SUPPLEMENTARY FILES

Supplementary Methods

Nasal wash procedure

Obtaining nasal wash sample: We atomize 2ml of warm (37°C) phosphate-buffered saline (PBS) solution into the child's nostril using a MAD Nasal® atomizer during breath-holding. The child is sitting, leaning slightly forward with the head bent slightly forward while holding a 15 mL centrifuge tube into which is placed the neck of a glass funnel (10-15 ml diameter). The funnel is placed below the nose while we atomize slowly the PBS aerosol into the nostril, ensuring that the child holds their breath. Once the syringe is emptied and removed from the nostril, the child blows strongly through the nose into the funnel while the opposite nostril is occluded. This same procedure is repeated in the other nostril and then we wash the funnel with 2ml of PBS solution before removing the 15ml centrifuge tube.

Processing of nasal wash sample: After shaking the sample gently on a mixer for 15 minutes, we centrifuge at 6000 RPM for 10 minutes. We then store some samples at -80°C and discard the remaining supernatant fluid. We place 250µl of pellet into two Cytospin funnels (125µl each) and centrifuge at 700 RPM for 4 minutes (Rotofix cytocentrifuge). We dry and stain slides with Wrights for direct observation under the microscope.

Spirometry estimations

The percentage of predicted spirometry values for age and height were estimated using Global Lung Initiative standards [1] and the FEV1 post-bronchodilator improvement was calculated as: (Post FEV1 - Pre FEV1 / Pre FEV1) x 100%.

Indications for starting inhaled corticosteroids (ICS)

The most updated Ecuadorian guidelines that we applied are based on the GINA 2008[2] and Spanish GEMA 2009[3] guidelines. They recommend controller ICS in children with persistent asthma or frequent episodic asthma (not more than 1 exacerbation every 5-6 weeks, with a maximum of 6-8 exacerbations per year and without symptoms between the exacerbations).

Statistical analysis:

Sample size estimation

We calculated that a cohort of 250 children with a severe asthma attack would provide 80% power to detect factors that reduce the proportion of children re-attending the emergency room within 6 months from 50% to 31.4% (hazard ratio of $\geq$1.46), and 90% power to detect factors that reduce the proportion of children re-attending emergency room within 1 year from 50% to 33.9% (hazard ratio of $\geq$1.37). The expected proportion of children suffering a subsequent asthma attack requiring emergency care was estimated to be 50% over the following 6 months, based on our previous findings in this same setting[4].

Missing data strategy

To investigate the effect of missing values for variables with greater than 5% missing data, we performed a sensitivity analysis using the "ice"[5] procedure for multiple imputation in Stata 13.1. The "mim" procedure in Stata[6] was then used to average the estimates of results across the 20 imputed data sets created, according to Rubin's rules[7]. The imputation models included all variables selected, the outcome of interest, and the Nelson Aalen estimator of the cumulative baseline hazard [8]. There was no difference in the final logistic regression and Cox regression multivariable models obtained when using the multiple imputation dataset compared to the original dataset (data not shown).

References

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Supplementary Results

With respect to food triggers, of the 93 children who reported food-induced asthma attacks, 70 reported cold drink or foods as triggers, 28 reported specific foods (milk, nuts, etc.), 5 reported both, and 2 did not specify the food trigger. The most common specific food triggers reported were artificial drinks and food colorants (both reported in 7 children). Allergen specific IgE for food mix was measured in a random sample of 59 children, with a positive result in 25 (42%) of them. There was no association between a positive food mix IgE and recurrence (OR: 1.08; 95% CI: 0.39-3.04). There was also no association between having reported a food trigger for asthma attacks and having a positive food mix IgE result (OR: 0.77; 95% CI:0.26-2.31).

Table S1: Exposures studied as potential predictors of recurrent asthma attacks, and available data out of 270 children that completed at least 2 weeks of follow-up (included in Cox regression analysis).

Exposure / predictor	Available data (N)	Method
Demographics		
- Age	270	Questionnaire
- Sex	270	Questionnaire
- Ethnicity	266	Questionnaire
- Siblings	269	Questionnaire
- Household location	268	Questionnaire
- Overcrowding	269	Questionnaire
- Monthly household income	248	Questionnaire
- Parental level of education	266	Questionnaire
Personal history		
- Gestational age	261	Questionnaire
- Birthweight	126	Questionnaire
- Breastfeeding	266	Questionnaire
- Bronchiolitis/pneumonia as infant	261	Questionnaire
Asthma history		
- Wheezing ever	267	Questionnaire
- Wheezing last 12m	266	Questionnaire
- Doctor's asthma diagnosis	266	Questionnaire
- Date last asthma attack	228	Questionnaire
- Number of severe exacerbations last year	265	Questionnaire
- ER attendance last year	268	Questionnaire
- Number of ER attendance/s last year	267	Questionnaire
- Hospitalization/s last year / ever	268	Questionnaire
- Admitted to ICU ever	267	Questionnaire
Asthma treatment previous year		
- Inhaled corticosteroids	266	Questionnaire
- Leukotriene inhibitors	266	Questionnaire
- Inhaled/nebulised SABA	266	Questionnaire
- No. oral corticosteroids courses	264	Questionnaire
- No. parenteral corticosteroids courses	264	Questionnaire
Asthma symptoms		
- Asthma control	267	C-ACT; ACT
- Quality of life	219	PAQLQ
- Triggers (number and specific triggers)	165	Questionnaire
- Total time last year with symptoms	268	Questionnaire
- Nocturnal symptoms	267	Questionnaire
- Symptoms with exercise	260	Questionnaire
- Pulmonary function	227	Lung function
Asthma knowledge		
- Poor asthma knowledge	253	NAKQ score
- Asthma education sessions	269	Questionnaire
Family history		
- Maternal rhinitis/asthma/eczema	261	Questionnaire
- Paternal rhinitis/asthma/eczema	259	Questionnaire
Co-morbidities		
- Allergic rhinitis (Doctor's diagnosis)	267	Questionnaire
- Eczema (Doctor's diagnosis)	268	Questionnaire
- Obesity	249	BMI (weight and height)

Environmental exposures		
- Air pollution at home area	269	Questionnaire
- Tobacco exposure at home	268	Questionnaire
- Humid household	268	Questionnaire
- Mould in household	269	Questionnaire
- Carpets in household	269	Questionnaire
- Pets	268	Questionnaire
Inflammatory markers		
- Blood eosinophilia	261	Blood sample
- Nasal eosinophilia	157	Nasal wash
- Fraction of exhaled nitric oxide	229	FeNO measurement

BMI: Body Mass Index; C-ACT: Childhood Asthma Control Test; ACT: Asthma Control Test; NAKQ: Newcastle Asthma Knowledge Questionnaire; PAQLQ: Pediatric Asthma Quality of Life Questionnaire; FeNO: Fraction of exhaled nitric oxide.

Table S2: Asthma control, asthma knowledge and quality of life of 264 participants followed up for 6 months or until first asthma attack recurrence, stratified by readmission status at 6 months.

	Total Cohort	**Second asthma attack within 6 months**		
	(N=264)	**Yes (N=121)**	**No (N=143)**	**P**
C-ACT score (mean, SD)	16.0 (3.75)	15.4 (4.05)	16.5 (3.41)	0.077
ACT score (median, IQR)	16.0 (13-18)	16.0 (14-18)	15.5 (13-18)	0.936
NAKQ score (median, IQR)	**18 (16-20)**	**17 (15-20)**	**18 (16-21)**	**0.041**
PAQLQ total score (median, IQR)	3.5 (3.0-4.0)	3.5 (2.9-4.0)	3.5 (3.0-4.2)	0.275
PAQLQ symptom score (median, IQR)	3.5 (2.8-4.1)	3.6 (2.8-4.0)	3.5 (2.8-4.2)	0.479
PAQLQ activity score (median, IQR)	3.4 (2.6-4.0)	3.4 (2.6-4.0)	3.4 (2.6-4.2)	0.525
PAQLQ emotional score (median, IQR)	**3.7 (3.1-4.5)**	**3.5 (3.0-4.2)**	**3.9 (3.2-4.6)**	**0.030**

IQR: Interquartile range; C-ACT: Childhood Asthma Control Test; ACT: Asthma Control Test; NAKQ: Newcastle Asthma Knowledge Questionnaire; PAQLQ: Pediatric Asthma Quality of Life Questionnaire. Bold: statistically significant differences ($p<0.05$)