal (n = 1).

stove proportions with increasing quartile. Such an increase is apparent for all stove types.

Fig. 1 illustrates the concentration-response relationships for all stoves combined, based on a restricted cubic spline fit (solid blue line) and its uncertainty (grey area). The minimum measured concentration (11 $\mu g/m^3$) was used as the reference value. For comparison, the integrated exposure-response functions (red lines) for ALRI associated with $PM_{2.5}$ found in other studies are also shown (Burnett et al., 2014).

Results of adjusted conditional logistic regression for quartiles and as a continuous measure with units of 10 $\mu g/m^3$, on the natural log scale–for all participants combined and separately for participants whose families used the 4 primary stove types are shown in Table 3. Because no participant household with a primary biomass stove fell into Quartile 1, the electric primary stoves were combined with the biomass primary stoves for the purposes of the analysis of the concentration-response relationship with the biomass stoves. This may be justified if, as seems quite likely, most of the $PM_{2.5}$ in kitchens with electric stoves comes from biomass burning nearby, as there is only limited motor vehicle traffic within the city.

All stove types showed evidence of increasing quartile association with ALRI as exposure increased. This trend was strongest for kerosene stoves. Reflecting the supralinear shape of the curve in Fig. 1, the estimates from the analyses with continuous exposures on a log scale better reflected the quartile analysis than did continuous estimates on a linear scale (not shown). We examined the interaction for the difference in slopes for $PM_{2.5}$ on the log scale for kerosene primary stoves relative

Table 2
Households stratified by study participant case or control status, primary stove type and quartile (Q) of mean $PM_{2.5}$ concentration across 24 h of kitchen monitoring.

Main stove	Status	Number of participant households (row %)					$PM_{2.5}$ (µg/m^3)	
$PM_{2.5}$ range:		Total	Q1 < 55 µg/m^3	Q2 55– < 91 µg/m^3	Q3 91– < 215 µg/m^3	Q4 ≥ 215 µg/m^3	Mean (SD)	Median
All	Controls	431 (100)	137 (31.8)	112 (26.0)	95 (22.0)	87 (20.2)	196 (322)	78
	Cases	393 (100)	70 (17.8)	94 (23.9)	111 (28.2)	118 (30.0)	327 (712)	108
Electricity	Controls	111 (100)	63 (56.8)	29 (26.1)	15 (13.5)	4 (3.6)	68 (87)	44
	Cases	70 (100)	34 (48.6)	17 (24.3)	13 (18.6)	6 (8.6)	99 (123)	57
Gas	Controls	128 (100)	60 (46.9)	39 (30.5)	22 (17.2)	7 (5.5)	81 (70)	58
	Cases	110 (100)	29 (26.4)	45 (40.9)	26 (23.6)	10 (9.1)	124 (173)	70
Kerosene	Controls	83 (100)	14 (16.9)	36 (43.4)	25 (30.1)	8 (9.6)	117 (117)	79
	Cases	104 (100)	7 (6.7)	28 (26.9)	44 (42.3)	25(24.0)	210 (250)	123
Biomass	Controls	109 (100)	0	8 (7.3)	33 (30.3)	68 (62.4)	522 (494)	330
	Cases	109 (100)	0	4 (3.7)	28 (25.7)	77 (70.6)	791 (1197)	350

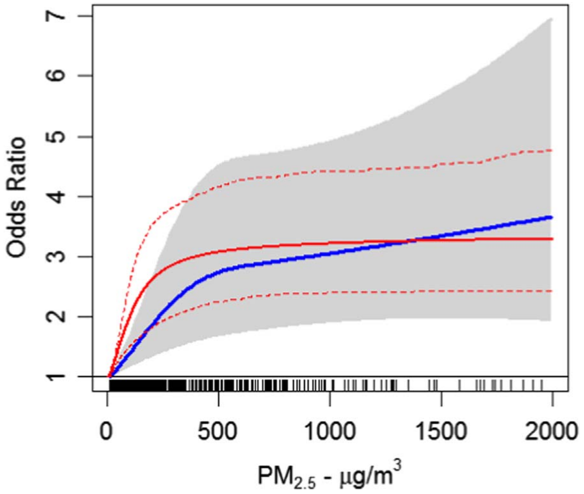

Fig. 1. The solid blue line shows the restricted cubic spline fit of the association between $PM_{2.5}$ and ALRI using the minimum concentration (11 µg/m^3) as the reference concentration, with uncertainty represented by the grey area. The rug plot along the x-axis shows the distribution of kitchen $PM_{2.5}$ concentrations for participants. The Integrated Exposure-Response function for child ALRI from Burnett et al. (2014) is displayed as a solid red line with uncertainty bounds (dashed red lines). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

to primary biomass and electric stoves combined. The OR for the main effect was 1.30 (1.10, 1.53) and for the interaction term 1.82 (1.08, 1.53). This supports the apparent difference between the two stove types seen in the quartile analysis.

Odds ratios for the $PM_{2.5}$ quartiles did not appear to be extensively confounded. For example, for the combined biomass and electricity category in Table 3, completely unadjusted matched odds ratios for quartiles 2–4 were 0.91, 1.65, and 2.11, respectively; after adding 21 demographic and socioeconomic variables (all of those in Table 1, other than child in kitchen and usual ventilation, which are likely to be on the causal pathway) to the model, the corresponding odds ratios were 0.90, 1.81 and 2.14, respectively.

Table 4 shows results of analyses similar to those in Table 3, but after eliminating households with biomass, kerosene or unknown secondary stoves. The concentration-response trends for biomass, kerosene and gas stoves all strengthened after eliminating from the analysis participants with pollutant-emitting secondary stoves in their households.

As previously shown (Bates et al., 2013), how much time the child spent in the kitchen was an independent predictor of risk. Table 5 shows that while many children in biomass-burning primary stove households are never or only sometimes in the kitchen during cooking, children in households where the primary stove is kerosene or gas were much more likely to spend all their time in the kitchen during cooking, particularly in kerosene stove households, where the proportion was about 90%. We carried out an analysis additionally excluding children who were reported never to spend time in the kitchen during cooking (Table 6).

Table 6 shows insufficient participant numbers for analysis of electric stoves and a possible slight strengthening of the concentration-response relationship for kerosene, but confidence intervals are too wide to conclude that there is any difference from the results in Table 4. Relative to results in Table 4, the relationships for gas and biomass stoves lost their monotonicity, perhaps because of reduced numbers.

The results displayed in the previous tables were based on quartiles derived from the entire distribution of household results. A consequence of this is that some of the quartile-specific results are based on very few participants (Table 2), with sometimes wide confidence intervals. As a check, we also calculated quartiles specific to each primary stove type. Stove-specific quartile results for the three participant restriction conditions (Tables 3, 4, 6) are shown in Table 7. This table additionally shows quartiles for biomass only, although quartiles based

Table 3
Adjusted $PM_{2.5}$ quartile-specific conditional logistic regression odds ratios and confidence intervals, for child ALRI, by primary stove type, for study participants, Bhaktapur, Nepal.

Primary stove type	Quartile (Odds ratio and 95% confidence interval)[a]				Continuous
(No. participants) Quartile $PM_{2.5}$ range	Q1 (reference) < 55 µg/m^3	Q2 55– < 91 µg/m^3	Q3 91– < 215 µg/m^3	Q4 ≥ 215 µg/m^3	Log_e (units: 10 µg/m^3)
All (N = 823)	1.00 -	1.51 (1.00, 2.27)	2.22 (1.47, 3.34)	2.48 (1.63, 3.77)	1.36 (1.19, 1.56)
Electric (N = 168)	1.00 -	0.77 (0.32, 1.85)	1.59 (0.60, 4.20)	1.98 (0.41, 9.46)	1.59 (0.99, 2.54)
Gas (N = 225)	1.00 -	2.40 (1.21, 4.77)	3.43 (1.51, 7.81)	2.98 (0.81, 10.9)	1.76 (1.12, 2.77)
Kerosene (N = 181)	1.00 -	1.85 (0.35, 6.22)	4.94 (1.49, 16.4)	5.36 (1.35, 21.3)	2.23 (1.31, 3.78)
Biomass and electric (N = 399)	1.00 -	0.93 (0.46, 1.89)	1.62 (0.87, 3.02)	2.00 (1.13, 3.02)	1.31 (1.10, 1.55)

[a] Adjusted for number of smokers in family, single or joint family residency, mother's occupation and mother's education.

Table 4
Adjusted $PM_{2.5}$ quartile-specific conditional logistic regression odds ratios and confidence intervals for child ALRI, by primary stove type, for study participants, Bhaktapur, Nepal, after eliminating participants from households with biomass, kerosene or unknown secondary stoves.

Primary stove type	Quartile (Odds ratio and 95% confidence interval)[a]				Continuous
(No. participants)	Q1 (reference)	Q2	Q3	Q4	Log_e (units: 10 μg/m^3)
Quartile $PM_{2.5}$ range	< 55 μg/m^3	55– < 91 μg/m^3	91– < 215 μg/m^3	≥ 215 μg/m^3	
Electric (N = 44)	1.00 -	0.20 (0.01, 7.38)	1.20 (0.13, 11.2)	1 -[b]	2.46 (0.53, 11.5)
Gas (N = 186)	1.00 -	2.49 (1.20, 5.15)	3.52 (1.40, 8.88)	4.45 (1.00, 19.8)	1.92(1.15, 3.22)
Kerosene (N = 166)[c]	1.00 -	2.88 (0.68, 12.3)	7.89 (1.88, 33.1)	15.2 (2.64, 87.1)	2.10 (1.21, 3.66)
Biomass and electric (N = 330)[d]	1.00 -	1.38 (0.60, 3.16)	1.75 (0.86, 3.57)	2.34 (1.22, 4.49)	1.32 (1.10, 1.59)

[a] Adjusted for number of smokers in family, single or joint family residency, mother's occupation and mother's education.
[b] Insufficient number for confidence interval calculation.
[c] Only biomass and unknown secondary stove households eliminated.
[d] Only kerosene and unknown secondary stove households eliminated.

Table 5
Distribution of the amount of time child participants spent in the kitchen during cooking, by stove type, as reported by adults in household.

Child in kitchen during cooking?	Number with primary stove at home (column %)				
	Electric	Gas	Kerosene	Biomass	All
Never	39 (21.6)	51 (21.4)	8 (4.3)	85 (40.0)	183 (22.2)
Sometimes	57 (31.5)	43 (18.1)	11 (5.9)	69 (31.7)	180 (21.8)
All the time	85 (47.0)	144 (60.5)	168 (89.8)	64 (29.4)	461 (56.0)
Total	181 (100)	238 (100)	187 (100)	218 (100)	824 (100)

on biomass and electricity combined are retained for comparison with the previous results. Generally, Table 7 shows patterns similar to when quartiles were based on all households combined, but confidence intervals are usually narrower because of the better balance of participants across quartiles.

4. Discussion

This paper extends our earlier analysis (Bates et al., 2013), which was focused on associations with household cooking fuel type. Both papers add to emerging evidence of health problems associated with household kerosene use. Also, but perhaps unexpectedly, both papers show an association with ALRI in households that use gas stoves.

As the tables show, the slopes of the $PM_{2.5}$ concentration-response relationships in households using kerosene stoves are much steeper than those in households using biomass for cooking. This is likely to be because all quartile concentrations for biomass-stove households (Table 7) fall in the concentration range associated with the flatter parts of the curves in Fig. 1. However, there is evidence, at least for other health outcomes, that there may be variability in the toxicity of $PM_{2.5}$, depending on its source. Diesel emissions of $PM_{2.5}$, which have similarity to kerosene emissions, have been associated with higher cardiotoxicity than $PM_{2.5}$ from biomass sources (Thurston et al., 2016).

In Fig. 1 it is noteworthy that the basic supralinear shape of the study data resembles the integrated exposure-response function for ALRI associated with $PM_{2.5}$ found in other studies (Burnett et al., 2014). This comparison tends to confirm the validity of our measurements although, given the width of the confidence interval around our data, the similarity should not be overstated. In particular, our curve "flattens" at about 450–500 μg/m^3, whereas the curve from the other studies flattens at about 200–250 μg/m^3. That the much higher $PM_{2.5}$ concentrations associated with biomass-burning stoves are not associated with higher odds ratios than found for $PM_{2.5}$ concentrations associated with kerosene and gas stoves may reflect that the biomass-derived $PM_{2.5}$ concentrations are on the flatter part of the curve, where a concentration decrease is associated with a lesser relative risk reduction. A second factor very likely to be influencing the difference between kerosene or gas and biomass stove-using households is the fact that children are much less likely to be absent from the kitchen when cooking with kerosene or gas than when cooking with biomass (Table 5). This strongly reinforces the need in future studies to obtain personal exposure measurements, rather than just micro-environment (room) measures when comparing the relative harm-inducing potencies of $PM_{2.5}$ from different sources.

As we previously showed (Pokhrel et al., 2015), the mean kitchen $PM_{2.5}$ concentrations in μg/m^3 associated with the 4 primary stove types were 80 (electric), 101 (gas), 169 (kerosene) and 656 (biomass). One implication, given the results presented in this paper, is that fuel-specific $PM_{2.5}$ may be of varying toxicity. The evidence suggests that particulate matter from kerosene may be much more toxic than that from biomass. If so, then it may be due to finer particulates from kerosene reaching further into the lungs or it may be something to do with composition of the kerosene particulates, or a combination of the two. Sahu et al. (2011) have shown that kerosene produces large numbers of fine particles, not reflected by the emitted $PM_{2.5}$ mass; and

Table 6
Adjusted $PM_{2.5}$ quartile-specific conditional logistic regression odds ratios and confidence intervals for child ALRI, by primary stove type, for study participants, Bhaktapur, Nepal, after eliminating households with biomass, kerosene or unknown secondary stoves and those who reported the child as never being in the kitchen during cooking.

Primary stove type	Quartile (Odds ratio and 95% confidence interval)[a]				
(No. participants)	Q1 (reference)	Q2	Q3	Q4	Continuous Log_e (units: 10 μg/m^3)
Quartile $PM_{2.5}$ range	< 55 μg/m^3	55– < 91 μg/m^3	91– < 215 μg/m^3	≥ 215 μg/m^3	
Electric (N = 34)	1.00 -	-[b]	-[b]	-[b]	5.00 (0.30, 84.6)
Gas (N = 140)	1.00 -	2.49 (1.08, 5.75)	6.65 (1.92, 23.1)	5.43 (1.08, 27.3)	2.59 (1.36, 4.92)
Kerosene (N = 152)[c]	1.00 -	3.34 (0.65, 17.3)	8.85 (1.69, 46.3)	15.6 (2.21, 109)	3.09 (1.52, 6.28)
Biomass and electric (N = 217)[d]	1.00 -	2.41 (0.88, 6.54)	1.32 (0.54, 3.25)	2.12 (0.95, 4.75)	1.26 (0.99, 1.60)

[a] Adjusted for number of smokers in family, single or joint family residency, mother's occupation and mother's education.
[b] Not calculable because of small participant number.
[c] Only biomass and unknown secondary stove households eliminated.
[d] Only kerosene and unknown secondary stove households eliminated.

Table 7
Adjusted conditional logistic regression odds ratios and confidence intervals, for child ALRI, by primary stove type and $PM_{2.5}$ quartiles specific to each primary stove type, for study participants, Bhaktapur, Nepal.

Primary stove type	Number	Quartile[a] (Odds ratio, 95% confidence interval)[b]			
		Q1 (reference)	Q2	Q3	Q4
Electric					
$PM_{2.5}$ range		$< 34\ \mu g/m^3$	$34– < 53\ \mu g/m^3$	$53– < 80\ \mu g/m^3$	$\geq 80\ \mu g/m^3$
All participants	168	1.00 -	2.00 (0.68, 5.90)	1.68 (0.57, 4.95)	2.58 (0.87, 7.65)
Sec. stoves out[c]	44	1.00 -	8.10 (0.28, 235)	6.32 (0.24, 169)	3.15 (0.14, 70.8)
Child in kitchen	34	1.00 -	-[f]	-[f]	-[f]
Gas					
$PM_{2.5}$ range		$< 46\ \mu g/m^3$	$46– < 63\ \mu g/m^3$	$63– < 98\ \mu g/m^3$	$\geq 98\ \mu g/m^3$
All participants	225	1.00 -	0.97 (0.44, 2.18)	1.60 (0.71, 3.58)	3.05 (1.32, 7.05)
Sec. stoves out[c]	186	1.00 -	1.10 (0.46, 2.63)	1.78 (0.75, 4.23)	3.53 (1.38, 9.05)
Child in kitchen	140	1.00 -	1.09 (0.38, 3.07)	2.27 (0.82, 6.29)	6.80 (2.00, 23.1)
Kerosene					
$PM_{2.5}$ range		$< 73\ \mu g/m^3$	$73– < 100\ \mu g/m^3$	$100– < 180\ \mu g/m^3$	$\geq 180\ \mu g/m^3$
All participants	181	1.00 -	2.56 (0.96, 6.79)	3.87 (1.46, 10.2)	4.90 (1.79, 13.4)
Sec. stoves out[d]	167	1.00 -	2.60 (0.94, 7.21)	3.77 (1.35, 10.6)	4.76 (1.65, 13.7)
Child in kitchen	152	1.00 -	3.02 (1.00, 9.15)	4.35 (1.44, 13.2)	9.30 (2.56, 33.8)
Biomass					
$PM_{2.5}$ range		$< 177\ \mu g/m^3$	$177– < 350\ \mu g/m^3$	$350– < 788\ \mu g/m^3$	$\geq 788\ \mu g/m^3$
All participants	214	1.00 -	1.17 (0.50, 2.76)	0.91 (0.39, 2.08)	1.69 (0.73, 3.90)
Sec. stoves out[e]	190	1.00 -	1.01 (0.41, 2.48)	0.99 (0.41, 2.39)	1.44 (0.59, 3.49)
Child in kitchen	104	1.00 -	0.66 (0.17, 2.49)	0.62 (0.16, 2.36)	1.27 (0.34, 4.80)
Biomass and electric					
$PM_{2.5}$ range		$< 56\ \mu g/m^3$	$56– < 134\ \mu g/m^3$	$134– < 459\ \mu g/m^3$	$\geq 459\ \mu g/m^3$
All participants	399	1.00 -	1.26 (0.69, 2.28)	1.54 (0.83, 2.86)	2.06 (1.11, 3.81)
Sec. stoves out[e]	330	1.00 -	1.74 (0.86, 3.53)	1.81 (0.90, 3.63)	2.45 (1.22, 4.95)
Child in kitchen	216	1.00 -	1.95 (0.84, 4.52)	1.48 (0.63, 3.49)	2.04 (0.83, 4.98)

[a] Quartiles are fuel-specific.
[b] Adjusted for number of smokers in family, single or joint family residency, mother's occupation and mother's education.
[c] Biomass, kerosene and unknown secondary stoves eliminated.
[d] Only biomass and unknown secondary stove households eliminated.
[e] Only kerosene and unknown secondary stove households eliminated.
[f] Not calculable because of small participant numbers.

increasing evidence suggests that polycyclic aromatic hydrocarbons (PAH), which are among kerosene combustion emissions, have potent immunosuppressant properties in animals and possibly in humans (Hew et al., 2015; Klingbeil et al., 2014; Liu et al., 2013; Nadeau et al., 2010; Padula et al., 2015).

Another possibility is confounding of the particulate associations by co-emitted chemical(s) from the kerosene, although it is not clear at present what those would be. Nitrogen oxides (NOx) produced from atmospheric nitrogen and oxygen by the high temperatures of gas combustion, however, is a plausible candidate for confounding the results for the gas-related particulates. Other possibilities are formaldehyde and ultra-fine particles, both produced by gas combustion. Also deserving of consideration is particles of food or cooking oil, produced by the high temperatures of gas stoves (Lunden et al., 2015).

Other sources of confounding, as well as selection and information biases, need to be considered as possible explanations for our results. In general, the type of cooking fuel used in a household is related to its socio-economic status. Low socio-economic status is associated with ALRI, perhaps through a number of mechanisms. There may be uncontrolled confounding in our results from socio-economic factors, but within strata defined by different stove types (Table 7) substantial confounding would not be expected. We examined a wide range of covariates and none of them had more than a minimal effect on our odds ratios. Of course, we can never rule out an unknown confounding factor, but to account for some of our results, particularly those for kerosene, the unknown confounder would need to be extremely strong (Axelson, 1980)

ALRI was clinically confirmed, interviews were carried out in homes, permitting verification of stove reporting, and the $PM_{2.5}$ exposure measures are objective and were obtained using standard procedures. This makes information bias less likely, but the $PM_{2.5}$ measurement period was only 24 h. It is perhaps remarkable that such a short monitoring period should provide such strong associations and reinforces arguments that epidemiologic studies of stove use should incorporate HAP monitoring, rather than just relying on reported stove use (West et al., 2013; Lam et al., 2012a). Considering intra-household daily variation in cooking practices, if we had been able to carry out monitoring for longer, and particularly if we had been able to carry out personal monitoring, then associations may have strengthened. However, in traditional households, such as those in our study, daily variation in cooking practices can be limited and 24 h may be reasonably representative of usual practice.

A possibility to be considered, since $PM_{2.5}$ concentrations were measured after case diagnoses, is that families might have altered household cooking and heating behaviors in order to lower $PM_{2.5}$ exposures. If this were so, it would have affected only case families and, therefore, could not have accounted for the positive associations we found. We think this possibility unlikely, however, as at the time of this study there was no awareness in the community of a possible link between household smoke exposure and ALRI.

Although other emission sources in or outside of the house could impact $PM_{2.5}$ measurements in kitchens of families using any stove type, their impact is likely to be greatest in kitchens using electricity or gas—and might account for the concentration-response trend found for children in homes with gas stoves. That we did not find such a trend for homes with electric primary stoves could reflect lower local emissions associated with neighborhood socioeconomic characteristics.

Although we did not have measures of $PM_{2.5}$ exposure during the time children spent outside their homes, this would most likely have attenuated household concentration-response relationships and be unlikely to explain the trends observed in this study. In fact, it suggests that the true exposure-response slopes may be even steeper than those we obtained.

Selection bias has been previously discussed (Bates et al., 2013), but must be further considered because not all participating households had $PM_{2.5}$ measurements conducted. As earlier explained, $PM_{2.5}$ was not measured in 93 homes. A comparison of Table 1 in this publication with the corresponding Table in our earlier publication (Bates et al., 2013), shows comparable distributions of variables and similar unadjusted odds ratios. This comparison suggests that not having air pollution monitoring data for all households is unlikely to have introduced substantial selection bias into our data. Cases of ALRI who had received antibiotics during the 48 h before assessment were excluded from the study (Bates et al., 2013). This was for reasons related to the underlying study (Valentiner-Branth et al., 2010). This exclusion would have tended to eliminate severe cases. The implications for interpretation of our results are uncertain. However, it might in part account for the absence of a strong exposure-response relationship for biomass stoves, which might be expected if biomass stoves are more likely to be associated with severe ALRI in children.

The striking concentration-response relationships shown here for $PM_{2.5}$ in kerosene stove-using households add to the growing evidence that this fuel may be much more harmful than previously assumed (Bates et al., 2013; Lam et al., 2012a; Pokhrel et al., 2010; Epstein et al., 2013). Despite well over a century of use as a household fuel, kerosene has largely been overlooked by previous studies, probably because, unlike solid fuels, it does not produce extensive visible smoke. Although kerosene has been subsidized as a household fuel in many countries, this is becoming less the case, for several reasons—its diversion to black market sales, the increasing availability of liquefied petroleum gas, risks of poisoning and burns, and rising awareness of its potential health risks. Growing recognition of its potential impact on climate may also be a factor (Lam et al., 2012b).

Although the association between use of solid cooking fuels and ALRI in infants and children is well-established (Dherani et al., 2008), an association with kerosene is much less investigated. A recent analysis of ALRI in pooled datasets of the Demographic and Health Surveys for sub-Saharan Africa countries obtained for kerosene cookfuel an OR of 1.64 (95% CI: 0.99, 2.71) (Buchner and Rehfuess, 2015). Kerosene appeared to be a stronger ALRI risk factor than biomass. An earlier study carried out in New Delhi slums obtained conflicting results for the association of kerosene cooking fuel with ALRI in infants (Sharma et al., 1998). Calculated from the data, unadjusted ORs for two slums were 0.95 (0.61, 1.48) and 1.96 (1.17, 3.29). The authors could not explain the difference between the two communities. Choi et al. (2015) found kerosene cooking was associated with respiratory conditions, including bronchitis, in women and children in Bangalore, India, but did not specifically address ALRI.

The concentration-response trends for $PM_{2.5}$ in households that cook with gas provide support for our previous finding that having a gas stove was associated with increased ALRI risk (Bates et al., 2013). As we previously mentioned, most studies of ALRI in relation to household fuel use in traditional communities have used LPG as the reference fuel category. There is, however, some evidence associating LPG use with increased respiratory risk (Moshammer et al., 2010; Ng et al., 1993; Willers et al., 2006; Wong et al., 2004). Our finding reinforces the need for other studies of gas, such as LPG, with electricity as the baseline cooking category, perhaps with more ambient and personal monitoring, to see whether these results from Bhaktapur are confirmed.

Whether or not results from further studies become available, our data reinforce the WHO recommendation that kerosene be actively discouraged as a household fuel (WHO, 2014). Also, gas stoves produce NOx and should only be used with adequate ventilation, particularly a hood, as is recommended in most developed countries.

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