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Widespread Clean Cooking Fuel Scale-Up and under-5 Lower Respiratory Infection Mortality: An Ecological Analysis in Ecuador, 1990–2019

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BACKGROUND: Nationwide household transitions to the use of clean-burning cooking fuels are a promising pathway to reducing under-5 lower respiratory infection (LRI) mortality, the leading cause of child mortality globally, but such transitions are rare and evidence supporting an association between increased clean fuel use and improved health is limited.

OBJECTIVES: This study aimed to investigate the association between increased primary clean cooking fuel use and under-5 LRI mortality in Ecuador between 1990 and 2019.

METHODS: We documented cooking fuel use and cause-coded child mortalities at the canton (county) level in Ecuador from 1990 to 2019 (in four periods, 1988–1992, 1999–2003, 2008–2012, and 2015–2019). We characterized the association between clean fuel use and the rate of under-5 LRI mortalities at the canton level using quasi-Poisson generalized linear and generalized additive models, accounting for potential confounding variables that characterize wealth, urbanization, and child health care and vaccination rates, as well as canton and period fixed effects. We estimated averted under-5 LRI mortalities accrued over 30 y by predicting a counterfactual count of canton-period under-5 LRI mortalities were clean fuel use to not have increased and comparing with predicted canton-period under-5 LRI mortalities from our model and observed data.

RESULTS: From 1990 to 2019, the proportion of households primarily using a clean cooking fuel increased from 59% to 95%, and under-5 LRI mortality fell from 28 to 7 per 100,000 under-5 population. Canton-level clean fuel use was negatively associated with under-5 LRI mortalities in linear and nonlinear models. The nonlinear association suggested a threshold at approximately 60% clean fuel use, above which there was a negative association. Increases in clean fuel use between 1990 and 2019 were associated with an estimated 7,300 averted under-5 LRI mortalities (95% confidence interval: 2,600, 12,100), accounting for nearly 20% of the declines in under-5 LRI mortality observed in Ecuador over the study period.

DISCUSSION: Our findings suggest that the widespread household transition from using biomass to clean-burning fuels for cooking reduced under-5 LRI mortalities in Ecuador over the last 30 y. https://doi.org/10.1289/EHP11016

Introduction

Lower respiratory infections (LRIs) are the leading cause of death for children under 5 y old (hereafter, "under-5") globally, with the largest burden of morbidity and mortality occurring in low- and middle-income countries (LMICs).[1] The factors that contribute to LRI mortality are primarily related to poverty and include malnutrition and micronutrient deficiency; poor health care access; inadequate use of health care resources; low vaccine coverage; inadequate water, sanitation, and hygiene; and elevated air pollution exposure.[2,3] Under-5 LRI incidence and mortality have declined globally over the last 30 y, with modeling studies suggesting these improvements are likely due to advances in economic welfare and changes in modifiable risk factors like air pollution, hygiene, and vaccine coverage.[2] Improving the evidence base for changes in modifiable risk factors to reduce under-5 LRI incidence or mortality can help to guide investments in addressing the persistently large LRI burden of disease among children.

Exposure to household air pollution (HAP) from burning biomass inefficiently for daily cooking and heating needs is a leading environmental risk factor for under-5 mortality around the world.[1,4] Although results from cookstove intervention trials have not yielded improved health in intention-to-treat analyses in large part[5] (one exception being study in Guatemala where a biomass stove with a chimney reduced physician-diagnosed severe pneumonia incidence),[6] they have established a robust exposure–response relationship showing that higher HAP exposure is associated with increased risk of children's respiratory infections.[7–9] One main hypothesis for the nonexistent or smaller-than-expected observed health benefits is that air pollution exposure reductions were insufficient due to *a*) households continued use of polluting fuels and/or *b*) elevated ambient concentrations from continued polluting fuel use among non-study households in the community or other noncooking emissions sources (e.g., trash burning, road sources, dust).[5,10–12] Still, evidence from randomized controlled trials and observational studies shows that, when clean-burning fuels like gas and electricity largely displace the use of polluting fuels like firewood, dung, and charcoal, personal air pollution exposures can be dramatically reduced—and even be close—to exposures designated in health-based exposure guidelines.[6,11,13–20] These studies are supported by laboratory- and field-based emissions estimates that indicate that the magnitude of health-damaging pollutants released during cooking is dramatically reduced when using gas stoves vs. biomass stoves.[21,22]

Existing studies also suggest that residential biomass burning contributes significantly to ambient air pollution.[23–27] A recent modeling study exemplified the implications of this source apportionment, showing that completely mitigating household biomass

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burning in India can effectively allow for the population-weighted ambient exposure to particulate matter (PM) with aerodynamic diameter $\leq 2.5\ \mu m$ ($PM_{2.5}$) to fall to the Indian annual ambient air quality standard ($40\ \mu g/m^3$), in the absence of other control measures.[28] Therefore, widespread community transitions to clean-burning cooking fuels (CFs) may be a strategy to address elevated ambient air pollution. Nevertheless, a household that reduces its own cooking-related air pollution may still face high air pollution–related health risks if ambient air pollution concentrations remain elevated in a community. Given that the risk of key health outcomes like LRIs decline nonlinearly with lower air pollution exposure,[7] persistently elevated ambient air pollution concentrations could curb the potential health benefits of household-level displacement of polluting CFs with clean-burning fuels.

Given this evidence, a central policy challenge has been facilitating situations where clean fuel adopters can drastically reduce their polluting fuel use. However, for many in LMICs, clean fuels are too costly and difficult to access to use consistently, and an estimated 2 billion people will continue to rely on biomass fuels for their household energy needs in 2030.[29–32] Around the world, there are very few examples of nationwide transitions to clean CFs in recent history when reliable census and mortality data have been recorded.[33] As a result, there is a paucity of evidence related to the long-term population health impacts of such clean energy transitions.

The results of policy changes in Ecuador provide a unique research opportunity to address this evidence gap. Universal direct-to-consumer government subsidies for liquified petroleum gas (LPG), first introduced in the 1970s and later increased and stabilized in 2000, have reduced the cost of LPG for household uses to approximately 10% of market price, with most households paying between USD $2.50 and USD $3.50 for a 15-kg cylinder refill, representing <1% of total monthly expenditures for the majority of households.[34,35] Although in the 1970s 80% of households cooked primarily with biomass (generally firewood), by 2010 just 9% of all households and 19% of rural households reported cooking primarily with biomass fuels.[36] High LPG use in Ecuador contrasts with that of neighboring countries like Peru, where 80% of rural households cooked primarily with biomass fuels in 2012.[37]

Whether Ecuador's nationwide household transition from firewood to LPG for cooking has yielded health benefits remains a crucial open question. We studied the association between historical increases in clean fuel use on under-5 LRI mortality in Ecuador between 1990 and 2019 and quantified health benefits. These results have important implications for the potential health benefits of ongoing clean fuel promotion programs globally, such as those in India, Ghana, and Peru, among others.

Materials and Methods

Our analysis aimed to model the association between increased clean fuel use and under-5 LRI mortality in Ecuador at the canton-level over the past 30 y. To do this, we aggregated public use data on mortality, clean fuel use, and household and individual characteristics into 5-y periods (1988–1992, 1999–2003, 2008–2012, and 2015–2019), using national census data and regionally representative surveys that combine to provide national coverage of all cantons in the country (data sources described in Table S1 and below). These time periods center around the three most recent full national censuses (1990, 2001, 2010) and the 5 most recent years during which there have been regular surveys that can be combined to provide national coverage of all cantons in the country.

Since the first period, several cantons split into two or more cantons, largely due to population growth and political motivations. In each of these cases, no external borders were altered, so we rejoined the split cantons into the original cantons to maintain a consistent population for analysis. Therefore, although there are now 224 cantons in Ecuador, in our analysis we used 173 cantons, as there were in 1990, because we cannot allocate cantonal data from 1990 to present-day divisions. In addition, we considered four cantons to be missing data: three areas that are considered "Nondelimited zones" (those that do not belong to a province) and that do not have corresponding administrative data (equivalent to three cantons; the combined population in 2010 was approximately 4,580 children under 5 y old and 33,000 total), and one that was a part of Peru in 1990 and did not have data from that time period. Additionally, two cantons had no observed under-5 LRI mortalities throughout the entire study period and were thus dropped from the analysis. According to our socioeconomic and demographic variables (described in the "Results" section titled "Exposure–Response Relationship"), these two cantons were somewhat less populated, more rural, and less economically developed than the cantons with observed under-5 LRI mortality (Table S2). The final sample size was 167 cantons across four time periods ($n = 668$ canton-period observations).

Mortality Data and Outcome Definition

We accessed publicly available mortality data that aim to record every individual death in Ecuador since 1990 (50,000–68,000 deaths/year), including date of birth, date of death, location of death, and sex. These data are collected from physical or digital reports of all individual deaths in Ecuador each year and are managed by the National Statistical and Census Institute (INEC). Deaths were coded according to the *International Classification of Diseases* (ICD). Following the Global Burden of Disease classifications,[2] we defined deaths caused by LRIs in children under 5 y old using ICD-9 codes 73, 79, 466–470, 480–489, 513, and 770 (1990–1996) and ICD-10 codes A48, A70, B97, J09–J22, J85, P23, and U04 (1997–2019) (causes and distribution shown in Table S3). Although the sensitivity and specificity of ICD codes to assess LRIs in children have not been widely determined, existing evidence suggests that this combination of ICD codes has high sensitivity for detecting LRIs.[38–40] Previously identified limitations of detecting LRIs using ICD codes are often due to chronic comorbidities unlikely to exist in children, suggesting higher accuracy for this study's outcome (under-5 LRI mortality).[41] Ecuador's mortality registry, which was used in this study, is classified as "Medium-High Quality" in an evaluation of vital statistics based on completeness of death reporting, quality of death reporting, level of cause-specific detail, internal consistency, quality of age and sex reporting, and data availability and timeliness.[42]

Clean Cooking Fuel Data

We estimated the fraction of households in a canton using a clean CF as their primary CF (%CF) in each of our time periods using *a*) the national censuses collected in 1990, 2001, and 2010 covering the full Ecuadorian population and *b*) the "Survey of Employment, Unemployment, and Subemployment" [Encuesta de empleo, desempleo, y subempleo (ENEMDU)], a survey administered to a rotating panel of households three times per year regularly between 2015 and 2019. In both surveys, respondents were asked, "What is the primary fuel or energy source that this household uses for cooking?" ("Cuál es el principal combustible o energia que utiliza este hogar para cocinar?"). Responses to this question have no bearing on obtaining subsidies or other government benefits. Based on existing literature on HAP concentrations or personal exposures when a household relies primarily on a given CF, we coded gas, gas (tank or cylinder), centralized/piped gas, and electricity as clean fuels and all other fuels [firewood, kerosene (locally known as kerex), diesel, gasoline, agricultural residues, and animal dung] as not clean fuels.[11,12,43] In the census years, we divided the number of households using a clean fuel by the total number of households responding to the question to estimate %CF at the canton level. When using the ENEMDU, we pooled all available data collected from 2015 to 2019 (14 surveys) and used the "srvyr" package in R (version 4.2.2; R Development Core Team) to leverage expansion factors provided by the Ecuadorian INEC to yield population-weighted canton-level estimates of %CF and other covariates.

Potential Confounders

The outcome in this study is aggregated counts of under-5 LRI mortalities per canton and study period; given that the unit of analysis is canton-period, potential confounders can only be those that vary from year to year and across cantons and that covary with both the outcome (count of under-5 LRI mortalities) and the exposure (% CF). We focused on the domains of urbanization, improved infrastructure, and socioeconomic development as potential drivers of both increased clean CF access and use and improved child health at the canton level. For example, these factors could improve the availability of clean CFs (i.e., LPG cylinder refill distribution networks), household economics to increase the affordability of clean CFs, and labor market participation, which in turn could increase the relative importance of using time-saving clean CFs. At the same time, these factors could increase the availability of health care resources (e.g., antenatal care, vaccines) and improve nutrition. After adjustment, we assume that variation in %CF is random with respect to other risk factors for under-5 LRI mortality, implying that we provide an unbiased estimate of the association between 5-y canton-period % CF and average under-5 LRI mortality.

We assembled a consistent set of variables from a variety of nationally representative surveys and surveys representative of cantons that intend to cover and serve as proxies for these domains, including household conditions, sociodemographics, and health care access and usage. For covariates related to urbanization, infrastructure, and socioeconomic development, we assigned estimates from the 1990, 2001, and 2010 decennial census to the 1988–1992, 1999–2003, and 2008–2012 study periods, respectively, and combined all ENEMDU surveys from 2015 to 2019 to establish canton-level estimates for the 2015–2019 study period. We combined three additional surveys, namely the Living Conditions Survey [Encuesta de condiciones de vida (ECV)], the Maternal and Child Health Survey [Encuesta demografica de salud maternal e infantil (ENDEMAIN)], and the National Survey of Health and Nutrition [Encuesta nacional de salud y nutricion (ENSANUT)], on fecundity, women's health, and infant health and used them to estimate canton-period child vaccination status and antenatal care usage. In particular, we used ENDEMAIN 1989, ENDEMAIN 1994, and ECV 1995 for the 1988–1992 period; ECV 1998, ECV 1999, ENDEMAIN 1999, and ENDEMAIN 2004 for the 1999–2003 period; ECV 2006, ENSANUT 2012, and ECV 2014 for the 2008–2012 period; and ENSANUT 2018 for the 2015–2019 period.[44–47] As with canton-period %CF, for the census-derived estimates, we simply divided the number of relevant responses by the total number of canton-period observations; for the other surveys, we combined all relevant observations and estimated, using the provided expansion factors.

Table 1 summarizes the potential confounders considered. These potential confounders included the percentage of households in a canton that were rural, percentage having available grid electrification, household building materials (e.g., the percentage of households with a dirt floor), household water and sanitation practices (e.g., the percentage of households with municipal piped water into the home), adult women's literacy, girls' school attendance rates, the percentage of households in which an Indigenous language was spoken, childhood vaccination rates, average age of mothers at birth, and antenatal care usage. We used principal components analysis (PCA) to separately construct indices for *a*) household materials; *b*) household hygiene and water practices; and *c*) under-5 vaccination rates. Canton-period indices were produced by subtracting a given canton-period estimate from the overall parameter mean, dividing by the scaling factor, multiplying by the first principal component, and then summing across all component variables. The household materials index was composed of the percentage of households whose homes use the highest-quality roof, wall, and floor materials. The household hygiene index was composed of the percentage of households with the highest-quality household water source, household toilet and solid waste disposal, household trash removal, and household exclusive shower. The vaccine index was composed of the percentage of children under 5 y old receiving the appropriate number of doses for the tuberculosis vaccine; the trivalent diphtheria, pertussis, and tetanus vaccine; the measles vaccine; and the polio vaccine. We tested the correlations between all potential confounding variables and the exposure and outcome over time and space (see Supplemental Information, Section 3).

Including all available potential confounders in our model could risk multicollinearity (leading to unstable coefficient estimates based on the inclusion or exclusion of variables) or overspecification of the model, leading to inflated standard errors. We developed a parsimonious model with limited correlation between variables (Figure S1), while still retaining important potential confounders in each of the relevant domains. Namely, we did not include multiple measures of household building materials or household water and sanitation practices in our preferred models because of multicollinearity. Our preferred model adjusted for the percentage of households in a canton that were rural; percentage of households that were not electrified via the grid; an index of household materials; percentage of households with a modern toilet connected to the municipal sewers or a septic tank, a cesspool, or a latrine; percentage of adult women who were literate; percentage of girls under 18 y old who reported attending school; percentage of households in which an individual in the household or the respondent spoke an Indigenous language; an index of vaccines administered among children under 5 y old; percentage of children under 5 y old receiving three doses of the pneumococcal conjugate vaccine; percentage of women who received formal antenatal care prior to delivery; and the median number of antenatal care visits among women receiving any antenatal care. Table S4 describes potential confounders included in alternative specifications.

We observed some implausible and missing canton-period variable estimates. Given our limited number of canton-periods overall, we sought to address these cases and to include all available data to maximize our power to detect an association between %CF and under-5 LRI mortality. Some cantons were relatively small, and some surveys contained relatively few observations (like vaccinations, antenatal care, and those in the 2015–2019 period). As a result, there were some covariates for which the canton-period estimates were implausibly zero ($n = 4$, 0.6% of all canton-period observations for all potential covariates). We approached these cases in one of two ways. When the canton-period was in 1999–2003 or 2008–2012, we linearly interpolated between the preceding and following canton-period estimates. When the canton-period was either the first or last period, we replaced the zero estimate with the closest canton-period estimate for that covariate. There were some cases in which there were no observations for a given variable in a canton-period (0.3% of all canton-period observations). These primarily occurred for questions related to vaccinations or antenatal care visits in smaller cantons. In those cases, we provided the canton with the province-level average values across the relevant period.

Table 1. Descriptive statistics of cantonal under-5 lower respiratory infection mortality, clean fuel use, and covariates in Ecuador from 1988–1992 to 2015–2019.

	Overall ($n = 676$ cantons)	1988–1992 ($n = 169$ cantons)	1999–2003 ($n = 169$ cantons)	2008–2012 ($n = 169$ cantons)	2015–2019 ($n = 169$ cantons)
Under-5 lower respiratory infection mortalities [mean (SD)][a]	6.18 (21.3)	12.71 (33.2)	5.59 (17.5)	3.79 (15.5)	2.48 (10.4)
Total under-5 population [mean (SD)][b]	9,482 (25,733)	8,880 (23,333)	9,398 (25,397)	9,872 (27,273)	9,779 (26,958)
Under-5 lower respiratory infection mortalities, per 100,000 under-5 population [mean (SD)]	58.95 (111.70)	137.13 (184.86)	50.48 (70.41)	28.88 (33.19)	17.54 (23.59)
Proportion of households primarily using a clean-burning cooking fuel [mean (SD)][c]	0.71 (0.25)	0.41 (0.18)	0.70 (0.19)	0.83 (0.14)	0.91 (0.10)
Proportion of households that are rural [mean (SD)]	0.63 (0.22)	0.68 (0.22)	0.64 (0.22)	0.62 (0.23)	0.59 (0.22)
Proportion of households not connected to electricity grid [mean (SD)]	0.15 (0.20)	0.39 (0.22)	0.19 (0.15)	0.00 (0.01)	0.03 (0.03)
Materials index [mean (SD)][d]	0.00 (1.42)	−0.98 (1.52)	−0.37 (1.28)	0.42 (1.11)	0.93 (0.88)
Household hygiene index [mean (SD)][d]	0.00 (1.85)	1.86 (1.19)	0.56 (1.18)	−0.32 (1.14)	−2.10 (1.13)
Proportion of adult women who are literate [mean (SD)]	0.83 (0.09)	0.79 (0.10)	0.85 (0.08)	0.88 (0.06)	0.81 (0.09)
Proportion of girls under 18 y old attending school [mean (SD)]	0.83 (0.10)	0.74 (0.06)	0.75 (0.05)	0.89 (0.03)	0.94 (0.04)
Proportion of households where an Indigenous language is spoken [mean (SD)]	0.07 (0.15)	0.06 (0.12)	0.08 (0.16)	0.08 (0.15)	0.09 (0.18)
Proportion of children under 5 with three doses of the pneumococcal conjugate vaccine [mean (SD)][d]	0.22 (0.27)	0.00 (0.00)	0.00 (0.00)	0.27 (0.15)	0.60 (0.16)
Vaccine index [mean (SD)][e]	0.00 (1.72)	−0.32 (2.35)	0.39 (1.19)	0.74 (0.98)	−0.82 (1.57)
Average age of mother at delivery in years [mean (SD)]	25.5 (1.2)	26.3 (1.0)	25.8 (0.9)	25.1 (0.8)	25.2 (1.4)
Proportion of pregnant women receiving formal antenatal care [mean (SD)]	0.86 (0.15)	0.74 (0.14)	0.82 (0.14)	0.92 (0.15)	0.95 (0.07)
Median number of antenatal care visits, if any [mean (SD)]	5.88 (1.56)	5.07 (1.43)	5.19 (1.36)	6.25 (1.43)	7.01 (1.13)
Mean ambient $PM_{2.5}$ ($\mu g/m^3$) [mean (SD)]	16.6 (2.8)	NA	14.8 (2.1)	17.8 (2.7)	17.2 (2.7)

Note: PM, particulate matter; $PM_{2.5}$, PM with aerodynamic diameter ≤ 2.5 μm; SD, standard deviation.

[a] Under-5 lower respiratory mortalities represent the yearly average of the years covered in the time period (1990–1992, 1999–2003, 2008–2012, 2015–2019). Therefore, it is possible for a canton-period estimate to not be a whole number.

[b] We estimate under-5 population in the 1988–1992, 1999–2001, and 2008–2012 time periods by counting the number of children under age 5 y in the 1990, 2001, and 2010 censuses, respectively. Because there has not been a survey with national coverage since 2010, we rely on age-specific population estimates produced by the Ecuadorian National Statistical Agency (INEC) that are based on the most recent census, the national birth and death registries, and data on migration and immigration, among other factors. These can be found freely at https://sni.gob.ec/proyecciones-y-estudios-demograficos. We average the yearly estimates from 2015 to 2019 to produce the canton-period estimates.

[c] Cooking fuel options included: piped/centralized gas, gas cylinders, electricity, kerosene (locally referred to as kerex), firewood, coal, and gasoline. Clean fuel options included piped gas, gas cylinders, and electricity.

[d] Indices are produced using the first component from principal components analysis. Canton-period indices are produced by subtracting a given canton-period estimate from the overall parameter mean, dividing by the scaling factor, and multiplying by the first principal component. Then, all parameters are summed to produce the index. The household materials index is comprised of roof, wall, and floor materials as specified in d-f; positive values indicate higher quality materials. The household hygiene index is comprised of the household water source, household toilet and solid waste disposal, household trash removal, and household exclusive shower; more negative values indicate more hygienic practices. The vaccine index is composed of all vaccines other than the pneumococcal conjugate vaccine–3.

[e] The pneumococcal conjugate vaccine–3 did not exist prior to the 2010 time period in Ecuador. Given that there was no similar vaccine, we assigned a 0% coverage value to all cantons in the 1988–1992 and 1999–2003 periods. We do not have data on which of the multiple pneumococcal conjugate vaccines were administered in the 2008–2012 and 2015–2019 periods in Ecuador.

Statistical Analyses

First, we modeled the association between %CF and under-5 LRI mortality linearly in generalized linear models (GLMs), presenting the association as a mortality rate ratio (MRR) per 10 percentage point increase in canton-period clean fuel use. We used quasi-Poisson regression to account for overdispersion in the under-5 LRI mortality data (allowing the variance of the outcome to be greater than its mean) and included canton-level under-5 population as an offset term. Beyond the potential confounding variables, we also included canton fixed effects to control for potential unobserved spatial confounding and fixed effects for study period (1988–2002, 1999–2003, 2008–2012, and 2015–2019) to account for potential unobserved temporal confounding (i.e., trends in development not captured by the measured potential confounders). Our use of fixed effects assumed that association between %CF and under-5 LRI mortality is the same for all cantons and periods but allowed the intercepts to vary without imposing any distribution on the estimated intercepts. Models were run using the "fixest" package in R (version 4.2.2; R Development Core Team)[48]; standard errors were clustered at the canton level.

Next, we relaxed the assumption of linearity in the relationship between %CF and under-5 LRI mortality using generalized additive models (GAMs). This model included a penalized spline for %CF, fixed effects for canton and period, and the aforementioned potential confounding variables. The optimal number of degrees of freedom for the curve was selected using the generalized cross-validation criterion.[49] We presented a canton- and period-averaged exposure–response relationship relative to the mean of %CF and estimated MRRs relative to increases of 10 percentage points at different points of the %CF distribution (i.e., from 45% to 55% and from 75% to 85%) to characterize the shape of the detected association.

Visual inspection of the nonlinear model output appeared to indicate a threshold in the relationship between %CF and under-5 LRI mortality. To further explore the possibility of such a "breakpoint," we conducted a segmented regression using the "segmented" package in R,[50] accounting for the same confounders and fixed effects for canton and period as our preferred specification. Such a breakpoint would imply a change in the magnitude of the association between clean fuel use and under-5 LRI at a certain level of %CF, which could provide a policy-relevant target for canton clean fuel penetration. Previous work hypothesized that a critical level of clean fuel adoption may be needed to result in health benefits,[51] and, thus, we sought to investigate whether such a phenomenon could be observed in our empirical analysis. The segmented regression model assumes a piecewise linear relationship between %CF and under-5 LRI mortality and can detect a breakpoint in generalized linear models (GLMs). Results from the fitted GAM indicated that this assumption of linearity on either side of a threshold was reasonable. A range of initial breakpoint values were tested based on the GAM exposure–response plot. If a breakpoint were detected, the model provided the breakpoint and coefficient estimates for both sides.

Throughout this study, we considered $p < 0.05$ as a threshold for statistical significance.

Estimating Averted under-5 LRI Mortalities from Increased Clean Fuel Use

We estimated the change in under-5 LRI mortalities over the study period attributable to changes in %CF. To enable year-by-year accrual of health benefits over the full study period, we constructed a cantonal data set for each year since 1990 by linearly interpolating %CF and all covariates between the middle years of each period (1990, 2001, 2010, and 2017); covariates in 2018 and 2019 were assigned 2017 values. Then, we used the exposure–response relationship modeled in the preferred GAM specification to predict the expected number of under-5 LRI mortalities in each canton-year based on the %CF in that canton-year ($\text{LRI}_{\%\text{CF\_current\_year}}$). We then made the same prediction based on %CF in 1990 but with the contemporaneous linearly interpolated canton-year covariates (i.e., when using 1992 under-5 LRI counts, we used 1992 covariates but 1990 %CF), providing a counterfactual estimate of the number of under-5 LRI mortalities if %CF had remained fixed at 1990 levels ($\text{LRI}_{\%\text{CF\_1990}}$). Therefore, subtracting $\text{LRI}_{\%\text{CF\_current\_year}}$ from $\text{LRI}_{\%\text{CF\_1990}}$ estimated the averted under-5 LRI mortalities attributable to changes in %CF in that canton-year; we then summed together these canton-year estimates to yield the full number of averted under-5 LRI mortalities attributable to changes in %CF between 1990 and 2019.

We additionally estimated the total declines in under-5 LRI mortalities across the full study period to determine the proportion attributable to changes in %CF ($\text{LRI Decline}_{\%\text{CF}}$). To do this, we predicted yearly under-5 LRI mortalities holding all covariates and %CF fixed at their 1990 levels but retaining increases in under-5 population between 1990 and 2019 ($\text{LRI}_{\%\text{CF\_Covariates\_1990}}$). Hence, $\text{LRI Decline}_{\%\text{CF}}$ was calculated by Equation 1:

$$\text{LRI Decline}_{\%\text{CF}} = \frac{(\text{LRI}_{\%\text{CF\_1990}} - \text{LRI}_{\%\text{CF\_current\_year}})}{(\text{LRI}_{\%\text{CF\_Covariates\_1990}} - \text{LRI}_{\%\text{CF\_current\_year}})}. \tag{1}$$

Associations by Sex, Study Period, and Region

We conducted analyses to assess sex-, study period–, and region-specific associations. Analyses mirrored our preferred GLM and GAM specifications. In sex-stratified analyses, we grouped the counts of under-5 LRI mortalities by sex and used sex-specific under-5 population offsets per canton-period. We stratified the study sample by study period (1988–1992, 1999–2003, 2008–2012, and 2015–2019). In this analysis, we did not include fixed effects for study period or canton but did adjust for all other confounders. We used the Cochran's Q-test to assess effect modification on the multiplicative scale.[52] For region, we interacted %CF with a dummy variable for region of the country (the Amazonian region, the Andean region, and the Coastal region), retaining fixed effects for study period and canton and covariates from the preferred specification.

Clean Fuel Use and Ambient Air Pollution

We investigated the associations between canton clean CF use, ambient air pollution, and under-5 LRI mortality. First, we used ambient $PM_{2.5}$ concentrations for South America derived from satellite-retrieved aerosol optical depth, chemical transport modeling, and ground-based measurements at a $0.1^{\circ} \times 0.1^{\circ}$ resolution (roughly $1.1\text{ km} \times 1.1\text{ km}$), available since 1998, to estimate mean canton ambient $PM_{2.5}$ concentrations in the three most recent study periods (1999–2003, 2008–2012, 2015–2019).[53] Within canton polygons, we estimated calendar-year mean $PM_{2.5}$ concentrations and then averaged across years of the period. We linearly modeled the association between canton %CF and mean canton ambient $PM_{2.5}$ concentrations in an empty model with only fixed effects for canton and period and then in an adjusted model using the potential confounding variables from our primary specification, minus those related to children's health and health care. In an additional specification, we included ambient $PM_{2.5}$ concentrations in both our empty and preferred adjusted model of the association between %CF and under-5 LRI mortality.

Sensitivity Analyses and Robustness Checks

We conducted a range of additional analyses to assess the sensitivity and robustness of our results to alternative specifications. We conducted four regressions with alternative potential confounder combinations. We also tested all combinations of potential confounders in quasi-Poisson GLMs (excluding combinations that included indices and their components). In another specification, we allowed for nonlinear confounding relationships using penalized splines with two knots for covariates that indicated nonlinearities when tested one by one in adjusted models (percentage of households that are rural and percent of households with grid electricity). We also tested alternative model specifications that *a*) allowed an additional degree of freedom for the spline assessing the association between %CF and under-5 LRI; *b*) modeled the outcome in a negative binomial vs. quasi-Poisson regression; *c*) used random intercepts vs. fixed effects for canton to use information from both within and between cantons for estimates, whereas coefficients from the fixed effects approach are effectively within-canton estimates; *d*) included regional fixed effects in the main specification; *e*) excluded the Galapagos Islands, which may have meaningfully different health, socioeconomic, or fuel use conditions due to their isolation; *f*) excluded the cantons that contain Ecuador's two most populous cities (Quito and Guayaquil) because they may be influential in the results because of higher variance in the outcome (see plot of residuals from the main model in Figure S2); and *g*) analyzed the association between %CF and under-5 LRI mortality at province level rather than the canton level. Finally, we assessed the possibility that incomplete mortality registry data might confound the relationship between clean CF use and under-5 LRI mortality. To do so we estimated the association between mortality registry completeness, obtained from Peralta et al.,[54] and %CF at the province level from 2001–2013 in a linear model with province and period fixed effects.

Results

Study Sample Characteristics

Our data show that clean CF increased and under-5 LRI mortalities declined over the study period (Figure 1; Excel Table S1). The mean canton-level %CF in the first period (1988–1992) was 41% (median and interquartile range: 39%, 26% to 55%). In the final period (2015–2019), %CF had increased to 91% (median and interquartile range: 95%, 87% to 97%). Nationwide, %CF increased from 59% to 95% over the study period. Between 1990 and 2019, we observed 179,976 under-5 mortalities, of which 29,897 were attributable to LRIs. In the first study period (1988–1992), we observed an average of 10,962 total under-5 mortalities each year, of which 2,146 were attributable to LRIs. Between 2015 and 2019, the final study period, we observed an average of 3,941 under-5 mortalities each year, of which 401 were attributable to LRIs. We also observed improvements in cantonal wealth, sanitation, education, and health care access and usage over the study periods (Table 1; Table S5).

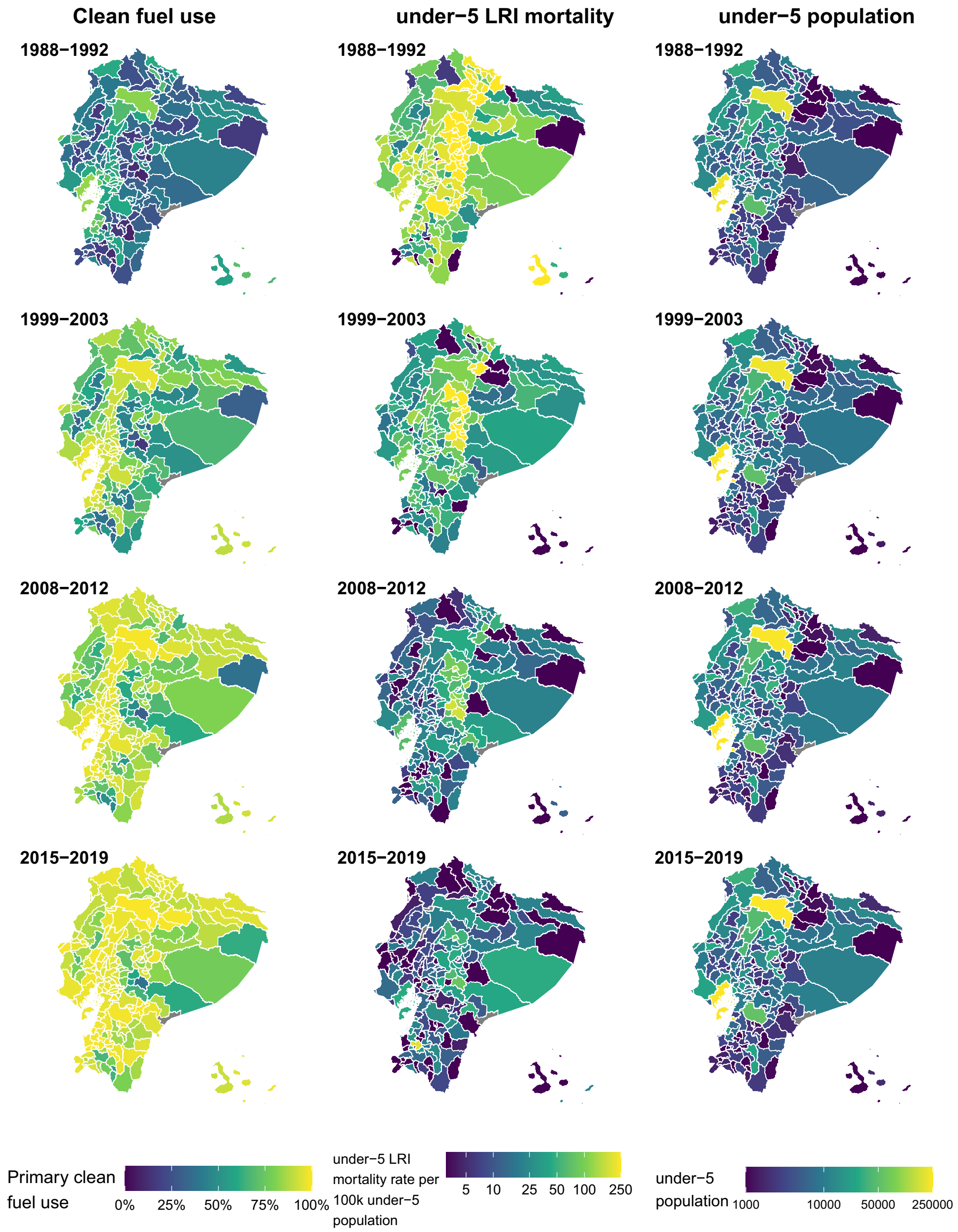

Figure 1. Clean fuel use, under-5 lower respiratory infection mortality, and under-5 population in 1988–1992, 1999–2003, 2008–2012, and 2015–2019. Left panel shows canton-level primary clean fuel use. Middle panel shows canton-level rates of under-5 lower respiratory infection mortality per 100,000 under-5 population. Right panel shows under-5 population. Thicker borders represent modern-day provinces, and thinner borders represent cantonal borders in 1990 ($n = 173$). The Galapagos islands are shown in an inset in the bottom right—they are otherwise found 560 mi west of the western coast of Ecuador. Cantons not included in the analysis are shown in gray ($n = 4$) (see Section 2). See Table 1 for summaries of period-specific data and Excel Table S1 for raw data.

Exposure–Response Relationship

Results from our generalized linear quasi-Poisson regression models showed a negative association between %CF and under-5 LRI with a MRR estimate of 0.79 [95% confidence interval (CI): 0.72, 0.87] per 10 percentage point increase in %CF in the unadjusted models that only included fixed effects for canton and time period and 0.90 (95% CI: 0.79, 1.02) per 10 percentage point increase in %CF in the preferred adjusted specification (Figure S9). Using the same preferred adjusted specification, we also found a nonlinear relationship between %CF and under-5 LRI mortality, from which we estimated an MRR of 0.94 (95% CI: 0.86, 1.04) for an increase in %CF from 45% to 55% and an MRR of 0.82 (95% CI: 0.79, 0.85) for an increase in %CF from 75% to 85% (Figure 2; Excel Table S2). Segmented regression analyses detected a threshold of 61% clean fuel use (95% CI: 52%, 70%), with a nonstatistically significant relationship below the %CF threshold (MRR: 0.99 per 10 percentage point increase in %CF, 95% CI: 0.88, 1.10) and a significant negative relationship above the threshold (MRR: 0.81 per 10 percentage point increase in %CF, 95% CI: 0.72, 0.92). Figure S3 shows the cantons that reached 61% clean fuel use in each study period; overall, 32% of all observations are below the 61% threshold.

Sex-, Study Period–, and Region-Specific Associations

There was no difference in the linear or nonlinear association between %CF and under-5 LRI across sex-stratified subsets (MRR for females per 10 percentage point increase in %CF: 0.90,

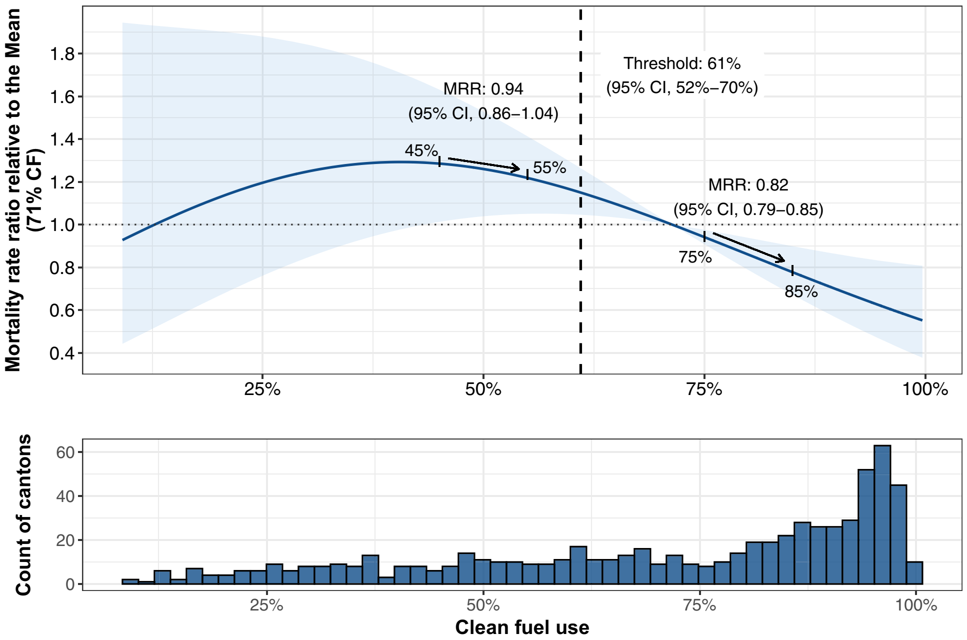

Figure 2. Adjusted nonlinear association between canton-level clean fuel use and under-5 LRI mortality rate. The top panel shows the MRR of under-5 LRI mortality spline response function and 95% confidence interval from the generalized additive model relative to the mean of %CF (71%), holding all else constant. Annotated MRRs estimate an increase in %CF from 45% to 55% and from 75% to 85%, respectively, holding all else constant from models like the main model, but with the lower value as the reference as opposed to the mean. The annotated threshold (dashed vertical line at 61%) is estimated from segmented regressions based on linear associations, rather than the nonlinear association shown on this plot. The bottom panel is a histogram showing the distribution of $n = 668$ canton-period %CF estimates. This preferred specification adjusted for percent of households in a canton that are rural; percent of households that are not grid electrified; an index of household materials; household has a modern toilet connected to the municipal sewers or a septic tank, a cesspool, or a latrine; adult women's literacy; under 18 y of age girls' school attendance rate; an individual in the household or the respondent speaks an Indigenous language; an index of vaccines administered among children under 5 y of age; coverage of the pneumococcal conjugate vaccine (three doses) among children under 5 y old; percent of women that received formal antenatal care prior to delivery; and the median number of antenatal care visits if attended. See Excel Table S2a for effect estimates and Excel Table S2b for canton-period %CF estimates. Note: CF, cooking fuel; LRI, lower respiratory infection; MRR, mortality rate ratio.

95% CI: 0.79, 1.02; MRR for males: 0.91, 95% CI: 0.82, 1.02; Cochran's Q-test $p = 0.90$) (Table S6; Figure S4). The negative association between %CF and under-5 LRI mortality was stronger in more recent periods, with no significant linear association observed in the first period (MRR 1.03; 95% CI: 0.91, 1.17) and MRRs between 0.83 and 0.65 observed in the subsequent three time periods (Cochran's Q-test $p < 0.01$) (Table S6; Figure S5). Given the increasing proportion of cantons reaching 60% of households primarily using a clean CF over the study periods (Figure S3), these period-specific results are generally consistent with the observed threshold effect. The similarity of nonlinear associations at high levels of %CF suggests that differences are driven in part by the range in %CF in each period (Figure S6). In the Andean and Coastal regions, we observed linear and nonlinear associations between %CF and under-5 LRI mortality that were similar to those in the main model (Table S6; Figure S6; Cochran's Q-test $p = 0.86$). There was no observed association between %CF and under-5 LRI mortality in the Amazonian region (Figure S6).

Estimated Averted under-5 LRI Mortalities

We estimated that increases in clean fuel use were associated with 7,343 averted under-5 LRI mortalities (95% CI: 2,555; 12,131) between the first (1988–1992) and final period (2015–2019). Increases in %CF were estimated to have averted under-5 LRI mortalities in 94% of cantons; estimates for total under-5 LRI averted were significantly different from 0 in 41% of cantons. The averted under-5 LRI mortalities attributable to increased %CF account for 19% (95% CI: 7%, 31%) of all declines in under-5 LRI mortality observed during study period (Table S7; Figure S7), with spatial heterogeneity observed (Figure 3; Excel Table S3).

Ambient Air Pollution and Clean Fuel Use

Canton average ambient $PM_{2.5}$ concentrations increased in Ecuador over the final three study periods from an average of $14.8\,\mu g/m^3$ in 1999–2003 to $17.2\,\mu g/m^3$ in 2015–2019 (Table 1; Figure S8). An increase of 10 percentage points in canton %CF was associated with a $0.25\,\mu g/m^3$ (95% CI: 0.14, 0.36) reduction and a $0.20\,\mu g/m^3$ (95% CI: 0.08, 0.33) reduction in ambient $PM_{2.5}$ in the empty and adjusted models, respectively. In a three-period model with only canton and period fixed effects, a $1\text{-}\mu g/m^3$ increase in canton average ambient $PM_{2.5}$ was associated with an MRR of 1.29 (95% CI: 0.98, 1.69). Adding canton average ambient $PM_{2.5}$ somewhat attenuated the association between %CF and under-5 LRI mortality in unadjusted and adjusted three-period models and was not itself significantly associated with under-5 LRI mortality (Figure S8). An increase of 10 percentage points in canton %CF was associated with an MRR of 0.77 (95% CI: 0.62, 0.94) in a three-period model with only canton and period fixed effects; when ambient $PM_{2.5}$ was included the MRR for %CF was 0.82 (95% CI: 0.72, 0.93). In the adjusted model, an increase of 10 percentage points in canton %CF was associated with an MRR of 0.88 (95% CI: 0.72, 1.08); when ambient $PM_{2.5}$ was included the MRR for %CF was 0.90 (95% CI: 0.74, 1.10).

Sensitivity Analyses and Robustness Checks

Our results were robust to alternative specifications. The linear and nonlinear associations modeled for a selection of alternative

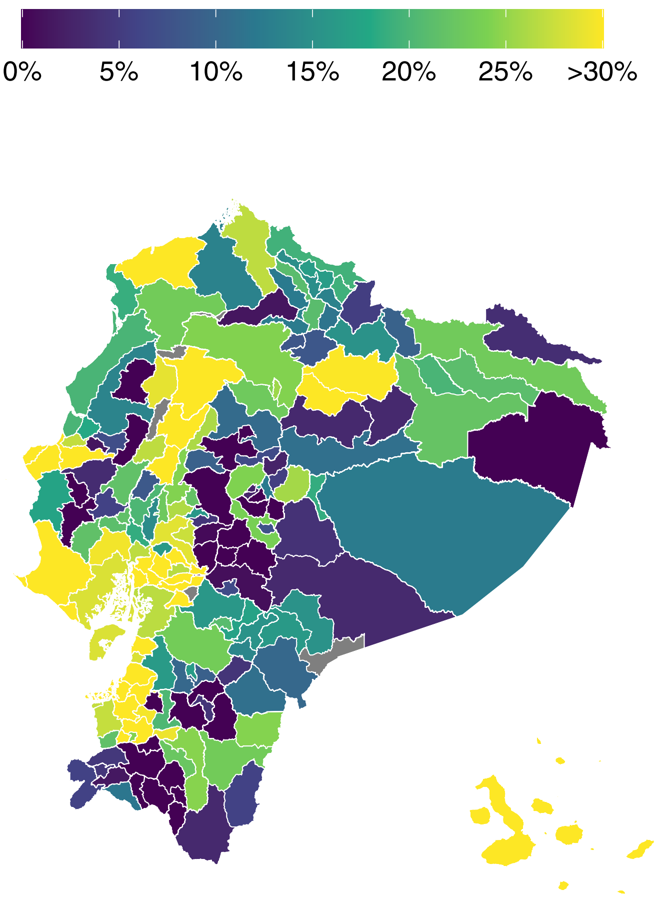

Figure 3. Percentage of all reduced under-5 LRI mortality from 1990 to 2019 attributable to increased clean fuel use at the canton level. The Galapagos islands are shown in an inset in the bottom right—they are otherwise found 560 mi west of the western coast of Ecuador. Cantons not included in the analysis are shown in gray ($n=4$). See Excel Table S3 for raw data.

potential confounding variable specifications demonstrated consistency in the magnitude and shape of the association between % CF and under-5 LRI mortality, especially above ~60% clean fuel use (the determined breakpoint from segmented regressions) (Figures S9 and S10). Segmented regressions applied to these alternative specifications estimated nearly identical thresholds and MRRs similar to those from the preferred specification (Table S8). Estimates of total averted under-5 LRI mortalities attributable to increased %CF between 1990 and 2019 were similar across alternative specifications, ranging from 6,236 (95% CI: 2,400; 10,072) to 9,061 (95% CI: 3,813; 14,308) deaths averted (Table S7). Canton %CF was negatively associated with under-5 LRI mortality in 99% of 73,818 models with different potential confounders, and the CI for MRRs did not cross 1.00 in 70% of models (Figure S11; Table S9). Results were robust to allowing nonlinear confounding relationships (Figure S12), to modeling the outcome as a negative binomial distribution (Figure S13), to using random intercepts rather than fixed effects for cantons (Figure S14), to including a fixed effect for region of the country (Figure S15), to omitting the Galapagos islands (Figure S16), and to omitting the cantons that contain Guayaquil and Quito (Figure S17). We also observed negative linear and nonlinear associations between %CF and under-5 LRI mortality at the province level in both unadjusted and adjusted models (Figure S18). We observed no significant association between changes in %CF and mortality registry completeness at the province level from 2001 to 2013 (Figure S19).

Discussion

Well-documented, large-scale clean household energy transitions are uncommon in the modern era. We capitalized on one such cooking energy transition to empirically estimate the health benefits of widespread clean CF adoption and use. Using publicly available mortality data, we found a robust, nonlinear association between clean fuel use and under-5 LRI mortality at the canton level over the last 30 y in Ecuador. Notably, we observed statistically significant declines in under-5 LRI mortality associated with increased clean fuel use only when >60% of households in a canton cooked primarily with a clean fuel (LPG or electricity). In total, we estimate that increased clean fuel use averted 7,340 under-5 mortalities from LRIs (95% CI: 2,560; 12,130), accounting for 19% of observed declines in under-5 LRI mortalities over the same time frame.

To date, there have been few studies estimating the health benefits of large-scale transitions to clean CF use. One study found that an 80% reduction in kerosene use, replaced with LPG, between 2008 and 2012 in Indonesia yielded a decrease of 1 percentage point in infant mortality rate.[55] Other studies have estimated the theoretical cost-effectiveness of potential clean cookstove programs to improve health using existing exposure–response associations between $PM_{2.5}$ exposure and health outcomes, exposure contrast scenarios between baseline traditional stove use and clean cookstove use, and underlying population demographics and disease rates.[17,56–65] These theoretical studies offer general guidance by assessing potential benefits and costs of clean cooking transitions, but they have several key limitations, including: *a*) assumptions that personal air pollution exposure scenarios, which are typically based on few, if any, in-country measurements, are consistent across time and space; *b*) use of relatively fixed background disease data that fail to capture spatiotemporal trends; and *c*) use of modeled disease data. Considering these limitations, our study offers advancement by using observed data on household fuel choice, household economics and demographics, and cause-coded deaths over three decades to establish a context-specific empirical relationship between increased clean fuel use and child mortality.

Our observation of a threshold effect suggests that nearly complete community-wide interventions may be needed to adequately achieve personal air pollution exposure reductions that yield health benefits. One potential interpretation of the threshold is that when approximately 60% of a canton uses clean fuels, there is sufficient community adoption to decrease household contributions to community-level air pollution, such that personal exposure is meaningfully reduced by the combination of reduced exposure at both household and community scales and, thus, health benefits accrue. Previous studies in which clean cooking interventions were provided to only a few households in a community observed smaller-than-expected exposure reductions perhaps because of persistently elevated community-level air pollution concentrations, potentially due to the remainder of households in the community using biomass for their household needs.[10–12,18,66] The threshold may also represent the point at which many households *a*) use LPG nearly exclusively, *b*) have sufficiently phased out traditional biomass stove use, and/or *c*) have attained and sustained personal exposure reductions beneficial to health. The observed threshold could also result from a pattern whereby relatively earlier clean fuel adopters were at lower risk of under-5 LRI mortality than later adopters were, and, thus, as %CF increases in cantons where >60% of households already primarily cook with a clean fuel, the benefits of clean fuel use are finally observed. Given these uncertainties and the relatively few observations below the threshold in our own data, it is possible that other locations or time periods would either have a threshold effect at a different level of clean fuel adoption and use or have no threshold effect at all.

Our investigation of ambient $PM_{2.5}$ levels is noteworthy for two reasons. First, the association we found persists—and is only slightly attenuated—after accounting for ambient $PM_{2.5}$ concentrations, suggesting a significant independent relationship between clean fuel use and under-5 LRI mortality at the canton level. Second, the negative association between clean fuel use and ambient $PM_{2.5}$ concentrations provides suggestive evidence that household biomass burning for cooking and heating contributes to ambient air pollution, extending previous findings that have primarily been based on emissions inventories and chemical transport modeling or highly localized air pollution measurement studies.[24,67–69] Although modeled ambient $PM_{2.5}$ concentrations have increased in Ecuador by $\sim 2.5\ \mu g/m^3$ between 1999 and 2019 (Table 1), we estimate that increased clean fuel use has been associated with a reduction in ambient $PM_{2.5}$ concentrations of $\sim 0.5\ \mu g/m^3$ over the same time period. This association represents an unaccounted-for externality of widespread clean fuel scale-up and could imply additional benefits for investments in expanding the use of clean CFs.

In this study we consider gas to be a clean CF; however, evidence suggests that cooking with gas can still increase indoor air pollution, especially nitrogen dioxide (NO_2).[70,71] Given that elevated NO_2 concentrations are associated with negative respiratory health outcomes,[72] it is worth considering the potential limitations of a transition from biomass to gas. Still, in comparison with cooking with polluting fuels like firewood and even considering the emissions from gas cooking, transitioning to gas and phasing out polluting biomass fuels is likely to be beneficial, with studies observing reduced levels of $PM_{2.5}$, carbon monoxide, and NO_2 in such transitions.[12,18,19,73] However, to our knowledge, there have been no studies directly comparing transitions from polluting biomass fuels to gas vs. electric cooking, which can be considered a cleaner alternative to gas because it produces no emissions at the point of use.

Limitations

This study relies on publicly available administrative data for all analyses. Although such data were not collected with the intention of being used for epidemiological analyses and have less precision than other sources of prospectively collected data that more directly measure outcomes, the findings from this study suggest that they may have high utility for retrospective analyses of countrywide changes in health and indicators of environmental exposures in countries with consistent and extensive administrative data collection mechanisms. Taking advantage of such data, which were previously collected, validated, and repeated throughout time, facilitates analyses of the type performed here. A related factor is that we lack direct measures of economic indicators (e.g., canton-level GDP, percentage of residents living below the poverty line), which have not been collected in a manner that facilitates canton-level estimates in each of our study periods using publicly available data.

A key limitation of our study is the lack of individual-level data on CF status and other risk factors that can be matched with available mortality data, thus limiting us to an ecological analysis. Therefore, it is important to consider that although a transition from using polluting fuels for cooking to clean fuels is a household-level change, in this study we are conducting an area-level analysis, and thus we can make no inference about the individual household-level impacts of such a transition on under-5 LRI mortality risk.

An additional limitation of our analysis is that we lack data on secondary CF use. Existing evidence suggests that fuel stacking (i.e., the use of multiple fuel types to meet all cooking needs) is common, especially when a clean CF has been recently acquired. Although there are no nationwide CF stacking data in Ecuador, our previous work indicates that biomass use secondary to LPG may be common in rural Andean and Coastal regions.[35] Nevertheless, we also found a high contrast in air pollution exposure dependent on whether the household primarily cooked with a clean fuel or firewood, suggesting substantial health-risk reduction when LPG is used primarily instead of firewood.[74]

The lack of publicly available mortality data prior to 1990 limited our analysis to a time period when Ecuador's population had already begun to transition toward use of clean fuel. Fewer canton-period observations at the lowest ends of clean fuel use have resulted in wide CIs for the association between %CF and under-5 LRI mortality rate. It is plausible that the lack of data at the lowest ends of %CF reduced our power to detect an association. Thus, our analysis was limited in its ability to fully capture the health benefits of the Government of Ecuador's investment in cooking gas subsidies because increases in clean fuel use had already occurred by 1990.

Although the mortality registry intends to capture all deaths in Ecuador, there may be some data missingness. Nevertheless, the mortality registry broadly agrees with Global Burden of Diseases, Injuries, and Risk Factors (GBD) estimates, which aim to estimate true morbidity and mortality by statistically correcting for reporting errors and biases.[2] For example, the GBD estimates that in 1990 there were 2,223 under-5 LRI mortalities in comparison with 2,250 under-5 LRI mortalities observed in our data and 795 under-5 LRI mortalities in 2017 in comparison with 405 observed in our data in 2017.[1] Given our use of canton and period fixed effects, incomplete mortality records could present a problem in our estimated association only if reporting differences covaried over time and across cantons with changes in clean fuel use; however, we found no association between changes in a measure of mortality registry completeness and %CF at the province level from 2001 to 2013. In any case, our estimates would be biased toward the null in the event that underreporting of under-5 LRI mortalities is not associated with our exposure.

Although under-5 LRI mortality is the leading cause of child mortality in Ecuador, the median number of cases per year in each canton-period was 1.3, and 48% of observations had ≤ 1 case per year. This relatively low sample size and relatively low variation in the outcome may lead to wide CIs and limit our ability to detect an association between %CF and under-5 LRI mortality. Nevertheless, we observe a consistent negative association between %CF and under-5 LRI mortality across a range of specifications, including when aggregating cantons to provinces.

Conclusions

Modeled evidence from global burden of disease studies suggests that reduced HAP has been the leading contributing factor to recent observed declines in under-5 LRI mortality worldwide. Existing evidence suggests that transitions to clean-burning CFs that reduce air pollution exposure could significantly reduce under-5 mortality, but real-world evidence estimating the impacts of such transitions is limited. Nevertheless, clean CFs are being adopted by biomass-using households around the world because of widespread programmatic efforts by governments and other organizations. Using data on mortality and CF use across 30 y of clean fuel scale-up in Ecuador, our results, despite the limitations of ecological studies, provide among the first empirical observations of the benefits of increased clean CF use at a nationwide scale over several decades. These findings are relevant to other regions with similarly increased clean CF use and to regions that are currently developing and implementing large clean cooking policies. Providing estimates of child health improvement from these transitions may inspire greater evidence-based investment in clean CFs.

Acknowledgments

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All data that support the findings presented in this article are publicly available from the Instituto Nacional de Estadistica y Censos (https://www.ecuadorencifras.gob.ec/estadisticas/). Code and data necessary to replicate the findings presented in this article are available at https://doi.org/10.7910/DVN/6XYZLM.

C.F.G. worked on conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, visualization, and manuscript production (original draft writing, review, and editing). M.L.B. reviewed and edited the manuscript. M.A.K. conducted funding acquisition, methodology, and manuscript writing, review, and editing. A.G.L. conducted funding acquisition and worked on manuscript writing, review, and editing. A.P. worked on funding acquisition; methodology; and writing, review, and editing. S.B.S. performed data curation; investigation; and manuscript writing, review, and editing. E.T. worked on funding acquisition and manuscript preparation (writing, review, and editing). A.V. performed manuscript review and editing. D.W.J. worked on conceptualization, funding acquisition, investigation, methodology, and manuscript writing, review, and editing.

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