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ORIGINAL ARTICLE

Air pollution control and the occurrence of acute respiratory illness in school children of Quito, Ecuador

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Abstract Because of air quality management and control, traffic-related air pollution has declined in Quito, Ecuador. We evaluated the effect of a city-wide 5-year air pollution control program on the occurrence of acute respiratory illness (ARI). We compared two studies conducted at the same location in Quito: in 2000, 2 years before the policy to control vehicle emission was introduced, and in 2007. Each study involved ~ 730 children aged 6–12 years, observed for 15 weeks. We examined associations between carboxyhemoglobin (COHb) serum concentration—an exposure proxy for carbon monoxide (CO)—ambient CO, and ARI in both cohorts. In 2007, we found a 48% reduction in the ARI incidence (RR 0.52; 95% CI 0.45–0.62, $p < 0.0001$), and 92% decrease in the percentage of children with COHb > 2.5% as compared to the 2000 study. We found no association between COHb concentrations above the safe level of 2.5% and the ARI incidence ($p = 0.736$). The decline in air pollution due to vehicle emissions control was associated with a lower incidence of respiratory illness in school children.

Keywords Acute respiratory illness · Policy emission control · Carboxyhemoglobin

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Introduction

Traffic-related air pollution has been associated with harm to respiratory health worldwide [1–11]. Children are highly prone to harmful effects of air pollutants on lung function [12–14] due to the small size of their airways and immaturity of defense mechanisms [12, 15]. Reduction of several pollutants, especially particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2), and ozone (O_3) has been associated with improvement of lung function [16, 17] plus the reduction of respiratory symptoms, bronchitis, allergic disorders in children with and without asthma, and in the number of daily asthma events [18–22]. In contrast, some studies have demonstrated that the reduced exposure to traffic-related air pollutants has little effect on lower respiratory symptoms [23] and did not affect the prevalence of respiratory/allergic symptoms in school children [24]. The reasons for such discrepancies are not clear, but might be attributed to effects of several confounding factors such as exposure misclassification, temporal, and spatial trends in exposure, health, socioeconomic status, and smoking [25], as well as population susceptibility, life style changes, or the use of statistical methods that bypass the link-by-link approach of classical accountability in evaluating the regulatory impacts [26].

In several Latin American countries, including Brazil [6, 27], Mexico [2, 28], Chile [29, 30], Colombia [31], and Ecuador [32–34] researchers have demonstrated associations between respiratory problems and urban air pollution. These countries have created programs for air pollution management and control. Studies are lacking on the effects of such programs on respiratory health in children.

The city of Quito is the most polluted city in Ecuador, due to the number of cars contributing to air pollution and to the mountain range that impedes airflow to reduce contamination [35, 36]. From January through April of 2000, we studied 616 children, aged 6–12 years, attending schools located in areas with different traffic intensities—moderate in the North and high in the Center. We found that 90% of school-aged children in the high-traffic area of Quito, and 43% of children in the city area with moderate traffic had blood concentrations of COHb higher than the safety level of 2.5% [33]. Trained pediatricians identified ARI episodes in about 70% of children in the high-traffic area and 30% of children in the moderate-traffic area. Children with COHb > 2.5% were 3.25 [95% CI 1.65, 6.38) times more likely to present with ARIs than children with COHb ≤ 2.5% [33]. Our study served as the foundation for city-wide public policies: creation of the Metropolitan Atmospheric Monitoring Network Quito (REMMAQ), plus vehicular emissions control in Quito with technical inspection of vehicles in 2002 [34]. By 2007, the annual average concentrations of sulfur dioxide (SO_2), CO, and PM_{10} decreased to acceptable levels. CO was reduced by 35% (from 1.29 to 0.83 μg/m^3) [37]. Such drastic reduction in air pollution seemed likely to lead to improvements in the respiratory health of city residents.

Was the reduction of traffic-related pollutant levels, specifically in CO exposure between 2000 and 2007, associated with both the incidence of ARI and COHb levels in school-aged children? We conducted a 15-week prospective study

of 730 children attending elementary schools in the North and Center areas of Quito and compared the findings with results of the 2000 study of ARI and the COHb levels in children attending schools in the same locations [33].

Methods

Study design and participants

The design and methods followed in the 2007 study, described in this section, were similar to those in the 2000 study [33] with the additional analysis of associations of ARI incidence and ambient CO measurements. In both studies, a pediatrician visited each child in the school twice weekly to examine the child's respiratory signs and symptoms and to determine the presence of upper acute respiratory illnesses and lower acute respiratory illnesses.

Out of 736 recruited children attending public elementary schools in the two areas of Quito, 6 (< 1%) children withdrew from their school for various reasons (change of address or presence of varicella). Between February and June 2007, we measured the incidence of ARI and COHb levels in remaining 730 children. To ensure comparability between the studies, we conducted the 2007 study in the winter season (see weather description in https://nutrition.tufts.edu/sites/default/files/documents/ENaumova-SupplementalMaterialCOHbARIpaper_09-24-18.pdf) (1) and in two schools located in the immediate vicinity of the previously studied schools (Center and North areas). The selected schools had similar characteristics: building, number of children, and socioeconomic status of the children.

During the screening period, we delivered detailed information about the study to teachers and parents of each child. We excluded three children due to presence of asthma ($n = 1$), congenital cardiopathy ($n = 1$), and major chest deformity ($n = 1$). A total of 736 children met the inclusion criteria: 6–11 years of age (age was confirmed by birth certificate), formal written consent freely signed by parents, and child assent.

Carboxyhemoglobin status

Before starting the follow-up period, we obtained a 5-mL venous blood sample from each child using a plastic syringe and placing the sample in a collecting tube with Ethylenediaminetetraacetic acid (EDTA). These tubes were refrigerated until transported for the analysis to a laboratory at Universidad Católica del Ecuador. (This laboratory also measured COHb in the 2000 study.) We measured COHb levels by spectrometry [38] within 24 h, and expressed results as a percentage of plasma hemoglobin. COHb concentration of 2.5% was considered the reference value, the level below which no symptoms would be found [39].

Acute respiratory illness measurements

Trained practitioners visited each child weekly at her/his school by to monitor respiratory symptoms and signs, and to determine the presence of acute upper and lower respiratory illnesses. Children who presented with respiratory illness were treated, but not necessarily removed from school, and followed until the resolution of the episode. A new case could be identified after 2 weeks free of respiratory illness. Acute upper respiratory illness was defined as the presence of two or more of the following signs/symptoms: cough, nasal secretion, fever > 37.5 °C (axillary temperature), inflammation of pharynx, and anterior cervical lymphadenitis. Presence of otitis (local pain, aural pus, and eardrum congestion) was also considered as acute upper respiratory illness. Acute lower respiratory illness was defined by tachypnea (respiratory rate > 20) and/or lower respiratory tract secretions (alveolar or bronchoalveolar) assessed by thoracic auscultation, plus one or more of the following: fever, cough, and chest retractions [40].

Anthropometric measurements

We measured each child's weight and height by standard procedures [41] using instruments calibrated by the Ecuadorian Institute of Normalization. Weight was measured with a DETECTO balance (New York), that included a height gage graduated in cm. Weight was recorded to the nearest 0.1 kg. Height was recorded to the nearest 0.1 cm.

Nutritional status

Weight-for-age Z-score (WAZ), and height-for-age Z-score (HAZ) were determined for each child using Nutstat software [Epi Info(TM) CDC, 2004]. Children having a WAZ < –2 SD were classified as underweight. Children having a HAZ < – 2 SD were classified as stunted.

Exposure to pollution

Household survey

To determine the indoor CO contamination, we sent a survey to the parents of study children in the first 3 weeks of the study. It asked about the type of fuel used for cooking (kerosene, gas, alcohol, firewood), and the presence of smokers. Ninety-four % of the surveys were completed.

Air quality measurements

In 2004, 4 years after the 2000 study was completed, Quito started city-wide routine air quality monitoring. To provide CO proxies for both time intervals, we obtained from two monitoring stations located in the Center and North areas all available monthly records

for CO levels during the period 2004–2007. Using monthly records, we interpolated CO average values from 2004 for COHb measurements in 2000 by direct assignment of the closest available monthly measurements in 2004 (4.5 mg/m^3 for CO level). We used these interpolated values in our analysis. For 2007, we obtained daily records of environmental CO, SO_2, and $PM_{2.5}$ levels, collected now as part of the automatic network of passive monitoring maintained by Quito Air Corporation (CORPAIRE). We supplemented the analysis with daily records for ambient temperature and precipitation from the National Institute of Meteorology and Hydrology (INAMHI), Quito, Ecuador [42].

Statistical analysis

We compared descriptive statistics about children from the 2000 and 2007 studies. Continuous variables were described as the mean and standard deviation; categorical variables as absolute frequency and percentages. We compared the distributions of the studied parameters with *t* Student and chi-squared tests for continuous and categorical variables, respectively.

We calculated the incidence rates (episodes/1000 child-weeks (CW) for the follow-up period) of acute respiratory illness and the annual frequency of ARI episodes/child in both 2007 and 2000 study groups. We estimated the average concentrations for the selected environmental air pollutants measured during the 15-week study.

The relationships between COHb levels and environmental CO were assessed by several regression models, using the CO values from the day of and the day prior to the COHb measurement. The models were gradually adjusted for individual characteristics (age, sex, underweight, stunting), variables for the household sources of indoor air pollution (indoor firewood use and smoking), and meteorological characteristics (see https://nutrition.tufts.edu/sites/default/files/documents/ENaumova-SupplementalMaterialCOHbARIpaper_09-24-18.pdf) (2). To evaluate the association of COHb, as a marker for CO exposure, with the presence of respiratory illness, we used two logistic regression models. In the first model, the explanatory variable, COHb, was used as a continuous variable (concentrations) and in the second as a binary variable (0, if COHb $\leq$ 2.5%; and 1, if COHb > 2.5%). We expressed the results in Adjusted Odds Ratios (AOR) with 95% confidence intervals.

To allow for multiple episodes of ARI in a child, we applied the Generalized Estimating Equation (GEE) for Poisson regression models to evaluate the association between COHb level and the incidence of ARI (ARI/1000 child-weeks). We applied the same model to examine the relationship between ambient CO concentrations and ARI incidence. We also explored the relationship between ARI incidence and COHb levels and between ARI incidence and ambient CO concentrations, using the classic Poisson regression model (see https://nutrition.tufts.edu/sites/default/files/documents/ENaumova-SupplementalMaterialCOHbARIpaper_09-24-18.pdf) (3). The results are expressed in rate ratios with 95% confidence intervals.

Logistic and GEE regression models were adjusted for age, sex, nutritional status (underweight and stunted), fire wood use for cooking, and presence of smokers in the households. Regression coefficients for study parameters were considered statistically significant if the corresponding two-sided *p* value was equal to or below 0.05.

Finally, we constructed a Poisson regression model for ARI occurrence for 2007 with CO, SO_2, and $PM_{2.5}$ concentration values (same day of COHb measurements) and adjusted for individual covariates.

We entered and managed data using the ACCESS program (version 11.5614.5602, 2003). We analyzed these data using the SPSS program (Version 22. 0, Lead Technologies Inc., SPSS Inc., Chicago, Illinois, USA). The complete database contained information from both 2007 and 2000 study.

Ethics approval and consent to participate

We obtained ethical approval for the study from the Ethical Committee of the Corporación Ecuatoriana de Biotecnología (CEB). We obtained voluntary formal written consent from parents, plus assent from each child.

Results

General characteristics of participants

In 2000, 616 children aged 6–12 years were studied [33]. Thirty-one percent (196/616) of the children had COHb measured, and 87.5% completed the survey. There were a total of 7337 weekly visits. In 2007, we enrolled 730 children aged 6–12 years in the study. All children had COHb measured and 98% completed the survey. A total of 10,683 child-weeks of observation were accumulated in the 2007 study. As compared to 2000, average age, the proportion of females, stunted, and underweight children were significantly higher in the 2007 study. Between the two study years, there were no significant differences in the percentage of home smokers and the use of firewood in households (Table 1).

Environmental contaminants

In the study of year 2000, there was no systematic monitoring of contaminants by areas in the city of Quito. Ambient CO levels were steadily declining over the period, based on city-wide routine monitoring, from 4.5 mg/m^3 in 2004 to 0.78 mg/m^3 in 2007 (Fig. 1a). During the study period in 2007, the maximum daily concentration of consecutive 8-h moving averages for CO and O_3 and the maximum daily concentration of consecutive 24-h moving averages for $PM_{2.5}$, NO_2, and SO_2 in north and center monitoring stations were within desirable and acceptable limits, as permitted by Ecuadorian Air Quality Standards (NECA) [37, 43] (Fig. 1b).

ARI incidence and carboxyhemoglobin levels

While there was no difference in the percentage of children who presented with ARI in 2007 and 2000, the number of ARI episodes and the annual frequency of ARI per child were significantly lower in 2007 as compared to 2000 (Table 2). Similarly, the

Table 1 Baseline characteristics of children in 2000 and 2007 studies

Study parameters	2000 ($n=616$)	2007 ($n=730$)	p value
Baseline characteristics			
Age (years)	8.64 ± 1.01	9.39 ± 1.53	< 0.0001
Females (%)	242 (39.4)	388 (53.2)	< 0.0001
Weight (kg)	27.38 ± 5.6	28.05 ± 7.71	0.074
Underweight[1]	17 (2.8)	95 (13.1)	< 0.0001
Height (cm)	127.5 ± 8.15	126.34 ± 12.42	0.067
Stunted[2]	56 (9.1)	233 (31.9)	< 0.0001
BMI (kg/m^2)[3]	16.74 ± 2.42	17.25 ± 2.42	< 0.0001
Survey			
Completed surveys	539 (87.5)	718 (98.4)	< 0.0001
Households with kerosene use	11 (2.17)	0 (0.0)	
Households with fire wood use	5 (0.9)	2 (0.2)	0.111
Households with smokers	128 (25.2)	159 (22.2)	0.22

Data are mean ± SD or *n* (%)

[1]Underweight was defined as weight-for-age *Z*-score < –2SD

[2]Stunted was defined as height-for-age *Z*-score < –2SD

[3]*BMI*—body mass index

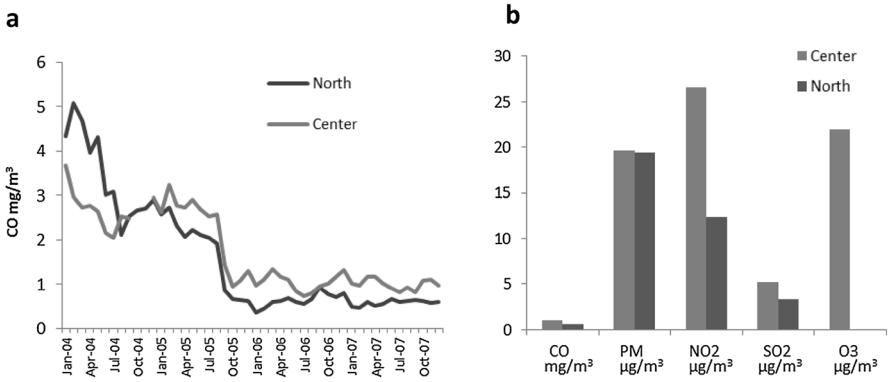

Fig. 1 Air quality in Quito (2004–2007). **a** Declining trend in the outdoor CO ambient concentration (mg/m^3) measured at the North and Center stations; **b** Maximum daily concentration of consecutive 8-h moving averages for CO and O_3, and maximum daily concentration of consecutive 24-h moving averages for $PM_{2.5}$, NO_2, and SO_2 in Center and North monitoring stations in 2007

incidence rate of ARI in 2007 was significantly lower than in 2000 (43.52 per 1000 CW vs. 83.14 per 1000 CW), equivalent to a 48% lower rate of ARI (RR 0.52; 95% CI 0.45–0.62, $p \leq 0.0001$).

In 2007, the average level of COHb was below 2.5%, in contrast to 2000, when it exceeded that safety level. Furthermore, in 2007, the fraction of children with COHb > 2.5% was significantly lower as compared to the 2000 study (4.9% vs. 64.9%) (Table 2).

Table 2 Incidence of acute respiratory illness and exposure measurements for children in 2000 and 2007 studies

Study parameters	2000 ($n=616$)	2007 ($n=730$)	p value
Outcome			
Children with ARI	308 (50.0)	357 (48.9)	0.689
ARI episodes	610	465	< 0.0001
Annual frequency of ARI/child	4.35	2.33	< 0.0001
Incidence rate of ARI/1000 child-weeks	83.14	43.52	< 0.0001
Blood tests (n)	196	730	
COHb levels (%)[1]	3.88 ± 1.93	1.90 ± 0.39	< 0.001
COHb > 2.5%[2]	136 (69.4)	36 (4.9)	< 0.001

Data are mean ± SD or n (%)

ARI acute respiratory illness

[1]COHb: Carboxyhemoglobin as percentage of CO fixed to hemoglobin

[2]COHb over the safe level of 2.5%

ARI incidence, carboxyhemoglobin, and CO

In 2007, neither ambient CO concentrations (Table 3) nor levels of COHb (Table 4) were associated with the risk of having ARI as compared to 2000 study. In 2007, having COHb levels > 2.5% was not associated with ARI (adjusted OR 1.29; 95% CI 0.65–2.53, $p=0.468$), in contrast to 2000 when AOR was 5.44 (95% CI 2.38–12.42, $p<0.0001$) (Table 5). Similarly, in 2007, levels of COHb were not associated with presence of ARI (adjusted OR 1.30; 95% CI 0.89–1.91, $p=0.187$), in contrast to 2000 when AOR was 1.57 (95% CI 1.28–1.93, $p<0.0001$).

ARI incidence in center and north areas of Quito

In 2007, the number of episodes of ARI, the percentage of children with ARI, and the annual frequency of ARI per child were comparable across the schools in the North and Central areas. The percentage of children with COHb > 2.5% was significantly lower in the Center school. The percentage of underweight children was significantly higher in the Center area school. While most characteristics of the study children in two schools were comparable, children at the Center area school were, on average, 1 year older as compared to those from the North area and there were more girls (Table 6).

In the Center area of Quito in 2007 as compared to 2000, there were significantly lower values for the percentage of children with ARI, the number of acute respiratory illnesses, annual rate of respiratory illness, COHb levels, and percentage of children with COHb > 2.5%. The children in 2007 were also significantly older, with more females, stunted children, and underweight children than those in the 2000 study (Table 6). The North area of Quito had a significantly higher percent of

Table 3 Risk factors associated with acute respiratory illness incidence in 2000 and 2007 studies and overall

	All RR (95% CI)	*p* value	2000 RR (95% CI)	*p* value	2007 RR (95% CI)	*p* value
CO (mg/m^3)[1]	1.23 (1.13,1.34)	< 0.0001	10.65 (4.66,24.37)	< 0.0001	1.12 (0.91,1.35)	0.290
Age (year)	0.93 (0.86,0.97)	0.017	1.06 (0.848,1.13)	0.585	0.95 (0.89,1.00)	0.097
Female	1.04 (0.87,1.36)	0.657	1.10 (0.72,1.67)	0.641	1.07 (0.89,1.28)	0.446
Underweight[2]	1.02 (0.79,1.33)	0.832	0.59 (0.215,1.66)	0.325	1.06 (0.81,1.39)	0.654
Stunted[3]	1.21 (0.98,1.50)	0.066	1.30 (0.68,2.51)	0.422	1.18 (0.97,1.45)	0.096
Indoor fire wood use	1.46 (0.42,5.05)	0.544	1.89 (0.86,4.13)	0.110	0.66 (0.16,2.72)	0.566
Indoor smokers	1.07 (0.88,1.30)	0.466	1.04 (0.64,1.58)	0.950	1.13 (0.92,1.39)	0.234

Rate Ratio (RR)—results from the Log-linear Poisson Generalized Estimating Equation model

[1]CO, Carbon monoxide as continuous variable on the day of COHb measurement

[2]Underweight was defined as weight-for-age *Z*-score < –2SD

[3]Stunted was defined as height-for-age *Z*-score < –2SD

Table 4 Risk factors associated with acute respiratory illness incidence in 2000 and 2007 studies and overall

	All RR (95% CI)	*p* value	2000 RR (95% CI)	*p* value	2007 RR (95% CI)	*p* value
COHb levels[1]	1.26 (1.17,1.34)	< 0.0001	1.24 (1.10,1.38)	< 0.0001	1.13 (0.94,1.36)	0.165
Age (year)	0.94 (0.89,1.00)	0.059	0.89 (0.72,1.09)	0.285	0.95 (0.89,1.04)	0.129
Female	1.06 (0.89,1.26)	0.472	1.48 (0.66,1.66)	0.842	1.07 (0.89,1.29)	0.434
Underweight[2]	1.48 (0.80,1.36)	0.729	0.75 (0.22,2.04)	0.578	1.08 (0.82,1.42)	0.570
Stunted[3]	1.17 (0.95,1.45)	1.200	1.33 (0.67,2.64)	0.403	1.18 (0.96,1.45)	0.099
Indoor fire wood use	1.72 (0.48,6.18)	0.402	3.13 (0.72,12.72)	0.110	0.65 (0.16,2.54)	0.528
Indoor smokers	1.23 (0.92,1.36)	0.245	1.02 (0.64,1.75)	0.799	1.13 (0.92,1.39)	0.241

Rate Ratio (RR)—results from the Log-linear Poisson Generalized Estimating Equation model

[1]COHb, as continuous variable

[2]Underweight was defined as weight-for-age *Z*-score < –2SD

[3]Stunted was defined as height-for-age *Z*-score < –2SD

children with ARI, more ARI episodes, and a higher annual ARI rate, yet significantly lower values for COHb levels. The percentage of children with COHb > 2.5% observed in 2007 was low compared to 2000. Again, children in 2007 were significantly older and the percentage of stunted and underweight children was higher as compared to 2000.

For indoor CO contamination factors, the use of firewood as fuel was comparable across the time and locations, while the use of kerosene declined (Table 6). For the 2007 study, in a multi-pollutant model, daily CO and SO_2 levels were significantly associated with number of episodes of ARI (see https://nutrition.tufts.edu/sites/

Table 5 Risk factors associated with the presence of acute respiratory illness in children in 2000 and 2007 studies

	2000 AOR (95% CI)	*p* value	2007 AOR (95% CI)	*p* value
COHb > 2.5%[1]	5.44 (2.38–12.42)	< 0.0001	1.29 (0.65–2.53)	0.468
Age/year	0.91 (0.61–1.34)	0.626	0.95 (0.86–1.05)	0.278
Female	1.76 (0.82–3.79)	0.146	1.13 (0.84–1.52)	0.431
Underweight[2]	2.53 (0.37–17.17)	0.342	0.92 (0.57–1.49)	0.743
Stunted[3]	1.94 (0.62–6.06)	0.254	1.21 (0.85–1.73)	0.278
Indoor fire wood use	1.30 (0.07–25.76)	0.865	0.83 (0.05–13.52)	0.895
Indoor smokers	0.85 (0.36–1.96)	0.696	1.14 (0.79–1.64)	0.484

Adjusted odds ratios (AOR) result from binary logistic regression model

[1]COHb, Carboxyhemoglobin over the safe level of 2.5%, as binary variable

[2]Underweight was defined as weight-for-age *Z*-score < –2SD

[3]Stunted was defined as height-for-age *Z*-score < –2SD

default/files/documents/ENaumova-SupplementalMaterialCOHbARIpaper_09-24-18.pdf) (Table S7).

Discussion

Five years of vehicle emissions control effectively and significantly decreased mean COHb levels, percent of children with COHb above the safety level > 2.5%, and incidence of ARI. The strongest evidence of the relation between declining of CO air pollution and respiratory health is that the RR for the association COHb > 2.5% and incidence of ARI decreased by 67.5% in this period. In 2007, the average value of COHb in blood of study children was below the safety level of 2.5%, in contrast to 2000 study when the average exceeded the safety level. Furthermore, the percentage of children with COHb > 2.5% decreased by 92%, and the annual frequency of ARI/child declined 46% compared to the year 2000 study. We suggest that reduced ambient levels of CO resulted in reduced COHb concentration and increased number of children with the safe COHb level. Did this environment lead to decreased susceptibility to ARIs in children residing in areas with high micronutrient and oxygen deficiency?

This evidence is consistent with other limited trials that have demonstrated benefits in child respiratory health from air pollution reduction policies, and other actions implemented to improve air quality. Although those studies were not specific for CO reduction, overall declining trends in several air pollutants were associated with a decrease of medical visits for asthma and lower respiratory infections [44], decrease of bronchitis symptoms [19], improvements in lung function [16–18], less pulmonary inflammation [45], and reduction in asthma prevalence [20]. School bus retrofits—used to reduce tailpipe and engine emissions—are associated with large reductions in bronchitis, asthma, and pneumonia incidence among children [46].

Table 6 Incidence of ARI and exposure measurements for children at Center and North in 2000 and 2007 studies

Variables	Center 2000 ($n=313$)	Center 2007 ($n=359$)	North 2000 ($n=303$)	North 2007 ($n=371$)	p value[1]
Outcome					
Children with ARI	219 (70.0)	169 (47.0)	90 (29.7)	189(50.9)	a, b, c, d, e
No. of ARI episodes	496	224	114	241	a, b, c, d, e
Annual rate of ARI	6.89	2.25	1.63	2.41	a, b, c
Baseline characteristics					
Age (years)	8.36 ± 1.08	9.56 ± 1.56	8.94 ± 0.84	9.23 ± 1.49	a, b, c, d, e, f
Females	92 (29.5)	204 (56.8)	150 (49.5)	184 (49.6)	a, b, c
Weight (kg)	27.0 ± 5.97	28 ± 8.12	27.75 ± 5.21	28.04 ± 7.30	
Underweight[2]	10 (3.2)	61 (17.0)	7 (2.31)	34 (9.16)	a, c, d, e, f
Height (cm)	126.46 ± 8.5	126.79 ± 11.7	128.57 ± 7.65	125.89 ± 13.1	d
Stunted[3]	27 (8.26)	116 (32.31)	29 (9.57)	117 (31.53)	a, c, d, e
BMI (kg/m^2)	16.75 ± 2.3	17.11 ± 2.5	16.7 ± 2.4	17.3 ± 2.3	c, d
Survey					
Completed surveys	238 (76)	348 (96.93)	301 (99.34)	370 (99.73)	a, b, c
Households with kerosene use	7 (2.94)	0 (0.0)	4 (1.68)	0 (0.00)	a, c
Households with fire wood use	1 (0.42)	1 (0.29)	4 (1.34)	1 (0.27)	
Households with smokers	37 (15.14)	74 (21.26)	91 (30.54)	85(22.97)	b, d
Blood tests	106	359	90	371	
COHb levels (%)[4]	5.09 ± 1.7	1.88 ± 0.29	2.55 ± 1.20	1.91 ± 0.46	a, b, c, d, e
COHb > 2.5%[5]	97 (91.50)	12 (3.34)	39 (43.33)	24 (6.47)	a, b, c, d, e

ARI acute respiratory illness

[1] p value < 0·05: a (Center 2000 vs. Center 2007), b (Center 2000 vs. North 2000), c (Center 2000 vs. North 2007), d (North 2000 vs. North 2007), e (North 2000 vs. Center 2007), f (North 2007 vs. Center 2007)

[2] Underweight was defined as weight-for-age Z-score < –2SD

[3] Stunted was defined as height-for-age Z-score < –2SD

[4] COHb, as continuous variable

[5] COHb, Carboxyhemoglobin over the safe level of 2.5%

It is important to mention that some studies did not show definite effects of air pollution regulation on respiratory illnesses in children [23, 24]. We believe that changes might better be attributed to the difference in pollutant exposure between subjects, the type of the policy that was implemented, or differences in study designs. Some studies on air pollution and health suggest that the variability in the relationship between decreases in pollution and respiratory symptoms may be due to unexplored heterogeneity between and within communities [18], measurement errors associated with instrument precision, spatial variability of pollutants [47, 48], and the lack of direct measurements of how emissions are changing and/or how they are responding to specific regulations [26].

Although lessening of both outdoor CO and COHb levels were seen in both study areas in 2007, the large reduction (67%) in the annual rate of IRA/child was detected only in the school located at the Center. This reduction was related to a marked decrease in the average of COHb levels in those children (63% reduction seen in Table 6). Other risk factors for acute respiratory infection, such as underweight and stunting [49–52] were not related to ARI (Tables 3 and 4). Potentially, this could indicate that ambient CO levels affect children independently of the nutritional status.

In the North area, the annual rate of ARI/child was 32% higher than in 2000 despite a 25% reduction of COHb levels observed in 2007 (Table 6). It is possible that other factors, such as immune status or other outdoor pollutants, that were not evaluated in this study, explain this finding. In fact, in the 2004–2007 period, the CO levels recorded in the North area were within desirable limits, and the pollutants of greatest concern were O_3 and $PM_{2.5}$ because they increased annually albeit within acceptable levels. Our hypothesis that the increase of PM in the north of Quito in 2007 may explain the rise in the incidence of respiratory illness becomes more plausible because of other factors that could influence the presence of such illness. Those factors that were not associated with the increase in ARIs include male sex, younger age, presence of underweight, or stunting.

Even if overall air quality showed improvement from January to April 2007, $PM_{2.5}$ levels had an increasing trend in the North of Quito. During February, levels were above the maximum levels allowed by the national standard (19.67 $\mu g/m^3$) [37]. Such increases reflect a significant increase in the car fleet with which the city of Quito has experimented across the years (7% per year or ~ 30,000 vehicles per year) [35].

It is worth mentioning that in the peripheral areas of Quito, such as in the north, the residential population has grown as has the number of commuters, with a resulting increase in heavy vehicular circulation, especially diesel buses [43]. Diesel combustion is known to generate approximately ten times more nanoparticles than the combustion of gasoline [53]. Even low levels of PM cause asthma and other respiratory diseases [46]. Diesel exhaust particles induce alveolar macrophages to produce nitric oxide which can combine with superoxide anions to produce peroxy-nitrite, a potent oxidizing compound that alters body cells, any somatic cells [54]. As indicated by a multi-pollutant model in 2007, CO and SO_2 levels were associated with the number of episodes of ARI. The high rate of respiratory illness in 2007 in neighborhoods charged with nanoparticles, suggests that control of CO emission and other pollutants, like SO_2, were not sufficient to prevent illnesses associated with chronic respiratory inflammation.

Due to the differences in study designs and measurements of both ambient pollutants and respiratory outcomes, direct comparisons of our findings with studies addressing the benefit for respiratory health of short- or long-term air pollution reduction are not completely feasible. Nevertheless, our findings support those studies, demonstrating that improvements in respiratory health can be expected when there are significant reductions in environmental pollution, even for the short periods.

The 48% reduction in the incidence of ARI (RR = 0.52, 95% CI 0.45, 0.62, $p < 0.0001$) that we found after 5 years of vehicle emission control might be comparable to the 37–40% drop in pneumonia cases due to reduced emissions of diesel-related toxics particulates from school buses reported by Beatty and Shimshack in 2011 [46]. Similarly, the reduced prevalence of common cold (OR = 0.78; 95% CI 0.68, 0.89) in children aged 6–15 years related to the decline in PM_{10} levels that was found by Bayer et al. in 2015 [21]; and with the decreased prevalence of respiratory symptoms (bronchitis, cough, and phlegm) in adolescents with asthma due to decreases of NO_2, $PM_{2.5}$, PM_{10}, and O_3 that Gilliland et al. demonstrated in 2017 [18]. Those studies were carried out in developed countries where children are less exposed to environmental risks than children in developing countries, such as Ecuador. Our findings are needed if we are to alert developing countries to the importance of having healthy environments to prevent respiratory problems.

Ecuador has been listed as a country with a high level of air pollution, but there are others whose populations are also at risk: Peru, Colombia, Venezuela, Mexico, Honduras, Chile, and Guatemala comprise the top Latin American countries with the worst air pollution [55]. Our findings suggest that policies intended to abate vehicle air pollution may be appropriate in other parts of the developing world with similar geographic conditions and where the impact of air pollution on respiratory health is severe. In addition, such control strategies are likely to be sustainable, as Quito has already demonstrated feasibility in a developing country.

Taken together, these findings show a strong relationship between CO, COHb, and ARI, explained by biologically plausible mechanisms. They indicate a benefit of the lower concentration of environmental CO on the respiratory health of children achieved by vehicle exhaust control. CO, one of the principal polluting gases from vehicular emissions [56], affects respiratory mucosae from the nose to the alveoli, causing respiratory infections—from colds to bronchospasm and pneumonia [4, 57]; and these infections increase hospitalizations [4, 57–59]. When CO enters the blood stream it reacts with hemoglobin to form COHb. This compound does not allow an adequate supply of oxygen to reach tissues and organs of the human body in a dose-dependent manner [60, 61]. Thus, an increase in ambient CO could lead to a potential increase in an individual's COHb level indicative of a condition that poses a risk for respiratory illness.

The major strengths of our study include (a) the representative sample size for Quito city, making the results relevant to other Andean countries, (b) the objective measure of CO exposure through COHb levels, (c) the direct detection of ARI cases by experienced pediatricians who examined each child every week, and (d) the inclusion of factors important for the development of acute respiratory illness. Furthermore, we compared our findings with the results of a 2000 study to determine whether a policy change had a long-term effect on a similar population. These strong points are responsible for robust analyses and trustworthy results.

The study has several limitations. Because CO monitoring was not available in 2000, it was not possible to evaluate directly the change of CO concentrations. For the analysis, we used conservative estimates based on the observed trend in measurements collected after 2004, when routine monitoring started. We compensated for the lack of measurements in 2000 with a more detailed analysis of CO lagged by 1 day with data available for 2007. We chose the lag of 1 day because during exposure to a fixed CO concentration, COHb levels increase rapidly over the first 2 h, and then begin to plateau at around 3 h, reaching an equilibrium steady state at 4–6 h. To maintain COHb below 2.5%, CO exposure cannot exceed 10 ppm [62]. In blood samples collected in tubes containing EDTA or heparin and stored at room temperature or at 4 °C, COHb concentrations were stable for at least 5 days [38]. The analysis of the CO concentration from the same day and a day prior COHb measurements reached similar conclusions.

We reconstructed the time series of CO measurements and demonstrated a trend in CO levels over time in two city areas. We have demonstrated that the ambient CO levels were strongly associated with the individual's COHb concentration (see https://nutrition.tufts.edu/sites/default/files/documents/ENaumova-SupplementalMaterialCOHbARIpaper_09-24-18.pdf) (2–3). Reduction of COHb levels observed in 2007 might indicate the effect of the reduced outdoor CO level. In addition, CORPAIRE [37] reported that the annual average concentrations of CO was reduced by 35% in the period 2004–2007 (from 1.29 to 0.83 μg/m^3), while the traffic density of light vehicles increased by approximately 47% (250,000 vs. 368,000 vehicles) [35].

Although we selected children from the same schools studied in 2000, the 2007 population had slightly different mean ages and nutritional status. Our multivariate models demonstrated that these variables were not associated with ARI occurrence. Unfortunately, we did not consider other factors that could have influenced ARI occurrence, such as physical activity, the use of transportation, or socioeconomic status. We did not evaluate what changes in lifestyle or immune status of each child that could have influenced the respiratory health status of the children.

While Quito's population increased from ~ 1,820,000 [63] to ~ 2,120,000 [64] during the period 2000–2007, there was no evidence that other factors affected the health outcomes, such as substantial changes in healthcare, or whether children stayed home when sick. Perhaps the same number of children developed ARIs, but less frequently, or there was a dramatic improvement in indoor air quality.

In September 2006, the National Congress approved a law to regulate the use and consumption of tobacco and its derivatives; however, the law was never enforced. In July 2011, the National Congress banned smoking in public places, but not within households [65].

Over the study period, no specific emission control measures were implemented and it is unlikely that other sources of CO (industry, smoking) were reduced. As expected, the vehicle fleet increased in the city and in the northern area there were more buses fueled by diesel than in the downtown area. This might have increased ARI episodes in the North school area.

In light of these findings, we believe that broad policies should be implemented to improve air quality throughout our city to reduce the health problems due to environmental contaminants. Sustainable community-wide campaigns to raise awareness

of the need for systematic controls of public and private motor vehicles can be useful preventive health actions. Our findings suggest that local pollution policies, such as control of exhaust emission from gasoline engine vehicles, and the gradual removal of old-fashioned carburetor vehicles from the circulation can contribute to the reduction of respiratory illnesses in children. These policies are likely to decrease the risk of school absenteeism and to reduce health care costs (45, 46). A comprehensive policy analysis may further demonstrate the benefits of the improved catalytic converters, the reduction of diesel emissions, and the use of biofuel in rapidly growing Latin American cities.

Conclusions

Our findings show that a substantial decline in ambient carbon monoxide level that resulted from a city-wide 5-year vehicular emission control program is associated with reduction of both incidence of respiratory illnesses and carboxyhemoglobin levels in school-aged children. Our study, along with others, supports the value of implementing preventive policies, and the need for sustained long-term programs in countries with poor air quality.

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